



Ministry of Public Health and Sanitation

# **REPORT ON POST-MARKET SURVEILLANCE OF FIRST LINE ANTI-TUBERCULOSIS MEDICINES IN KENYA**

**October 2012**



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# Abbreviations and Acronyms

CDC	Centres for Disease Control
DLTLD	Division of Leprosy, Tuberculosis and Lung Disease
E	Ethambutol
FDC	Fixed Dose Combination
H	Isoniazid
HCSM	Health Commodities and Services Management Program
ICH	International conference on Harmonization
KEMSA	Kenya Medical Supplies Agency
KNPDP	Kenya National Pharmaceutical Drug Policy
MDRTB	Multi Drug Resistant Tuberculosis
MOPHS	Ministry of Public Health and Sanitation
MOMS	Ministry of Medical Services
MSH	Management Sciences for Health
NQCL	National Quality Control laboratory
PPB	Pharmacy and Poisons Board
PMS	Post Market Surveillance
PV	Pharmacovigilance
R	Rifampicin
RH	Rifampicin/Isoniazid
RHZ	Rifampicin/Isoniazid/Pyrazinamide
RHZE	Rifampicin/Isoniazid/Pyrazinamide/Ethambutol
RHE	Rifampicin/Isoniazid/Ethambutol
S	Streptomycin
TB	Tuberculosis
USAID	United States Agency for International Development
WHO	World Health Organization
XDR TB	Extensively Drug Resistant Tuberculosis
Z	Pyrazinamide

# Definitions

**Active pharmaceutical ingredient:** The chemical substance responsible for a product's pharmacological effect.

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

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

**Clinical trial:** A systematic study on a pharmaceutical product in human subjects (including patients and other volunteers) in order to discover or verify the effects of and/or identify any adverse reaction to investigational 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:** A combination of two or more different classes of antiretroviral medicines with unrelated mechanisms of action.

**Drug / 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 product includes the presentation, packaging and the accompanying information.

**Drug resistance:** The World Health Organization (WHO) defines resistance to a medicines as the ability of a microorganism 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.

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

**Formulation:** The administration form of a completed pharmaceutical product, inclusive of the strength of the active pharmaceutical ingredient per unit dose e.g. isoniazid 100mg tablet, rifampicin 150mg capsule.

**Generic medicine:** A pharmaceutical product that is manufactured without a licence 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 Rifampicin) or under a branded name (such as Rifadin).

**National pharmacovigilance Centre:** A single, governmentally 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 drug safety.

**Pharmaceutical product:** Any medicine intended for human use, presented in its finished dosage form that is subject to control by pharmaceutical legislation (registered). A product may be sold under a brand name or under a generic name.

**Prescription event monitoring:** A system created to monitor adverse drug events in a population. Prescribers are requested to report all events, regardless of whether they are suspected adverse events or for identified patients receiving a specified drug.

**Sample:** For the purposes of this study, each of the medicines found in each facility on the day of the survey was given a sample number.

**Treatment failure:** Failure to achieve the desired therapeutic response after the initiation of therapy. Treatment failure is not synonymous with drug resistance.

# Foreword

Tuberculosis is the third major cause of morbidity (106,083) and mortality (15/100,000) in Kenya, with its prevalence and incidence rates at 283/100,000 and 305/100,000<sup>1</sup>. It affects all age groups, but has its greatest toll in the most productive age group of 15 to 44 years. The major contributing factor to the large TB disease burden in Kenya is the concurrent HIV pandemic. Other contributing factors include poverty and social deprivation that has led to mushrooming of peri-urban slums, congestion and limited access to general health services.

Recently, there have been increasing concerns about the emergence of drug resistant TB, a challenge which threatens to reverse the gains achieved in the fight against TB. In Kenya, the cumulative number of drug resistant TB cases diagnosed as at the end of 2010 was 525. Of these, 112 cases were diagnosed in 2010 alone. Drug resistant TB is attributed to man-made causes mainly lack of adherence to treatment; poor accessibility and quality of first line anti-TB drugs and limited knowledge among health care workers and the community.

To mitigate the challenges posed by tuberculosis and drug resistant TB in the face of the HIV epidemic and the socio-economic environment, the Ministry of Public Health and Sanitation, Ministry of Medical Services through the DLTD and PPB undertook a post market survey of first line anti-TB medicines with the aim of establishing the availability, quality and registration status in the Kenyan market. This survey was conducted through collaboration and support from various stakeholders; the key ones being CDC, WHO, MSH, PPB and NQCL.

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<sup>1</sup> WHO Global Tuberculosis Control WHO Report 2010

The findings of this survey will go a long way in designing appropriate strategies to ensure quality, safety and efficacy of anti-TB medicines for the public sector as proposed in the Ministry of Medical Services 2008-2012 and Ministry of Public Health and Sanitation 2008-2012 strategic plans. In addition, the findings of this survey have informed the design of interventions incorporated in the DLTLD Strategic Plan 2011-2015. It is envisaged that this survey will be carried out routinely to inform policy in drug regulation, quality assurance and procurement and ultimately ensure that patients receive high quality pharmaceutical care for better treatment outcomes.

Signed

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# Abstract

**Background:** The number of TB cases notified in Kenya has increased tenfold since 1990 while the incidence of all forms of TB increased from 11,625 in 1990 reaching a peak of 116,723 in 2007. A slow decline to 106,083 in the year 2010 has since been noted.

Kenya has made significant progress in the prevention and control of tuberculosis. Notably, it achieved the WHO medium term targets of case detection rate of 70% and treatment success rate of 85% in 2006<sup>2</sup>. It has continually improved on these targets reaching a case detection rate of 85% and treatment success rate of 85.86% as at the end of 2010.<sup>3</sup>

Despite the significant gains in the prevention and control of TB, there are other emerging challenges such as multi-drug resistant strains of tuberculosis. Scientific evidence suggests that development of resistant strains may result from irrational use and poor quality of medicines.

It is therefore important that anti-TB medicines are safe, efficacious, of high quality and administered according to the Directly Observed Therapy, Short-course (DOTS). In Kenya, there are limited reports on the quality of fixed dose combinations for anti-TB drugs available in public and private health facilities.

## Aims and Objectives

The aim of this survey was to establish baseline data on availability, range; quality and registration status of anti-tuberculosis medicines in Kenya's public, mission and private health sectors. The objectives were:

1. To establish the *availability and range* of anti-TB drug formulations in Kenya.

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<sup>2</sup> WHO Global Tuberculosis Control WHO Report 2008

<sup>3</sup> DLTLD Annual Report 2010

2. To determine the *quality* of anti-TB drugs at public, mission and private sector health facilities in Kenya.
3. To determine the *registration* status of the first line anti-TB medicines in Kenya.

**Methods:** A cross sectional survey was carried out at 77 TB treatment sites sampled across the country. Questionnaires were administered to obtain qualitative data on storage and distribution of anti-TB medicines. In addition, 400 batches were sampled randomly from all these sites and out of these, 120 samples randomly selected and sent to the National Quality Control Laboratory for quality control tests.

**Results:** The recommended first line medicines used for the treatment of TB were generally available in all the eight provinces in Kenya. Notably unavailable in the sites visited was streptomycin in two provinces and EH in one province. Current treatment guidelines, however, do not advocate use of EH in the management of TB. The entire recommended oral fixed dose combinations used in both the intensive and continuation phases of TB treatment were available in all the sites in the country. 25% of the anti-TB formulations were RHZE fixed dose combination. 88% were adult anti-TB formulations whereas 12% percent were pediatric dosage forms.

Overall, most facilities (78%) had acceptable storage conditions with the exception of those in North Eastern Province where significantly high storage temperatures were recorded. All regions had relative humidity levels (33-62%) within the recommended range. Most facilities had inadequate storage infrastructure and lacked pallets and appropriate shelving.

A total of 120 product samples were analyzed. **Ten** failed to comply with one or more of the test parameters, representing a failure rate of **8.3%**. All the non-compliant products were two- component fixed dose combination samples with RH combination accounting for **80%** of non-compliance and the EH combination accounting for the remaining **20%** of failures.

Out of the 26 RH samples that were submitted for laboratory analysis, 8 (31%) failed assay tests because of having higher average content of active ingredients than specified.

All the sampled medicines had current registration status at the Pharmacy and Poisons Board except one sample of EH whose registration certificate was later issued in September 2009.

**Conclusions and Recommendations:** Healthcare facilities in Kenya generally have the first line medicine formulations recommended for the treatment of TB. Most of the samples analyzed were of good quality with an overall failure rate of 8.3%. 31% of RH samples did not have the required content and thus there is need for follow up on the failed batches for corrective action. It is recommended that, to ensure good quality medicines, all technical specifications guiding procurement should include WHO pre-qualification status for all products and manufacturers. In addition, local batch testing of anti-TB medicines should be instituted as a routine practice in all sectors. This should be augmented with regular post marketing surveillance at least every two years. There is also need to renovate storage areas in health facilities or build new ones where required so as to maintain quality of procured medicines. This should be supported by good distribution and storage practices. It was commendable to note that all anti-TB medicines available are registered by the Pharmacy and Poisons Board.

# 1. Background and Introduction

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## 1.1 Tuberculosis in Kenya

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Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* bacilli. Occasionally, *Mycobacterium bovis* transmitted through contaminated milk and *Mycobacterium africanum* bacilli also cause the disease. The bacillus is transmitted from person to person through aerosolized droplet nuclei generated through coughing- the most important mode of transmission of TB. The bacillus may also be transmitted by other aerosol generating processes including laughing, talking, sneezing, singing and spitting. An infectious tuberculosis patient is one with a positive TB sputum smear result<sup>4</sup>.

### Trends of Tuberculosis

The rapid increase in Tuberculosis cases notified in Sub Sahara Africa (SSA) has reached epidemic levels and created a major public health problem not witnessed before. In 2007, there were more than 9.27 million cases of tuberculosis reported to World Health Organization with more than 2 million deaths. Most of the estimated numbers of cases in 2007 were in Asia (55%) and Africa (31%). Although the total number of incident cases of TB is increasing in absolute terms as a result of population growth, the number of cases per capita is falling<sup>5</sup>.

Kenya is among the 22 countries that for a long time has been collectively contributing to 80% of the global burden of TB disease. In 2009 the country was ranked 13th among the 22 TB high burden countries. The absolute number of TB cases notified increased more than tenfold since 1990 while the TB case notification rates for all cases increased from below 50/100,000 in 1990 to a maximum of 271/100,000 population in 2010. The incidence of all forms of TB increased from 11,625 in 1990 reaching a peak of 116,723 in 2007. A slow decline to 106,083 in the year 2010 has since been

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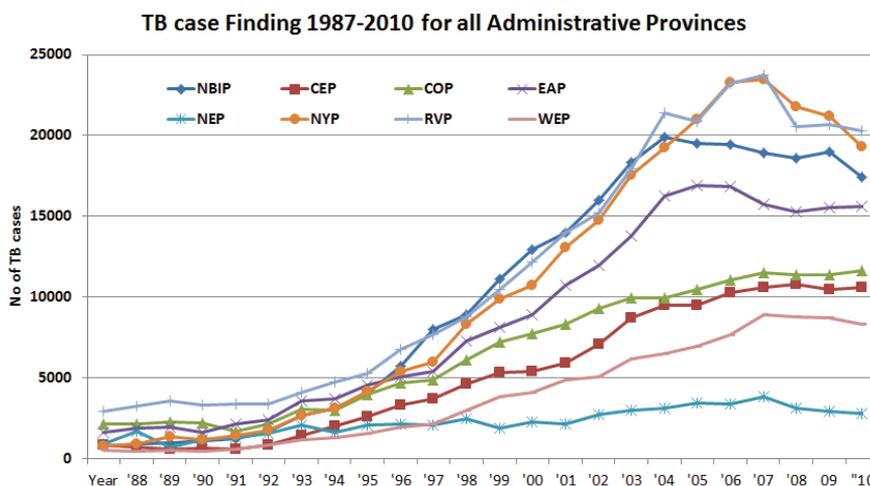
<sup>4</sup> DLTLD Treatment Guidelines 2009

<sup>5</sup> WHO Global Tuberculosis Control Report WHO Report 2009

noted. This decline may reflect a slowing down of the rate of growth of the epidemic or the beginning of the decline in the incidence of TB due to the efforts made over the past decade. At this stage with the information available, it is impossible to know which of these options is true.

