MINISTRY OF HEALTH

Pharmacy and Poisons Board

And

National Malaria Control Program

Monitoring the Quality of Antimalarial Medicines Circulating in Kenya: Round 4

November 2015

NATIONAL MALARIA CONTROL PROGRAM
MINISTRY OF HEALTH, KENYA

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[1] NMCP = National Malaria Control Program

Executive Summary

Malaria remains the leading cause of morbidity and mortality in Kenya and accounts for the highest proportion of outpatient visits in the Kenyan health care system. Availability of good quality medicines is essential in ensuring prompt and effective treatment of malaria according to the current national malaria strategy. This report presents the findings of the fourth round and compares it with first, second, and third rounds of monitoring of the quality of anti-malarials that have been done over the last four years.

One hundred antimalarial samples were targeted in each of the five sentinel sites. The purposive sampling of anti-malarials included artemisinin-based combination therapy (ACT) and Sulfadoxine-Pyrimethamine (SPs), among others, based on their availability. Sampling was done in the public, private and informal sectors.

Basic testing using the Global Pharma Health Fund (GPHF) Minilab™ was performed on most collected samples at the sentinel sites. This was followed by verification analysis of 10 percent 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 confirmatory testing using compendial analysis at the NQCL.

The results indicate that the presence of unregistered and substandard anti-malarials in the market was very low in the year 2014. 100% of samples that underwent compendial testing passed the test as per the requirements. In addition 99.3% of the samples collected from the market were found to be medicines registered by the Pharmacy and Poisons Board. The results show that ACTs in the public, private and informal sectors were of good quality, though their presence in the informal market is undesirable.

The results also show the convenience of utilizing minilabs as a safe, rapid and cost-effective way of screening anti-malarial medicines in the field.

Acronyms and Abbreviations

ACTm	Artemisinine-based Combination Therapy for malaria
AL	Artemether Lumefantrine
AMFm	Affordable Medicines for Malaria
HCSM	Health Commodities and Services Management
MCU	Malaria Control Unit
MSH	Management Sciences for Health
MIP	Medicines Information and Pharmacovigilance
NQCL	National Quality Control Laboratory
PMS	Post Market Surveillance
PQM	Promoting the Quality of Medicines
PPB	Pharmacy and Poisons Board
TLC	Thin-Layer Chromatography
USAID	United States Agency for International Development
USP	United States Pharmacopeia
USP-NF	United States Pharmacopeia-National Formulary
USP PQM	United States Pharmacopeia-Promoting Quality of Medicines

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1. INTRODUCTION

1.1. Malaria in Kenya

Malaria is a major public health problem in Kenya and accounts for 31 percent of outpatient consultations and five percent of hospital admissions. Malaria transmission and infection risk are determined largely by altitude, rainfall patterns, and temperature. High levels of transmission are seen on the coast and around Lake Victoria but rarely in the highlands. Approximately 70 percent of the Kenyan population is at risk for malaria, of whom the majority live in areas of epidemic and seasonal transmission [(1)].

A decline in the burden of malaria in Kenya has been observed in recent years due to aggressive efforts to scale up malaria control measures. This has reduced malaria transmission intensity in most parts of the country. In spite of this, moderate-to-high levels of transmission persist in certain endemic zones; the 2010 Kenya Malaria Indicator Survey [(2)] (MIS) confirmed that malaria prevalence remains more than twice as high in rural areas (12%) compared to urban areas (5%). Malaria prevalence around Lake Victoria is particularly high at 38%, even as prevalence in other epidemiological zones has dropped to less than 5%. Consequently, as part of Kenya's revised National Malaria Strategy 2009–2017 (NMS), prevention and control interventions are tailored to the current epidemiology of malaria, with efforts concentrated in the lake-endemic zone [(3)].

1.2. Quality of Anti Malarials in Kenya

Several studies to assess the quality of anti malarials in Kenya have been undertaken in the last decade that continue to inform current and future initiatives towards a comprehensive post –marketing surveillance (PMS) system. The main findings of some of these previous studies include:

- A nationwide study of anti-malarials by the Pharmacy and Poisons Board in collaboration with DOMC in May 2006, found that a wide range of anti-malarials existed in the market, and the majority were not included in the national malaria treatment guidelines. A large proportion (42.6%) were not registered, and some of those did not meet quality standards. The survey enabled an innovative approach to the regulation of medicines for priority diseases, with the regulator and the disease control program working collaboratively to address an issue of great public health importance (Ministry of Health, 2007).
- In 2008, PPB and DOMC collaborated in a multi-country study on quality of anti-malarials in Africa (QAMSA). Results from the study showed that 96% 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 Sulfadoxine/ Pyrimethamine samples were compliant with specifications (WHO, 2010).
- In 2010, a nationwide survey of anti-malarials by the PPB and Malaria Control Unit (MCU) found that 93% of the 535 samples collected were registered in the country;

91.8%, (n=451), 76.3% (n=80) and 84.1% (n=44) of the samples analyzed passed Level 1, Level 2 and Level 3 analysis respectively.

- In 2011, another nationwide survey of anti-malarials by the PPB and Malaria Control Unit (MCU) found that 96.8% of the 499 samples collected were registered in the country; 97%, (n=496), 100% (n=65) and 76% (n=25) of the samples analyzed passed Level 1, Level 2 and Level 3 analysis respectively.
- The results of the most recent survey of the quality of anti-malarials in Kenya, conducted by the PPB and MCU in 2012, showed that 99.1% of the 545 samples collected were registered in the country; 94.6%, (n=514), 90% (n=71) and 90% (n=20) of the samples analyzed passed Level 1, Level 2 and Level 3 analysis respectively.

The above results show that over the past few years there was a general improvement in the quality and registration status of anti-malarial products in the Kenya market.

1.3. Aims and Objectives

The primary objective of post marketing surveillance is to monitor the safety of medicines and their conformity with the specifications for quality declared in the registration dossier or recognized in the pharmacopeias. When conducted regularly, this exercise helps provide continuous information on the quality of medicines circulating in the country.

The specific objectives of the PMS exercise were:

- To identify unregistered products in the selected sites
- To determine the quality of medicines in the selected sites
- To develop a medicine's quality database, for trend analysis of circulating medicines
- Disseminate information on medicines' quality 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 strategies and implementation plans to address problems identified in the study

2. METHODOLOGY

2.1. Sampling Strategy and Training

The sampling strategy involved collecting smaples from various levels operating in the distribution chain, including public sector facilities (KEMSA, public health facilities, health centers), non-governmental organizations (NGOs), faith-based organizations (such as Mission of Essential Medicines Services (MEDS), private for-profits dispensing sites

(pharmacies), hospitals (private and public), and the illicit (informal) markets. Samples were also collected from the two refugee camps of Daadab and Kakuma that receive large amounts of donated medicines

Samples in the private sector were collected using the "mystery shopper" approach, to avoid alerting traders by simulating the real life situation of how patients access medicines. For the purpose (?) of the malaria control program, samples were collected from the five sentinel sites defined in the sample site selection section. This strategy ensured that samples were obtained from all sectors where patients are most likely to be exposed to medicines.

