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Ministry of Medical Services

POST MARKET SURVEY OF ANTIRETROVIRAL MEDICINES IN KENYA

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Abbreviations and Acronyms

ABC	Abacavir
AIDS	Acquired Immune Deficiency Syndrome
API	Active Pharmaceutical Ingredient
ART	Antiretroviral Therapy
ARV	Antiretroviral
AZT	Zidovudine
°C	Degrees Centigrade
CDC	Centre for Disease Control
cGMP	Current Good Manufacturing Practice
cm	centimetre
DAR	Daily Activity Register
ddI	Didanosine
DLTLD	Division of Leprosy, Tuberculosis and Lung Diseases
EFV	Efavirenz
FEFO	First Expiry First Out
FIFO	First In First Out
FTC	Emtricitabine
GSK	Glaxo Smithkline
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
HCSM	Health Commodities Services Management Program
ICH	International Conference on Harmonization
KAIS	Kenya AIDS Indicator Survey
KEMSA	Kenya Medical Supplies Agency
Kg	Kilogram
KNASP	Kenya National AIDS Strategic Plan
KNPP	Kenya National Pharmaceutical Policy
3TC	Lamivudine

MEDS	Mission for Essential Drug Supplies
MSD	Merck Sharp and Dohme
MOMS	Ministry of Medical Services
MOPHS	Ministry of Public Health and Sanitation
MSH	Management Sciences for Health
NACC	National AIDS Control Council
NASCOP	National AIDS STI Control Program
NQCL	National Quality Control Laboratory
NVP	Nevirapine
PLHIV	People Living with HIV
PMS	Post Market Surveillance
PPB	Pharmacy and Poisons Board
PV	Pharmacovigilance
RH	Relative Humidity
d4T	Stavudine
SA	South Africa
SPS	Strengthening Pharmaceutical Systems (Program)
SPSS	Statistical Product and Service Solutions
TB	Tuberculosis
TDF	Tenofovir
UK	United Kingdom
USA	United States of America
USP/DQI	United States Pharmacopoeia/Drug Quality and Information
WHO	World Health Organization

Glossary of Terms

Active Pharmaceutical Ingredient: The chemical substance responsible for a product's pharmacological effect.

Adverse Event/Adverse Experience: Any untoward medical occurrence that may present during treatment with a pharmaceutical product but does not necessarily have a causal relationship with the treatment.

Brand name: Name given to a pharmaceutical product by the manufacturer e.g. Stocrin is the brand name for Efavirenz. Brand names may also be used for generic products (branded generics).

Clinical trial: A systematic study on pharmaceutical products in human subjects (including patients and other volunteers) in order to discover or verify its effects of and/or identify any adverse reaction related to it the products, and/or to study the absorption, distribution, metabolism and excretion of the products with the objective of ascertaining their efficacy and safety. Clinical trials are generally classified into phases I to IV.

Phase IV trials are studies performed after marketing of the pharmaceutical product. They are carried out on the basis of the product characteristics for which the marketing authorization was granted and are normally in the form of post-marketing surveillance.

Combination: Pharmaceutical product containing two or more medicines.

Dosage form: The form in which a completed pharmaceutical product is administered e.g. tablet, capsules, injection.

Drug: See medicine.

Drug resistance: The World Health Organization (WHO) defines antiretroviral resistance as the ability of a virus strain to multiply despite the administration and absorption of a medicine given in doses equal to or higher than those usually recommended but within the tolerance of the subject, provided drug exposure

at the site of action is adequate. Resistance to antiretrovirals arises because of the selection of viruses with genetic mutations or gene amplifications that confer reduced susceptibility to the medicine.

Generic medicine: A pharmaceutical product that is manufactured without a license from the innovator manufacturer and marketed after the expiry of patent or other exclusive rights. A generic medicine may be marketed under a non-proprietary name (such as efavirenz) or under a branded name (such as emcure, a branded generic of efavirenz).

Formulation: The administration form of a completed pharmaceutical product, inclusive of the strength of the active pharmaceutical ingredient per unit dose e.g. efavirenz 600mg tablets, lamivudine 10mg/ml syrup.

Medicine: Any substance in a pharmaceutical product that is used to modify or explore physiological systems or pathological states for the benefit of the recipient. The term medicinal product, includes the presentation, packaging, and accompanying information.

National pharmacovigilance centre: A single, government recognized centre or integrated system within a country with the clinical and scientific expertise to collect, collate, analyze and give advise on all information related to medicine safety.

Pharmaceutical product: Any medicine intended for human use, presented in its finished dosage form, that is subject to registration and control by pharmaceutical legislation.

Prescription event monitoring: A system created to monitor adverse drug events in a population based on prescriptions received.

Quality assurance: Refers to the management activities required to ensure that the medicines that reach patients are safe, effective and of acceptable quality. These activities may include, but are not limited to product evaluation for registration, manufacturers' pre-qualification, and quality control.

Quality control: Refers to the testing of samples as specified by the product monographs.The quality of ARVs is in fact an issue of global concern as evidenced by the emphasis placed by World Health Organization (WHO).

Sample: For the purposes of this study, sample refers to each of the medicines collected from the facility meeting the sampling criteria.

Treatment failure: Inability to achieve the desired therapeutic response after the initiation of therapy at the recommended dosages. Treatment failure is not synonymous with drug resistance.

Foreword

Kenya is currently experiencing a mixed HIV/ AIDS epidemic with characteristics of both a 'generalized' epidemic among the mainstream population, and a 'concentrated' epidemic among specific most-at-risk populations (MARPs) and geographies.

HIV/AIDS is one of the leading causes of death in Kenya and its control remains a challenge. It was declared a national disaster and a public health emergency in 1999 by the Government of Kenya. Since then, the Government has put in place structures to ensure scaling up of HIV prevention, care and treatment services. To ensure improvement in the quality of life, reduction of morbidity and mortality due to HIV and AIDS, access to appropriate treatment plays a pivotal role. Quality, safety and efficacy of antiretrovirals need to be considered to ensure that a patient receives optimal benefits from the prescribed treatment and resistance to antiretrovirals is contained. Quality of the medicinal product not only needs to be assured during manufacture, but also during storage and dispensing. Moreover, access to quality, effective treatment remains the core mandate of any public health program and this needs to be complemented with an effective regulatory system.

To mitigate the challenges in the management of HIV and drug resistant HIV, National AIDS/STI Control Program (NASCOP) and the Pharmacy and Poisons Board (PPB),the National Drug Regulatory Authority, conducted a post market survey of antiretrovirals in the Kenyan market. The aim of the survey was to provide baseline information on availability, registration status, quality of ARV medicines and conformity to national ART guidelines in public, private and faith-based health sectors in Kenya.

The survey demonstrated the commitment of the parent Ministries of Health towards ensuring patient safety. Its findings will go a long way in designing appropriate strategies to ensure quality, safety and efficacy of antiretrovirals for the public as proposed in the Ministry of Medical Services 2008-2012 and Ministry of Public Health and Sanitation 2008-2012 strategic plans.

To ensure that patients continuously receive high quality pharmaceutical care, it is envisaged that this type of survey will be conducted periodically in order to inform policy in drug regulation, quality assurance, procurement and other applicable strategies.

It is hoped that the report will inform actions to be taken by regulators, other relevant policy makers and stakeholders to eradicate poor quality, sub-standard, counterfeit and unregistered antiretroviral medicines from Kenya.

We recognise and applaud the multi-stakeholder collaboration and support from CDC, WHO, MSH, PPB, NASCOP and NQCL for their technical expertise and financial commitment in the execution of the survey, finalization of the report and dissemination of the findings. We look forward to their partnership in the implementation of the proposed recommendations.

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Abstract

Background: HIV and AIDS was declared a national disaster in 1999 by the government of Kenya which then established the National AIDS Control Council (NACC) to coordinate the multi-sectoral response to this public health threat. Currently, approximately 1.5 million people are estimated to be living with HIV virus in Kenya[1]. The national prevalence of HIV is 7.4 % in those aged 15-49 years and 7.1 % in the population aged 15-64 years.[2] About 800,000 Kenyans are eligible for antiretroviral therapy.[3]

Kenya has made significant progress in the prevention and management of HIV since the initiation of its national HIV/AIDS program. Over 500,000 PLHIV were receiving ART by December 2011.

Kenya adopted the gold standard for ART, Highly Active Antiretroviral Therapy (HAART), which is a combination of at least 3 antiretroviral medicines (ARVs) selected from at least 2 different ARV classes. Availability and access to appropriate, safe and quality antiretrovirals is essential to support effective prevention and treatment of HIV and AIDS.

The supply of quality antiretroviral products is a major concern at both national and international levels. Ineffective, poor quality and harmful medicines lead to negative public health impacts such as exacerbation of disease, resistance to medicines, therapeutic failure and even death. Consequently, these lead to diminished confidence in the health system as a whole and wastage of resources.

Aim: The aim of this survey was to establish and document baseline data on the availability and quality of ARV medicines as well as determine conformity of prescribing practices to national ART guidelines in Kenya's public, private and faith-based health sectors and propose corrective recommendations.

[1] Kenya National AIDS Strategic Plan (KNASP) III 2009/10 – 2012/3

[2] Kenya AIDS Indicator Survey (KAIS) 2007

[3] National AIDS Control Council (NACC) 2009

Objectives

The specific objectives were to:

1. Establish the range and availability of all ARVs in Kenya.
2. Determine the registration status of the sampled ARVs with PPB.
3. Assess the quality of key 1st line, alternative 1st line and selected 2nd line ARVs.
4. Assess the storage conditions of ARVs at the study facilities.
5. Determine conformity of prescribing practices to national treatment guidelines.

Methodology

A cross sectional survey was carried out in August and September 2009 and a total of 92 ART treatment sites and 55 community pharmacies were sampled across the country.

Questionnaires were administered in the sample sites and community pharmacies to obtain qualitative data on storage and distribution of antiretroviral medicines. 272 samples of antiretroviral medicines were randomly selected and sent to the National Quality Control Laboratory for quality control tests.

A total of 1558 sample of ARV preparations were collected from the market. These comprised of 95 products, 73 formulations and 14 APIs. Of the 73 formulations, 12 were capsules, 9 oral solutions and 52 tablet formulations.

Results

13 formulations, of which three were pediatric FDCs, were not available in 50% of the provinces.

Of the 95 products sampled, 69 (72.6.3%) were registered while 26 (27.47%) were not registered in Kenya. The unregistered products were from multiple manufacturing companies i.e. Abbot (2), Aurobindo (7), Cipla (8), Hetero (1), Matrix (4), Ranbaxy (1), Roche (1), Strides Arcolab (2).

In total 99.63% (n=272) of the samples analyzed passed laboratory tests.[4] Only one product(0.37%) failed tests of uniformity of weight and dissolution but complied on the assay. This product was AZT 300mg (manufactured by Hetero Drugs Limited, India), Batch No. A7276, MFD Date December 2007, Exp Date: November 2009, Client No. T1F4602.

The most common type of ventilation was one sided at 49.5% while air conditioning was the least at 8.7%. Most of the facilities had shelves and pallets in their storage areas. Five provinces recorded the highest indoor temparture (320 C). The minimum recorded indoor temperature was 180 C in Central and Rift Valley provinces. Humidity levels in most of the provinces were within acceptable range i.e. maximum 65% (ICH guidelines). Coast province had the highest humidity (72%).

Of the 14 API contained in the products found in the market, 7 (50%) were not in the Kenya National ART guidelines 2005 Edition. The majority (99.1%) of patients were on the recommended national ART regimens. However, only 47% and 41% of facilities had current adult and pediatric ART guidelines respectively.

Conclusions and Recommendations: One third of the products sampled from the market were not registered by the PPB. Storage conditions in majority of the sampled facilities were satisfactory. The laboratory results indicate that the samples analyzed were of good quality. Prescribing practices conformed to the national ART guidelines although availability of the guidelines was limited. Availability of pediatric FDC formulations was limited which could be attributed to their recent introduction by the national ART program.

In view of the findings on the registration status of the products, there is need to strengthen enforcement of drug regulatory activities especially drug registration. Further, there is need to conduct regular PMS to augment other product quality assurance measures. Current National ART guidelines should be disseminated widely to healthcare providers working in both private and public sectors.

[4] One product failed tests of uniformity of weight and dissolution but complied on the assay. This product was AZT 300mg (Hetero Drugs Limited, India), Batch No: A7276, MFD date: Dec-07, Exp. date: Nov-09, Client No: T1F4 602. However this product had already expired at the time of analysis and was therefore excluded from the analysis results.

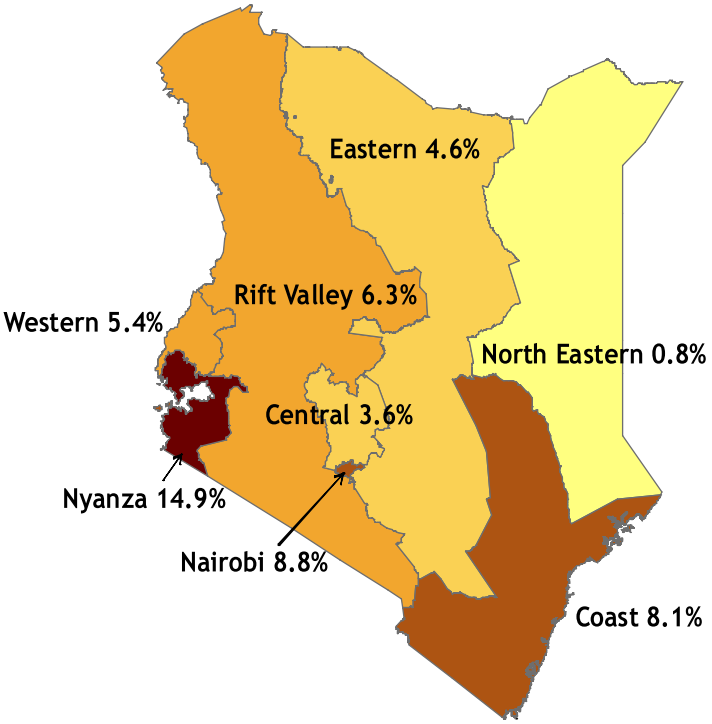
Introduction

Background

HIV and AIDS is a global disaster, and one of the most devastating health challenges facing many developing countries including Kenya. It was declared a national emergency in 1999 by the Government of Kenya.

Approximately 1.5 million people are estimated to be living with HIV virus in Kenya. The Kenya AIDS indicator Survey (KAIS) conducted in 2007 showed a prevalence of 7.4 % in those aged 15-49 years and prevalence of 7.1 % in the population aged 15-64 years. This prevalence varies greatly from one geographical region to another with figures ranging from 1% to 15% across provinces as shown in Figure 1.0 below.

Figure 1: Kenya HIV prevalence by province



(Source; KAIS 2007)

About 800,000 Kenyans are estimated to be in need of antiretroviral therapy . Of these, over 440,000 were receiving ART by end of December 2010 with children aged less than 14 years accounting for 36,000 of those on treatment .

[5] NACC 2009
[6] NASCOP National Monthly ART Commodity Stock Status Report (2- Pager) December 2010

ART in Kenya was first introduced in the private sector in the late 80's to early 90's and in the public sector in 2003. About 1200 health facilities in Kenya are currently providing ART The national ART program goal is to achieve universal access i.e. reach at least 80 % of those in need of treatment by 2013 according to KNASP III, 2009.

Kenya adopted the gold standard for ART, Highly Active Antiretroviral Therapy (HAART), which is a combination of at least 3 antiretroviral medicines (ARVs) selected from at least 2 different ARV classes. These are defined in the "Guidelines for Antiretroviral Drug Therapy in Kenya". The availability of these ARV medicines is therefore a vital component for the success of HIV and AIDS prevention and control strategies as they have proven to prolong and improve the quality of the lives of People Living with HIV and AIDS (PLHIV).