The average annual increase of notified cases over the past decade is 5% for all forms of TB. Since 2006 the average rate of increase of notified cases has declined to -1% per year.

**Figure 1: TB case finding data 1987 – 2010**



There are many reasons for the continued large burden of TB, despite the long presence of a strong programme. These factors include little change in poverty levels, delays in TB diagnosis from both patient and health system related factors, which facilitates TB transmission, and as already mentioned the concurrent HIV epidemic. In 2010, the national average of HIV prevalence in TB patients was 41%, but with considerable variation across Kenya.

Kenya is considered to be a low prevalence MDRTB setting. In 2010 a total of 112 MDR TB cases were identified and notified to the WHO. The increasing notification of MDR TB and XDR TB is threatening to reverse all the gains that have been achieved by the country.

TB remains one of the frequent causes of death among adults despite being nearly 100% curable. The current global strategy is to prevent infection through efficient case finding and treatment (6). Control continues to elude mankind more than a century after the causative organism was identified and more than half a century since effective anti-TB drugs were introduced.

Kenya adapted the Directly Observed Treatment Short-course (DOTS) over fifteen years ago to improve on treatment adherence and efficient use of anti-TB medicines. It was however only until 2006 that Kenya achieved the WHO set TB control targets of 70/85 i.e. Case Detection Rate (CDR) of 70% and the treatment success rate of smear positive TB patients of 85%.

Kenya has made significant progress in the prevention and control of tuberculosis. Notably, it achieved the WHO medium term targets of case detection rate of 70% and treatment success rate of 85% in 2006<sup>6</sup>. The country has continually improved on these targets reaching a case detection rate of 82% for all forms of tuberculosis and treatment success rate of 86.85 as at the end of 2009.<sup>7</sup>

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## 1.2 Anti-TB Drug Policy in Kenya

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Tuberculosis treatment involves the use of multiple drugs taken in combination. This is done to prevent the emergence of drug resistance to any of the individual drugs. When single drugs are used (monotherapy), the tubercle bacilli quickly develop resistance to the drug used and hence anti-TB drugs should always be used in combination. Most anti-TB drugs are available as tablets containing multiple drugs in Fixed Dose Combinations (FDC). There are currently five primary drugs used to treat TB: Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), Ethambutol (E) and Streptomycin (S). Anti-TB drugs should be taken in the right combinations and doses, and their correct schedules for the appropriate duration. To promote total adherence to treatment, an individualized patient centered approach should be developed<sup>8</sup>.

In the first two months of treatment of tuberculosis, four drugs (RHZE) are used to rapidly reduce the number of tubercle bacilli (bacillary load) in the body. This phase

<sup>6</sup> WHO Global Tuberculosis Control WHO Report 2008

<sup>7</sup> DLTLD Annual Report 2010

<sup>8</sup> DLTLD Treatment Guidelines 2009

is called the Intensive phase of anti-TB treatment. After these first two months, two drugs are used for 4-6 months (RH or EH) and this phase is called the Continuation Phase of anti-TB treatment.. Table 1-3 below provide a summary of the Kenya national recommended treatment guidelines for management of TB in adults, pediatrics and relapse patients.

**Table 1: Treatment regimen for new adult TB patients**

Abbreviation of regimen <b>2RHZE/4RH</b>		
Phase	Intensive Phase	Continuation Phase
Duration	Daily treatment with appropriate patient support, including DOT, for two months	Daily treatment with appropriate treatment support, including DOT, for four or six months
Drugs used	Rifampicin (R) + Isoniazid (H) + Pyrazinamide (Z) + Ethambutol (E)	Rifampicin (R) and Isoniazid (H), 4 months.

**Table 2: Treatment regimen for retreatment patients**

Abbreviation of regimen <b>2SRHZE / 1RHZE / 5RHE</b>			
Phase	Intensive Phase		Continuation Phase
Duration	Daily treatment with appropriate patient support for two months	Daily treatment with appropriate patient support for one month	Daily treatment with appropriate patient support for five months
Drugs used	Streptomycin (S) + Ethambutol (E) + Rifampicin (R) + Isoniazid (H) + Pyrazinamide (Z)	Ethambutol (E) + Rifampicin (R) + Isoniazid (H) + Pyrazinamide (Z)	Ethambutol (E) + Rifampicin (R) + Isoniazid (H)

**Table 3: Treatment regimen for children**

Abbreviation of regimen	2 RHZ	4RH
Phase	Intensive Phase	Continuation Phase
Duration	Daily treatment with appropriate patient support for two months	Daily treatment with appropriate patient support for four months

### 1.3 Drug Regulation in Kenya

The PPB is the drug regulatory authority of the ministries of health in Kenya. It was 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 and veterinary medicines and medical devices. In addition, PPB advises the Government on all aspects on medicines regulation and pharmacy practice in order to safeguard the health of all Kenyans.

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

The Pharmacovigilance Unit under the Directorate of Product evaluation and registration at the PPB is responsible for all post-market surveillance activities. Prior to a drug being registered for use in the country, analysis of its quality, efficacy and specifications should be carried out by PPB in conjunction with 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. Post market surveillance was started actively in 2006 by the Pharmacy and Poisons Board following the creation of the Pharmacovigilance Unit.

The Pharmacovigilance unit works together with the Pharmaceutical Inspectorate Department and other departments as necessary.

NQCL is the technical arm responsible for evaluating the quality of medicines and medical devices in Kenya. It carries out examination and testing of drugs and medical devices by use of chemicals, physical, pharmacological and other pharmaceutical evaluation. NQCL is a WHO prequalified laboratory and has the capacity to serve national and regional medicine quality control needs.

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## 1.4 Substandard Medicines

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Sub-standard anti-TB drugs may lead to a number of consequences. These include treatment failures, drug resistance, mortality or morbidity, development of Multi-Drug Resistant TB and Extensively drug resistant TB resulting in increased cost of treatment of TB, prolonged disease transmission and suffering of the TB patient.

WHO estimates that up to 25% of the medicines used in developing and developed countries are counterfeit or substandard. It is important to establish the quality of anti-TB drugs that DLTLTD provides to health facilities batch by batch through Kenya Medical Supplies Agency (KEMSA). KEMSA is the Kenya Government agency entrusted with the responsibility of procuring, warehousing and distribution of drugs, non-pharmaceuticals and equipment of high quality.

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## 1.5 Study Justification

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One of the key components of the STOP TB strategy is to ensure that there is an effective drug supply and management system. Therefore there is need to put in place measures to ensure that anti-TB medicines are of high quality and efficacy.

Regular post-marketing surveillance for pharmaceuticals in Kenya is not being undertaken and therefore the risk of poor quality drugs finding their way into the public health care system is possible.

Information on the quality of fixed dose anti-TB drugs in Kenya is lacking and therefore the need for FDC's quality assessment along the supply chain/distribution channels. No concise study and continuous monitoring of the quality of anti-TB medicines in Kenya has been done to establish their safety and effectiveness.

## 2. Methodology

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### 2.1 Scope and Duration

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The survey sought to determine the availability, range, quality and registration status of all the first line TB medicines in the market in all eight provinces in Kenya. The quality parameters that the survey sought to establish were:

1. Quality of storage conditions for anti TB medicines i.e. temperature, humidity, ventilation and infrastructure e.g. use of shelving and pallets.
2. Conformity to compendia specifications on uniformity of weight, friability, disintegration, dissolution, identification and assay for content.

Data was collected from public, faith-based and private sector health facilities. The inclusion criteria for selecting facilities were:

- Facilities offering TB treatment
- KEMSA depots
- Retail chemists

The survey was conducted in June 2009 and laboratory analysis took place between July and November 2009.

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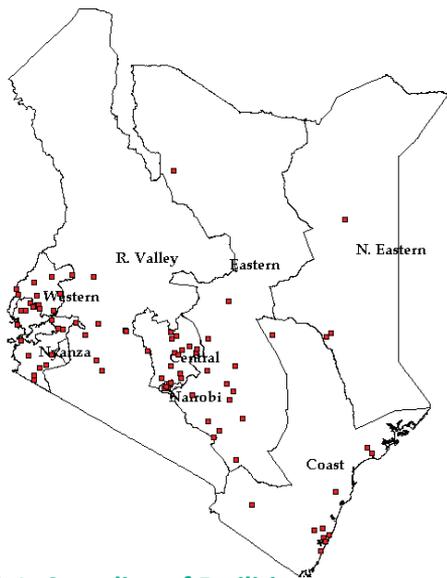
### 2.2 Sampling

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Stratified random sampling was used where the country was stratified into 12 strata corresponding to the TB control provinces (See Figure 2 below). There were three levels of sampling:

- Sampling of facilities
- Sampling of medicines
- Sampling of medicines for laboratory analysis.