The participants were trained before the sampling and testing was carried out,. The training was facilitated by PQM with support from the Malaria Control Unit (MCU), PPB and NQCL.

2.2. Site Selection

Sites for sample collection were identified in collaboration with PPB, NQCL, and PQM, based on several factors such as epidemiological data showing prevalence of the disease, medicines availability and accessibility, freely circulating medicines originating from border towns, ports of entry, refugee camps and availability of human resources.

2.3. Medicines Selected for Sampling

The selection of antimalarial medicines for sampling was based on MCU'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-line 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/Proguanil
- Other ACTs
    - Artesunate Amodiaquine
- Monotherapies

- Monotherapies were not tested; they were collected only for the purpose of monitoring the shift from monotherapies to ACTs and to evaluate their availability in the market.

2.4. Sample Definition

For the purpose of this study, a sample was defined as a medicine containing a defined API, dosage form, strength, and lot number from a particular level in the distribution chain. Samples with the same attributes described above and the same lot number were only collected if they were found in a different level in the distribution chain, such as wholesaler versus retailer, etc. Medicines with the same lot number were not collected from similar or same level facilities (for example, two pharmacies or retailers).

2.5. Number of Units to Collect per Sample

The number of units collected per sample was determined by the required tests to be performed on the samples. Refer to table below.

The following example of sample collection applies only to solid dosage forms (tablets and capsules).

Table 1: Field Sampling Strategy for Tablets

Minimum Units	Maximum Units	Comments
Initial Sampling		
20	40	If the minimum of 20 units is not feasible, collect what is available but no less than 5 units
Re-Sampling for Compedial Testing		
50	100	If the —minimum of 50 units is not feasible, refer to the Number of Units Needed in "*Guidelines for Compendial Testing*"

2.6. 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 counterfeits or sub-standard or for which adverse drug events had been reported.

2.7. 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)

2.8. 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 larger amounts.

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 sample's identity should it fail or results 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.

2.9. 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.

2.9.1. Level 1 Basic Tests utilizing the 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*[2]
- 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.

2.9.2. 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).

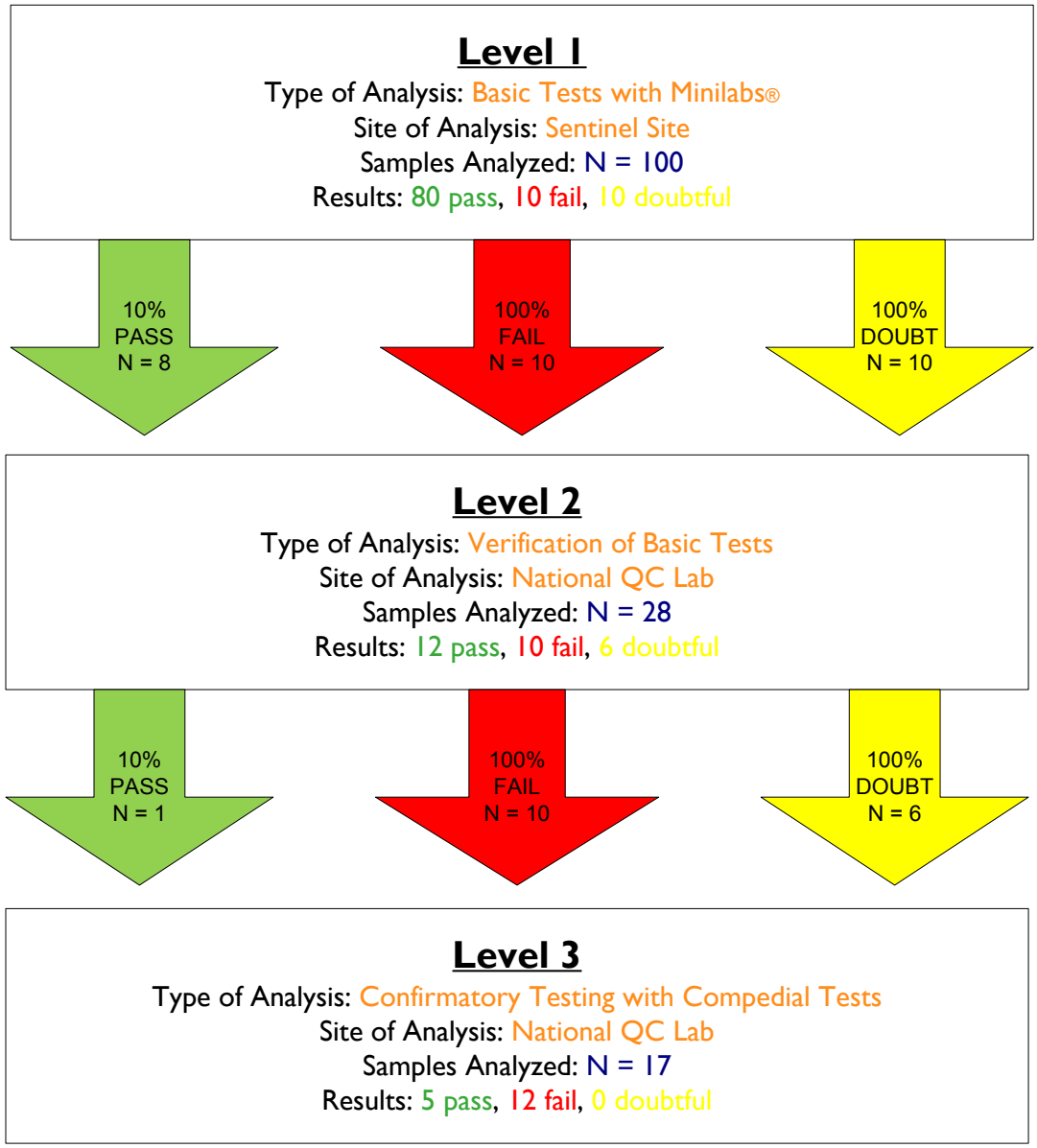
For any samples that failed or were doubtful, they continued to the third stage of analysis for complete compendial testing.

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 precedents of dissolution failures.

[2] * Pass: Conforms to all 3 tests; ** Fail: Does not conform to at least one of the three tests; Doubtful: Conflicting or inconclusive results for at least one of the three tests

Figure 1: Example of Sample Flow for Quality Testing



2.9.3. 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.

3. RESULTS

3.1. Sample Description

3.1.1. Sampling by Sector

The sampling was done in three sectors namely the private, public and informal sectors. Sampling in the private sector was highest owing to the wider range of anti-malarials. The sample sizes are compared across the four rounds of sampling (i.e. from 2011 – 2014).

Table 2: Sampling by Sector

Sector	Round 1	Round 2	Round 3	Round 4
Private	312	373	301	415
Public	169	118	229	157
Informal	55	8	15	33
Total	**536**	**499**	**545**	**605**

3.1.2. Sampling by API

AL was the most sampled antimalarial followed by SPs which is consistent with their availability.