Appropriate medicines are essential to support effective prevention and treatment of HIV and AIDS. Some of the major critical issues that need continuous monitoring in ART commodity supply programs include:

- Quality assurance of the ARVs
- Conformity to the National ART treatment guidelines
- Availability and accessibility of the ARVs to those who need them.

The supply of antiretroviral products that are effective and of acceptable quality has become a major concern at both national and international levels. Quality supplies go a long way in preventing wastage of resources, ensuring good treatment outcomes and averting treatment failure.

The use of ineffective, poor quality and harmful medicines leads to negative public health impacts such as exacerbation of disease, resistance to medicines, therapeutic failure and even death. Consequently, these lead to diminished confidence in the health system as a whole and wastage of resources in terms of money spent on the ineffective poor quality medicines both by consumers and the government.

Along with the quality of the medicines consumed, it is important to ensure that only registered and approved medicines are available at all times in the market.

The Pharmacy and Poisons Board (PPB) plays a fundamental role in ensuring the provision of quality, safe and efficacious pharmaceutical

products and services. In addition, PPB has a responsibility to ensure that all medicines in the market are registered prior to availability. As part of the registration requirements, it is mandatory that the site of manufacture is inspected for current good manufacturing practice (cGMP) compliance and that samples of the medicines are tested to ensure quality. Unregistered medicines pose a serious threat to the overall efforts of ensuring safety, efficacy and quality since they are not authorized for sale in the market by the regulatory authority nor their quality established by the same.

In line with the above, the PPB has established a national pharmacovigilance system and developed a strategy for Post-Market Surveillance (PMS) of medicines upon which the survey on the quality of ARVs is anchored. PMS encompasses the pro-active and reactive collection of information on quality, safety and performance of medicines, medical devices, cosmetics, herbal medicines and related substances after they are placed in the market.

Previous and regular proactive and reactive post-market surveillance activities have shown presence of un-registered antimalarial medicines, cough and cold remedies and antibiotics in Kenya (PMS Anti-malarial Medicines Report, 2007). As at the time of the survey, none of the documented post market surveillance activities had focused on antiretroviral medicines. This survey, conducted in September 2009, was specifically designed to assess the availability, quality of antiretroviral and conformity of prescribers to national ART guidelines in Kenya.

Drug Regulation in Kenya

The PPB is the drug regulatory authority of the ministries responsible for health in Kenya, established in 1957 under the Pharmacy and Poisons Act, Chapter 244 of the laws of Kenya. PPB has the mandate to regulate pharmaceutical services, ensure the quality, safety and efficacy of human, veterinary medicines and medical devices. Additionally it advises the Government on all aspects on medicines regulation and pharmacy practice in order to safeguard health of all Kenyans.

One of the objectives of the Kenya National Pharmaceutical Policy 2010 (KNPP) is to ensure that the quality of drugs that are locally manufactured and imported meet internationally accepted quality standards.

The Pharmacovigilance section under the Directorate of Product Evaluation and Registration at the PPB is responsible for post-market surveillance activities. Prior to a drug being registered for use in the country, it has to be evaluated for standards of quality, efficacy and specifications by PPB in conjunction with a laboratory such as the National Quality Control Laboratory (NQCL). The primary objective of the post market surveillance is to ensure safety of medicines and conformity with the specifications as declared in the registration dossier at the time of initial drug registration.

The Pharmacovigilance section works together with the Directorate of Inspectorate, Surveillance and Enforcement specifically divisions of Good Distribution Practices (GDP), Good Manufacturing Practices (GMP) and Ports Of Entry.

The NQCL is responsible for evaluating the quality of medicines and medical devices. NQCL is a WHO prequalified laboratory and has the capacity to serve national and regional medicines quality control needs. Other laboratories include: Mission for Essential Drugs and Supplies (MEDS), which has a WHO prequalified laboratory and the Drugs Analysis and Research Unit (DARU).

Substandard Medicines

Substandard medicines lead to a number of consequences that include drug resistance leading to treatment failures, increased morbidity and mortality and wastage of available limited resources.

It is important to establish the quality of medicines in Kenya since it has been found through previous surveillance activities that substandard medicines are present in the market.

The Kenya Medical Supplies Agency (KEMSA) has been entrusted with the responsibility of procuring, warehousing and distributing medicines, non-pharmaceuticals, medical devices and equipment of high quality on behalf of the Government. The Pharmacy and Poisons Board works with KEMSA to ensure that the relative mandates of the two institutions are met. Moreover, the section of Pharmacovigilance ensures continuous communication and feedback on medicine quality issues to healthcare providers, policy makers, pharmaceutical industry and the public.

Literature Review

Appropriate quality medicines are essential to promote public health disease management approach. According to a survey conducted by WHO in some African countries, 30-50% of samples tested were of poor quality. Samples that failed quality assurance were 18% from Cameroon, Madagascar and Chad, 17% from Tanzania and Zimbabwe and 48% from Nigeria. 16% of the samples from Cameroon, Madagascar and Chad were counterfeit. [7]

In another study on quality of anti-malaria medicines in six sub-Saharan countries, the quality of anti-malarial medicines was reasonably under control in Kenya and Tanzania. Nigeria had the highest incidence of failing samples at 63.9%. This situation is confounded by the fact that in some African countries, medicines are sold in open market places, are smuggled or imported illegally into the countries and some domestic manufacturers do not meet cGMP. In addition, storage and distribution conditions of the medicines are inappropriate and corruption is still a challenge.[8]

Several anecdotal reports indicate that substandard ARVs are available in the global market. Quality of medicines, especially ARVs, was a key concern to the partners involved in the 3 by 5 strategy. For this reason, the partners established the WHO pre-qualification scheme as a prerequisite to procurement of ARVs. The prequalification scheme anchors on the principle that *'Quality cannot be assessed, tested or inspected into the product. It has to be built into it.'* [9]

Globally, WHO has been receiving reports on cases of counterfeit medicines since 1982. Some of these reports revealed that about 70% of the cases were reported by developing countries whereas less than 30% came from developed countries. The counterfeiting of medicines is a global scourge, which is particularly serious in the African continent.

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[7] WHO, http://www.who.int/entity/medicines/services/counterfeit/impact/impactF_S/en/).

[8] The WHO "Survey of the quality of selected antimalarial medicines circulating in six countries of sub-Sahara Africa"was conducted as part of a collaborative study with the United States Pharmacopeia (USP) Drug Quality and Information Programme, known as the "QAMSA Study". February 2011

[9] Dr Lembit Rago, (2005), Update on UN prequalification of medicines, http://www.who.int/bloodproducts/animal_sera/L.RagoWHO-QSM.pdf

According to WHO estimations, whereas counterfeit medicines represent 1% of the market in developed countries, up to 30% of the medicines sold in African countries are counterfeits. Several factors may explain this high rate in Africa, from the weaknesses of legislation and controls, to the lack of affordability of medicines and the attitude of governments. [10]

A counterfeit medicine represents different levels of risk, depending on whether the active ingredient is present or not, whether the dosage is right or whether the product contains toxic substances

The final quality of a manufactured product is determined by the raw materials used, formulation, manufacturing process and equipment, technical capability for producing and packaging, transportation and storage conditions.[11]

Treatment of HIV/AIDS in Kenya is based on recommendations in the national treatment guidelines formulated by the health ministries. These guidelines outline ARVs to be used as first line and also specify subsequent drug sequencing incase of treatment failure or adverse events. Since the number of treatment options can impact program effectiveness, conformity to these guidelines would ensure that the most appropriate regimen is chosen for a particular patient to prevent development of resistance and to give room for future treatment options.

HIV treatment involves the use of multiple ARVs taken in combination, commonly referred to as Highly Active Anti Retroviral Therapy (HAART). This is done to achieve maximum suppression of the virus and prevent the emergence of drug resistance to any of the medicines. The primary goal of ART is to achieve maximal and durable suppression of viral replication and induction of immune recovery leading to improved quality of life of the patients and reducing HIV related morbidity and mortality.

There are 4 classes of ARVs currently available in Kenya:

1. Nucleoside & Nucleotide reverse Transcriptase Inhibitors
2. Non-nucleoside reverse Transcriptase Inhibitors
3. Protease Inhibitors
4. Fusion Inhibitors

[10] M. Chauve (2008). The fight against counterfeit medicines in Africa: experience and role of pharmacists. Compte Rendus Biologies vol. 331, no. 12, p. 982-985

[11] USP 32 NF 27

The Ministries of Health through NASCOP have standardized the antiretroviral drug regimen in use taking into account the need for a public health approach, availability, accessibility, affordability and efficacy of the treatment. Fixed dose combinations are preferred over single drug formulations to promote adherence as well as for easier and more convenient planning by the program.

Study justification

Due to the magnitude of the HIV pandemic and the important role that ARVs play in the management of PLHIV, the quality of ARVs in the country is a matter of critical importance. Post market surveillance enables the detection of sub-standard, counterfeit and unregistered ARVs and the effects of storage conditions on the quality and stability of the ARVs.

Regular PMS of ARVs in Kenya has not been done before hence the need to establish the baseline information relating to quality and availability of ARV drugs in the country and propose appropriate interventions.

Aim of the Survey

The aim of this survey was to establish and document baseline data on the availability and quality of ARV medicines as well as determine conformity of prescribing practices to national ART guidelines in Kenya's public, private and faith-based health sectors and propose corrective recommendations.

Objectives of the survey

The objectives of the survey were to:

1. Establish the range and availability of all ARVs in Kenya.
2. Determine the registration status of the sampled ARVs with PPB.
3. Assess the quality of key 1st line, alternative 1st line and selected 2nd line ARVs.
4. Assess the storage conditions of ARVs at the study facilities.
5. Determine conformity of prescribers to national treatment protocols by ART providers.

Study Methodology

Study scope and duration

This was a nationwide study covering all the eight provinces.

The ARVs surveyed were 1st line, alternative 1st line and selected 2nd line as defined in the National ART Guidelines 3rd Edition 2006.

Data was collected from four defined sector outlets i.e. the public, faith-based and private health facilities as well as community pharmacies.

Data and sample collection was conducted between August and September 2009. Laboratory testing and analysis took place between October 2009 and June 2010.

Study Design

This was a descriptive cross-sectional survey using both qualitative and quantitative data collection methods.

Study Population

The study population included all health facilities and community pharmacies providing ARVs in Kenya. These consisted of public facilities (level 2 to 6), faith based health facilities, private hospitals and community pharmacies dispensing ARVs drugs to the public.

Sampling

The country was stratified into 8 regions corresponding to the administrative provinces. The samples were allocated proportional to the caseload of HIV patients receiving care as per the reported patient numbers by end 2008. In each stratum, samples were reallocated to four categories i.e. public, private, faith-based and community pharmacies. For the community pharmacies, a purposive sampling was done to pick the towns where the study was carried out. Major towns were selected based on corresponding caseload of health facilities providing ART.

The highest proportion (10%) of the study facilities selected were from Nairobi. This is due to the fact that Nairobi has the highest number of health facilities and community pharmacies providing ARVs.

Two sampling frames were used:

i. Pharmaceutical Society of Kenya (PSK) data-base of all registered

community pharmacies in Kenya. This was used to sample the community pharmacies

ii. NASCOP ART sites list for health facilities. This was used to sample public, faith-based and private health facilities.

The public facilities comprised provincial, district and sub-district hospitals, health centres and dispensaries. Faith-based sector outlets were hospitals and outlets dispensing ARVS. Private facilities comprised privately owned hospitals while community pharmacies were privately owned pharmaceutical retail outlets registered by Pharmacy and Poisons Board (PPB).

1. Inclusion Criteria and Exclusion Criteria for facilities and for the drugs

Inclusion criteria:

- Health facilities and community pharmacies stocking and dispensing ARVs.
- Facilities with more than one month of stock of antiretroviral medicines to be sampled.
- Samples with more than six months to expiry.

Exclusion criteria:

- Health facilities and community pharmacies not stocking and dispensing ARVs
- Samples with less than six months expiry
- Expired and damaged ARV medicines
- Facilities with less than one month of stock of the ARVs of interest
- ARVs requiring special storage conditions such as refrigeration.

2. Survey facilities sample size

A representative sample of 92 health facilities and 55 community pharmacies were included in the survey from a sampling frame of 750 and 1100 respectively (see Figure 2 and Table 1 below).

Figure 2: Geographical Distribution of Sampled Sites by Province

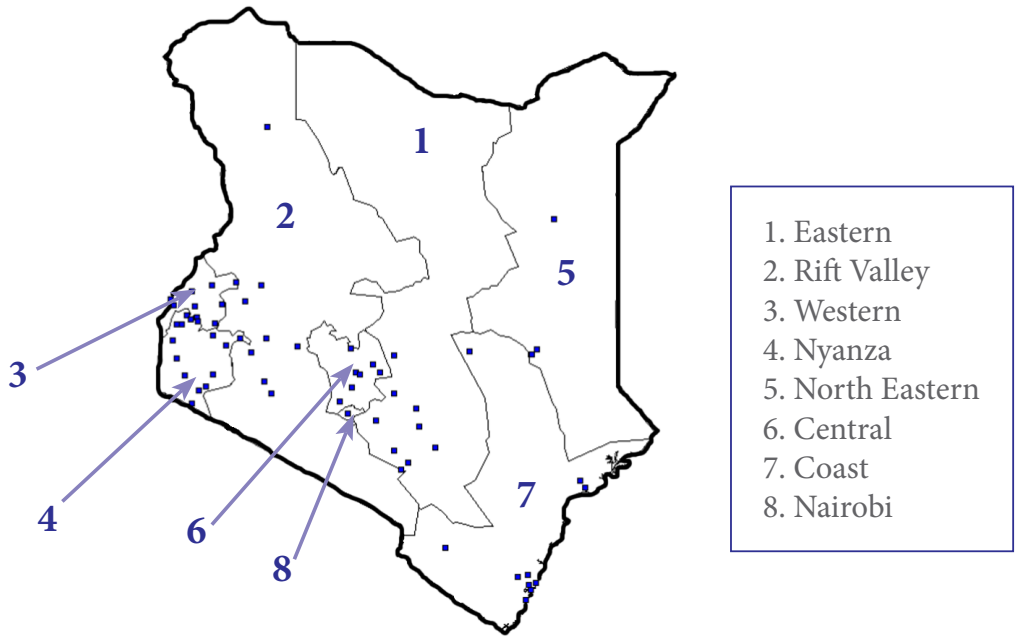


Table 1: Sample of Health Facilities and Community Pharmacies by Province

Province	Total Samples	Category 1 - Public Health facilities / regional store	Category 2 - Mission Health Facilities	Category 3 – Private health facilities	Category 4 - Community Pharmacies
Nairobi	29	7	2	2	18
Central	20	8	5	1	6
Coast	15	7	1	2	5
Eastern	19	10	2	1	6
North Eastern	3	2	0	0	1
Nyanza	27	18	3	1	5
Rift Valley	22	8	2	1	11
Western	12	7	2	0	3
Total	**147**	**67**	**17**	**8**	**55**

3. Sampling of Medicines at the Facilities

A stratified random sampling of medicines was done. All ARVs available in the facility were listed. For every product the number of batches available were identified and serialized. Using a table of random numbers, a batch was selected and predetermined quantities of the product were picked and coded. For each solid formulation a minimum of 100 tablets/

capsules were collected for laboratory analysis. However, for the purpose of this study the sampled quantities for liquid formulation were 5 bottles. Each sample was blinded by assigning a code to reflect the team and the facility it was obtained from e.g. T1F3 for team 1 facility 3.

4. Sampling of Prescriptions

Systematic random sampling was used to obtain five adult and five pediatric prescriptions. The sampling frame was all the available prescriptions for the three months prior to the study.