**Figure 2: Map of Kenya showing sites where the TB drugs were sampled**



### 2.2.1 Sampling of Facilities

Selection of facilities for survey was based on the caseload of TB in the region reported in the year 2007. To determine the sample size, the following parameters were used:-

- a) Total number of facilities providing TB related services: 2228
- b) Allowable error: 3.8%

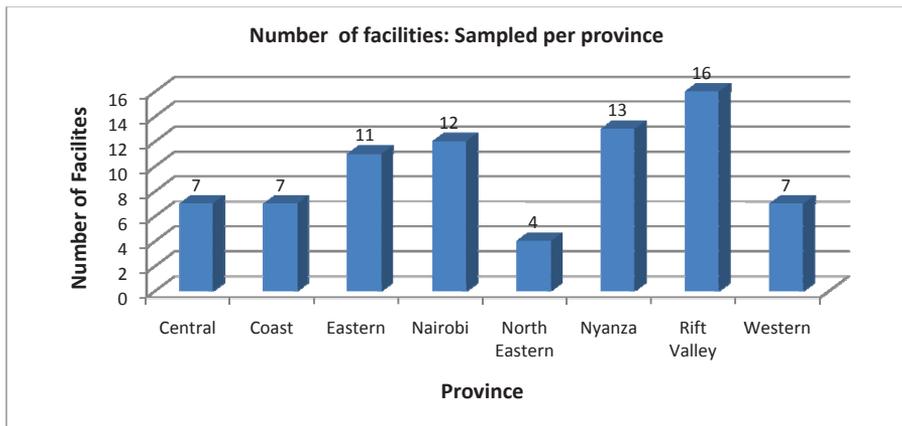
The sample size obtained was 77 sites comprising of 67 treatment centers / facilities and 10 regional stores. (See Table 4 and Figure 3)

**Table 4: Distribution of sampling sites**

REGION	Total No. of Sampling sites	Regional Stores	Category 1 -Public Health facilities	Category 2 - Mission Health Facilities	Category 3 – Private health facilities
COAST	8	1	5	1	1
CENTRAL	7	1	4	1	1

NORTH-EASTERN	4	1	1	1	1
RIFT VALLEY NORTH	7	1	4	1	1
RIFT VALLEY SOUTH	8	1	5	1	1
WESTERN	6	1	3	1	1
EASTERN	11	2	6	2	1
NYANZA	14	1	10	2	1
NAIROBI	12	1	4	4	3
TOTALS	77	10	42	14	11

**Figure 3: Number of facilities sampled per province (n=77)**



## 2.2.2 Sampling of Medicines from the Field

All first line anti-TB medicines found in the sampled facilities on the day of data collection were sampled. To qualify for sampling, the following criteria was used

### *Inclusion criteria*

- A minimum sample size of 100 tablets subject to availability of adequate stocks at the facility so as not to interfere with service delivery.
- A shelf life of at least 6 months at the time of sampling

### *Exclusion criteria*

- 1st line anti-TB drug having damaged packaging/seals
- Anti-TB drugs in supply boxes
- Expired anti-TB drugs

A total of 400 samples were collected from the field. Samples were coded by team and facility number e.g. T1 F 15 meant team 1 and facility 15 (Annex 2, 3 and 4: Tables on team composition and facilities visited)

## 2.2.3 Sampling of Medicines for Laboratory Analysis

Samples collected from the field were sorted by active ingredient and formulation out of which a total of 120 samples were randomly selected for analysis. The sample size selected was proportionate to the total number of samples in each category.

Coding of samples for analysis was performed centrally at the DLTLD/PPB offices. This was done by assigning a unique number to each product comprising of the team number, facility number and a three digit number to identify the formulation and batch. For example

T1 F15 101 would stand for sample 1 of the RHZE (150mg/75mg/400mg/275mg) tablet formulation collected by team 1, from facility 15. (See Annex 6: Coding of samples for analysis form)

Centralized sampling of medicines for laboratory analysis was to minimize bias by ensuring that at the time of sample collection in the field, the data collectors were unaware as to which batches would be analyzed.

A total of 120 batches out of 400 batches sampled from the field were selected for laboratory testing from 77 sampling sites (Tables 5 to 9). Laboratory analysis entailed physical tests, dissolution and assay for content.

**Table 5: Samples containing Rifampicin and Isoniazid submitted to NQCL for analysis**

S/ No	Brand name	Formulation	Manufacturer	Country of Manufacture	No. of Samples submitted
1.	RIFINAH – 300 tablets	RH (300/150mg)	Aventis Pharma (Pty) Ltd	South Africa	2
2.	RIHIDE – P PAEDIATRIC DISPERSIBLE TABLETS	RH (60/30mg)	Cosmos Ltd	Kenya	11
3.	RIHIDE FILM COATED TABLETS	RH (150/75mg)	Cosmos Ltd	Kenya	2
4.	AKURIT TABLETS	RH (150/75 mg)	Lupin Ltd	India	3
5.	RIFAMPICIN/ ISONIAZID TABLETS	RH (150/75mg)	Svizera Labs	India	8

**Table 6: Samples containing Ethambutol and Isoniazid submitted to NQCL for analysis**

S/ No	Brand name	Formulation	Manufacturer	Country	No. of Samples submitted
1	ECONEX – 400 TABLETS	EH (400/150 mg)	Macleods Pharmaceuticals	India	9
2	ETHAMBUTOL/ ISONIAZID TABLETS	EH (400/150mg)	Svizera Labs	India	15

**Table 7: Samples containing Rifampicin, Isoniazid and Ethambutol submitted to NQCL for analysis**

S/ No	Brand name	Formulation	Manufacturer	Country	No. of Samples submitted
1	RIFAMPICIN/ ISONIAZID/ ETHAMBUTOL TABLETS	RHE (150/75/275mg)	Lupin Ltd	India	21

**Table 8: Samples containing Rifampicin, Isoniazid and Pyrazinamide submitted to NQCL for analysis**

5S/ No	Brand name	Formulation	Manufacturer	Country	No. of Samples submitted
1	RIHAZ FILM COATED TABLETS	RHZ (150/75/400mg)	Cosmos Ltd	Kenya	15
2	RIMCURE PAED 3 FDC TABLETS	RHZ (60/30/150mg)	Sandoz (Pty) Ltd	South Africa	9

**Table 9: Samples containing Rifampicin, Isoniazid, Ethambutol and Pyrazinamide submitted to NQCL for analysis**

5S/ No	Brand name	Formulation	Manufacturer	Country	No. of Samples submitted
1	RIFAMPICIN / ISONIAZID / ETHAMBUTOL / PYRAZINAMIDE	RHZE (150/75/275/400 mg)	Svizera labs	India	9
2	AKURIT 4 TABLETS	RHZE (150/75/275/400 mg)	Lupin Ltd	India	7

3	FORECOX – TRAC TABLETS	RHZE (150/75/275/400 mg)	Macleods Pharmaceuticals	India	8
4	RIHAZ – E tablets	RHZE (150/75/275/400 mg)	Cosmos Ltd	Kenya	1

## 2.3 Coding of Samples

There were two levels of coding done i.e. coding of samples collected from the field and coding of samples selected for laboratory analysis.

## 2.4 Data Collection

### 2.4.1 Data Collection Tools

#### Questionnaires

A semi structured questionnaire for data collection was developed and pre- tested to check clarity of questions and ease of administration (See Annex 2). The questionnaire was designed to collect information on storage conditions for anti TB medicines at facility level and contained a list of all anti-TB medicines presumed to be in the market with the allowance to add any additional products not listed.

#### Sample Collection Form

A sample collection form was designed to enable collection of samples from the field and was structured to collect the following information per sample; name of TB medicine; name of facility; brand name; unit of issue; type of packaging; batch number; label claim/strength; formulation, manufacturing date; expiry date and country of manufacture (See Annex 5).

#### Data Collectors

There were three survey coordinators and nine data collectors for the survey comprising pharmaceutical personnel and program officers from both PPB and DLTL. A pre-survey training was carried out in Nairobi to orientate the data collectors on the rationale and methodology of the survey. The Chief Pharmacist issued each data collector with a letter of introduction to facilitate the collection of data and samples from the sites. (See Annex 1)

### 2.4.2 Data Collection Process

Three teams comprising of three members visited the 77 facilities in assigned regions. Data was collected between the 26th of April to 15th of May 2009. The questionnaires and the sample collection forms were administered by the data collectors on site. Where the samples available in the site met the selection criteria, they were obtained free of charge or purchased. Samples collected each day were labeled and recorded appropriately.

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## 2.5 Data Analysis

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The questionnaires, sample collection forms and samples were received at the PPB, verified for completeness and accuracy and appropriately coded. The samples were sorted according to presentation and batch number, recorded and kept in a secure store within the PPB premises.

Data was entered into a prepared database after which data analysis was done using SPSS software version 16. Descriptive statistics was used to organize, summarize collected data and analysis of variance to assess if there is any significant deviation from the set standards.

The registration status of the TB samples was verified at the PPB through their database.

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## 2.6 Laboratory Analysis

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Analysis of samples was by methods obtained from official compendia i.e. British Pharmacopoeia (B.P.) 2007 Volume IV and United States Pharmacopoeia (USP 31 NF 26) Convention (2008). The following tests were done for each of the samples: uniformity of weight, friability (for dispersible tablets), dissolution, identification and assay.

A certificate of analysis was issued for each sample analyzed and a detailed report of actual method used to test each sample and results obtained produced.

## 3. Results

### 3.1 Availability of Anti-TB Drug Formulations

*Table 10: Regional availability of first line anti-TB medicines in Kenya*

Formulation / Province	RHZE	RH	EH	S	RHZ	RHE
Central	Y	Y	Y	Y	Y	Y
Coast	Y	Y	N	Y	Y	Y
Eastern	Y	Y	Y	Y	Y	Y
North Eastern	Y	Y	Y	Y	Y	Y
Nairobi	Y	Y	Y	Y	Y	Y
Nyanza	Y	Y	Y	N	Y	Y
Rift Valley	Y	Y	Y	Y	Y	Y
Western	Y	Y	Y	N	Y	Y

Key: Y – Available N – Not available

In Coast province all the facilities visited did not have the fixed dose combination of ethambutol with isoniazid (EH). In both Nyanza and Western provinces all the sites visited did not have streptomycin injection. It's worth noting that previous guidelines cited that RH could be used in place of EH and that in all the sites where EH was unavailable, RH was in stock. Currently however, EH is no longer used in the management of TB.

All the 77 TB treatment sites visited had in stock the recommended first line anti-TB medicines. 22 of the 77 sites visited representing 28.57% had one medication not available in the pharmacy and these were EH and streptomycin. Streptomycin was the more common unavailable medicine.

### 3.2 Range of Anti-TB Drug Formulations

Table 11 below shows the range of anti-TB medicines, fixed dose combinations and formulations available in the sites visited.

	Formulation 1	Formulation 2	Formulation 3
RHZE	Tablet, (150/75/400/275)mg	Tablet, (60/30/150/104) mg*	
RH	Tablet, (300/150)mg	Tablet, (150/75)mg*	Tablet, (60/30)mg *
EH	Tablet, (400/150)mg		
S	Vial, 1g		
RHZ	Tablet, (150/75/400)mg	Tablet, (60/30/150)mg*	
RHE	Tablet, (150/75/275)mg		
H	Tablet, 100mg		
E	Tablet, 400mg		

\*Paediatric formulation

The assessment team visited 77 health facilities. Sixty eight of the 77 TB treatment sites visited were able to give samples to the assessment team. A total of 307 samples for anti-TB formulations were collected from 60 health facilities, 6 KEMSA depots and 2 retail pharmacies. Twenty five percent of the anti-TB formulations were RHZE fixed dose combination. Eighty eight percent were adult anti-TB formulations whereas 12% percent were paediatric dosage forms.

### 3.3 Quality of Anti-TB medicines

#### 3.3.1 Storage Conditions

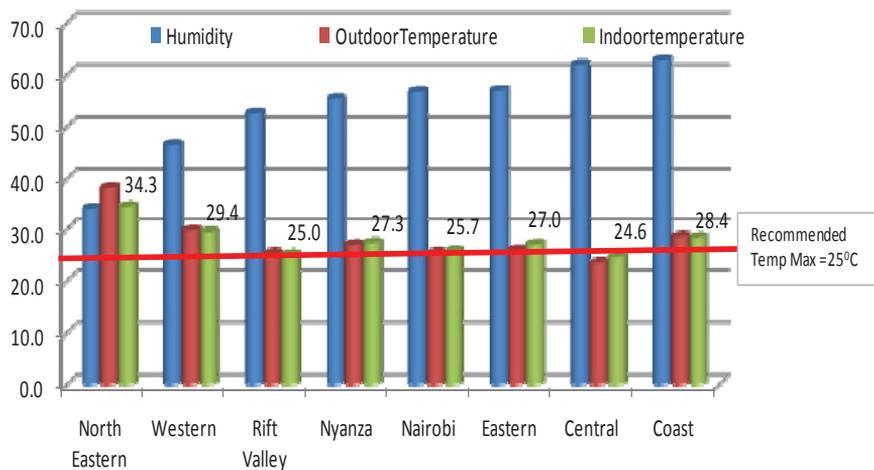
##### 3.3.1.1 Temperatures

With regard to temperature, the survey found that in North Eastern province, both indoor and outdoor temperatures were above the recommended range of 28-32oC. Other provinces with relatively higher temperatures (above 25oC but below 30oC) were Western, Nyanza, Eastern and Coast. (See Figure 4)

##### 3.3.1.2 Humidity

All the provinces had acceptable relative humidity ranges based on the ICH Guidelines Zone IVA which recommend that the relative humidity for storage of tablets should be less or equal to 65+5%.