Table 3: Distribution of Samples by Active Pharmaceutical Ingredient (API)

API	Round 1	Round 2	Round 3	Round 4
Artemether/ Lumefantrine	290	258	288	349
Sulfadoxine/ Pyrimethamine	101	105	106	133
Quinine Sulphate	83	85	77	77
Artesunate/ Amodiaquine	14	40	21	42
Quinine Dihydrochloride	-	-	3	4
Sulfamethopyrazine/Pyrimethamine	-	11	-	-
Dihydroartemisinin Piperaquine	19	-	49	-
Other	29	-	1	-
Total	**536**	**499**	**545**	**605**

3.1.3. Sampling by Region

During Round 4, the largest number of samples was collected in the Rift Valley region followed in decreasing order by Western, Nyanza, Nairobi and Coast regions in that order.

Table 4 shows the number of samples in the various regions from Round 1 to Round 4

Table 4: Distribution of Samples by Region

Region	Round 1	Round 2	Round 3	Round 4
Coast	107	99	115	100
Rift Valley	128	100	105	102
Nairobi	100	100	108	101
Nyanza	101	100	100	101
Western	100	100	117	101
Garissa	-	-	-	49
Turkana	-	-	-	52
Total	**536**	**499**	**545**	**606**

3.1.4. Summary of Sampling

Table 5: Summary of sampling and analysis for the four rounds

Round	Total # of Samples Collected	# of samples analyzed in the field using Minilab (Level 1)	# of Samples analyzed at NQCL using Minilab (Level 2)	# of samples analyzed at NQCL using compendial methods (Level 3)
Round 1	536	451	80	44
Round 2	499	496	65	25
Round 3	540	514	71	20
Round 4	606	117	112	115

3.2. Registration with the Pharmacy and Poisons Board

Figure 2 shows the registration status of the samples over the four rounds of post marketing surveillance. The percentage of unregistered samples has consistently decreased over time.

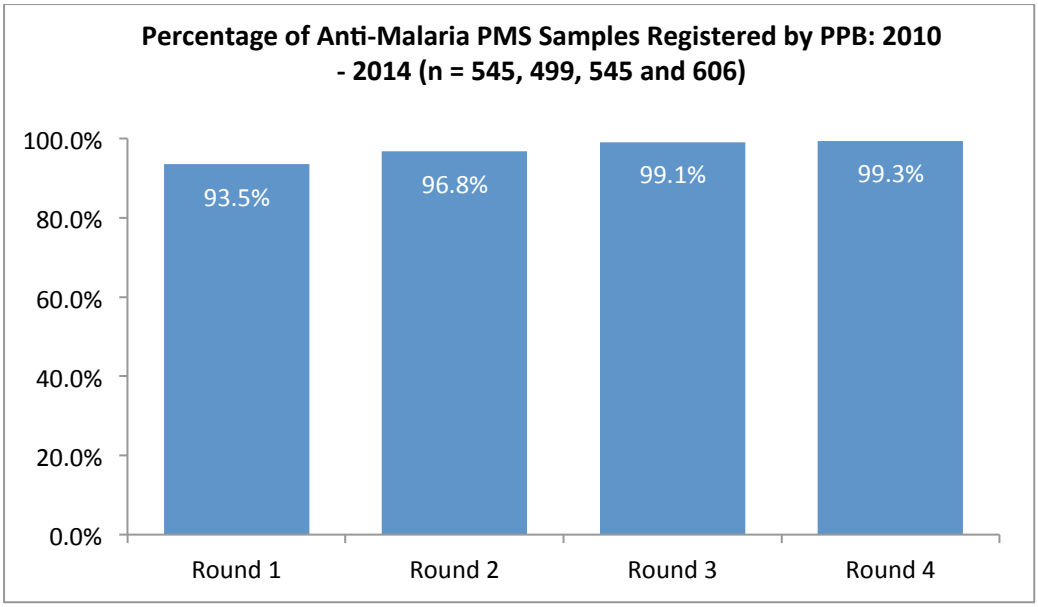


Figure 2: Registration status of PMS samples over time

3.3. Basic and Compendial Test Results

3.3.1. Level I Screening Test Results

The proportion of samples in Round 4 failing the level one screening test (minilab tests) was 1% - largely unchanged from the previous round. However, the proportion of samples that passed level one testing (82%) dropped to values below 90% for the first time since 2010. Conversely, 17% of the samples were 'doubtful', an increase from the 3 to 4.6% range observed in the previous three rounds.

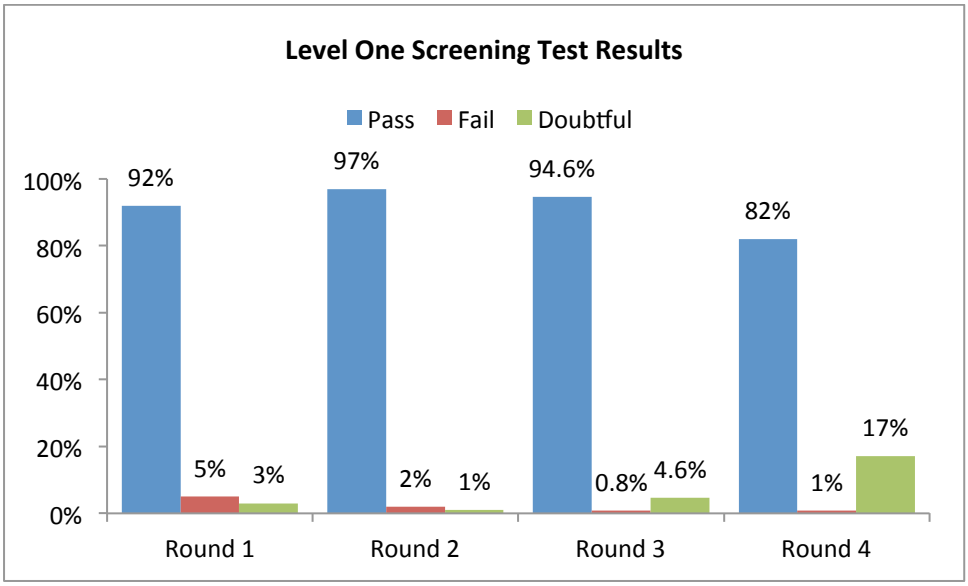


Figure 3: Results of Level I Testing

The reasons for doubtful results are summarized in figure 4.