5. Sampling of products for laboratory analysis

Product sampled underwent some verification for completeness of data requirements and expiry status. The samples were then categorized according to active ingredients, strength and formulation. Each category was assigned a code (see Annex 5)

Sampling for laboratory analysis was a two stage process. In the initial step, all samples were subjected to stratified random sampling. However, for products where only one sample was collected from the field, all were taken for analysis. All the samples obtained from community pharmacies were included in the final sample for analysis. A representative sample of 272 samples out of a sampling frame of 1558 was obtained for laboratory analysis.

Data Collection

Data Collection tools

Two sets of tools were used for the survey.

1. Sample collection form

The collection form was designed to collect data on name of the product, the active pharmaceutical ingredient, the batch code, date of manufacture and expiry, name of manufacturer and country of origin (see Annex no 8).

2. Semi-structured questionnaire

The questionnaire was designed to collect data on sources of ARV medicines; transportation mode, storage conditions and conformity of the prescriptions to the National ART Treatment guidelines (Annex no 1).

Pre-testing of the data collection tools

A one day pre-survey training was carried out in Nairobi to orientate the data collectors on the survey process and the tools. The questionnaire and the sample collection forms were pretested in a public and a Faith-based hospital and two community pharmacies in Nairobi and Central provinces. Findings from the pre-test were incorporated and the tool finalized.

Data Collection Teams

There were six teams (T1 to T6) each comprising of three members drawn from health facilities, NASCOP and PPB. (Annex 4: List of Team Members and Health Facilities Listed).

Data Collection Process

Quantitative and qualitative data collection methods were used. A semi-structured questionnaire was administered to a health care provider in each health facility visited. A checklist was used to record observations.

Laboratory analysis

The ARV samples for analysis were submitted to the NQCL in October 2009 and analysis of the samples was completed in June 2010. 272 samples were submitted for analysis. The samples analyzed comprised both solid and liquid formulations; 230 solid and 42 liquid formulations. All tablets were subjected to the tests of uniformity of weight, friability, dissolution and determination of content of the active pharmaceutical ingredient (assay). Liquid formulations were tested for microbial load and assay.

Methods Used

Solid Formulations

1. Uniformity of weight British Pharmacopoeia (B.P) 2007 Volume 4, Appendix XIIG.
2. Dissolution and Assay: Both compendia and adapted in house methods of analysis.
3. Friability: British Pharmacopoeia (B.P) 2007 Volume 4, Appendix XVIIG.
4. Disintegration: British Pharmacopoeia (B.P) 2007 Volume 4, Appendix XIIA.

5. API Determination: Compendia APIs: United States Pharmacopoeia (U.S.P) 32NF27, Non compendia APIs-adapted manufacturers in house methods of analysis

Liquid Formulations

1. Microbial Load: British Pharmacopoeia (B.P) 2007 Volume 4, Appendix XVIB Plate Count Method.
2. Assay: Non Compendial APIs-adapted manufacturers in house methods of analysis; Compendial APIs: United States Pharmacopoeia (U.S.P) 32NF27.

National Quality Control Laboratory (NQCL) issued a certificate of analysis for the samples tested.

Data Analysis

The data collection forms and samples were received at the PPB and verified for completeness and accuracy. The registration status of the ARV samples was determined. Data was entered into Access based database after which data was analyzed using SPSS software version 16. Descriptive statistics was used to express the finding.

Results

All the targeted health facilities (100%, n=92) were visited and surveyed whereas only 42% (n=55) of community pharmacies were surveyed.

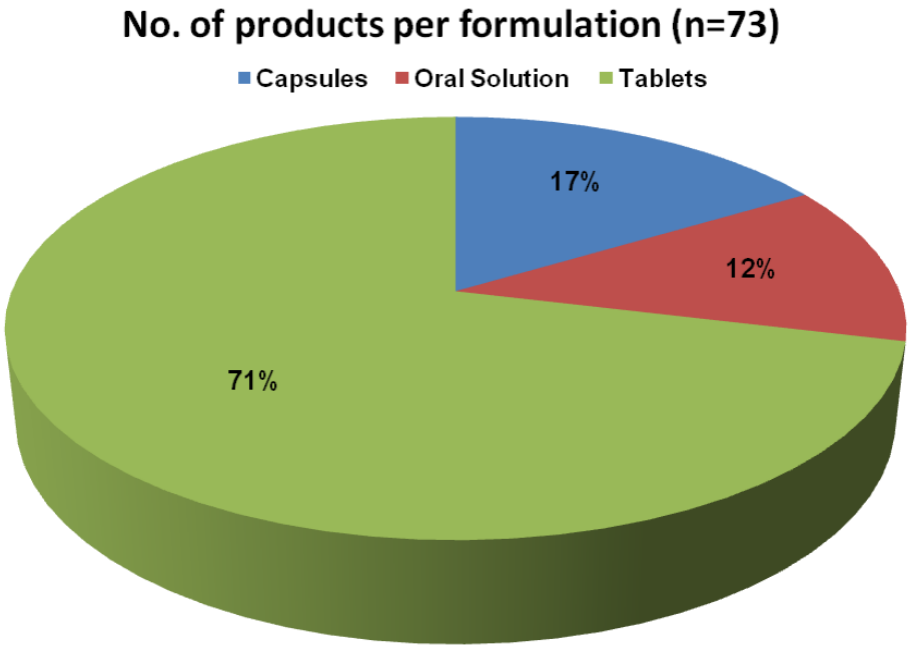
The results are categorised in 5 sections

I. Range and availability of ARV medicines
II. Registration status of sampled products
III. Quality of sampled ARV medicines
IV. Storage conditions of ARV medicines in study facilities
V. Conformity of prescribed ARVs to national ART guidelines.

1. Range and availability of ARV medicines in Kenya

A total of 1558 sample of ARV preparations were collected from the market. These made up 95 brands, 73 formulations and 14 APIs. Of the 73 formulations, 12 were capsules, 9 oral solutions and 52 tablet formulations (Figure 3). The oral solution was available in syrup, suspension or powder for reconstitution. Tablets were available as plain, film-coated and dispersible forms.

Figure 3: Percentage of sampled products by formulation



13 formulations were not available in 50% of the provinces. These were:

i. Abacavir 60mg/Lamivudine 30mg
ii. Didanosine 250mg
iii. Didanosine 400mg
iv. Didanosine 50mg
v. Efavirenz 600mg/Emtricitabine 200mg/Tenofovir 300mg
vi. Indinavir 500mg
vii. Lamivudine 30mg/Nevirapine 50mg/Zidovudine 60mg
viii. Lopinavir 100mg/ritonavir 25mg
ix. Nelfinavir 250 mg
x. Saquinavir 200mg
xi. Stavudine 12mg/Lamivudine 60mg/Nevirapine 100mg
xii. Stavudine 40mg/Lamivudine 150mg/Nevirapine 200mg
xiii. Tenofovir 300mg/Emtricitabine 200mg

a) Availability of dosage formulations by province

Availability of dosage formulations per province indicated that oral solid dosage forms formed the largest proportion with an average of 78.9% countrywide. However, there was regional variation in the distribution of the oral solid dosage forms ranging from 75.2% in Coast and 87.5% in North Eastern. Liquid dosage formulations were 21.1% of the total samples collected (Table 2 below).

Table 2: Availability of dosage formulations by province

Dosage form	REGION								
	Central	Coast	Eastern	Nairobi	North Eastern	Nyanza	Rift Valley	Western	Total
Capsules % (n)	6.2% (14)	14.0% (25)	8.8% (15)	6.7% (11)	2.5% (1)	12.9% (58)	9.7% (17)	6.4% (10)	**9.7% (151)**
Liquid % (n)	19.5% (44)	24.7% (44)	21.6% (37)	21.5% (35)	12.5% (5)	20.3% (91)	18.8% (33)	25.6% (40)	**21.1% (329)**
Tablets % (n)	74.3% (168)	61.2% (109)	69.6% (119)	71.8% (117)	85.0% (34)	66.7% (299)	71.6% (126)	67.9% (106)	**69.2% (1078)**
Total % (n)	**100.0% (226)**	**100.0% (178)**	**100.0% (171)**	**100.0% (163)**	**100.0% (40)**	**100.0% (448)**	**100.0% (176)**	**100.0% (156)**	**100.0% (1,558)**

b) Availability of Single and Fixed Dose Combination (FDC) by province

The single formulations were the most common (71.9%) across the country followed by the double combinations at 17.1%. The triple combination represented only 11% of the formulations. (Table 3 below)

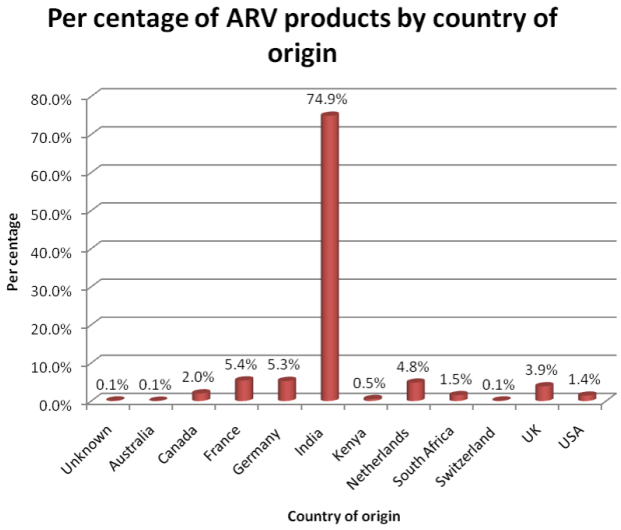
Table 3: Availability of Single and Fixed Dose Combination (FDC) by province

Combination	REGION								
	Central	Coast	Eastern	Nairobi	North Eastern	Nyanza	Rift Valley	Western	Total
Single % (n)	71.2% (161)	71.9% (128)	65.5% (112)	73.6% (120)	55.0% (22)	74.6% (334)	73.9% (130)	72.4% (113)	**71.9% (1120)**
Double % (n)	17.7% (40)	16.9% (30)	18.7% (32)	15.3% (25)	27.5% (11)	16.1% (72)	15.9% (28)	17.9% (28)	**17.1% (266)**
Triple % (n)	11.1% (25)	11.2% (20)	15.8% (27)	11.0% (18)	17.5% (7)	9 .4% (42)	10.2% (18)	9.6% (15)	**11.0% (172)**
Total % (n)	100.0% (226)	100.0% (178)	100.0% (171)	100.0% (163)	100.0% (40)	100.0% (448)	100.0% (176)	100.0% (156)	**100.0% (1558)**

c) Percentage of ARV Products by Country of Origin

The study showed that ARVs products found in the country were manufactured from 11 countries with the majority (74.9%) from India. Only 0.5% of the ARV products were manufactured locally (Figure 4). However, it was not possible to establish the country of origin for two of the products found in Coast and Central provinces (Annex7: Country of Origin of ARV Products by Province).

Figure 4: Percentage of ARV Products by Country of Origin (n=95)

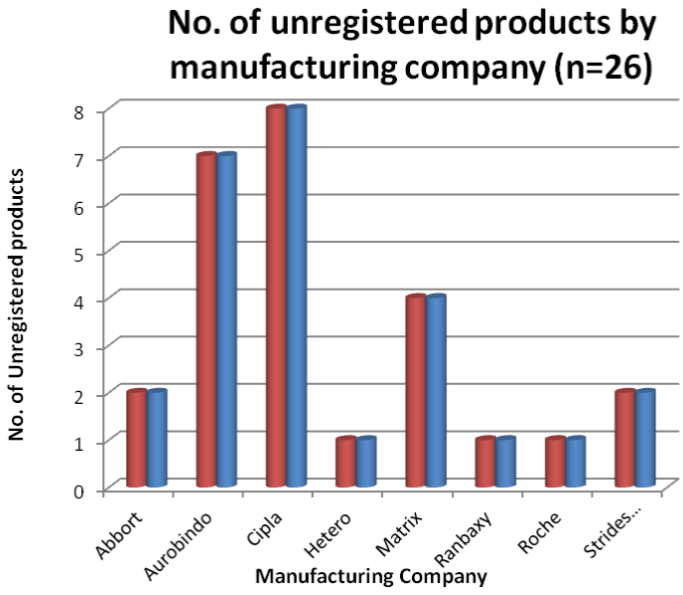


2. Registration status of the sampled ARVs

The registration status of all products was determined by searching through the Pharmacy and Poisons Board (PPB) drug registration database as at June 2010.

Of the 95 products, 69 (72.6%) were registered while 26 (27.4%) were not registered in Kenya. The unregistered products were from multiple manufacturing companies as shown below (Figure 5).

Figure 5: Number of unregistered products by manufacturing company



The countries of origin of the unregistered products included India, South Africa, Germany and Switzerland. 88.5% (n=26) of the unregistered products were from India, manufactured by Aurobindo, Cipla, Strides Arcolab Ltd, Ranbaxy, Hetero Drugs Ltd and Matrix Labs.

3. Quality of sampled ARV medicines

In total 99.63% (n=272) of the samples analyzed complied (Annex 8: Results of samples analyzed). 100% of the liquid formulations (n=42) and 99.56% of the solid formulations (n=230) analyzed complied (Tables 3 and 4 below). Only one product (0.37%) failed tests of uniformity of weight and dissolution but complied on the assay (Table 5). This product was Zidovudine 300mg, Batch No: A7276, MFD date: Dec-07, Exp. date: Nov-09, Client No: T1F4 602.

Table 4: Uniformity of weight, dissolution and assay results for solid ARV formulations

Tests	Method	Specifications	Test results (passed)	Conformity
Uniformity of weight	Weight	Tablets/capsules deviate by more than 5% from mean tablet weight	229 out of 230	99.56%
Dissolution	HPLC	No tablet less than 70% (n=6)	229 out of 230	99.56%
Assay	HPLC	90.0-110.0%	230 out of 230	100.00%

Table 5: Microbial load and assay results for liquid ARV formulations

Tests	Method	Compendia	Specifications	Test results	Conformity
Microbial Load	Plate Count Method	B. P 2007 Vol.Iv App. XVI B	5x102 Colony Forming Unit (CFU) per Ml	42 out of 42	100.00%
Assay (Identification)	HPLC	Adopted In-House Method	92.0--108.0%	42 out of 42	100.00%

Table 6: Results of the failed product

Tests	Method	Compendia	Specifications	Determination	Remarks
Uniformity of weight	Weight	B.P 2007 Vol. IV App XII G	Tablets/capsules deviate by more than 5% from mean tablet weight	Four deviates (9.0%, -6.1%, -8.4%, 5.6%)	Does not comply
Dissolution	HPLC	U.S.P 32 N.F 27 Vol 3 page 3890	No tablet less than 70% (n=6)	73.2% (n=12; RSD=10.7%)	Does not comply
Assay	HPLC	U.S.P 32 N.F 27 Vol 3 page 3890	90.0-110.0%	107.8% (n=7; RSD=1.8%)	Complies

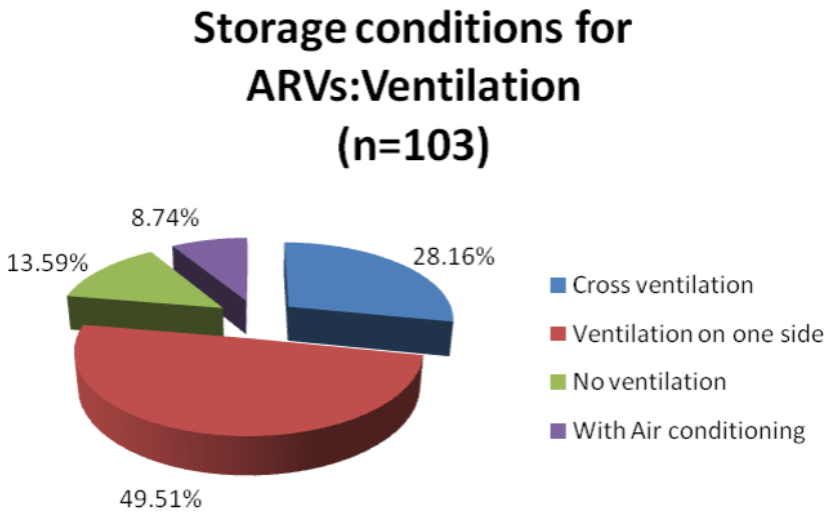
4. Storage conditions of ARVs at the study facilities.