**Figure 4: Mean storage temperatures and humidity by province**



### 3.3.1.3 Ventilation

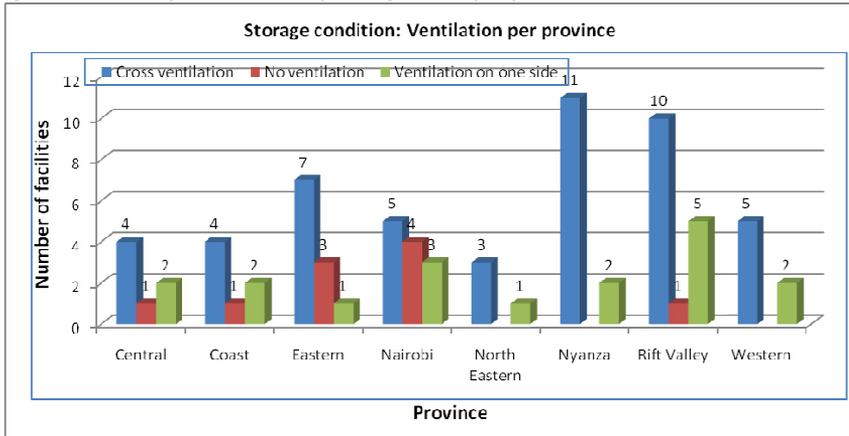
In Central, Coast, Eastern, Nairobi and Rift valley there were a number of facilities which lacked ventilation in their storage facilities. (See Figure 5)

### 3.3.1.4 Storage Infrastructure

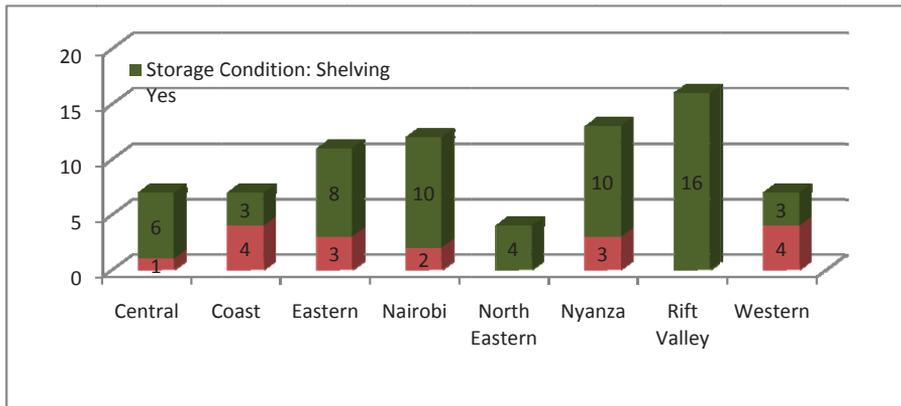
#### *Shelving and use of pallets*

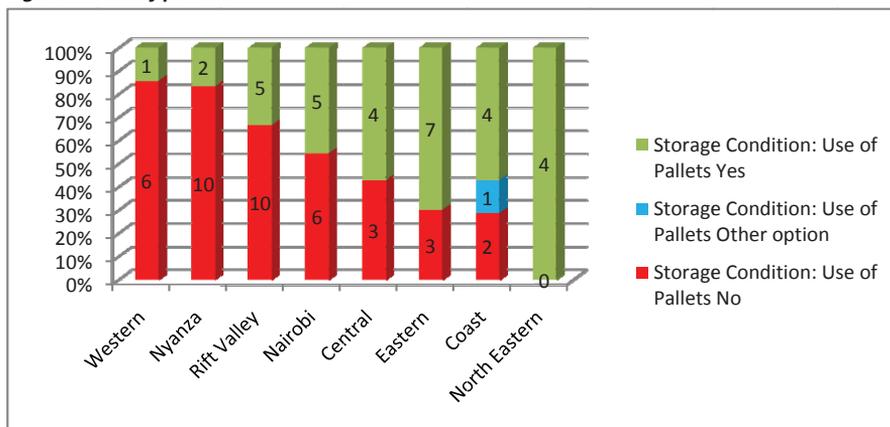
Use of shelves and pallets promotes good storage practices. Except for North-Eastern province, all the provinces had facilities that were without pallets for storage. In Central, Coast, Eastern, Nairobi, Nyanza and Western provinces, some facilities did not have adequate shelving (See Figures 6 and 7).

**Figure 5: Summary - ventilation of storage areas per province**



**Figure 6: Summary of shelving**



**Figure 7: Use of pallets**

### 3.3.2 Laboratory Analysis

#### 3.3.2.1 Physical Tests

All 120 samples complied with specifications for uniformity of weight and identification tests. For paediatric dispersible tablets additional tests for friability and disintegration were done for which all 11 samples passed.

#### 3.3.2.2 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. All tablet formulations passed this test with the exception of EH where 2 (13%) of the 15 samples submitted for analysis failed.

#### 3.3.2.3 Assay Tests

This involved determination of the average content of active ingredient in the samples submitted. A total of 26 fixed dose combinations (FDCs) of RH samples were assayed of which 8 (30.8%) failed. 75% of these samples that failed were paediatric RH formulations as shown in figure 8 below. All the RHE (21 samples) and RHZ (24 samples) submitted complied with the specifications for all the tests performed. All the 25 samples of RHZE submitted for assay passed.

**Table 12: Analysis results for 2 component FDC (Rifampicin/Isoniazid) tablets**

S/N	Brand Name	Formulation	No. of Samples Submitted	Results		Tests failed	Registration Results
				Samples failed	Samples passed		
1	RIFINAH – 300 TABLETS	RH (300/150mg)	2	2 (100%)	0	Assay	Registered
2	RIHIDE-P PAEDIATRIC DISPERSIBLE TABLETS	RH (60/30mg)	11	6 (55%)	5	Assay	Registered
3	RIHIDE FILM COATED TABLETS	RH (150/75mg)	2	0	2	-	Registered
4	AKURIT TABLETS	RH (150/75 mg)	3	0	3	-	Registered
5	RIFAMPICIN / ISONIAZID TABLETS	RH (150/75mg)	8	0	8	-	Registered

**Table 13: Analysis results for 2 component FDC (Ethambutol/Isoniazid) tablets**

S/N	Brand Name	Formulation	No. of Samples Submitted	Results		Tests failed	Registration Results
				Samples failed	Samples passed		
1	ECONEX-400 TABLETS	EH (400/150 mg)	9	0	9	-	Registered
2	ETHAMBUTOL / ISONIAZID TABLETS	EH (400/150mg)	15	2 (13%)	13	Dissolution	*Registered

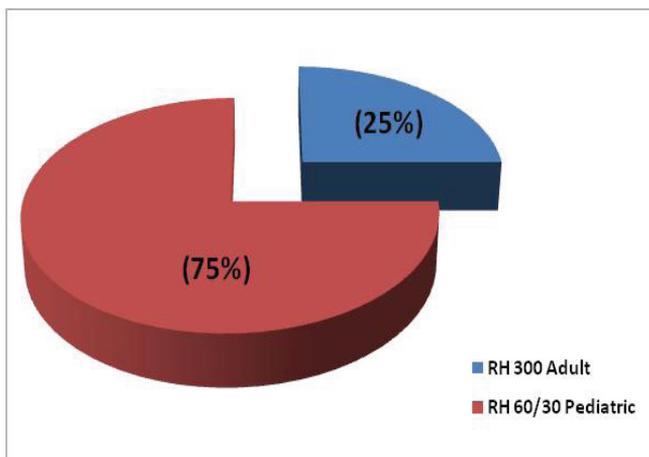
**Table 14: Analysis results for 3 component FDC (Rifampicin / Isoniazid / Ethambutol) tablets**

S/N	Brand Name	Formulation	No. of Samples Submitted	Results		Tests failed	Registration Results
				Samples failed	Samples passed		
1	RIFAMPICIN / ISONIAZID / ETHAMBUTOL TABLETS	RHE (150/75/275mg)	21	0	21	-	Registered
2	RIHAZ FILM COATED TABLETS	RHZ (150/75/400mg)	15	0	15	-	Registered
3	RIMCURE PAED 3 FDC TABLETS	RHZ (60/30/150mg)	9	0	9	-	Registered

**Table 15: Analysis results for 4 component FDC (Rifampicin/Isoniazid /Pyrazinamide/ Ethambutol) tablets**

S/N	Brand Name	Formulation	No. of Samples Submitted	Results		Tests failed	Registration Results
				Samples failed	Samples passed		
1	RIFAMPICIN / ISONIAZID / THAMBUTOL/ PYRAZINAMIDE	RHZE (150/75/275/400 mg)	9	0	9	-	Registered
2	AKURIT 4 TABLETS	RHZE (150/75/275/400 mg)	7	0	7	-	Registered
3	FORECOX-TRAC TABLETS	RHZE (150/75/275/400 mg)	8	0	8	-	Registered
4	RIHAZ – E TABLETS	RHZE (150/75/275/400 mg)	1	0	1	-	Registered

**Figure 8: Distribution of RH samples that failed assay tests (n=8)**



### 3.4 Registration Status of First Line Anti-TB Drugs in Kenya

From the study, 13 out of 14 different brands of anti-TB medicines found in the market had current registration status. However EH (400/150mg)\* that was unregistered at the time of the survey got registered in September 2009 (See Table 16).

**Table 16: Registration status of the anti-TB medicines in Kenya by June 2009**

S/N	Brand Name	Formulation	Manufacturer	Registration Results
Samples containing Rifampicin and Isoniazid				
1	RIFINAH – 300 tablets	RH (300/150mg)	Aventis Pharma (Pty) Ltd	Registered
2	RIHIDE – P PAEDIATRIC DISPERSIBLE TABLETS	RH (60/30mg)	Cosmos Ltd	Registered
3	RIHIDE FILM COATED TABLETS	RH (150/75mg)	Cosmos Ltd	Registered
4	AKURIT TABLETS	RH (150/75 mg)	Lupin Ltd	Registered
5	RIFAMPICIN/ISONIAZID TABLETS	RH (150/75mg)	Svizera Labs	Registered
Samples containing Ethambutol and Isoniazid				
6	ECONEX – 400 TABLETS	EH (400/150 mg)	Macleods Pharmaceuticals	Registered

7	ETHAMBUTOL/ ISONIAZID TABLETS	EH (400/150mg)	Svizera Labs	*Registered
Samples containing Rifampicin, Isoniazid and Ethambutol				
8	RIFAMPICIN / ISONIAZID / ETHAMBUTOL TABLETS	RHE (150/75/275mg)	Lupin Ltd	Registered
Samples containing Rifampicin, Isoniazid and Pyrazinamide				
9	RIHAZ film coated tablets	RHZ (150/75/400mg)	Cosmos Ltd	Registered
10	Rimcure Paed 3 FDC tablets	RHZ (60/30/150mg)	Sandoz (Pty) Ltd	Registered
Samples containing Rifampicin, Isoniazid, Ethambutol and Pyrazinamide				
11	RIFAMPICIN/ISONIAZID/ ETHAMBUTOL/ PYRAZINAMIDE	RHZE (150/75/275/400 mg)	Svizera labs	Registered
12	AKURIT 4 TABLETS	RHZE (150/75/275/400 mg)	Lupin Ltd	Registered
13	FORECOX – TRAC TABLETS	RHZE (150/75/275/400 mg)	Macleods Pharmaceuticals	Registered
14	RIHAZ – E TABLETS	RHZE (150/75/275/400 mg)	Cosmos Ltd	Registered

(Source: Pharmacy and Poisons Board website)

## 4. Discussion, Conclusions and Recommendations

Generally the five primary medicines recommended for first line use in the treatment of TB were available in all the eight provinces in Kenya at the time of the study. Not only were these available but also in the appropriate combinations for both adult and paediatric TB treatment. This is indeed a true reflection of the treatment success rate of the TB program in Kenya.