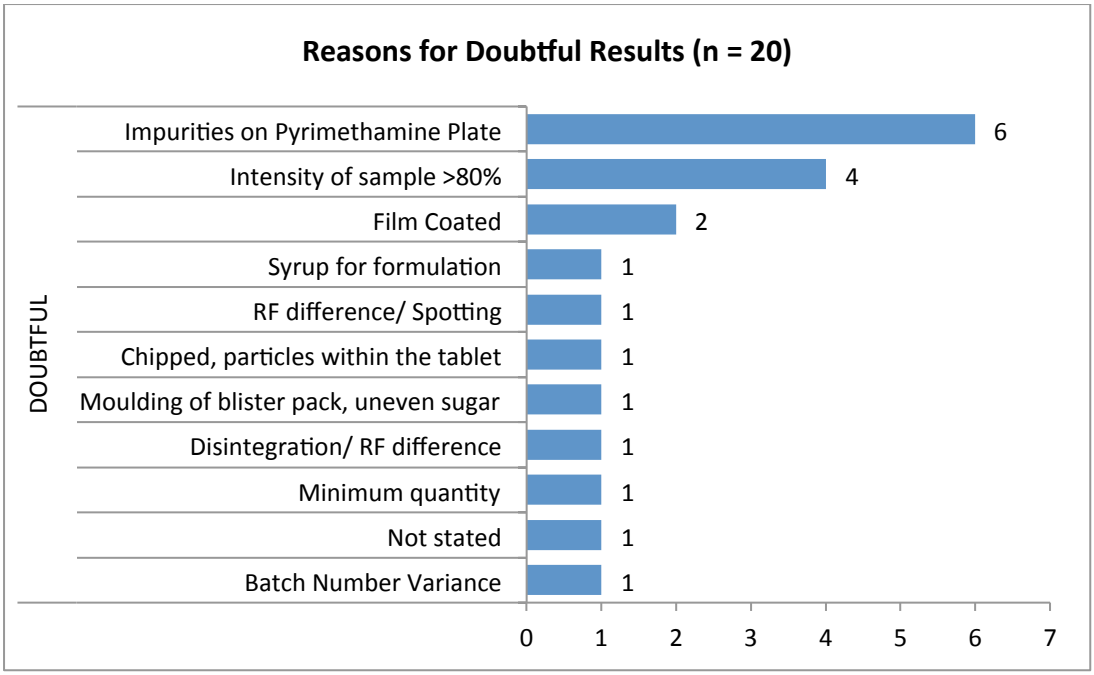


Figure 4: Reasons for 'doubtful' Results in Level I Testing

3.3.2. Level 2 Screening Test Results

The proportion of samples that passed level 2 screening test was 94%, a slight increase from 90% observed in Round 3. No samples failed the level 2 screening test and 6% of the samples were doubtful.

The reasons for doubtful results were: presence of impurities (2 samples), intensity of sample <80% (3 samples), uneven sugar coating (1 sample) and chipped tablets (1 sample).

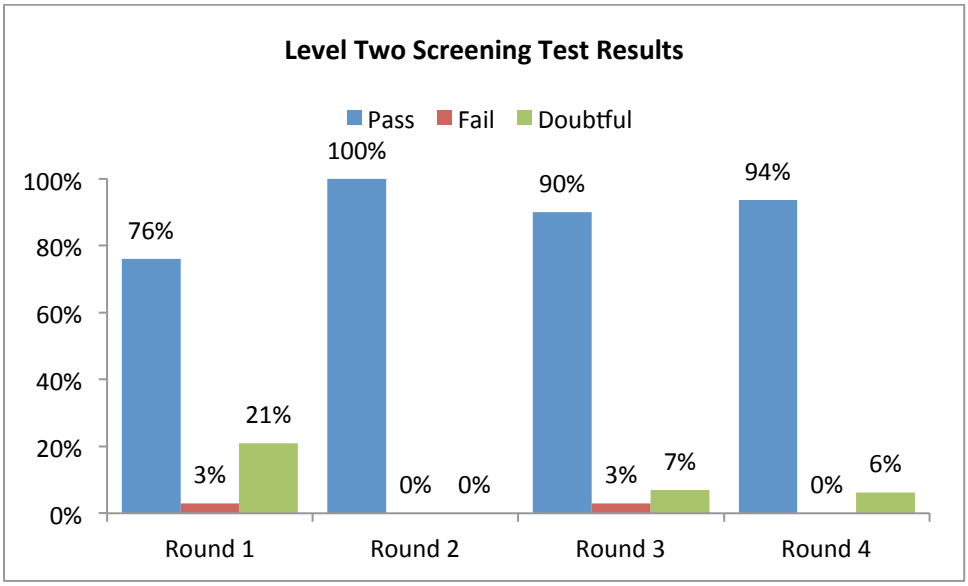


Figure 5: Results of Level 2 Testing

3.3.3. Level 3 Compedial Test Results

All 115 samples that were subjected to compendial testing passed. This is the first time that a 100% pass rate has been accomplished since 2010.

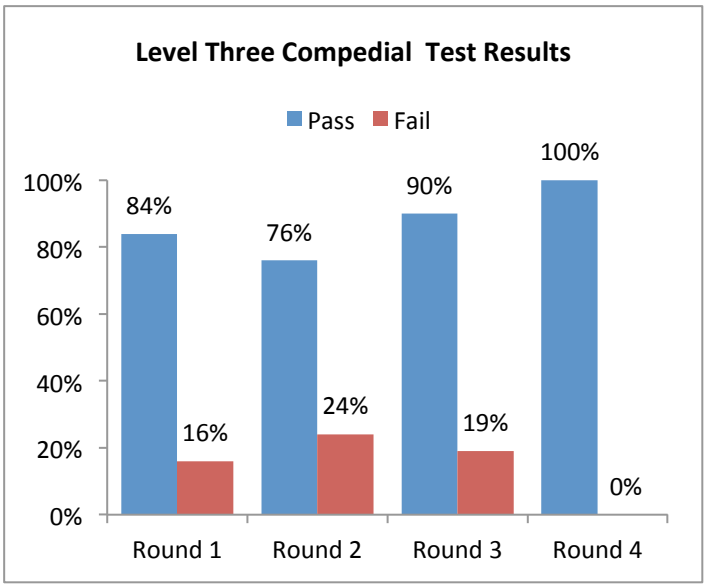


Figure 6: Results of Compedial Testing

Table 6: APIs Analyzed: Round 4

Active Pharmaceutical Ingredient (API)	# of samples
Artemether/ Lumefantrine	66
Sulfadoxine/ Pyrimethamine	24
Quinine Sulphate	14
Artesunate/ Amodiaquine	7
Quinine Dihydrochloride	4
Total	**115**

3.4. Determinants of Conformity

3.4.1. Sector of Health

Public sector and private/ informal sector samples had almost equal chances of passing the level I screening test with a prevalence ratio for public vs private/ informal samples of just 1.03 (table 6). This is in contrast to the previous round where public sector samples were 1.3 times more likely to pass.

Table 7: Sector and Conformity

Sector	Level I Test Results		Total
	Pass	Fail/ Doubtful	
Public	26 (83.9%)	5	**31**
Private/ Informal	70(81.4%)	16	**86**
	96(82%)	**21**	**117**

3.4.2. Artemesinine-based Combination Therapy (ACTm) vs. non-ACTm

Passing ACTm samples were 1.2 times higher than passing non-ACTm samples.