Majority of health facilities had acceptable storage conditions.

a) Ventilation

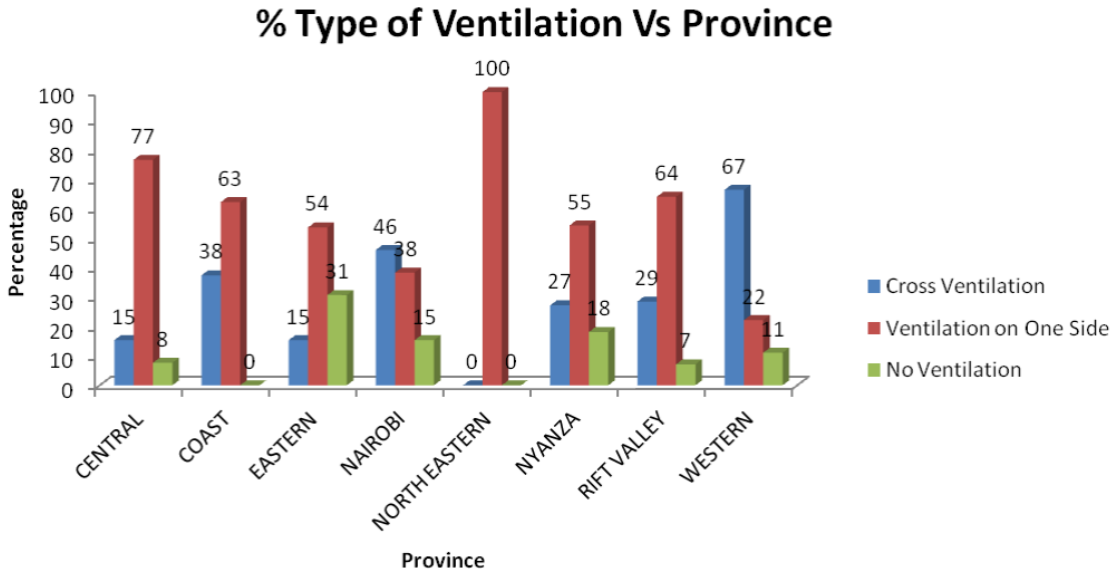
49.51% of the facilities had their storage areas with ventilation on one side. The most common type of ventilation was one sided at 49.5% while air conditioning was the least at 8.7% (Figure 6).

Figure 6: Type of Ventilation in ARV Storage Areas



Western province had the highest proportion (67%) of storage area with the cross ventilation while 50% of facilities studied in North Eastern province had air conditioning. Eastern province recorded the highest proportion (31%) of storage areas that lacked ventilation. (Figure 7)

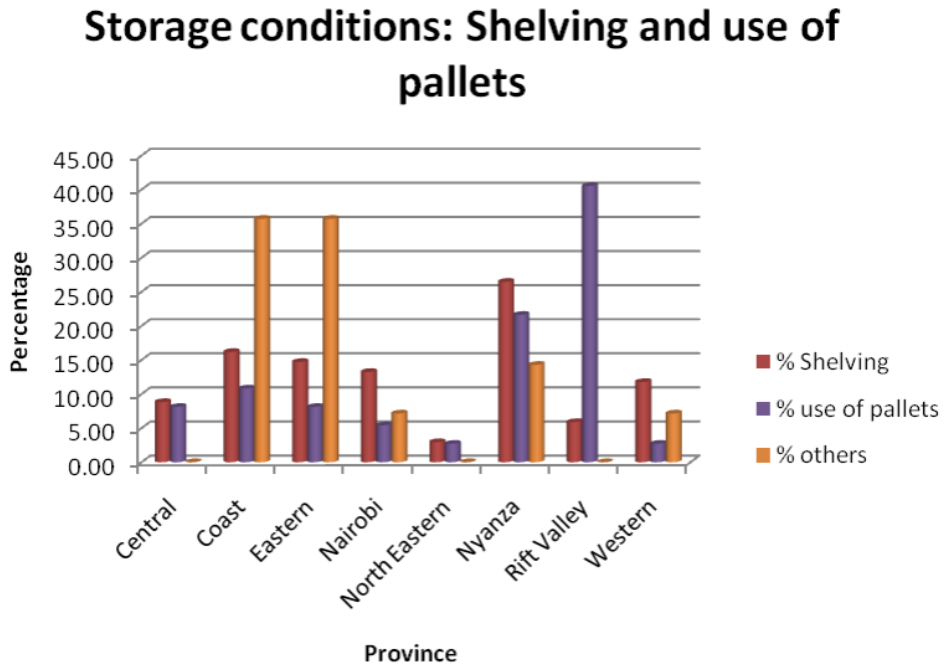
Figure 7: Summary of type of ventilation of ARV medicines storage facilities by province



b) Shelving and use of pallets

Most of the facilities complied with good storage practices on use of shelves and pallets. A number of facilities had other alternatives such as metal cabinets and wooden cupboards.

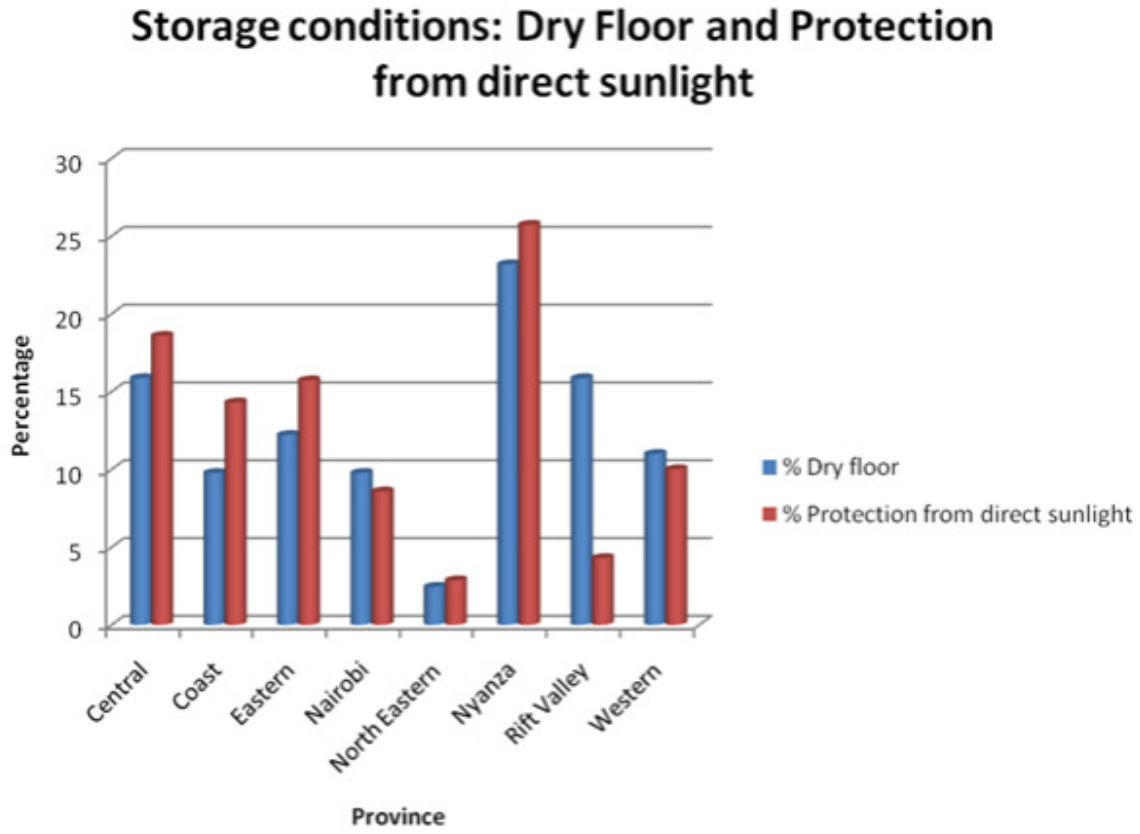
Figure 8: Percentage of facilities using shelving, pallets and other storage fittings



c) Dry floor and protection from direct sunlight

Most of the facilities complied with good storage practices on maintenance of dry floors and protection from direct sunlight (Figure 10).

Figure 9: Percentage of facilities with dry floor and protection from direct Sunlight

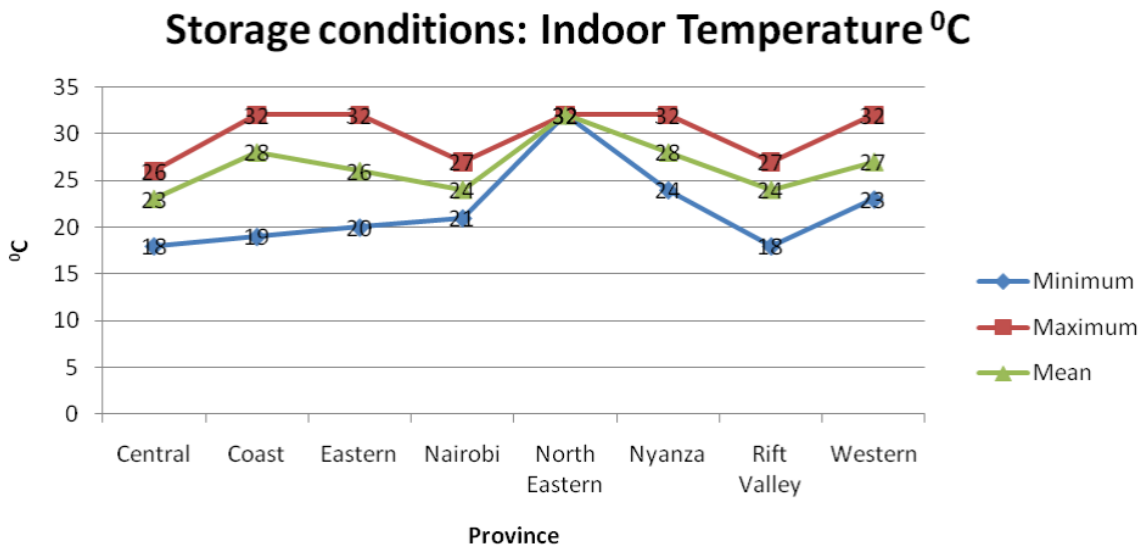


d) Temperature

i) Indoor Temperature

Five provinces recorded the highest indoor temparture (320 C). The minimum recorded indoor temperature was 180 C in Central and Rift Valley provinces(Figure 10 below).

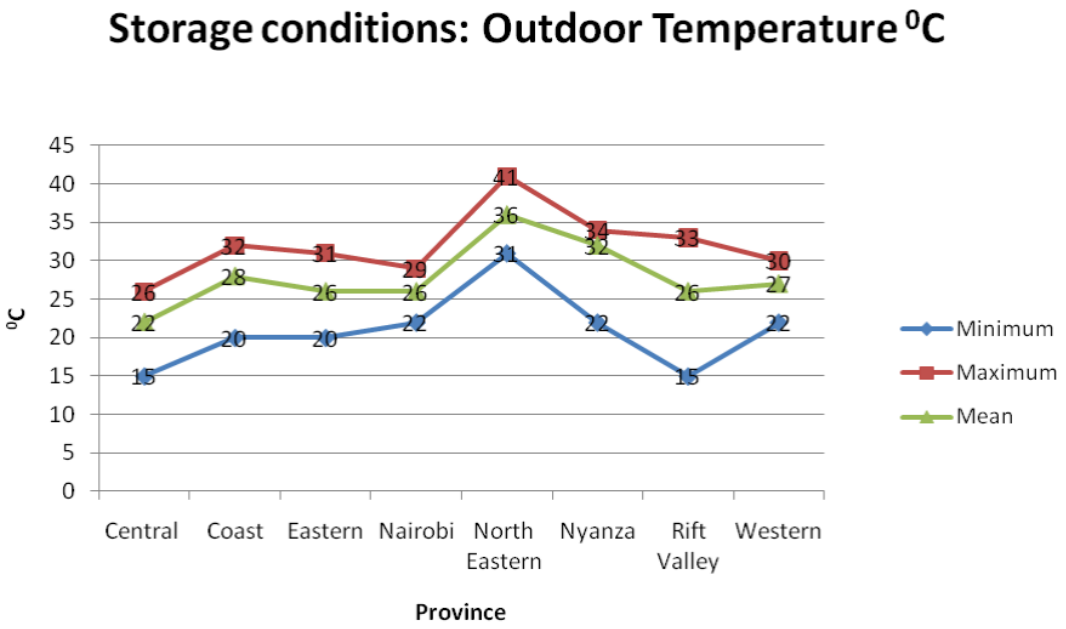
Figure 10: Indoor Temperature



ii) Outdoor temperature

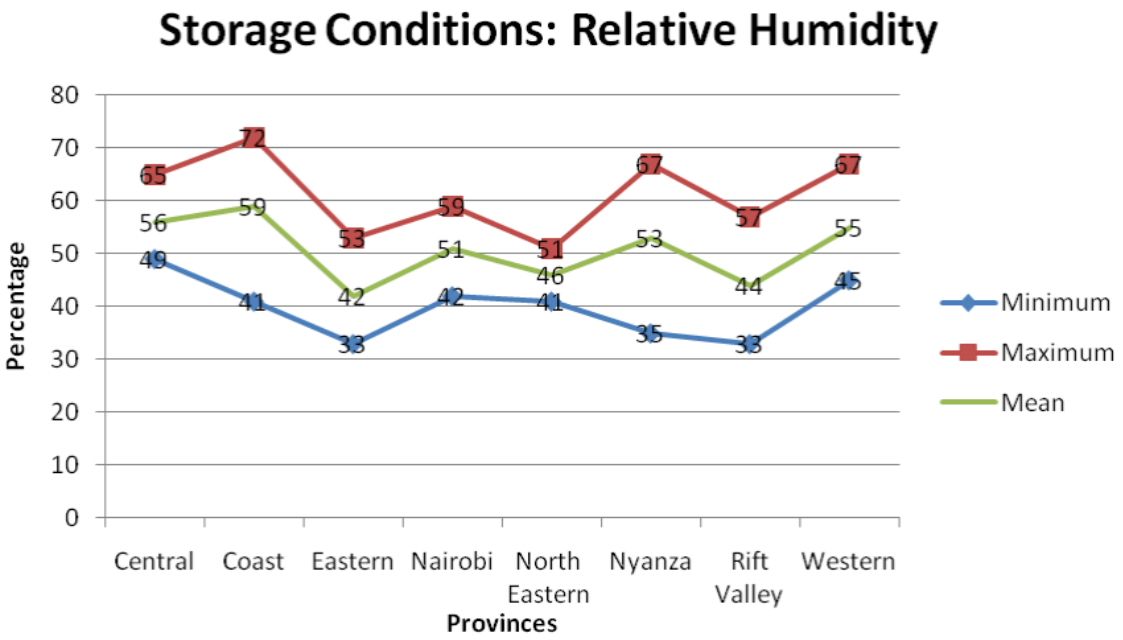
North Eastern province recorded the highest outdoor temparture (410C) while Central and Rift Valley provinces recorded the lowest outdoor temperature at 150 C(Figure 12 below).