Generally most facilities visited had good storage practices. Temperature control was found to be a major challenge in North Eastern province with indoor temperatures of storage areas averaging 34.3oC. Four other provinces had relatively high temperatures that have the potential to affect medication quality if not controlled adequately.

With all the sites visited having acceptable relative humidity levels, medicines that failed dissolution and disintegration tests must have been due to other causes that may not be detectable by this study.

Although a number of storage areas in five provinces lacked ventilation, this does not directly affect the quality of medications. Ventilation is a determinant for indoor storage temperatures and should be considered especially in provinces with borderline to high temperatures. With the exception of North Eastern, all the other provinces had a number of facilities that lacked pallets and adequate shelving. Good shelving and use of pallets in storing medicines contributes to ensuring that potency is retained for their specified shelf-life.

Laboratory analyses performed revealed that generally all samples complied with specifications for uniformity of weight and identification tests. This means that the samples contained the active ingredients indicated on the labels. In addition, all the 11 paediatric dispersible tablets passed tests for friability and disintegration. This is a favorable finding considering that paediatric anti-TB medicines are not available in

liquid formulations. All samples passed dissolution tests except two EH fixed dose combinations. This implies that there is poor bioavailability of the active ingredients in these formulations.

Out of the 26 RH samples that were submitted for laboratory analysis, 8 (31%) failed assay tests due to higher average content of active ingredients than specified. It was realized that among these samples was the original brand Rifinah-300®. Traditionally, branded products have set the benchmark for quality. Furthermore, 75% of the samples that failed assay tests were RH paediatric dispersible tablets. This finding is unfavourable since it increases chances of occurrence of adverse drug reactions, drug interactions and toxicities. The problem is further compounded by the fact that tuberculosis is a criterion for starting ARVs in HIV co-infected patients and some drugs used in treatment of both conditions share common toxicities. Interestingly in this study, it was found that only products from manufacturers who are not WHO prequalified failed the specified laboratory tests.

Out of the 14 different brands of anti-TB medicines found during the survey, only one product was not registered at the time of the survey. An application for registration with PPB had already been submitted for the unregistered EH and the applicant was in the course of responding to some queries by PPB at the time of the survey. The product was later registered in September 2009.

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## Conclusions

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- 4.1 The recommended first line medicines and formulations for the treatment of TB are available in Kenyan healthcare facilities.
- 4.2 Temperature control in medication storage areas countrywide needs to be improved and especially North Eastern province.
- 4.3 The relative humidity levels in medication storage areas countrywide are within acceptable limits and thus humidity is not expected to contribute to affecting the quality of anti-TB medicines in Kenya.
- 4.4 Poor ventilation is common in many medication storage areas in Kenya.
- 4.5 Use of pallets and shelving for medicines is not up to desired standards in Kenya.

- 4.6 The failure rate in laboratory analysis for anti-TB medicines in Kenya is 8.3% and mainly related to paediatric formulations.
- 4.7 All anti-TB medicines sampled during the survey have current registration with PPB.

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## Lessons Learned

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- 1 Collaboration and communication between the DLTLD, PPB and NQCL to be improved.
- 2 Procedures in procuring of laboratory testing services to analyse drug samples should be determined early through an open tender system.
- 3 The turnaround time should be clearly indicated in the tender document.
- 4 Regulatory action for failed samples should be put in place by the relevant authority and communicated to the responsible department.
- 5 The procedures for conflict resolution among aggrieved manufacturers should be well laid down before the exercise.
- 6 More capacity building is required in the area of Pharmacovigilance activities.

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## Limitations of the Study

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- 1 Some sampling sites did not have adequate stocks and therefore did not meet the inclusion criteria.
- 2 Personnel in some facilities were hostile and did not allow data collectors to collect samples.
- 3 Geographical limitations.
- 4 Private health facilities were not adequately represented in the survey due to budgetary constraints. (Minimal budgetary allocation for purchase of samples in these facilities.)

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## Recommendations

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### Pharmacy and Poisons Board (PPB)

- 1 Should regularly monitor the quality of pharmaceuticals in the market and support all PMS activities within the ministries of health and inform all stakeholders.

- 2 Procedures for handling failed analysed samples and subsequently batches i.e. quarantine, recall, withdrawal etc. should be shared with the DLTLTD and Manufacturers before the PMS. A feedback mechanism should be in place to user departments on appropriate action taken.
- 3 To develop guidelines on effective execution of PMS exercises.
- 4 PMS results should be used to inform policies regarding drug regulation in Kenya.
- 5 Develop procedures for corrective and regulatory actions to be taken following post market surveillance activities

#### **National Quality Control Laboratory (NQCL)**

- 1 Review the cost of analyses for samples submitted for post-marketing surveillance.
- 2 Reduce the turn-around time to ensure that the results are relevant at the time of dissemination.

#### **Division of Leprosy, Tuberculosis and Lung Disease**

- 1 Dissemination strategies should be stipulated and done within one year after the survey.
- 2 PMS should be a regular exercise (every 2 years) and the focus should be on establishing PMS activities in sentinel sites through the mini-laboratory type of surveillance (USP project).
- 3 Second-line anti-TB drugs should be incorporated in subsequent PMS activities.
- 4 To increase budgetary allocation for purchase of PMS samples from the private sector.
- 5 Should involve pharmaceutical personnel in the management of commodities at the health facilities.
- 6 Should improve on support supervision to facilities from the national level.
- 7 Advocate for a multi-country survey quality of anti-TB medicines in the region.

## **Ministry of Public Health and Sanitation / Ministry of Medical Services**

### **Department of Pharmacy**

- 1 To lobby for resources for rehabilitation and construction of medical stores within health facilities.
- 2 To advocate for more involvement of pharmaceutical personnel in management of TB medicines at all levels of care.
- 3 To advocate for joint PMS surveys among programmes to guide policy.
- 4 To integrate the PMS activities within the two ministries to reduce the cost.
- 5 Renovation or building of new medicine stores in facilities where there are gaps.

### **Development Partners**

- 1 To continually provide technical and financial support for post marketing surveillance activities.
- 2 To provide support for operational research in quality control and assurance of medicines.
- 3 Involvement of DPs to assure patients of high quality drugs in line with PMS findings.

### **Pharmaceutical Manufacturers, Importers and Distributors**

- 1 To ensure their products comply with PPB guidelines.
- 2 To take responsibility for product recalls and replacements.

### **Kenya Medical Supplies Agency**

Enhance quality assurance activities

### **Consumers**

Should communicate any quality issue regarding medicines to the appropriate authorities.

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# Annexes

## Annex 1: Letter of Introduction

**REPUBLIC OF KENYA**  
**MINISTRY OF MEDICAL SERVICES**  
**PHARMACY AND POISONS BOARD**

Telegram: "MINHEALTH" Nairobi  
Telephone: 020-2716905/6, 020-3562107  
Mobile No. 0733 884411/0720 608811  
Fax: 2713431  
Email: info@pharmacyboardkenya.org



PHARMACY & POISONS  
BOARD HOUSE  
LENANA ROAD  
P.O. BOX 27663-00506  
NAIROBI

When replying please quote

PPB/PVIGI/09/24

15<sup>th</sup> April 2009

To,

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.....

.....

**Re: Post-Market Surveillance of First Line Anti-TB Medicines**

The Pharmacy and Poisons Board (PPB) and Division of Leprosy, TB and Lung Disease (DLTLD) are carrying out surveillance on the quality and availability of first line Anti-TB medicines. The survey is being carried out in the public and private sector health facilities in Kenya. Your facility has been chosen by randomization.

The survey requires the collection of basic information (such as pertaining to the site and storage) and sampling the first line Anti-TB medicines. The information will be recorded by the data collectors in the questionnaire attached. The data collectors are from PPB, DLTLD, Ministry of Medical Services and Ministry of Public Health and Sanitation. The survey will be undertaken over a three week period from the 26<sup>th</sup> April to 15<sup>th</sup> May 2009.

Anonymity of individual facilities and personnel will be maintained at all times by means of a facility code during data analysis and report writing. The samples will also be coded with a product code.

I will be grateful for your cooperation through transparent provision of the required information and sampling needed for the survey.

The list of appointed data collectors is as below:

Dr. Chris Masila	Mr. Alywn Kimalael
Dr. Richard Muthoka	Dr. Irene Muchoki
Mr. George Muthuri	Dr. Joel Mwova
Dr. Mikal Ayiro	Mr. Hillary Kipruto
Ms. Albina Imbuka	Dr. Jayesh Pandit

Thanking you in advance.

  
Dr. K. C. Koskei  
Registrar, Pharmacy and Poisons Board

## Annex 2: Team 1 Members and Facilities Visited

<b>Team 1</b>
<p><b>Members</b></p> <ol style="list-style-type: none"> <li>1. Dr. Chris Masila (Team leader)</li> <li>2. Mr. Alwyn Kimalel</li> <li>3. Dr. Irene Njeri Muchoki</li> <li>4. Mr. Karimi (Driver)</li> </ol>
<p><b>Facilities visited</b></p> <p>South Rift Valley</p> <p>Maralal District Hospital; Langa Langa Health Centre; Njoro Health Centre; Suguta Health Centre; Care Chemist; Kemsal – Nakuru; Kajiado District Hospital; Entasopia Health Centre; St. Mary’s Mission Hospital – Nakuru; Lodung’okwe Dispensary; Valley Mission Hospital; Mau Narok Health Centre.</p> <p>Nairobi Region</p> <p>Mater Hospital; Mukunga Hospital; St. Mary’s - Lang’ata; Westlands Health Centre; Lower Kabete Dispensary; KEMSA – Nairobi; SOS Medical Centre Buruburu; Umoja Health Centre; Kam Pharmacy- Kimathi Street Branch; Pangani Clinic; St. Theresa Dispensary – Pangani; Coptic Mission Hospital; N.Y.S Health Centre; Guru Nanak Hospital; Blue House; Kariokor Clinic.</p> <p>Coast Region</p> <p>Ngao Sub-district Hospital; Kilifi District Hospital; Malindi District Hospital; Pandya Hospital – Mombasa; KEMSA – Mombasa; Diani Health Centre; Mazeras Dispensary Mewa Hospital; Mombasa Hospital; AAR Docks; Kakoneni Health Centre; Kakuyuni Health Centre; Ganjoni Health Centre.</p>

## Annex 3: Team 2 Members and Facilities Visited

<b>Team 2</b>
<p><b>Members</b></p> <ol style="list-style-type: none"> <li>1. Hillary Kipruto</li> <li>2. Joel Mwova</li> <li>3. Peter Kiptoo</li> </ol>
<p><b>Facilities visited</b></p>

**Eastern**

Embu PGH; Kangundo DH; Kitui DH; Thinu HC – Machakos; Gachuriri HC – Mbeere; Nyambene SDH; Isiolo TB-manyatta; Garbatulla SDH – Isiolo; Kibwezi SDH; Meru DH; and Kisasi HC – Kitui

**North Eastern**

KEMSA depot Garissa; Ifin SDH – Garissa; Daadab HC – Garissa and Police line dispensary – Garissa

**Central**

KEMSA depot Nyeri; Kangema SDH – Murang’a North; Kimbimbi SDH – Kirinyaga; Kirogo HC – Murang’a North; Othaya SDH – Nyeri South; St. Mulumba Hospital – Thika and Jamii Hospital – Karatina.