Table 8: Conformity of ACTm vs. non-ACTm Samples

Sector	**Level 1 Test Results**		**Total**
	Pass	**Fail/ Doubtful**	
ACTm	69(86.3%)	11	**80**
Non-ACTm	27(72.97%)	10	**37**
	96(82%)	**21**	**117**

3.5. Sensitivity and Specificity of the Minilab Tests

Sensitivity of a test refers to the percentage of samples that passed one level of testing and then went on to pass the next level of testing i.e. the proportion of samples that were correctly identified as conforming (true positives).

Specificity of a test refers to the percentage of samples that failed one level of testing and then went on to fail the next level of testing too i.e. the proportion of samples that were correctly identified as non-conforming (true negatives).

3.5.1. Level 1 Sensitivity and Specificity

The sensitivity of the level 1 test was 98% while the specificity was 35%. Four of the samples that either failed or were doubtful during level 1 testing did not undergo level 2 testing due to insufficient samples for analysis at NQCL

Table 9: Sensitivity and Specificity of Level 1 Testing

		Level 2		**Total**
		Pass	**Fail/ Doubtful**	
Level 1	Pass	94(97.8%)	2	**96**
	Fail/ Doubtful	11	6(35.3%)	**17**
	Total	**105**	**8**	**113**

3.5.2. Level 2 Sensitivity and Specificity

The sensitivity and sensitivity of the level 2 test were 100%. Insufficient quantities of one sample were received at NQCL thus analysis of this was not undertaken.

Table 10: Sensitivity and Specificity of Level 2 Testing

		Compendial Testing		**Total**
		Pass	**Fail/ Doubtful**	
Level 2	Pass	101(100%)	0	**101**
	Fail/ Doubtful	0	6(100%)	**6**
	Total	**101**	**6**	**107**

4. Discussion

4.1. Registration Status

In Round 4, 99.3% of the samples collected were registered by the Pharmacy and Poisons Board. This is the highest proportion registered since Malaria PMS started in 2010. One product – Artemether Lumefantrine tablets 40mg/ 240mg – was not registered in the country while two products, both containing Sulfadoxine/ Pyrimethamine tablets 500mg/ 25mg, were infringing on a tradename already registered in the country by another company. The three products that were not registered by PPB were manufactured in India.

4.2. Screening and Compedial Test Results

The proportion of samples failing or doubtful at level one (minilab) testing fell to 82% in Round 4 after consistently being above 90% on the previous three rounds. Impurities in the pyrimethamine plate and intensity of sample >80% accounted for more than half of the failed/ doubtful samples. Level 1 testing had high sensitivity and specificity rates for detection of poor quality anti-malarials. Considering the remarkably lower cost of minilab testing and how fast results are available compared to laboratory testing, these findings highlights the value of this approach and encourage its continued use. Furthermore, a possibly scale-up of minilabs across the country to conduct quality screening of anti-malarials and other medicines in the market is warranted.

Like in previous years, the proportion of samples passing level 2 testing continued to be high with zero failures and just 7 doubtful samples. Six of the seven doubtful samples went on to pass in the compendial testing. All 115 samples that were subjected to compendial testing passed.

Another positive finding was that a high proportion of anti-malarials, both in the public and private sectors, conformed to the requisite quality standards. The overall findings demonstrate the continued availability of good quality antimalarial medicines in the market- both ACTm and non-ACTm in the country.

4.3. Sensitivity and Specificity of the Minilab Tests

The sensitivity for level 1 (minilab) testing was 98% meaning that this proportion of samples had been correctly identified as conforming to quality standards. Just two samples that passed minilab screening went on to provide doubtful results in the level 2 test. The sampling strategy meant that the 11 samples that had been flagged as fail/doubtful during minilab testing and then passed level 2 testing posed no risk to patients.

Specificity of minilab testing was 35% meaning that this testing detected just ¾ of the samples that ended up being doubtful in level 2 testing. The ideal specificity is 100%, i.e. the screening test should not 'pass' any non-conforming samples. However, it is worth noting that both samples that passed minilab screening but were doubtful in level 2 testing went on to pass the compendial test.

4.4. Regulatory Actions Undertaken by PPB

The three products that were not registered in the country were withdrawn from the market. PPB also instituted investigations to trace the source of these products.

5. Conclusion and Recommendations

5.1. Conclusion

The proportion of poor quality anti-malarials continues to decline with the increased surveillance, improved regulation and the scale up of the AMFm program. Almost all the antimalarials in the market are registered and meet quality standards. Of particular importance is that all the ACTs, including those locally manufactured, meet quality standards.

The results obtained with the minilab show that this cost effective and rapid methodology is of value and it is recommendable of institutionalize its use for post market surveillance, especially in border towns and areas prone to substandard medicines

5.2. Recommendations

- The AMFm initiative should be sustained to ensure the availability of good quality anti-malarial medicines in the private sector
- Regular post market surveillance should be institutionalized at the county level, preferably using minilabs for screening purposes, to ensure that all anti-malarials available to the population meet the required quality standards
- Quality assurance mechanisms should be put in place for minilab testing to ensure that only reliable results are reported
- Prompt and decisive regulatory action needs to be taken on failed samples to rapidly take them out of the market and on manufacturers whose products do not meet regulatory requirements

6. REFERENCES

1. **President's Malaria Initiative.** President's Malaria Initiative: Fighting Malaria and Saving Lives. [Online] [Cited: May 19, 2015.] http://www.pmi.gov/where-we-work/kenya.

2. **Division of Malaria Control [Ministry of Public Health and Sanitation], Kenya National Bureau of Statistics,and ICF Macro.** *2010 Kenya Malaria Indicator Survey.* Nairobi : DOMC, KNBS and ICF Macro, 2011.

3. **President's Malaria Initiative (PMI).** *Malaria Operational Plan FY 2015.* 2015.

7. ANNEXES

7.1. Sampling Checklist

Before departing for sentinel sites with the intention of sampling for a Medicine Quality Monitoring (MQM) program, check that you have all the items listed below.

Task
1. Sufficient Sampling Forms *Fill out one form for each sample.*
2. Sampling Plan *Prepare a sampling plan in accordance with the MQM protocol and plan ahead for each day of sampling.*
3. Sampling Tools *Each sampling team must have the following tools:*
• New plastic or glass, opaque, clean containers to store and transport samples
• Map for the designated site with listed sources of sample collection
• Scissors, gloves, clean spatula or spoon, forceps, tape, watch, labels
• Indelible markers for labeling the sampling containers
• Indelible pens to complete forms
• Cardboard box(es) to store collected samples.
4. Notebook *(one per sampling team)* *Use a notebook dedicated to only MQM collections to record additional information about sampling activities.*
5. Logistics *Money for transportation, purchasing samples, food, lodging, and other incidentals.*
6. Optional items *Digital or conventional camera, mobile phone, global positioning system device, and other items as necessary.*

7.2. Sample Collection Form

Date (day/month/year)	
Name of Site	
Name of Collector	
Signature of Collector	

SAMPLE INFORMATION	
Sample code [1]	
Complete site address *(Name of location, street address, contact information, if applicable)*	
Sector of site (public, private or informal)	
Description of dispensing site (pharmacy, health clinic, hospital, warehouse, etc.)	
Commercial drug name	
INN[2]	
Pharmaceutical presentation (tablet, capsule, injectable, etc.)	
Dosage (mg)	
Manufacturer name	
Manufacturer's batch or lot number	
Manufacturing date (if present)	
Expiry date	
Registration or license number (if applicable)	
Manufacturer address	
Number of units collected[3]	
Package description: • Type of package (blister pack/card, bottle, others specify) • Number of units/pack • Presence of insert/leaflet	
Check one:	taken in original package taken from bulk container
Instructions to store sample (e.g., keep medicine away from light and at 25◦)	
Storage conditions at site[4]	

[1] Adapt according to program or country needs, suggested will be (A/B/C/D/E): A: Name of Country, B: INN/API, C: Collection Site; D: Date of Collection; E: Sequential Number.