Figure 11: Outdoor Temperature



e) Relative Humidity

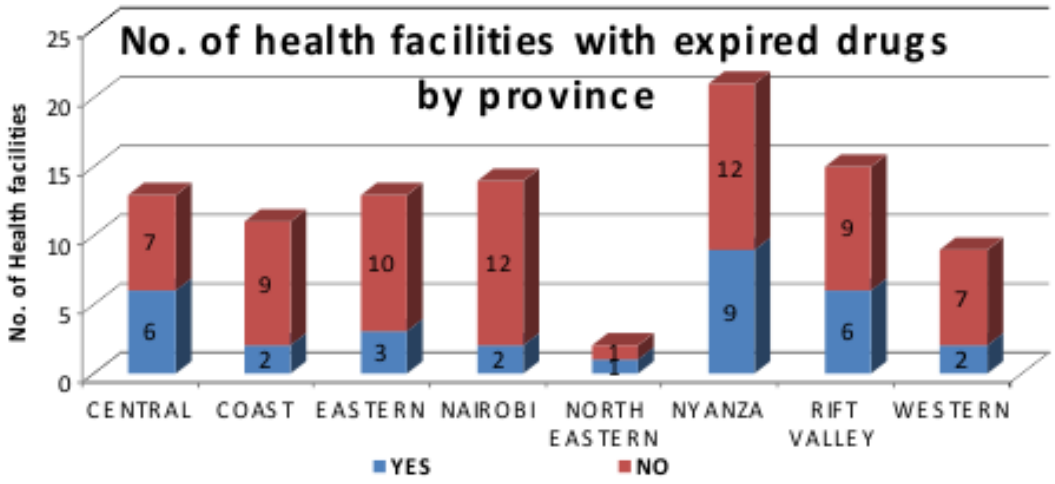
Figure 12: Percentage relative humidity by province



Coast province had the highest humidity (72%) at the time of the study as shown above, while Eastern and Rift Valley recorded the lowest humidity levels (33%). However humidity levels in most of the provinces had acceptable ranges i.e. maximum 65% + 5% (ICH guidelines)

f) Presence of Expired ARVs in health facilities

Figure 13: Presence of Expired ARVs by Province (n=98)



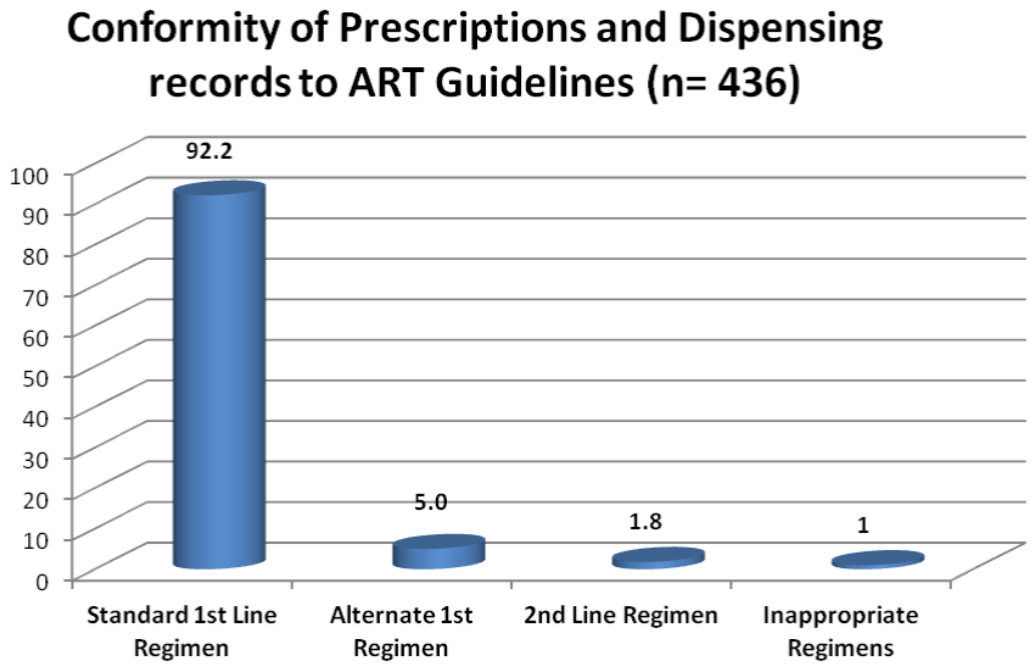
All the provinces had expired drugs at the time of the visit. Some of the expired drugs found were Abacavir tablets , Zidovudine Syrup, Liponavir/ Ritonavir syrup, AZT/3TC/NVP FDC tablets, Stavudine capsules.

5. Conformity to national treatment protocols by ART providers.

a) Conformity of Prescriptions and Dispensing records to ART Guidelines

The data collectors sampled and assessed 436 prescriptions and dispensing records for conformity to ART treatment guidelines. Majority (99%) of patients were on the recommended national ART regimens. 92.2% of the patients were on the standard 1st line regimen, 5.0 % were on alternate 1st line regimen and 1.8% on 2nd line ART regimens. One percent of patients were found to be on inappropriate ART combinations.

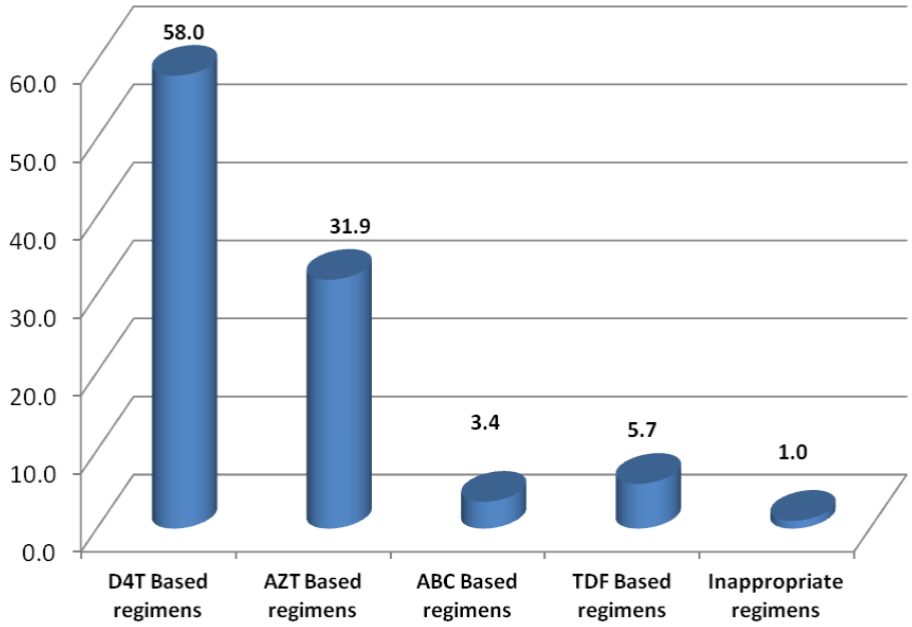
Figure 14: Conformity of Prescriptions and Dispensing records to ART Guidelines



b) Commonly used ART regimens

The most commonly used regimens were stavudine-based regimens (57.9%) and AZT-based regimens (31.8%).

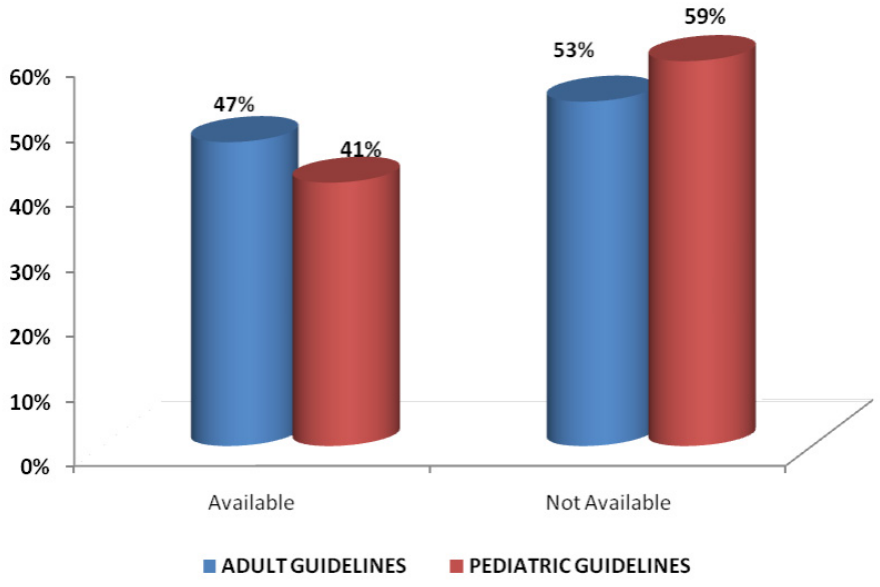
Figure15: Percentage distribution of commonly used ART regimens (n= 436)



c) Availability of Adult and Pediatric ART Guidelines

Of the study sites visited, 96 facilities were interviewed for availability of adult and pediatric ART guidelines. Only 47% and 41% of facilities had adult and pediatric guidelines respectively (Figure 16).

Figure 16: Percentage availability of adult and pediatric ART guidelines



Discussion

All the targeted health facilities (100%, n=92) were visited and surveyed whereas only 42% (n=55) of community pharmacies were surveyed. The number of community pharmacies surveyed was small due to the fact that at the time of the study majority of them did not stock ARVs.

The discussions will be in five parts based on the objectives of the study namely:-

- Range and availability of ARV medicines
- Registration status of sampled products
- Quality of sampled ARV medicines
- Storage conditions of ARVs in study facilities
- Conformity of prescribed ARVs to the national ART guidelines

1. Range and availability of ARV medicines

A total of 14 ARV APIs were found in the market in different strengths and combinations. These were Abacavir, Zidovudine, Lamivudine, Didanosine, Stavudine, Emtricitabine, Tenofovir, Efavirenz, Nevirapine, Indinavir, Lopinavir, Ritonavir, Nelfinavir and Saquinavir. Of these 14 APIs, Emtricitabine, Indinavir, Nelfinavir and Saquinavir do not form part of the recommended 1st line, alternative first line or 2nd line regimens. Availability in the market of APIs that are not in the national treatment guidelines could be due to, among other reasons, use of alternative protocols in the private sector that are largely influenced by emerging global trends. Other factors could be the use of these APIs within research settings and for the purpose of continuum of care for patients initiated on therapy outside the country.

There was a varied distribution of the APIs in the study regions with Nyanza province having all the 14 APIs present and North Eastern having the least. This could be attributed to the HIV prevalence patterns in the regions (with Nyanza bearing the heaviest burden) and the influence of non-governmental organizations that support HIV treatment.

The 14 APIs were found in 40 different combinations, 73 different formulations and 95 different products. Whereas availability of a wide range of brands of APIs increases accessibility to treatment, ensuring the quality

poses a challenge. Having a multiplicity of brands imposes challenges on the health system such as additional requirements for regulation and lack of cost-effectiveness because numerous small quantities of different brands are sourced and procured separately. In addition, this may cause confusion among patients and health providers thereby adversely affecting the quality of care and ultimately treatment outcomes.

Majority of the formulations in the regions were oral solid dosage forms i.e. 78.9% of the total. Liquid formulations constituted 21.1% of the total. Whereas it is a positive finding that majority of the formulations existed as tablets, most were in single dose formulations (71.9%). Fixed dose combinations (FDCs) are desirable and recommended by the WHO as these promote treatment adherence by reducing the pill burden as well as easing inventory management of commodities by health care workers. Only 11% of the formulations were available as triple FDC while 17.1% were dual FDC.

Availability of pediatric FDCs was poor with 50% of the provinces (Coast, Nairobi, North Eastern, Rift Valley and Western) not having the following products: Abacavir 60mg/Lamivudine 30mg; Lamivudine 30mg/Nevirapine 50mg/Zidovudine 60mg and Stavudine 12mg/Lamivudine 60mg/Nevirapine 100mg. This can be attributed to the fact that pediatric formulations were introduced into the system within the same year the survey was conducted.

2. Registration status of sampled products

Registration of products serves to ensure that all medicines allowed to be marketed/sold meet required quality standards and are of assured efficacy and safety. Out of the 95 products found in the market 72.6% were registered by the PPB.

88.5% (n=26) of the unregistered products were from India, manufactured by Aurobindo, Cipla, Strides Arcolab Ltd, Ranbaxy, Hetero Drugs Ltd and Matrix Labs.

Other countries of origin of the unregistered products were South Africa, Germany and Switzerland.

The findings on the registration status was comparable to the findings of the survey on Antimalarial Medicines in Kenya (2007), which found out that 42.6% of the sampled antimalarial medicines were not registered.

In another study (QAMSA, 2011), only three unregistered brands out of the 154 samples of antimalarial medicines were identified at different distribution levels.

The presence of unregistered products within the market is undesirable as this potentially compromises patient care and safety as the quality of these medicines is not assured.

3. Quality of sampled ARV medicines (Laboratory analysis results)

All the sampled ARVs complied with the laboratory tests performed with the exception of one.

a) Physical tests

All 272 samples complied with specifications for identification tests. Only 1 sample (AZT 300mg manufactured by Hetero Drugs Limited, India) failed the uniformity of weight test as this was submitted for analysis one month to expiry and was analyzed after seven months. The sample was collected with a shelf life of 3 months, a breach of the sample selection criteria. In addition the average turnaround time for samples submitted for analysis at the NQCL is 6 months. For pediatric dispersible tablets additional tests for friability and disintegration were done for which all 10 samples passed.

b) Dissolution test

The dissolution test was carried out as a means of determining the in vitro release of active ingredients in the tablet formulations over a specified duration under carefully regulated conditions of pH and agitation. Of the 220 samples submitted for analysis, only one (0.45%) failed the dissolution test. This was the same sample that had failed the uniformity of weight test i.e. AZT 300mg by Hetero Drugs Limited, India.

c) Assay tests

Assay testing involved determination of the average content of active ingredient in the samples submitted. All samples submitted passed.

It is a positive finding that 99.63% of the samples passed all the laboratory tests despite the fact that 27.4% were unregistered. However, this coincidence should not diminish the importance of drug registration and

regular post marketing surveillance as these are critical quality assurance measures. In addition, most ARVs in the market are procured by the National Aids and STI Control Program (NASCOP) with donor funding. These funding agencies impose stringent procurement conditions i.e. requirements for WHO pre-qualification for all suppliers, hence the low failure rates.

4. Storage conditions of ARVs in study facilities

The storage conditions of pharmaceutical products influence their physical and chemical properties which in turn affects their effectiveness and safety. According to ICH Guidelines for Zone IVA, the recommended relative humidity and room temperature for storage of tablets is less or equal to 65+5% and 30±2oC respectively. To maintain the quality of pharmaceutical products, storage should comply with the recommended conditions. Consequently, the storage areas should be designed to ensure good storage conditions. In particular, drug stores should be clean, dry and temperatures maintained within acceptable limits. Measures that can be employed to ensure adequate storage conditions include ventilation, air conditioning, dehumidification and use of pallets.

This study evaluated the storage conditions for first line ARVs which mostly requires storage at room temperature and dry conditions. From the available data, most sites (90%, n=115) had adequate levels of ventilation. However, Eastern province had the highest number of facilities with no ventilation, with 4 out of 13 facilities not compliant (31%). This observation is significant since this province was found to have high outdoor temperatures (max 32oC), which would necessitate measures to ensure adequate ventilation.

The relative humidity in most provinces was within the recommended range (55-65%) for storage of drugs except Coast province that had the highest at 72%. Relative humidity in Nyanza and Western provinces were 67% each. It was notable that Coast province had high indoor temperatures (max 32oC) and high relative humidity. A combination of high storage temperatures and high relative humidity is undesirable as this affects product stability. Storage conditions in such settings should therefore be improved and regularly monitored.

It was notable that all 8 provinces had facilities whose indoor temperatures

were within ICH temperature recommendations of 30±2oC. North Eastern province recorded the highest outdoor temperature (41oC).

All the provinces except North Eastern had some facilities with drugs stored on the floor. Western, Rift Valley and Nyanza had a large proportion of facilities with drugs on the floor. It was commendable that one facility in Coast province had improvised pallets. Good storage practices require commodities to be kept off the floor to protect from temperature fluctuations, water spillage as well as allow for free air circulation.