**Annex 4: Team 3 Members and Facilities Visited****Team 3****Members**

1. George Muthuri
2. Dr. Richard Muthoka
3. Albina Imbuka
4. Ben Lodi

**Facilities visited****North Rift**

Eldoret KEMSA; Turbo HC - Uasin Gishu; Chembulet HC - Uasin Gishu; Suwerwa HC – Transzoia; Sigor HC - West Pokot; Mercy Mission Hosp – Koibatek and Cherangany Nursing Home – Transzoia.

**Nyanza**

Kisumu KEMSA; Makindu disp – Nyando; Awendo HC – Migori; Iranda disp - Kisii Central; Nyahera HC – Kisumu; Kibogo disp – Nyando; Sondu HC – Nyando; Kisii DH - Kisii Central; Etago HC – Gucha; Kusa HC – Nyando; Lambwe disp – Homabay; Ober Kamohit – Kisumu; Nyammagwa – Gucha and Segga Cottage Hospital – Siaya.

**Western Province**

Alupe Leprosy hospital; Ematundu disp - Butere/mumias; Lyanginga HC – Vihiga; Kapchamnani disp – Vihiga; Chelelemuk Hosp–Teso and Equator Hosp - Vihiga

**Annex 5: Selected SampleDetails Table**

Name of TB Drug	Dosage Form	Batch No	Label Claim	Mfg Date	Expiry Date	Country of Mfg	Name of manufacturer	Type of packaging (blister strip/ loose /container



## Annex 7

Table 1.1. Samples containing Rifampicin and Isoniazid (n=26)

No.	Brand	Manufacturer	Sample No. (NDQA200906-)	Client Ref.	Batch No.	Mfg. Date	Exp. Date
1.	RIFINAH - 300 TABLETS	Aventis Pharma (Pty) Ltd.	284	T <sub>1</sub> F <sub>1</sub> 802	A 8341	03/08	03/12
2.			285	T <sub>1</sub> F <sub>1</sub> 801	A 8341	03/08	03/12
3.	RIHIDE - P PAEDIATRIC DISPERSIBLE TABLETS	Cosmos Limited	331	T <sub>2</sub> F <sub>20</sub> 422	080651	06/08	05/10
4.			332	T <sub>2</sub> F <sub>4</sub> 414	080648	05/08	04/10
5.			333	T <sub>1</sub> F <sub>16</sub> 408	080331	03/08	02/10
6.			335	T <sub>1</sub> F <sub>4</sub> 429	080650	05/08	04/10
7.			334	T <sub>2</sub> F <sub>9</sub> 418	080651	05/08	05/10
8.			336	T <sub>1</sub> F <sub>8</sub> 403	080652	06/08	05/10
9.			337	T <sub>3</sub> F <sub>11</sub> 431	080650	05/08	04/10
10.			338	T <sub>3</sub> F <sub>10</sub> 430	080652	06/08	05/10
11.			339	T <sub>2</sub> F <sub>4</sub> 426	080648	05/08	04/10
12.			340	T <sub>2</sub> F <sub>4</sub> 416	080652	06/08	05/10
13.			341	T <sub>1</sub> F <sub>21</sub> 409	080651	06/08	05/10
14.	RIHIDE FILM COATED TABLETS	Cosmos Limited.	342	T <sub>2</sub> F <sub>21</sub> 637	072264A	11/07	10/10
15.			354	T <sub>1</sub> F <sub>20</sub> 621	080645	04/08	03/11
16.	AKURIT TABLETS	Lupin Ltd.	343	T <sub>2</sub> F <sub>5</sub> 627	AE80024	02/08	01/10
17.			344	T <sub>3</sub> F <sub>8</sub> 647	AE80031	02/08	01/10
18.			345	T <sub>3</sub> F <sub>19</sub> 635	AE80023	02/08	01/10
19.	RIFAMPICIN/ ISONIAZID TABLETS	Svizera Labs	346	T <sub>3</sub> F <sub>1</sub> 639	SL379	01/08	12/10
20.			347	T <sub>3</sub> F <sub>8</sub> 645	SL384	01/08	12/10
21.			348	T <sub>3</sub> F <sub>28</sub> 619	SL385	01/08	12/10
22.			349	T <sub>3</sub> F <sub>3</sub> 643	SL385	01/08	12/10
23.			350	T <sub>2</sub> F <sub>1</sub> 646	SL379	01/08	12/10
24.			351	T <sub>1</sub> F <sub>3</sub> 604	SL391	02/08	01/11
25.			352	T <sub>1</sub> F <sub>17</sub> 614	SL339	11/06	10/09
26.			353	T <sub>1</sub> F <sub>8</sub> 606	SL393	02/08	01/11

## Annex 8

Table 1.2. Samples containing Ethambutol and Isoniazid (n=24)

No.	Brand	Manufacturer	Sample No. (NDQA200906-)	Client Ref.	Batch No.	Mfg. Date	Exp. Date
1.	ECONEX 400 TABLETS	Macleods Pharmaceuticals	380	T <sub>3</sub> F <sub>14</sub> 514	ED714	02/07	02/10
2.			381	T <sub>3</sub> F <sub>24</sub> 532	ED704	02/07	02/10
3.			382	T <sub>3</sub> F <sub>19</sub> 527	ED706	02/07	02/10
4.			383	T <sub>3</sub> F <sub>9</sub> 518	ED710	02/07	02/10
5.			384	T <sub>3</sub> F <sub>17</sub> 525	ED705	02/07	02/10
6.			385	T <sub>3</sub> F <sub>15</sub> 521	ED709	02/07	02/10
7.			386	T <sub>3</sub> F <sub>16</sub> 526	ED707	02/07	02/10
8.			387	T <sub>3</sub> F <sub>20</sub> 514	ED706	02/07	02/10
9.			388	T <sub>3</sub> F <sub>5</sub> 508	ED701	02/07	02/10
10.	ETHAMBUTOL /ISONIAZID TABLETS	Svizera Labs	389	T <sub>3</sub> F <sub>15</sub> 523	SL836	05/06	04/11
11.			390	T <sub>3</sub> F <sub>23</sub> 531	SL889	06/06	05/11
12.			391	T <sub>3</sub> F <sub>12</sub> 520	SL875	05/06	04/11
13.			392	T <sub>3</sub> F <sub>11</sub> 510	SL910	07/06	06/11
14.			393	T <sub>3</sub> F <sub>26</sub> 503	SL881	05/06	04/11
15.			394	T <sub>3</sub> F <sub>21</sub> 515	SL905	07/06	06/11
16.			395	T <sub>3</sub> F <sub>8</sub> 507	SL909	07/06	06/11
17.			396	T <sub>3</sub> F <sub>20</sub> 513	SL912	07/06	06/11
18.			397	T <sub>3</sub> F <sub>12</sub> 511	SL909	07/06	06/11
19.			398	T <sub>3</sub> F <sub>7</sub> 506	SL895	07/06	05/11
20.			399	T <sub>3</sub> F <sub>10</sub> 509	SL908	07/06	06/11
21.			400	T <sub>3</sub> F <sub>11</sub> 519	SL874	05/06	04/11
22.			401	T <sub>3</sub> F <sub>21</sub> 529	SL908	07/06	06/11
23.			402	T <sub>3</sub> F <sub>3</sub> 504	SL911	07/06	06/11
24.	403	T <sub>3</sub> F <sub>2</sub> 533	SL904	07/06	06/11		

## Annex 9

Table 1.5. Samples containing Rifampicin, Isoniazid, Ethambutol and Pyrazinamide (n=25)

No.	Brand	Manufacturer	Sample No. (NDQA200906-)	Client Ref.	Batch No.	Mfg. Date	Exp. Date
1.	RIFAMPICIN/	Svizera Labs.	355	T <sub>1</sub> F <sub>19</sub> 120	SL1271	02/08	01/11
2.	ISONIAZID/		358	T <sub>1</sub> F <sub>15</sub> 113	SL1269	01/08	12/10
3.	ETHAMBUTOL/		362	T <sub>2</sub> F <sub>17</sub> 149	SL1256	01/08	12/10
4.	PYRAZINAMIDE		363	T <sub>1</sub> F <sub>21</sub> 121	SL1257	01/08	12/10
5.	TABLETS		364	T <sub>1</sub> F <sub>24</sub> 124	SL1257	01/08	12/10
6.			365	T <sub>1</sub> F <sub>2</sub> 106	SL1267	01/08	12/10
7.			366	T <sub>3</sub> F <sub>7</sub> 164	SL1247	01/08	12/10
8.			371	T <sub>2</sub> F <sub>1</sub> 130	SL1255	01/08	12/10
9.			376	T <sub>2</sub> F <sub>14</sub> 145	SL1244	01/08	12/10
10.	AKURIT-4	Lupin Ltd	356	T <sub>3</sub> F <sub>6</sub> 162	AH80112	02/08	01/10
11.	TABLETS		357	T <sub>3</sub> F <sub>20</sub> 153	AH80099	02/08	01/10
12.			359	T <sub>3</sub> F <sub>18</sub> 150	AH80100	02/08	01/10
13.			360	T <sub>3</sub> F <sub>8</sub> 165	AH80108	02/08	01/10
14.			361	T <sub>3</sub> F <sub>15</sub> 147	AH80098	02/08	01/10
15.			370	T <sub>1</sub> F <sub>13</sub> 109	AH80093	02/08	01/10
16.			378	T <sub>3</sub> F <sub>23</sub> 174	AH80108	02/08	01/10
17.	FORECOX-TRAC	Macleods Pharmaceuticals	367	T <sub>3</sub> F <sub>9</sub> 140	RF701	02/07	01/10
18.	TABLETS		368	T <sub>3</sub> F <sub>30</sub> 152	RF707	02/07	01/10
19.			369	T <sub>3</sub> F <sub>14</sub> 169	RF715	02/07	01/10
20.			372	T <sub>3</sub> F <sub>26</sub> 176	RF706	02/07	01/10
21.			373	T <sub>2</sub> F <sub>5</sub> 134	RF721	02/07	01/10
22.			374	T <sub>3</sub> F <sub>9</sub> 166	RF711	02/07	01/10
23.			375	T <sub>1</sub> F <sub>16</sub> 115	RF720	02/07	01/10
24.			379	T <sub>1</sub> F <sub>14</sub> 111	RF718	02/07	01/10
25.	RIHAZ-E	Cosmos Ltd	377	T <sub>1</sub> F <sub>26</sub> 126	081266	01/09	12/10
	TABLETS						