[2] INN is the International Non-proprietary Name of a drug product, also known as Active Pharmaceutical Ingredient (API)

[3] If fewer than the number required by the protocol, please explain.

[4] Please describe the general storage conditions of the sampling site (e.g., medicines exposed to sun and/or air, no temperature and/or humidity control, water visible in storage room, medicines stacked inappropriately, etc.)

* Sample collection form should be attached to the sample and additional copies should be retained as indicated in the project protocol.

7.3. Basic Tests Analysis Form for Sentinel Site Staff

Sample Code	
Date of Analysis (dd/mmm/yyy)	
Sentinel Site of Analysis	
Name of Analyst	
Signature of Analyst	

TEST 1: VISUAL & PHYSICAL INSPECTION	
Visual Inspection:	
Please confirm that all of the recorded information in the Sample Collection Form (Annex 2) is consistent with the packaging and labeling of the medicine. Correct the Sample Collection Form (Annex 2) if there are any errors and/or omissions.[3] Have any corrections and/or additions been made to Sample Collection Form (Annex 2): ☐ Yes ☐ No	
Other Comments (description of hologram, any print on the backing foil, etc.)	
Physical Inspection:	
Shape (circular, oval, flat sides, other)	
Uniformity of shape	
Uniformity of color	
No physical damage (cracks, breaks, erosion, abrasion, sticky)	
Other observations (no foreign contaminant, dirty marks, proper seal - for capsule)	

TEST 2: DISINTEGRATION[4]		
Time of observed disintegration (minutes) 1. _____ 2. _____ 3. _____	Did the drug pass the disintegration test? ☐ Yes ☐ No	

[3] If any corrections/ additions were made to the Sample Collection Form, initial and date all added information
[4] Disintegration tests are 30 minutes; for testing at sentinel sites perform only 3 tablets/capsules. If one or more units do not disintegrate classify the sample as failing basic tests and send for confirmatory tests. For confirmatory testing please refer to the testing protocol.

TEST 3: TLC	
Did the sample have a spot? ☐ Yes ☐ No Rf Standard: _____ Rf Sample: _____ Rf % Sample difference:[5] _____	Intensity of sample spot compared to standard: ○ Less than 80% ○ Between 80% and 100% ○ More than 100% Were there any contaminants/impurities present? ☐ Yes ☐ No Observations: _____

FINAL RESULTS

○ The sample conformed with basic tests

○ The sample did not conform with basic tests Reason: _____

○ The sample is considered doubtful Reason: _____

How many units are remained after basic tests? _____

REPORT REVIEWED BY[6]:

Name: _____ Signature: _____

Date: _____

[5] Rf % Sample Difference = $\frac{|\text{Rf (Standard)-Rf (Sample)}|}{\text{Rf (standard)}} \times 100$

In this formula $|Rf\ (Standard) - Rf\ (Sample)|$ represents the absolute value of the difference between the Rf's of the standard and the sample.

Ex: In a TLC run the following values are obtained: Rf (standard) = 0,55, Rf (sample) = 0,57; The Rf % Sample Difference = $\frac{|0.55\text{-}0.57|}{0.55} \times 100 = \frac{0.02}{0.55} \times 100 = 3.6\%$

[6] If applicable

7.4. Basic Tests Analysis Form for National Quality Control Laboratory Staff

Sample Code	
Date of Analysis (dd/mmm/yyy)	
Sentinel Site of Analysis	
Name of Analyst	
Signature of Analyst	

TEST 1: VISUAL & PHYSICAL INSPECTION		
Visual Inspection:		
Please confirm that all of the recorded information in the Sample Collection Form (Annex 2) is consistent with the packaging and labeling of the medicine. Correct the Sample Collection Form (Annex 2) if there are any errors and/or omissions.[7] Have any corrections and/or additions been made to Sample Collection Form (Annex 2): ☐ Yes ☐ No		
Other Comments (description of hologram, any print on the backing foil, etc.)		
Physical Inspection:		
Shape (circular, oval, flat sides, other)		
Uniformity of shape		
Uniformity of color		
No physical damage (cracks, breaks, erosion, abrasion, sticky)		
Other observations (no foreign contaminant, dirty marks, proper seal - for capsule)		
TEST 2: DISINTEGRATION[8]		
Time of observed disintegration (minutes) 1. _____ 2. _____ 3. _____	Did the drug pass the disintegration test? ☐ Yes ☐ No	
TEST 3: TLC		
Did the sample have a spot? ☐ Yes ☐ No Rf Standard: _____ Rf Sample: _____ Rf % Sample difference:[9] _____	Intensity of sample spot compared to standard: ○ Less than 80% ○ Between 80% and 100%	

[7] If any corrections/ additions were made to the Sample Collection Form, initial and date all added information

[8] Disintegration tests are 30 minutes; for testing at sentinel sites perform only 3 tablets/capsules. If one or more units do not disintegrate classify the sample as failing basic tests and send for confirmatory tests. For confirmatory testing please refer to the testing protocol.

[9] Rf % Sample Difference = $\frac{|\text{Rf (Standard)-Rf (Sample)}|}{\text{Rf (standard)}} \times 100$

In this formula $|Rf\ (Standard) - Rf\ (Sample)|$ represents the absolute value of the difference between the Rf's of the standard and the sample.