5. Conformity of prescribed ARVs to National ART guidelines

Treatment guidelines represent one approach to promoting therapeutically effective and economically efficient patient care. Guidelines are useful in ensuring that there is optimal care for improved treatment outcomes.

The study revealed that 98.9% of patients on ARVs were treated according to the recommended national ART guidelines at the time of the study, with 0.9% being treated with inappropriate regimens. The high conformity to the national ART guidelines can be interpreted as indicative of standard and quality care being provided at treatment centers. This is further supported by the fact that 92% of all patients on HAART are still on 1st line regimens, an indication of low treatment failure rates.

Moreover, in line with the national ART guidelines at the time of the study, the most commonly used regimens were stavudine-based regimens (57.9%) and AZT-based regimens (31.8%).

Although conformity to the national ART guidelines is high, availability of the guidelines themselves was relatively poor. Adult and pediatric ART guidelines were found in less than 50% of the facilities visited. This finding could be an indication of poor dissemination of the ART guidelines which could be due to shortages in quantities printed and poor distribution mechanisms.

Conclusion and Recommendations

Conclusion

The 92 products comprised of 14 APIs of which 7 were not in the national ART guidelines. Availability of APIs that are not in the national treatment guidelines in the market could be due to, among other reasons, use of alternative protocols in the private sector that are largely influenced by emerging global trends. One third of the products sampled from the market were not registered by the PPB. A large proportion of these were manufactured in India with a few being manufactured in South Africa and Switzerland. Storage conditions in the sampled facilities were satisfactory. Majority of the facilities had temperature and relative humidity within ICH recommendations for storage. The laboratory results indicate that most of the samples analyzed were of good quality with only one failing. This was because the analysis was done after the product had expired. Prescribing practices were conforming to the national ART guidelines although availability of the guidelines was limited.

In view of the findings on the registration status of the products, there is need to strengthen enforcement of drug regulatory activities especially drug registration. Further, there is need to conduct regular PMS to augment other product quality assurance measures.

Challenges and limitations of the study

Summary:

- Products/medicines requiring special storage conditions were not sampled.
- Some facilities could not be accessed and therefore were replaced by nearest accessible facility.
- The period the samples took to be analyzed was long (6 months from time of samples submission).
- PPB data base was not fully developed hence information required was not obtained on time.
- Use of inspection vehicles and pharmaceutical inspectors for the survey led to closure of facilities.
- Some sampled sites did not have adequate stocks therefore they did not meet the inclusion criteria.

- Some health facilities were adamant and refused to participate in the survey
- The private health facilities were not adequately covered.

Recommendations

PPB

- Prompt regulatory actions to mop up all unregistered products
- Regular PMS of ARVs and other medicines and medical devices such as those for opportunistic infections, contraceptive pills, condoms etc
- Greater collaboration with public health programs in the regulation of medicines
- Greater advocacy with parent ministries responsible for health for goodwill and support for medicine regulation
- Stringent quality assurance measures to ensure preservation of the limited therapeutic options currently available
- Enforcement of penalties for unregistered products in the market
- Regular update of PPB databases on registered products in the market
- Enforcement of CAP 244 provisions for sampling of products for PMS purposes
- Update Kenya's ICH zone from 4A to 4B due to high humidity levels observed in some regions which are outside Zone 4A limits
- Prompt documentation and dissemination of future post market survey findings

NASCOP

- Greater and continued collaboration with PPB in assuring quality of ARVs and other medicines
- Regular PMS of ARVs and other medicines and medical devices such as those for opportunistic infections, contraceptive pills, condoms etc
- Improve and standardize technical specifications for ARV procurement for use by all procuring entities

- Dedicate financial and participatory support on an annual basis for routine PMS.
- standardization of guidelines/ protocols across all sectors to preserve therapeutic alternatives for patients requiring second line and salvage regimens, and advocacy for adoption of uniform & standardized guidelines across all sectors
- Extensive dissemination of national guidelines for ART and training of staff of rational use
- Facilitate redistribution mechanisms for short expiry ARVs

NQCL

- Faster turn-around time in sample analysis
- Investment in state of the art analytical equipment

MOPHS/MOMS

- Better internal collaborations for such joint activities
- making it a requirement that all PHP medicines are part of the PPB's PMS strategy
- Increase support to the public health programs and PPB

Department of Pharmacy (DOP)

- Conduct PMS for essential medicines in collaboration with PPB and other stakeholders
- Strengthen systems for reverse logistics and redistribution
- Document and implement standards for good storage conditions at health facilities
- Strengthen supervisory mechanisms
- Promote appropriate use of ARVs

Development Partners

- Increase financial and technical support for Post Market Surveillance activities
- Compliance to local procurement and regulatory requirements

Pharmaceutical Manufacturers, Importers & Distributors

- Compliance to legal requirements
- Ensure their products comply with PPB guidelines

Consumers

- Communication of any quality issue regarding medicines to the appropriate authorities.

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Annexes

Annex 1: Questionnaire

1. Name of Province/District .....

2. Name of Health facility/Store/Pharmacy/Chemist .....

3. Name of sample/Data Collector .....

A) At the ARVs storage/distribution/dispensing area

1. Do you store/distribute/dispense ARVs at this facility?

Yes ☐

No ☐

(Proceed with interview if Yes, End the interview if No).

2. Drug particulars *(Find attached the table to fill per facility visited)*

3. Storage conditions: make observations (tick in the appropriate check box)

a) Ventilated *(Observe)*

Cross ventilation ☐

Ventilation on one side ☐

Air Conditioning ☐

No Ventilation ☐

b) Are drugs stored on shelves? *(Observe)*

Yes ☐

No ☐

Other (specify)……

c) Pallets used (at least 10cm) off the floor

Yes ☐

No ☐

Others (specify)……

d) Storage conditions in compliance with the labeling requirements
(Compare drugs storage requirements against the storage conditions)

i. Temperature /humidity conditions:-
Indoor Temperature…….
Out Door Temperature……..
Humidity ……% RH

ii. Dry Place: Yes ☐ No ☐

iii. Protect from direct sunlight Light: Yes ☐ No ☐

Comment on general storage conditions .....

.....

.....

e) Are there Antiretroviral drugs stored on the floor?

Yes ☐

No ☐

If Yes, please explain .....

.....

f) Are there expired Antiretroviral drugs?

Yes ☐

No ☐

If Yes, list the drugs and reasons .....

.....

g) Are there Antiretroviral drugs with damaged packs or broken seals?

Yes ☐

No ☐

If Yes, list the drugs and reasons .....

.....

h) Have you ever received medicines with anomalies: changed color, crumbling etc

Yes ☐

No ☐

If Yes please describe .....

.....

i) Where does the facility/chemist obtain or source the ARVs from? *(Ask to see evidence)*

- Kemsa
- MEDS
- Other (Specify)

.....

.....

.....

.....

j) Mode of transportation from Source (District store/Central site store/KEMSA/ MEDS) to health facility or chemist:-

Air ☐

Vehicle ☐

Motor-bike ☐

Bicycle ☐

Other ☐

Specify for Other.....

7. a) Do you inspect packages for damaged or expired drugs on receipt?

Yes ☐

No ☐

b) Is First-in/first-out procedure (FIFO) being used?

Yes ☐

No ☐

c) Is First Expiry First Out (FEFO) being followed?

Yes ☐

No ☐

8. Do you file/store copies of prescriptions for patients taking ARVs?

Yes ☐

No ☐

[If the answer is yes, sample 5 prescriptions and proceed to the clinic area to check for the patients in the ART register.

If the answer is No, ask for the next available dispensing record (e.g. DAR, dispensing tool, etc) and sample 5 patients from there, then proceed to the clinic to check for the patients in the ART register]

B) At the ART clinic area:

a. Tabulate the 5 sampled patients as follows using information obtained from the prescriptions or dispensing record.

Patient number	**Regimen**	**Age (Yrs)**	**Weight (Kg)**	**Height (cm)**	**Is the patient on 1st line, Alternative 1st line or 2nd line treatment?**	**Provider Conformity to National treatment guidelines- Yes or No?**	**Remarks**
1							
2							
3							
4							
5							

b. Interview a clinician/nurse at the clinic:

- What is the preferred adult ART regimens prescribed in this facility?
- List 3 regimen and doses for the same.
- Which is the fastest moving ART regimen? (For Pharmacy/ Community pharmacies)

Regimen	**Doses**
1.	
2.	
3.	

- What is the preferred pediatric ART regimens prescribed in this facility? List 3 regimen and doses for the same

Regimen	**Doses**
1.	
2.	
3.	

- Do you have National ART guidelines (3rd Edition 2005) at the clinic for reference? (If yes, ask to see a copy).

  Yes ☐

  No ☐

- Do you have the (October 2008) Paediatric Treatment Guideline (Circular) at the clinic for reference? (If yes, ask to see a copy.)

  Yes ☐

  No ☐

  [End of Interview]

  Thank the interviewee for his/her participation.

Annex 2: List of Health Facilities

NAME OF FACILITY	LOCATION
1. Langata Health Centre	Nairobi
2. Ngaira/Rhodes Health Centre	Nairobi
3. Stc Casino	Nairobi
4. Dandora Ii Health Centre	Nairobi
5. Mukuru Reuben Health Centre	Nairobi
6. Donholm Health Centre	Nairobi
7.K ariobangi Health Centre	Nairobi
8. St. Joseph Mukasa Faith-Based Hospital	Nairobi
9. Mater Hospital	Nairobi
10. Amurt Health Care Centre	Nairobi
11. Nazareth Faith-Based Hospital-Korogocho	Nairobi
12. Jomo Kenyatta University Of Agriculture And Technology	Thika
13. Ngorongo Health Centre	Thika
14. Mary Help Of The Sick Faith-Based Hospital	Thika
15. Garissa Provincial Hospital	Garissa
16. Wajir District Hospital	Wajir
17. Masimba Health Centre	Kajiado
18. Sher Agencies-Nakuru	Nakuru
19. Ololunga-Narok	Narok
20. Sogoo Health Centre	Narok
21. Iten-Keiyo	Keiyo
22. Lodwar District Hospital	Turkana
23. *Lanet 3Kr	Nakuru
24. Londiani Sub-District Hospital	Kericho
25. Eldoret Hospital (Private)	Eldoret
26. Christian Faith-Basedary Fellowship-Ewaso Nyiro	Ewaso Nyiro
27. Ct&Pc-Narok	Narok
28. Beacon Of Hope-Kajiado	Kajiado
29. Naivasha Faith-Based Hospital	Naivasha
30. Mary Immaculate Dispensary(Faith-Based)	Nyandarua
31. Nazareth Faith-Based Hospital	Tinganga
32. Mariakani Sub-District Hospital	Kilifi
33. Tiwi Health Centre	Kwale

34. Witu Health Centre	Lamu
35. Shimo La Tewa Health Centre	Mombasa
36. Kipini Hc	Tana River
37. Oda Dispensary	Tana River
38. Wesu District Hospital	Taita Taveta
39. Mikindani Cbhc-Mbungoni	Mombasa
40. Pandya Hospital	Mombasa
41. St. Lukes Faith-Based Hospital	Kilifi
42. Matiliiku District Hospital	Makueni
43. Nunguni Sub-District Hospital	Makueni
44. Katulani Health Centre	Kitui
45. Kauwi Health Centre	Kitui
46. Mutitu Health Centre	Kitui
47. Mutomo Faith-Based Hospital	Kitui
48. Runyenjes Sub –District Hospital	Runyenjes
49. Gatab Health Centre	Marsabit
50. Mbeere District Hospital	Mbeere
51. Giaki Health Centre	Meru Central
52. Nyambene District Hospital	Meru North
53. Mwea Faith-Based Hospital	Mwea
54. Family Health Options Clinic-Meru Central	Meru Central
55. Kimbimbi Health Centre	Mwea
56. Baricho Health Centre	Kirinyaga
57. Kiganjo Health Centre	Nyeri
58. Karaba Health Centre	Mwea
59. Outspan Hospital	Nyeri
60. Kangema Health Centre	Muranga
61. Kirogo Health Centre	Muranga
62. Marindi Dispensary	Homa Bay
63. Ndhiwa Sub-District Hospital	Homa Bay
64. Bugumbe Health Centre	Kuria
65. Mariwa Health Centre	Migori
66. Etago Health Centre (Merlin)	Gucha
67. Christa Mariane Health Centre (Merlin)	Kisii Central
68. Muhoroni Sub-District Hospital	Nyando

69. Katito Health Centre	Nyando
70. Family Health Options-Kisumu	Kisumu
71. Hongo Ogosa-Kisumu	Kisumu
72. Kisumu District Hospital	Kisumu
73. Tuungane-Kisumu	Kisumu
74. St. Monica Faith-Based Hospital-Town Clinic	Kisumu
75. Ugina-Suba	Suba
76. St. Camillus Faith-Based Hospital-Tagache	Migori
77. St. Josephs Faith-Based Hospital-Migori	Migori
78. Bumula Health Centre	Bungoma
79. Matayo's Health Centre	Busia
80. Kambiri Health Centre	Kakamega
81. Likuyani Sub-District Hospital	Lugari
82. Hamisi Health Centre	Vihiga
83. Busia District Store	Busia
84. Friends Lugulu Faith-Based Hospital (Lurende)	Bungoma
85. St. Mary's Faith-Based Hospital-Butere Mumias	Butere Mumias
86. Namasoli Ack Faith-Based Hospital	Butere Mumias
87. Uyawi Health Centre	Bondo
88. Boro Dispensary	Siaya
89. Siaya District Hospital	Siaya
90. Sigomere Health Centre	Siaya
91. Yala Sub-District Hospital	Siaya
92. Bama Nursing And Maternity Home	Siaya

Annex 3: List of Private Chemists

NAME OF CHEMIST	LOCATION
1. RAFIKI PHARMACEUTICALS	PUMWANI (KAMUKUNJI)
2. CITY LINK PHARMA LTD	KAMUKUNJI
3. TRANSCHEM PHARMACEUTICALS	NAIROBI CBD
4. HEALTHLINK	NAIROBI CBD
5. SURGIPHARM LTD	NAIROBI CBD
6. NICEWELL CHEMISTS	EMBAKASI
7. GRAND PHARMACY	LANGATA
8. APPLEGENIE PHARMACY	LANGATA
9. TRANSLAR CHEMIST	EMBAKASI
10. PHARMORE CHEMISTS	EMBAKASI
11. JOY CHEMISTS	EMBAKASI
12. ROYSAMBU CHEMIST	KASARANI
13. PHARMART UKAY	WESTLANDS
14. PENTAPHARM	WESTLANDS
15. DAN PHARMACY	WESTLANDS
16. UMMAH PHARMACY	GARISSA
17. RAMOGI CHEMIST	KISUMU
18. JACKS PHARMACY	KISII
19. LABOREX LTD	ELDORET
20. NAKURU MEDICAL STORES	NAKURU
21. TEALAND CHEMISTS	KERICHO
22. EASTERN CHEMISTS	MERU
23. MAKADARA CHEMISTS	MAKADARA

Annex 4: Final Route Allocation for ARV PMS

TEAM	MEMBERS	FACILITIES VISITED ART Treatment Sites	CHEMISTS
One (Nairobi and North Eastern)		• Langata HC • Ngaira/Rhodes HC • STC Casino • Dandora 11 HC • Mukuru Reuben HC • Don holm HC • Kariobangi HC • St. Joseph Mukasa Faith-Based Hospital • Mater Hospital • Amurt Health Care Centre • Jomo Kenyatta University of Agriculture and Technology-Thika • Ngorongo HC-Thika • Mary Help Of The Sick Faith-Based Hospital • Nazareth Faith-Based Hospital-Korogocho • PGH Garissa • Wajir DH	• Embakasi -3 • Langata -2 • Kasarani -2 • Pumwani -2 • Garissa -1
Two (Rift Valley)		• Masimba HC-Kajiado • Sher agencies-Nakuru • *Ololunga-Narok • Sogoo HC-Narok • Iten-Keiyo • Lodwar DH-Turkana • *Lanet 3KR-Nakuru • Londiani SDH-Kericho • Eldoret hospital (private)-Eldoret • Christian Faith-basedary Fellowship-Ewaso ngiro (CT&PC)-Narok • Beacon of hope-Kajiado • *Naivasha faith-based hospital • Mary Immaculate dispensary(faith-based)-Nyandarua • Nazareth faith-based hospital-Tinganga	• Eldoret - 4 • Nandi North (Kapsabet) - 2 • Nakuru Central (CBD) - 3 • Kericho -2