## Annex 10

Table 1.3 Samples containing Rifampicin, Isoniazid and Ethambutol (n=21)

No.	Brand	Manufacturer	Sample No. (NDQA200906-)	Client Ref.	Batch No.	Mfg. Date	Exp. Date
1.	RIFAMPICIN/ ISONIAZID / ETHAMBUTOL TABLETS	Lupin Ltd.	286	T <sub>1</sub> F <sub>3</sub> 301	GC 98001	01/09	12/11
2.			287	T <sub>1</sub> F <sub>3</sub> 302	GC 98001	01/09	12/11
3.			288	T <sub>1</sub> F <sub>3</sub> 303	GC 98001	01/09	12/11
4.			289	T <sub>1</sub> F <sub>3</sub> 304	GC 98001	01/09	12/11
5.			290	T <sub>1</sub> F <sub>13</sub> 305	GC 98002	01/09	12/11
6.			291	T <sub>1</sub> F <sub>14</sub> 306	GC 98001	01/09	12/11
7.			292	T <sub>1</sub> F <sub>18</sub> 307	GC 98001	01/09	12/11
8.			293	T <sub>1</sub> F <sub>19</sub> 308	GC 98001	01/09	12/11
9.			294	T <sub>1</sub> F <sub>28</sub> 309	GC 98002	01/09	12/11
10.			295	T <sub>2</sub> F <sub>7</sub> 310	GC 98001	01/09	12/11
11.			296	T <sub>2</sub> F <sub>3</sub> 311	GC 98001	01/09	12/11
12.			297	T <sub>2</sub> F <sub>9</sub> 313	GC 98002	01/09	12/11
13.			298	T <sub>2</sub> F <sub>15</sub> 315	GC 98001	01/09	12/11
14.			299	T <sub>2</sub> F <sub>16</sub> 316	GC 98001	01/09	12/11
15.			300	T <sub>2</sub> F <sub>18</sub> 317	GC 98001	01/09	12/11
16.			301	T <sub>2</sub> F <sub>20</sub> 318	GC 98002	01/09	12/11
17.			302	T <sub>2</sub> F <sub>22</sub> 319	GC 98001	01/09	12/11
18.			303	T <sub>3</sub> F <sub>6</sub> 320	GC 98002	01/09	12/11
19.			304	T <sub>3</sub> F <sub>8</sub> 321	GC 98002	01/09	12/11
20.			305	T <sub>3</sub> F <sub>9</sub> 322	GC 98002	01/09	12/11
21.			306	T <sub>3</sub> F <sub>10</sub> 323	GC 98002	01/09	12/11

## Annex 11

Table 1.4 Samples containing Rifampicin, Isoniazid and Pyrazinamide (n=24)

No.	Brand	Manufacturer	Sample No. (NDQA200906-)	Client Ref.	Batch No.	Mfg. Date	Exp. Date
1.	RIHAZ FILM- COATED TABLETS	Cosmos Ltd	307	T <sub>3</sub> F <sub>10</sub> 228	071892	09/07	08/10
2.			308	T <sub>3</sub> F <sub>10</sub> 218	071893	09/07	08/10
3.			309	T <sub>3</sub> F <sub>13</sub> 205	071894	11/07	10/10
4.			310	T <sub>3</sub> F <sub>17</sub> 222	061530	05/06	04/09
5.			311	T <sub>3</sub> F <sub>20</sub> 230	071892	09/07	08/10
6.			312	T <sub>3</sub> F <sub>2</sub> 215	071893	09/07	08/10
7.			313	T <sub>3</sub> F <sub>2</sub> 214	071893	09/07	08/10
8.			314	T <sub>3</sub> F <sub>17</sub> 229	071892	09/07	08/10
9.			315	T <sub>3</sub> F <sub>14</sub> 207	071893	09/07	08/10
10.			316	T <sub>3</sub> F <sub>2</sub> 212	071893	09/07	08/10
11.			317	T <sub>3</sub> F <sub>11</sub> 219	071893	09/07	08/10
12.			318	T <sub>3</sub> F <sub>23</sub> 226	071893	09/07	08/10
13.			319	T <sub>3</sub> F <sub>2</sub> 217	071894	11/07	10/10
14.			320	T <sub>3</sub> F <sub>2</sub> 203	071893	09/07	08/10
15.			321	T <sub>3</sub> F <sub>2</sub> 202	071893	09/07	08/10
16.	RIMCURE PAED 3 FDC TABLETS	Sandoz (Pty) Ltd.	322	T <sub>3</sub> F <sub>20</sub> 704	509514	09/07	03/10
17.			323	T <sub>3</sub> F <sub>13</sub> 709	509514	09/07	03/10
18.			324	T <sub>3</sub> F <sub>3</sub> 702	509362	09/07	03/10
19.			325	T <sub>3</sub> F <sub>3</sub> 705	509514	09/07	03/10
20.			326	T <sub>3</sub> F <sub>2</sub> 701	509546	09/07	03/10
21.			327	T <sub>3</sub> F <sub>14</sub> 703	509362	09/07	03/10
22.			328	T <sub>3</sub> F <sub>21</sub> 708	509362	09/07	03/10
23.			329	T <sub>3</sub> F <sub>15</sub> 706	509652	04/08	10/10
24.			330	T <sub>3</sub> F <sub>20</sub> 707	509362	09/07	03/10

## Annex 12 Coding of Samples for Analysis Form

		Sum of Squares		Df	Mean Square	F	Sig.
<b>Humidity * Province 1</b>	Between Groups	(Combined)	3,247.273	7	463.896	5.279	.000
		Linearity	1,284.945	1	1284.945	14.622	.000
		Deviation from Linearity	1,962.328	6	327.055	3.722	.003
	Within Groups		5,975.526	68	87.875		
	<b>Total</b>		<b>9222.799</b>	<b>75</b>			
<b>Outdoor Temperature * Province 1</b>	Between Groups	<b>(Combined)</b>	747.759	7	106.823	12.264	.000
		Linearity	27.838	1	27.838	3.196	.078
		Deviation from Linearity	719.920	6	119.987	13.775	.000
	Within Groups		583.596	67	8.710		
	<b>Total</b>		<b>1,331.355</b>	<b>74</b>			
<b>Indoor temperature * Province1</b>	<b>(Combined) .. 38</b>	<b>(Combined)</b>	388.798	7	55.543	6.826	.000
		Linearity	5.700	1	5.700	.701	.405
		Deviation from Linearity	383.098	6	63.850	7.847	.000
	Within Groups		561.429	69	8.137		
	<b>Total</b>		<b>950.227</b>	<b>76</b>			

## Annex 13: Means of Humidity and Temperature per Province

Province		Humidity	Outdoor Temperature	Indoor temperature
Central	Mean	61.957	23.429	24.557
	N	7	7	7
	Std. Deviation	9.8114	3.4707	3.8768
	Range	23.5	10.0	10.4
Coast	Mean	62.886	28.543	28.357
	N	7	7	7
	Std. Deviation	6.7945	2.0272	2.4979
	Range	17.2	5.5	7.4
Eastern	Mean	57.073	25.855	26.982
	N	11	11	11
	Std. Deviation	8.7652	2.8257	2.4935
	Range	27.0	8.4	8.2
Nairobi	Mean	56.767	25.275	25.650
	N	12	12	12
	Std. Deviation	7.4374	1.6896	1.7328
	Range	25.9	5.9	6.7
North Eastern	Mean	33.763	38.200	34.250
	N	4	4	4
	Std. Deviation	18.9265	3.4293	2.7538
	Range	39.6	8.0	6.0
Nyanza	Mean	55.317	26.896	27.292
	N	12	12	13
	Std. Deviation	10.0719	3.5895	3.6105
	Range	33.0	10.7	12.5
Rift Valley	Mean	52.606	25.231	25.031
	N	16	16	16
	Std. Deviation	9.1821	3.5472	3.1016
	Range	29.5	14.2	12.9

Western	Mean	46.514	29.683	29.371
	N	7	6	7
	Std. Deviation	6.9406	1.3906	1.5882
	Range	19.1	3.9	4.7
Total	Mean	54.593	26.785	26.921
	N	76	75	77
	Std. Deviation	11.0892	4.2416	3.5360
	Range	71.8	24.9	18.0

## Annex 14: Questionnaire

### Observation Check List

1. Name of Province/district -----
2. Name of Health facility/KEMSA depot-----
3. Name of sample/data Collector \_\_\_\_\_
4. Drug particulars (Find attached the table to fill per facility visited)
5. Storage conditions: make observations (tick in the appropriate check box)
  - a) **Ventilated**
    - Cross ventilation
    - Ventilation on one side
    - No ventilation
  - b) **Shelving**
    - Yes
    - No
    - Other option.....
  - c) **Pallets used (at least 10cm) off the floor**
    - Yes
    - No
    - Other option.....

**d) Storage conditions in compliance with the labeling requirements**

- i. Temperature /humidity conditions:  
Indoor Temperature.....  
Out Door Temperature.....  
Humidity .....% RH
- ii. Dry Place: Yes  No
- iii. Protect from Light: Yes  No

Comment on general storage conditions.....  
.....  
.....  
.....

**e) Are there anti-TB drugs stored on the floor?**

- Yes
- No
- If Yes, please explain.....  
.....

**f) Are there expired anti-TB drugs; with broken seals or damaged packs?**

- Yes
- No
- If Yes, list the drugs and reasons .....  
.....

**g) Are there anti-TB drugs with damaged packs?**

- Yes
- No
- If Yes, list the drugs and reasons.....  
.....

**h) Mode of transportation from district store/KEMSA to health facility:**

- Air
- Vehicle
- Motor-bike
- Bicycle

6.