Ex: In a TLC run the following values are obtained: Rf (standard) = 0,55, Rf (sample) = 0,57; The Rf % Sample Difference = $\frac{|0.55\text{-}0.57|}{0.55} \times 100 = \frac{0.02}{0.55} \times 100 = 3.6\%$

	○ More than 100% Were there any contaminants/impurities present? ☐ Yes ☐ No Observations: _____
FINAL RESULTS	
○ The sample conformed with basic tests ○ The sample did not conform with basic tests Reason: _____ ○ The sample is considered doubtful Reason: _____	
How many units are remained after basic tests? _____	
REPORT REVIEWED BY[10]:	
Name: _____ Signature: _____ Date: _____	

[10] If applicable

7.5. List of Sampled Facilities

	Name of Facility	Region	Sectory	Type
1.	Al-Iman Pharmacy	Coast	Private	Chemist
2.	Citadel Pharmaceuticals	Coast	Private	Wholesaler
3.	Coast Provincial General Hospital	Coast	Public	Hospital
4.	Dawamart Chemist	Coast	Private	Chemist
5.	Fariji Chemist	Coast	Private	Chemist
6.	Jashchem Pharmaceuticals	Coast	Private	Chemist
7.	Kohima Chemist	Coast	Private	Chemist
8.	Latecoast Pharma	Coast	Private	Chemist
9.	Latecoast Pharma	Coast	Private	Wholesaler
10.	Likoni District Hospital	Coast	Public	Hospital
11.	Limar Pharmacy	Coast	Private	Chemist
12.	Malindi District Hospital	Coast	Public	Hospital
13.	Medmatt Pharmacy	Coast	Private	Chemist
14.	Mijikenda Pharmacy	Coast	Private	Chemist
15.	Mikindani Medical Centre	Coast	Private	Clinic
16.	Moi District Hopital	Coast	Public	Hospital
17.	Msambweni District Hospital	Coast	Public	Hospital
18.	Oasis Medical Centre	Coast	Public	Hospital
19.	Old-Tana Pharmacy	Coast	Private	Chemist
20.	Otieno Chemist	Coast	Private	Chemist
21.	Palm Beach Hospital	Coast	Private	Hospital
22.	Palmland Pharmaceuticals Ltd	Coast	Private	Chemist
23.	Palmsea Pharmaceuticals	Coast	Private	Chemist
24.	Pamoja Chemists & Cosmetics	Coast	Private	Chemist
25.	Pharmart Chemist	Coast	Private	Chemist
26.	Psalmchem Pharmacy	Coast	Private	Chemist
27.	Romanyo Pharmaceuticals	Coast	Private	Chemist
28.	Rosky Chemist	Coast	Private	Chemist
29.	Sevenite Healthcare Ltd	Coast	Private	Wholesaler
30.	Tawfiq Hospital	Coast	Private	Hospital
31.	Waridi Pharmacy	Coast	Private	Chemist
32.	Al-Noor Pharmacy, Hagadera Refugee Camp	Garissa	Private	Chemist
33.	Asad - Medical Centre Hagadera	Garissa	Informal	Hospital
34.	Dadaab Islamic Relief World Wide Dadaab	Garissa	Private	Wholesaler
35.	Dadaab Sub District Hospital	Garissa	Public	Hospital
36.	Dagahaley Hospital (MSF Swiss)	Garissa	Private	Hospital
37.	Garissa Provincial General Hospital	Garissa	Public	Hospital
38.	Habib Pharmacy	Garissa	Informal	Chemist

Name of Facility	Region	Sectory	Type
39. Hagadera IRC Hospital	Garissa	Private	Chemist
40. Hagadera IRC Hospital	Garissa	Private	Hospital
41. IFO 1 Hospital C/O Islamic Relief Worldwide	Garissa	Private	Hospital
42. Iftin Subdistrict Hospital	Garissa	Public	Hospital
43. IRC Hagadera Hospital	Garissa	Private	Hospital
44. Islamic Relief Worldwide	Garissa	Private	Wholesaler
45. Madina Pharmacy	Garissa	Private	Chemist
46. Mash Pharmacy - Opp. Daghaley Hospital	Garissa	Informal	Chemist
47. Mash Pharmacy, Dental & Clinic	Garissa	Private	Clinic
48. Mash Pharmacy, Dental & Clinic	Garissa	Private	Chemist
49. Medina Pharmacy	Garissa	Private	Chemist
50. Police Line Dispensary, Garissa	Garissa	Public	Clinic
51. Safa Medical Clinic, Laboratories and Pharmacy	Garissa	Informal	Chemist
52. Tawakal Pharmacy - Buka Iftin Centre	Garissa	Informal	Chemist
53. Amylin Chemist	Kakamega	Private	Chemist
54. Bungoma District Hospital	Kakamega	Public	Hospital
55. Bungoma West Pharmacy	Kakamega	Private	Chemist
56. Busia District Hospital	Kakamega	Public	Hospital
57. Dagrich Pharmacy	Kakamega	Private	Chemist
58. Emuhaya Sub District Hospital	Kakamega	Public	Hospital
59. Garissa Pharmacy Drug Store	Kakamega	Private	Chemist
60. Guardian Chemists	Kakamega	Private	Chemist
61. Iguhu District Hospital	Kakamega	Public	Hospital
62. Kakamega PGH	Kakamega	Public	Hospital
63. Khunyangu District Hospital	Kakamega	Public	Hospital
64. Kima Mission Hospital	Kakamega	Public	Hospital
65. Kocholya District Hospital	Kakamega	Public	Hospital
66. Liberpharm Limited	Kakamega	Private	Chemist
67. Lichomo Chemist	Kakamega	Private	Chemist
68. Malaba Dispensary	Kakamega	Private	Chemist
69. Matayos Chemist	Kakamega	Private	Chemist
70. Mohini Chemist	Kakamega	Private	Chemist
71. New Amo Pharmacy and Laboratory	Kakamega	Private	Chemist
72. Oviwa Enterprises Limited	Kakamega	Private	Chemist
73. Pesi Medical Centre	Kakamega	Private	Chemist
74. Pramukh Chemist Limited	Kakamega	Private	Chemist
75. Riddhi Pharmacy	Kakamega	Private	Chemist
76. St Elizabeth Mukumu Hospital	Kakamega	Public	Hospital
77. Tiba Chemist, Chavakali	Kakamega	Private	Chemist

Name of Facility	Region	Sectory	Type
78. Uplands Pharmacy	Kakamega	Private	Chemist
79. Webuye District Hospital	Kakamega	Public	Hospital
80. Athi River Health Centre	Nairobi	Public	Health Centre
81. Chania S. Pharmacy	Nairobi	Private	Chemist
82. Coptic Hospital	Nairobi	Private	Hospital
83. Dase Chemist	Nairobi	Private	Chemist
84. Empire Pharmacy	Nairobi	Private	Chemist
85. Family Health Options Kenya	Nairobi	Private	Hospital
86. Gathiimaini Pharmacy	Nairobi	Private	Chemist
87. Jamia Clinic	Nairobi	Private	Clinic
88. Jolichem Pharmacy, Airport North Road	Nairobi	Private	Chemist
89. Machakos District Hospital	Nairobi	Public	Hospital
90. Magann Pharmaceuticals Ltd	Nairobi	Private	Chemist
91. Maresi Healthcare Ltd	Nairobi	Private	Chemist
92. Mathari Hospital	Nairobi	Public	Hospital
93. Melchizedek Hospital	Nairobi	Private	Hospital
94. Mica Pharmaceuticals Ltd	Nairobi	Private	Chemist
95. Mission For Essential Drugs and Supplies	Nairobi	Private	Wholesaler
96. Nicomed Pharmaceuticals	Nairobi	Private	Chemist
97. Omaera Pharmaceutical	Nairobi	Private	Chemist
98. Omaera Pharmaceuticals Ltd	Nairobi	Private	Chemist
99. Omaera Pharmaceuticals Ltd	Nairobi	Private	Wholesaler
100. Sage Pharmacy	Nairobi	Private	Chemist
101. Sage Pharmacy Ltd, Dagoretti	Nairobi	Private	Chemist
102. Sage Pharmacy, Kenyatta	Nairobi	Private	Chemist
103. Syokimau Pharmacy	Nairobi	Private	Chemist
104. Thika Level 5 Hospital	Nairobi	Private	Chemist
105. Thika Level 5 Hospital	Nairobi	Public	Hospital
106. Uchumi Hyper Pharmacy	Nairobi	Private	Chemist
107. Avenue Hospital Kisumu	Nyanza	Private	Hospital
108. Awang' Mach Chemist	Nyanza	Informal	Chemist
109. A-Z Pharmacy Limited	Nyanza	Private	Wholesaler
110. Bondo Medical Centre	Nyanza	Private	Clinic
111. Darhom Chemist and Shop	Nyanza	Informal	Chemist
112. Doorstep Pharmacy	Nyanza	Private	Chemist
113. Guchalabs Chemists	Nyanza	Private	Chemist
114. Jamige Chemist	Nyanza	Informal	Chemist
115. Nyanza PGH	Nyanza	Public	Hospital
116. Katito Gateway Pharmacy	Nyanza	Private	Chemist