TEAM	MEMBERS	FACILITIES VISITED ART Treatment Sites	CHEMISTS
Three (Coast and Eastern?)		• Mariakani Sub-District Hospital-Kilifi • Tiwi HC-Kwale • Witu HC-Lamu • Shimo La Tewa HC-Mombasa • Kipini HC-Tana River • Oda Dispensary-Tana River • *Wundanyi District Hospital-Taita Taveta • Mikindani CBHC-Mbungoni-Mombasa • Pandya Hospital-Mombasa • St. Lukes Faith-Based Hospital-Kilifi • Matiliiku DH-Makueni • Nunguni SDH-Makueni • Katulani-Kitui*** • *Kauwi-Kitui*** • *Mutitu-Kitui*** • Mutomo Faith-Based Hospital-Kitui	• Machakos -2 • Kitui -1 • Mombasa -3 • Kilifi -2
Four (Eastern, Central) Five (Nyanza) Six (Western)		• Runyenjes SDH-Embu • Gatab HC-Marsabit • Mbeere DH-Mbeere • Giaki HC-meru central • Nyambene DH-Meru North • Mwea faith-based hospital-Embu • Family health options clinic-Meru central • Kimbimbi HC-Kirinyaga** • Baricho HC-Kirinyaga • Kiganjo HC-Nyeri • Karaba HC-Nyeri • Outspan private hospital • Kangema HC-Muranga • Kirogo HC-Muranga	• Kiambu-2 • Nyeri -2 • Thika -2 • Meru -2 • Embu -1

TEAM	MEMBERS	FACILITIES VISITED ART Treatment Sites	CHEMISTS
Three (Coast and Eastern?)		• Marindi Dispensary-Homabay • Ndiwa SDH-Homabay • Bugumbe HC-Kuria • Mariwa HC-Migori • Etago HC (Merlin)-Gucha • Christa Mariane HC (merlin)-Kisii central • Muhoroni SDH-Nyando • Katito HC-Nyando • Family health options-Kisumu • *Hongo Ogosa-kisumu • Kisumu DH-Kisumu • *Tuungane-Kisumu • *Ugina-Suba • St. Monica faith-based hospital-Town clinic-Kisumu • *St. Camillus faith-based hospital-Tagache-Migori • St. Josephs faith-based hospital-Migori	• Machakos -2 • Kitui -1 • Mombasa -3 • Kilifi -2
Four (Eastern, Central) Five (Nyanza) Six (Western)		• Runyenjes SDH-Embu • Gatab HC-Marsabit • Mbeere DH-Mbeere • Giaki HC-meru central • Nyambene DH-Meru North • Mwea faith-based hospital-Embu • Family health options clinic-Meru central • Kimbimbi HC-Kirinyaga** • Baricho HC-Kirinyaga • Kiganjo HC-Nyeri • Karaba HC-Nyeri • Outspan private hospital • Kangema HC-Muranga • Kirogo HC-Muranga	• Kiambu-2 • Nyeri -2 • Thika -2 • Meru -2 • Embu -1

TEAM	MEMBERS	FACILITIES VISITED ART Treatment Sites	CHEMISTS
Five (Nyanza)		• Marindi dispensary-Homabay • Ndiwa SDH-Homabay • Bugumbe HC-Kuria • Mariwa HC-Migori • Etago HC (Merlin)-Gucha • Christa Mariane HC (merlin)-Kisii central • Muhoroni SDH-Nyando • Katito HC-Nyando • Family health options-Kisumu • *Hongo Ogosa-kisumu • Kisumu DH-Kisumu • *Tuungane-Kisumu • *Ugina-Suba • St. Monica Faith-Based Hospital-Town Clinic-Kisumu • *St. Camillus faith-based hospital-Tagache-Migori • St. Josephs Faith-Based Hospital-Migori	• Kisumu - 2 • Kisii - 2 • Migori - 1 • Westlands (Nairobi) -3
Six (Western)		• Bumula HC-Bungoma • Matayo's HC-Busia • Kambiri HC-Kakamega • Likuyani SDH-Lugari • Hamisi HC-Vihiga • Busia district store-Busia • Friends Lugulu faith-based hospital (Lurende)-Bungoma • St. Mary's faith-based hospital-Butere Mumias • Namasoli ACK faith-based hospital-Butere/mumias • Uyawi HC-Bondo • Boro dispensary-Siaya • Siaya DH-Siaya • Sigomere HC-Siaya • Yala SDH-Siaya • Bama Nursing and Maternity Home-Siaya	• Bungoma - 1 • Busia - 1 • Kakamega - 1 • CBD - Nairobi - 6

Annex 5: Coding of Laboratory Samples

Code	Product (Active Ingredients)	Start Series no.	End Series no.
2900'S	Lamivudine + Stavudine + Nevirapine (150mg/30mg/200mg)	2901	2995
3000'S	Lamivudine + Zidovudine + Nevirapine (150mg/300mg/200mg)	3001	3021
3100's	Lamivudine + Stavudine + Nevirapine (60mg/12mg/100mg)	3101	3101
3200's	Lamivudine + Nevirapine + Zidovudine (30mg/50mg/60mg)	3201	3202
3300's	Lamivudine + Stavudine + Nevirapine (30mg/6mg/50mg)	3301	3301
3400's	Lamivudine + Stavudine + Nevirapine (150mg/40mg/200mg)	3401	3402
3500's	Efavirenz + Emtricitabine + Tenofovir (600mg/200mg/300mg)	3501	3501
2200'S	Lamivudine + Stavudine (150mg/30mg)	2201	2249
2300'S	Lopinavir + Ritonavir (200mg/50mg)	2301	2343
2400'S	Lamivudine + Zidovudine (150mg/300mg)	2401	2443
2500'S	Lopinavir + Ritonavir (80mg/20mg)	-	-
2600'S	Tenofovir + Lamivudine (300mg/300mg)	2601	2611
2700'S	Lopinavir + Ritonavir (100mg/25mg)	2701	2702
2800'S	Abacavir + Lamivudine (60mg/30mg)	2801	2801
3800's	Didanosine (50mg)	3801	3801
3700's	Didanosine (250mg)	3701	3701
3600's	Didanosine (400mg)	3601	3601
2100'S	Stavudine (20mg)	2101	2120
2000'S	Efavirenz (200mg)	2001	2033
1900'S	Abacavir (300mg)	-	-
1800'S	Tenofovir (300mg)	1801	1828
1700'S	Didanosine (200mg)	1701	1702
1600'S	Stavudine (15mg)	1601	1615
1500'S	Abacavir (300mg)	1501 + 1901	1522 + 1909
1400'S	Nevirapine (50mg/5mL)	1401	1431
1300'S	Lamivudine (10mg/mL)	1301	1326
1200'S	Stavudine (30mg)	1201	1214
1100'S	Abacavir (20mg/mL	1101	1119
1000'S	Efavirenz (30mg/5mL)	1001	1001
900'S	Zidovudine (50mg/5ml)	901	939
800'S	Didanosine (100mg)	801	811
700'S	Didanosine (25mg)	701	702
600'S	Zidovudine (300mg)	601	622
500'S	Efavirenz (600mg)	501	566
400'S	Zidovudine (100mg)	401	439
300'S	Efavirenz (50mg)	301	330
200'S	Nevirapine (200mg)	201	286
100'S	Lamivudine (150mg)	101	154

Annex 6: Availability of ARV formulations per province

Active Ingredient(s) and Strength	Central	Coast	Eastern	Nairobi	North Eastern	Nyanza	Rift Valley	Western
Abacavir 20mg/ml	√	√	√	√	X	√	√	√
Abacavir 300mg	√	√	√	√	X	√	√	√
Abacavir 60mg/Lamivudine 30mg	X	X	X	X	X	√	X	X
Didanosine 100mg	√	√	√	√	√	√	√	√
Didanosine 200mg	√	X	X	√	√	√	√	√
Didanosine 250mg	X	X	X	X	X	√	X	X
Didanosine 25mg	√	X	√	√	√	√	X	√
Didanosine 400mg	X	X	X	X	X	√	X	X
Didanosine 50mg	X	X	X	√	√	√	X	X
Efavirenz 200mg	√	√	√	√	X	√	√	√
Efavirenz 30mg/ml	√	√	√	√	X	√	X	√
Efavirenz 50mg	√	√	√	√	√	√	√	√
Efavirenz 600mg	√	√	√	√	√	√	√	√
Efavirenz 600mg/Emtricitabine 200mg/ Tenofovir 300mg	X	√	X	√	X	√	√	X
Indinavir 500mg	X	√	X	X	X	X	X	X
Lamivudine 150mg	√	√	√	√	√	√	√	√
Lamivudine 150mg/Zidovudine 300mg	√	√	√	√	√	√	√	√
Lamivudine 150mg/Zidovudine 300mg/ Nevirapine 200mg	√	√	√	√	√	√	√	√
Lamivudine 30mg/Nevirapine 50mg/ Zidovudine 60mg	√	X	√	X	X	√	X	X
Lamivudine 50mg/5ml	√	√	√	√	√	√	√	√
Lopinavir 100mg/ritonavir 25mg	√	X	√	X	X	√	X	X
Lopinavir 200mg/ritonavir 50mg	√	√	√	√	√	√	√	√
Lopinavir 80mg/ritonavir 20mg	√	√	√	X	X	√	X	√
Nelfinavir 250 mg	√	X	X	X	X	X	X	X
Nevirapine 50mg/5ml	√	√	√	√	√	√	√	√
Nevirapine 200mg	√	√	√	√	√	√	√	√
Saquinavir 200mg	√	X	X	X	X	X	X	X
Stavudine 12mg/Lamivudine 60mg/ Nevirapine 100mg	√	X	√	X	X	X	X	X
Stavudine 15mg	√	√	√	X	X	√	√	√
Stavudine 20mg	√	√	√	√	X	√	√	X
Stavudine 30mg	√	√	√	√	√	√	√	√
Stavudine 30mg/Lamivudine 150mg	√	√	√	√	√	√	√	√
Stavudine 30mg/Lamivudine 150mg/ Nevirapine 200mg	√	√	√	√	√	√	√	√

Active Ingredient(s) and Strength	Central	Coast	Eastern	Nairobi	North Eastern	Nyanza	Rift Valley	Western
Stavudine 40mg/Lamivudine 150mg/ Nevirapine 200mg	X	X	√	√	X	√	√	X
Tenofovir 300 mg/Lamivudine 300mg	√	X	√	√	√	√	√	√
Tenofovir 300mg	√	√	√	√	√	√	√	√
Tenofovir 300mg/Emtricitabine 200mg	X	√	X	√	X	X	√	X
Zidovudine 100mg	√	√	√	√	X	√	√	√
Zidovudine 300mg	√	√	√	√	√	√	√	√
Zidovudine 50mg/5ml	√	√	√	√	√	√	√	√

Annex 7: Country of origin of ARV products by province

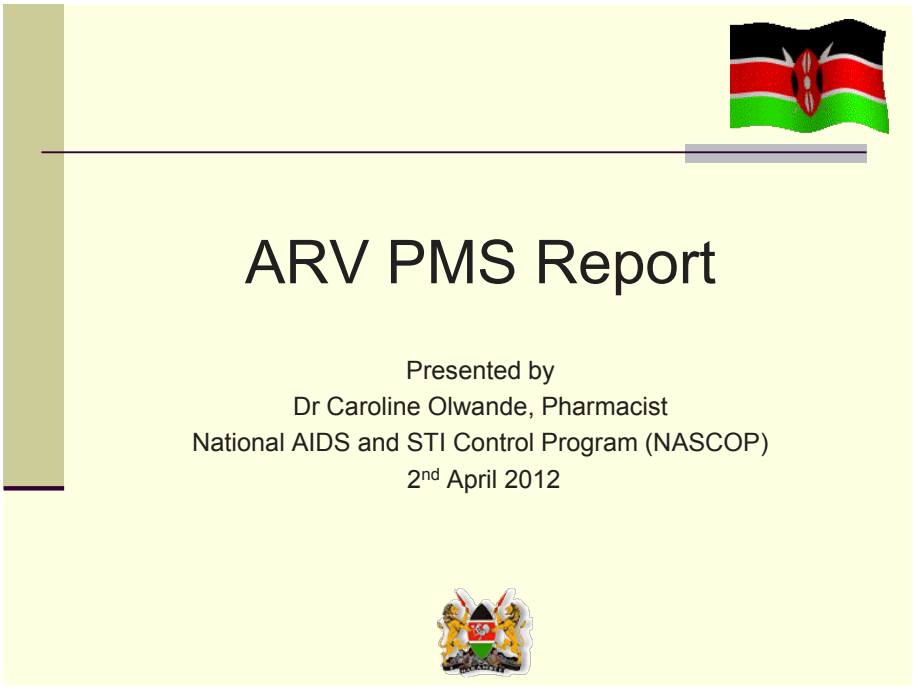
Country of Origin	REGION								
	Central	Coast	Eastern	Nairobi	North Eastern	Nyanza	Rift Valley	Western	Total
Unknown	0.4%(1)	0.6%(1)	0%(0)	0%(0)	0%(0)	0%(0)	0%(0)	0%(0)	**0.1%(2)**
Australia % (n)	0%(0)	0%(0)	0%(0)	0%(0)	0%(0)	0%(0)	0.6%(1)	0%(0)	**0.1%(1)**
Canada % (n)	2.2%(5)	3.4%(6)	0%(0)	3.1%(5)	0%(0)	2.0%(9)	0.1%(2)	2.6%(4)	**2.0%(31)**
France % (n)	5.3%(12)	4.5%(8)	5.8%(10)	5.5%(9)	0%(0)	4.7%(21)	9.7% (17)	4.5%(7)	**5.4%(84)**
Germany % (n)	2.7%(6)	5.1%(9)	3.5%(6)	6.7%(11)	7.5%(3)	7.1%(32)	6.2% (11)	2.6%(4)	**5.3%(82)**
India % (n)	79.6% (180)	65.2% (116)	83.0% (142)	68.7% (112)	87.5% (35)	72.5% (325)	71.6% (126)	84.0% (131)	**74.9% (1167)**
Kenya % (n)	0%(0)	3.9%(7)	0%(0)	0%(0)	0%(0)	0%(0)	0.6%(1)	0%(0)	**0.5%(8)**
Netherlands % (n)	3.5%(8)	6.7% (12)	2.3%(4)	8.6%(14)	5.0%(2)	6.2%(28)	0.6%(1)	3.8%(6)	**4.8%(75)**
South Africa% (n)	1.8%(4)	2.8%(5)	1.8%(3)	2.5%(4)	0%(0)	1.1%(5)	1.1%(2)	0.6%(1)	**1.5%(24)**
Switzerland % (n)	0.9%(2)	0%(0)	0%(0)	.0%(0)	0%(0)	0%(0)	0%(0)	0%(0)	**0.1%(2)**
UK % (n)	2.7%(6)	4.5%(8)	3.5%(6)	3.7%(6)	0%(0)	6.0%(27)	3.4%(6)	0.6%(1)	**3.9%(60)**
USA % (n)	0.9%(2)	3.4%(6)	0%(0)	1.2%(2)	0%(0)	0.2%(1)	5.1%(9)	1.3%(2)	**1.4%(22)**
Total % (n)	**100.0% (226)**	**100.0% (178)**	**100.0% (171)**	**100.0% (163)**	**100.0% (40)**	**100.0% (448)**	**100.0% (176)**	**100.0% (156)**	**100.0% (1558)**

Annex 8: Results of samples tested

	No. of samples tested	No of active ingredient(s) tested (API)	Samples failed	Test failed	No. of brands per sample
Abacavir sulphate 300mg	7	1	0	0	1
abacavir/lamivudine 60/30mg	1	2	0	0	1
didanosine 100mg	3	1	0	0	1
didanosine 200mg	2	1	0	0	1
didanosine 250mg	1	1	0	0	1
didanosine 25mg	2	1	0	0	1
didanosine 400mg	1	1	0	0	1
didanosine 50mg	1	1	0	0	1
efavirenz 200mg tablets	7	1	0	0	1
efavirenz 200mg capsules	1	1	0	0	1
efavirenz 50mg	9	1	0	0	1
efavirenz 600mg	21	1	0	0	3
efavirenz/emtricitabine/ tenofovir 600/200/300	1	3	0	0	1
lamivudine 150mg	17	1	0	0	3
lamivudine/stavudine 150/30mg	17	2	0	0	1
lamivudine/stavudine/ nevirapine 150/30/200mg	30	3	0	0	4
lamivudine/stavudine/ nevirapine 150/40/200mg	2	3	0	0	2
lamivudine/stavudine/ nevirapine 30/6/50mg	0	3	0	0	1
lamivudine/stavudine/ nevirapine 60/12/100mg	1	3	0	0	1
lamivudine/zidivudine 150/300mg	16	2	0	0	4
lamivudine/zidovudine/ nevirapine 150/300/200mg	8	3	0	0	3
lamivudine/zidovudine / nevirapine 30/60/50	1	3	0	0	1
nevirapine 200mg	29	1	0	0	1
stavudine 15mg	4	1	0	0	1
stavudine 20mg	4	1	0	0	1
stavudine 30mg	4	1	0	0	2
tenofovir disoproxil fumarate 300mg	5	1	0	0	2
tenofovir disoproxil fumarate/lamivudine 300/300mg	3	2	0	0	1

	No. of samples tested	No of active ingredient(s) tested (API)	Samples failed	Test failed	No. of brands per sample
zidovudine 100mg	12	1	0	0	3
zidovudine 300mg	7	1	1 (14.3%)	Uniformity weight and dissolution	2
nevirapine hemihydrate 50mg/5ml	11	1	0		
lamivudine 10mg/ml	10	1	0	0	2
abacavir 20mg/ml	7	1	0	0	1
efavirenz 30mg/ml	1	1	0	0	2
zidovudine 50mg/5ml	13	1	0	0	2
Lopinavir/ritonavir 200/50mg	13	2	0	0	2
				0	1
Total	**272**	**53**	**1**	1	**57**

Annex 9: Post Market Surveillance Dissemination meeting Presentation



Presentation Outline

- Background
- Methodology
- Objectives
- Sampling
- Tools, development and pre-testing
- Data collection and analysis
- Key findings
- Summary of Findings
- Recommendations
- Mini PMS report

Background

- HIV and AIDS declared a national disaster in 1999- establishment of the National AIDS Control Council (NACC) to coordinate the multi-sectoral response to the public health threat
- Approximately 1.5 million living with HIV in Kenya; national prevalence is 7.4 % in 15-49 years and 7.1 % 15-64 years; over I million in care and about 500,000 on ART as at end December 2011

Background

- ARVs have been used since late 90s in private health facilities and early 2000 in public health facilities
- Availability and access to appropriate, safe and quality antiretrovirals is essential to support effective prevention and treatment of HIV and AIDS.
- PMS for ARVs appropriate about 8 years post large scale us of the products

Aim

To establish the ***availability*** and the ***quality*** of ARV medicines in Kenya as well as determine their ***appropriate use*** in public, private and faith-based health sectors.

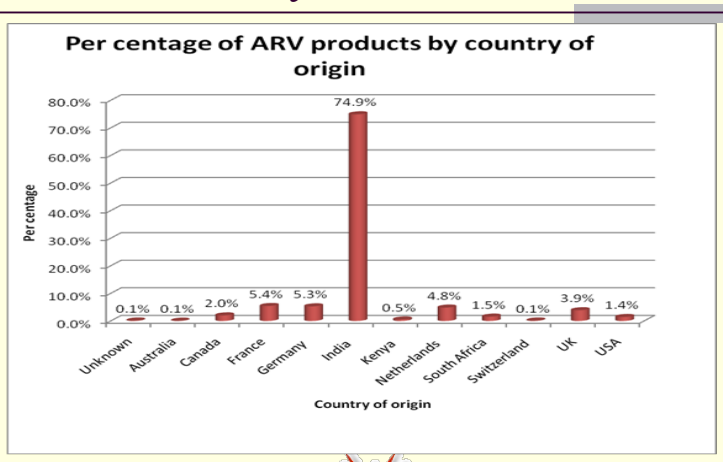
Objectives

- Establish the range and availability of all ARVs in Kenya.
- Determine the registration status of the sampled ARVs with PPB.
- Assess the quality of key 1st line, alternative 1st line and selected 2nd line ARVs.
- Assess the storage conditions of ARVs at the study facilities.
- Determine conformity of prescribing practices to national treatment guidelines.

Methodology

- A cross sectional survey
- Survey period: August and September 2009
- Survey facilities: 92 ART treatment sites and 55 community pharmacies
- Survey tools: A sample collection form and a questionnaire
- 1558 ARV preparations were collected -95 products, 73 formulations and 14 APIs
- 272 samples of antiretroviral medicines (230 solid and 42 liquid formulations) were randomly selected and sent to the National Quality Control Laboratory for quality control tests.

Findings: 1. Range and availability of ARVs in Kenya



Findings: 2. Local registration status of the sampled ARVs

Findings: 3. Quality of ARVs (Uniformity of weight, dissolution and assay results for solid ARV formulations)

Tests	Method	Specifications	Test results (passed)	Conformity
Uniformity of weight	Weight	Tablets/capsules deviate by more than 5% from mean tablet weight	229 out of 230	99.56%
Dissolution	HPLC	No tablet less than 70% (n=6)	229 out of 230	99.56%
Assay	HPLC	90.0-110.0%	230 out of 230	100.00%

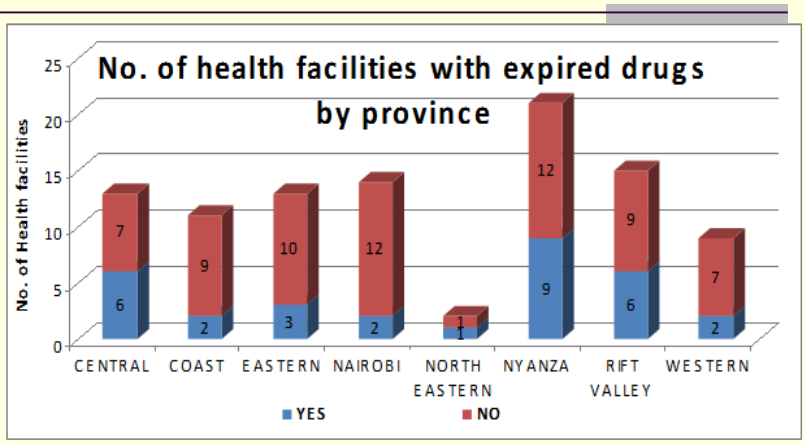
Findings: Quality of ARVs (Microbial load and assay results for liquid ARV formulations)

Tests	Method	Compendia	Specifications	Test results	Conformity
Microbial Load	Plate Count Method	B. P 2007 Vol.Iv App. XVI B	□ $5x10^2$ Colony Forming Unit (CFU) per Ml	42 out of 42	100.00%
Assay (Identification)	HPLC	Adopted In-House Method	92.0--108.0%	42 out of 42	100.00%

Findings: Quality of ARVs (Results of the failed product)

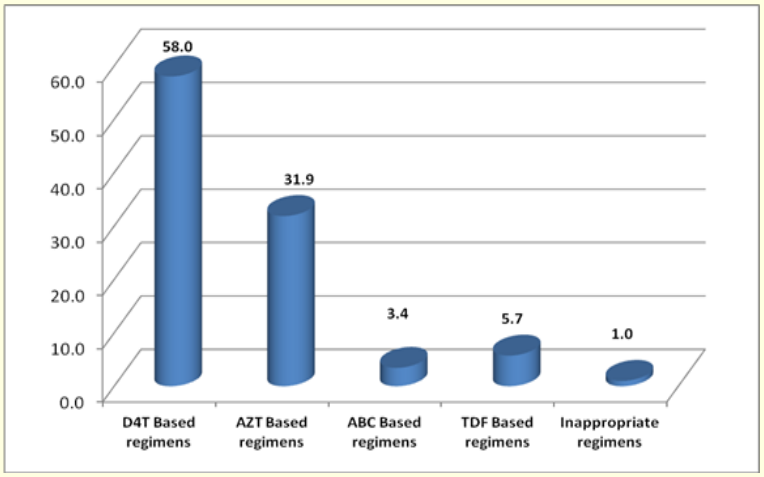
Test	Method	Compendia	Specification	Determination	Remarks
Uniformity of weight	Weight	B.P 2007 Vol. IV App XII G	tablets/capsules deviate by more than 5% from mean tablet weight	Four deviates (9.0%, -6.1%, -8.4%, 5.6%)	Does not comply
Dissolution	HPLC	U.S.P 32 N.F 27 Vol 3 page 3890	No tablet less than 70% (n=6)	73.2% (n=12; RSD=10.7%)	Does not comply
Assay	HPLC	U.S.P 32 N.F 27 Vol 3 page 3890	90.0-110.0%	107.8% (n=7; RSD=1.8%)	Complies

Findings: 4. Storage conditions of ARVs at the study facilities



Findings: 5. Conformity of prescribing practices to national treatment guidelines

Percentage distribution of commonly used ART regimens



Summary of findings

- 13 formulations, of which three were pediatric FDCs, were not available in 50% of the provinces.
- Of the 95 products sampled, 69 (72.6.3%) were registered while 26 (27.47%) were not registered in Kenya. The unregistered products were from multiple manufacturing companies i.e. Abbot (2), Aurobindo (7), Cipla (8), Hetero (1), Matrix (4), Ranbaxy (1), Roche (1), Strides Arcolab (2).

Summary of findings

- 99.63% (n=272) of the samples analyzed passed laboratory tests. Only one product(0.37%) failed tests of uniformity of weight and dissolution but complied on the assay. This product was AZT 300mg (manufactured by Hetero Drugs Limited, India), Batch No. A7276, MFD Date December 2007, Exp Date: November 2009, Client No. T1F4602.
- Most common type of ventilation was one sided at 49.5% while air conditioning was the least at 8.7%. Most of the facilities had shelves and pallets in their storage areas. Five provinces recorded the highest indoor temperature (32^0 C). The minimum recorded indoor temperature was 18^0 C in Central and Rift Valley provinces. Humidity levels in most of the provinces were within acceptable range i.e. maximum 65% (ICH guidelines). Coast province had the highest humidity (72%).

Summary of findings

- One product failed tests of uniformity of weight and dissolution but complied on the assay. This product was AZT 300mg (Hetero Drugs Limited, India), Batch No: A7276, MFD date: Dec-07, Exp. date: Nov-09, Client No: T1F4 602. However this product had already expired at the time of analysis and was therefore excluded from the analysis results.
- Of the 14 API contained in the products found in the market, 7 (50%) were not in the Kenya National ART guidelines 2005 Edition. The majority (99.1%) of patients were on the recommended national ART regimens. However, only 47% and 41% of facilities had current adult and pediatric ART guidelines respectively.

Conclusion

- One third of the products sampled from the market were not registered by the PPB.
- Storage conditions in majority of the sampled facilities were satisfactory.
- The laboratory results indicate that the samples analyzed were of good quality.
- Prescribing practices conformed to the national ART guidelines although availability of the guidelines was limited.
- Availability of pediatric FDC formulations was limited which could be attributed to their recent introduction by the national ART program.

Recommendations

- Strengthen enforcement of drug regulatory activities especially drug registration.
- Regular PMS to augment other product quality assurance measures.
- Current National ART guidelines should be disseminated widely to healthcare providers working in both private and public sectors.
- Enforce good storage practices at health facilities

Mini PMS in Nyanza and Nairobi

- Triggered by alert on falsified products (Zidolam N) by WHO and PPB – **September 2011**
- **Aim**: A quick surveillance of selected sites to establish the of presence and extent of use of implicated products as well as other poor quality ARV and OI medicines
- **Focus**: 26 sites in Homabay and Nyando districts and 4 sites in Nairobi (MSF France support)

Specific objectives of the mini PMS

- To establish the presence of and storage conditions of the falsified ARVs and/or other poor quality medicines at the selected health facilities
- To determine the extent of exposure of patients to the falsified ARVs and/or other poor quality medicines and the extent to which corrective measures had been undertaken
- To conduct a sensitization on Pharmacovigilance and Post Marketing Surveillance to the facility staff
- To orient health care workers on the standard operating procedure on reporting of poor quality ARVs and other medicines and client/patient education

Methodology

- Six teams were constituted consisting of staff from NASCOP, PPB and MSH
- Five teams visited facilities in Nyanza and one team visited the Nairobi sites
- The exercise was conducted between the **31st of October and 5th of November.**
- A half day meeting to familiarize the team members on the specific tasks at each facility and use of the data collection tool was held.
- A feedback meeting was held at the end of the exercise where each team reported on key findings for each facility as well as recommendations for the future

Summary of findings

- Homabay district
  - About 140,000 packs of Zidolam N were procured and dispensed to about 2000 patients in Homabay and Ndhiwa districts
  - MSF-F buffers stocks i.e. holds stocks to act as buffer to the DH in case of shortages, otherwise, the main supplier of ARVs to the facility is KP
  - MSF-F procures OI medicines for use in clinic B from CHMP (a French company).
  - MSF also procures pediatric & MDR TB medicines; laboratory commodities

Summary of findings

- Homa bay District
  - Manufacturing company of AZT/3TC/NVP FDC in stock at the time of visit was Matrix Laboratories Limited supplied by KP
  - Transporters of ARVs noted as : Kuber Agencies Limited; Kaiko Investment
  - The facility created a register to document clients who received the falsified Zidolam N (Between 24th Oct 2011 and 1st Nov 2011, a total of 44 patients had returned the medicines) for VL testing
  - Mop up of implicated batches was done in all facilities immediately following the alerts and were quarantined at the MSF-F store in Homabay DH

Summary of findings

- Nyando district
  - No facility visited had reported having received any falsified Zidolam N and that no patient was ever issued with the drugs or came across the falsified drugs in any of the facilities
  - Staffs in all the facilities visited were not familiar with the drug donations guideline and no facility had a copy of the guidelines
  - Some of the facilities (Kusa HC and Sigoti HC) had received donations of medicines without any documentation and staff were not aware who actually gave the donations

Summary of findings

- Nairobi district
  - All batches of Zidolam-N from Hetero had been quarantined and returned to supplier
  - Some commodities had registration from Tanzania, Botswana, and Zambia but not Kenya.

Conclusion and recommendations

- Audit of all implicated agencies – C-Mehta, CHMP, OGRA, Droplets, Pharma Trade
- Suspend all implicated companies until audit report is provided
- Discourage ARVs donations directly to health facilities, instead channel all ARVs supply via the two main pipelines i.e. KEMSA and KP. Any funding for ARVs procurement should be channeled through the two pipelines via NASCOP
- Collapse all parallel supply chains into the two national pipelines i.e. KEMSA and KP
- Conduct regular quality checks on the supply chains and PMS every two years