	Name of Facility	Region	Sectory	Type
117.	Kentons Limited	Nyanza	Private	Wholesaler
118.	Kiangoso (K) Chemists	Nyanza	Private	Chemist
119.	Kisii Level V Hospital	Nyanza	Public	Hospital
120.	Kisumu East District Hospital	Nyanza	Public	Hospital
121.	Leo Chemist Limited	Nyanza	Private	Chemist
122.	Meridian Four Pharmacy	Nyanza	Private	Wholesaler
123.	Mogwa Pharmaceuticals	Nyanza	Private	Chemist
124.	Nyakongo Pharmaceuticals Limited	Nyanza	Private	Wholesaler
125.	Nyalenda Health Centre	Nyanza	Public	Health Centre
126.	Nyangena Hospital	Nyanza	Private	Hospital
127.	Nyaranga Pharmacy	Nyanza	Private	Wholesaler
128.	Patridge Healthcare	Nyanza	Private	Chemist
129.	Port Florence Community Hospital	Nyanza	Private	Hospital
130.	Ram Hospital	Nyanza	Private	Hospital
131.	Ravitco Chemist	Nyanza	Informal	Chemist
132.	Shanob Pharmaceuticals	Nyanza	Private	Chemist
133.	St. Joseph's Hospital Nyabondo, Annex	Nyanza	Private	Chemist
134.	Tayyibah Medical Clinic	Nyanza	Private	Clinic
135.	Victoria Pharmaceuticals Limited	Nyanza	Private	Wholesaler
136.	Wilco Pharmacy	Nyanza	Private	Chemist
137.	Burnt Forest Private Clinic	Rift Valley	Private	Clinic
138.	Bwena Medical Services	Rift Valley	Private	Clinic
139.	Cheranganyi Nursing Home	Rift Valley	Private	Hospital
140.	Eldoret Intrenational Airport Dispensary	Rift Valley	Public	Health Centre
141.	Generation Afya Centre	Rift Valley	Private	Clinic
142.	Huruma Chemist	Rift Valley	Private	Chemist
143.	Huruma Subdistrict Hospital	Rift Valley	Public	Hospital
144.	Kabarnet DH	Rift Valley	Public	Hospital
145.	Kahosi Chemist	Rift Valley	Private	Chemist
146.	Kape Health Care Pharmacy	Rift Valley	Private	Chemist
147.	Kimalel Health Centre	Rift Valley	Public	Health Centre
148.	Kitale District Hospital	Rift Valley	Public	Hospital
149.	Kuinet Chemist	Rift Valley	Private	Chemist
150.	Laangoni Chemist	Rift Valley	Private	Chemist
151.	Lima Chemists Stores Ltd	Rift Valley	Private	Chemist
152.	Mana Chemist	Rift Valley	Private	Wholesaler
153.	Moi Teaching and Referral Hospital	Rift Valley	Public	Hospital
154.	Moschem Pharmacy Ltd	Rift Valley	Private	Chemist
155.	Mosoriot Health Centre	Rift Valley	Public	Health Centre

	Name of Facility	Region	Sectory	Type
156.	Mothers Pharmacy Ltd	Rift Valley	Private	Wholesaler
157.	Sarara Chemist	Rift Valley	Private	Wholesaler
158.	Stalom Chemist	Rift Valley	Private	Chemist
159.	Sugu Nanga Chemist	Rift Valley	Private	Chemist
160.	Tionybei Chemist	Rift Valley	Public	Hospital
161.	Tionybei Chemist	Rift Valley	Private	Chemist
162.	Total Medicare Ltd	Rift Valley	Private	Chemist
163.	Transwide Pharmaceuticals Ltd	Rift Valley	Private	Chemist
164.	Transwide Pharmaceuticals Ltd	Rift Valley	Private	Wholesaler
165.	Alpha Chemist & Vet	Turkana	Informal	Chemist
166.	Ishara Chemist, Lodwar	Turkana	Private	Chemist
167.	Ishara Chemist, Lodwar	Turkana	Private	Hospital
168.	Kakuma IRC Refugee Camp Hospital	Turkana	Private	Hospital
169.	Kakuma Mission Hospital	Turkana	Private	Hospital
170.	Lodwar Chemists	Turkana	Private	Chemist
171.	Lodwar District Hospital	Turkana	Public	Hospital
172.	Lokichar Chemist	Turkana	Private	Chemist
173.	Premier Medical Services	Turkana	Private	Clinic
174.	Tarachi Chemist, Kakuma	Turkana	Informal	Chemist
175.	Turkana Chemist, Lodwar	Turkana	Private	Chemist
176.	Winas Chemist	Turkana	Private	Chemist
177.	Winas Chemist (B)	Turkana	Private	Chemist

7.6. List of Data/ Sample Collection Team

Team #	Team Members	Counties Visited
1	Sarah Chesaro George Muthuri Beatrice Mutisya Lily Kipkeno	Nairobi Machakos Thika
2	Peter Kiptoo Gladwel Cheruiyot	Baringo Uasin Gishu Trans Nzoia West Pokot Elgeyo Marakwet
3	Peter Kiptoo Moly Okoth	Siaya Kisumu Kisii
4	Emily Siminyu Philip Mutinda Mercy Wandeto James Kingori	Taita Taveta Mombasa Kilifi Kwale
5	George Muthuri Sarah Chesaro Lilly Kipkeno Beatrice Mutisya	Daadab (Garissa)
6	George Muthuri Henry Ogeto	Kakuma (Turkana)
7	Patrick Kibiego Mary Kendi	Busia Bungoma Kakamega Vihiga,
8.	Andrew Nyandigisi George Wang'ang'a Stephen Kimatu Latifa El Hadry	Central Supervisory, M& E