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

Thank the interviewee for his/her participation

## Annex 15: Post Marketing Surveillance Dissemination Meeting Presentation



# POST MARKET SURVEILLANCE OF 1<sup>ST</sup> LINE ANTI- TUBERCULOSIS MEDICINES IN KENYA

DR RICHARD MUTHOKA,  
DIVISION OF LEPROSY, TB & LUNG DISEASE  
APRIL 2012

*To render Kenya and its communities free of Leprosy, TB and Lung Disease*



## Presentation outline

- Background
- Objectives
- Survey Design and Methodology
- Data collection and analysis
- Key findings
- Corrective and Regulatory actions
- Recommendations

*To render Kenya and its communities free of Leprosy, TB and Lung Disease*



## DLTLD



- Division of Leprosy, TB & Lung Disease was established in 1981. Previously called NLTP
- Under the Department of Disease Prevention & Control in the Ministry of Public Health & Sanitation
- Vision: To render Kenya and its communities free of leprosy, TB and Lung Disease
- Coverage: over 2,500 TB treatment and over 1,000 diagnostic facilities

To render Kenya and its communities free of Leprosy, TB and Lung Disease



## Background

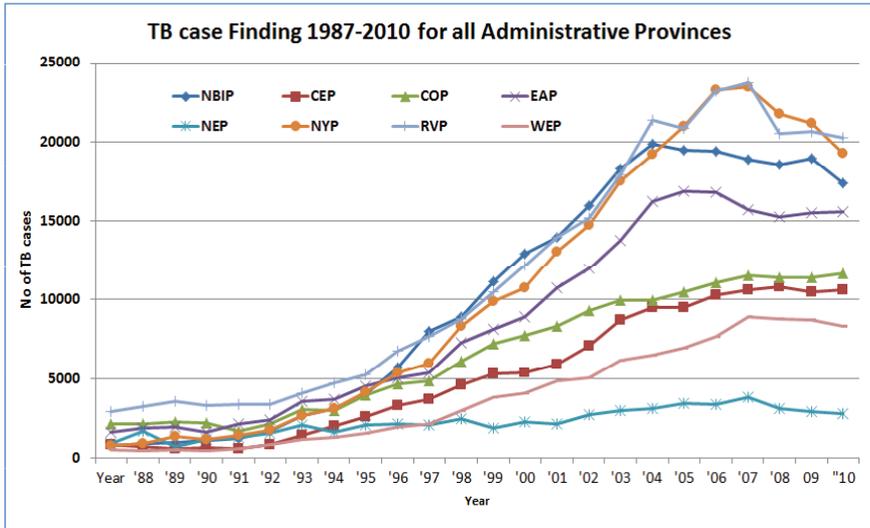


- TB is a public health problem in Kenya
- Kenya is ranked 13<sup>th</sup> among the 22 TB high burden countries.
- Estimates are 338 cases per 100,00 population (DLTLD annual report, 2009)
- A slow decline to 106,083 in the year 2010 has since been noted
- HIV /Aids is the main driver - 45% of TB patients found to be co-infected with HIV
- Multi Drug Resistant TB (MDR-TB) prevalence is low (<1%)but increasing

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## TB Case Finding 1987-2010



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## Quality TB care



- Kenya TB program achieved the WHO set TB targets i.e. detecting 70% of cases and treating successfully smear positives by 85%
- DOTS treatment in Kenya
  - First line TB treatment regimen – 2RHZE/4RH
  - Retreatment TB regimen -2SRHZE/1RHZE/5RHE
  - Treatment Regimen for children – 2RHZ/4RH

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## Objectives of the study



- To establish the *availability and range* of TB drug formulations in Kenya.
- To determine the *quality* of anti-TB drugs at public, mission and private sector health facilities in Kenya.
- To determine the *registration status* of the first line anti-TB medicines in Kenya.

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## Methodology



- There were three levels of sampling:
  - Sampling of facilities
  - Sampling of medicines
  - Sampling of medicines for laboratory analysis
- Stratified sampling of facilities was applied to correspond to the 12 TB control provinces as per caseload of TB cases reported in 2007
- 3 categories of facilities were considered i.e. public, private and mission based on the proportion of the facilities in the strata

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## Cont....

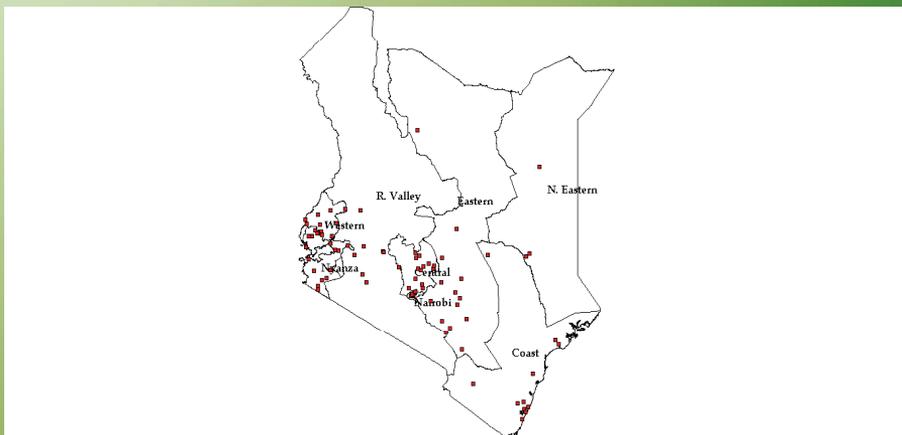


- 77 sites were sampled. These comprised of 67 treatment centers / facilities and 10 regional stores
- 400 batches were sampled randomly from the sites out of which a representative sample of 120 batches was selected for testing at the NQCL

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## Map showing sampled sites



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## Distribution of Sampled Sites

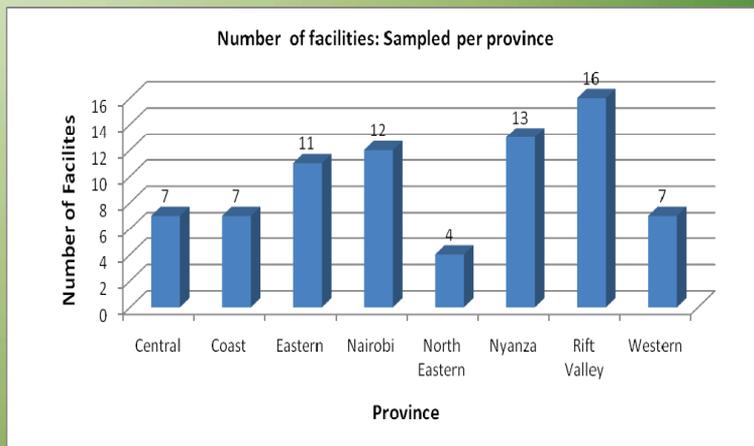


REGION	Total No. of Sampling site	Regiona l Stores	Category 1 - Public Health facilities	Category 2 - Mission Health Facilities	Category 3 - Private health facilities
COAST	8	1	5	1	1
CENTRAL	7	1	4	1	1
NORTH-EASTERN	4	1	1	1	1
RIFT VALLEY NORTH	7	1	4	1	1
RIFT VALLEY SOUTH	8	1	5	1	1
WESTERN	6	1	3	1	1
EASTERN	11	2	6	2	1
NYANZA	14	1	10	2	1
NAIROBI	12	1	4	4	3
<b>TOTALS</b>	<b>77</b>	<b>10</b>	<b>42</b>	<b>14</b>	<b>11</b>

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## Number of Facilities Sampled per Province (n=77)



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## Survey instruments



- A questionnaire was administered to capture qualitative data on all first line Anti-TB drugs
- A sample collection form was used to capture details of all the product samples from the facilities
- Thermo-hygrometers
- PPB Drug Registration Database

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## Laboratory analysis



- Analysis of samples was by methods obtained from official compendia i.e. British Pharmacopoeia (B.P.) 2007 Volume IV & United States Pharmacopeia (USP 31 NF 26) Convention (2008).
- Tests done included: uniformity of weight, friability (for dispersible tablets), dissolution, identification & assay
- A certificate of analysis was issued for each sample analyzed
- A report of actual method used to test each sample and results obtained was produced.

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## TB drug combinations analyzed



### 2 FDCs

- Rifampicin / Isoniazid (RH)
- Ethambutol / Isoniazid (EH)

### 3 FDCs

- Rifampicin/ Isoniazid/ Ethambutol (RHE)
- Rifampicin/ Isoniazid/ Pyrazinamide (RHZ)

### 4 FDCs

- Rifampicin/Isoniazid/Pyrazinamide/Ethambutol (RHZE)

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## Results & Discussion



- All 120 samples complied with the standard specifications for **uniformity of weight test**
- All the batches for paediatric RH tablets complied with BP specifications for **friability** and **Disintegration** tests
- **31% of the 2 FDC (RH combination)** failed to comply with the standard specifications for content of active ingredient (assay) i.e. had more content for either rifampicin and/or Isoniazid

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## Cont...



- **8% of the 2 FDC (EH combination)** failed to comply with the standard specifications (i.e. more content)
- All batches of **3 FDC (RHE Combination)** complied with the specifications for all the tests performed
- All batches of **3 FDC (RHZ Combination)** complied with the specifications for all the tests performed
- All batches of **4 FDC (RHZE Combination)** complied with the specifications for all the tests performed

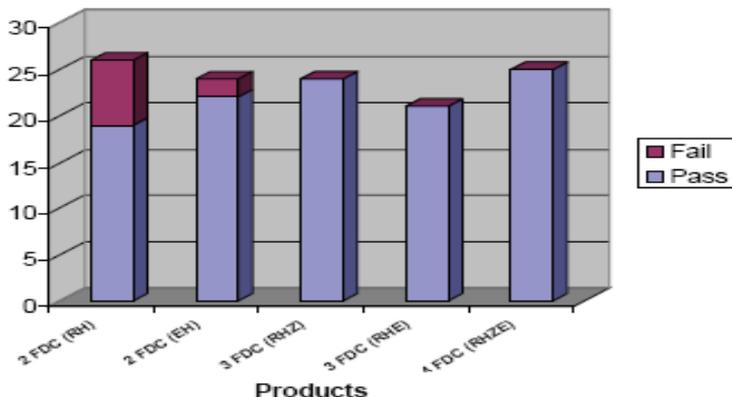
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## Summary



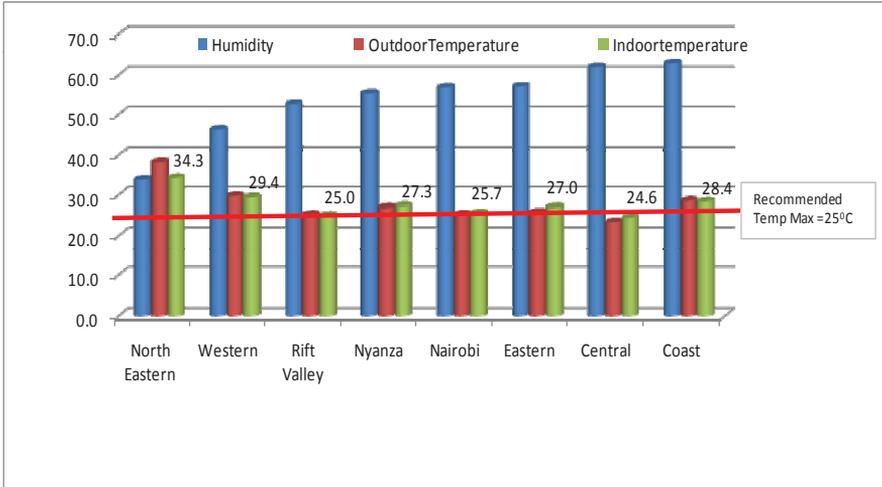
### Analysis Results



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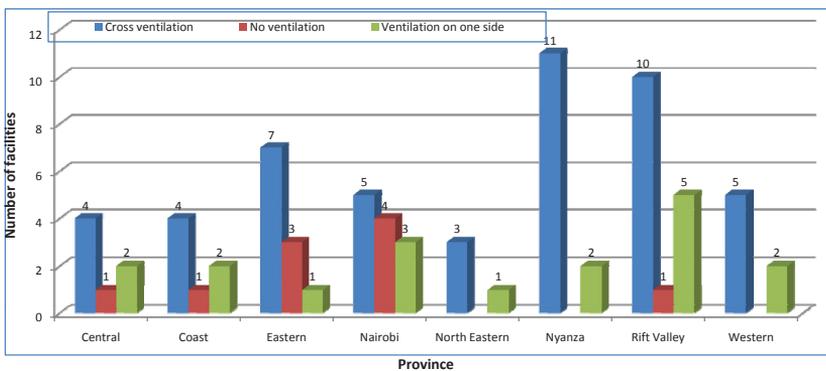
## Storage Conditions: Mean Temperature & Humidity by province



## Ventilation

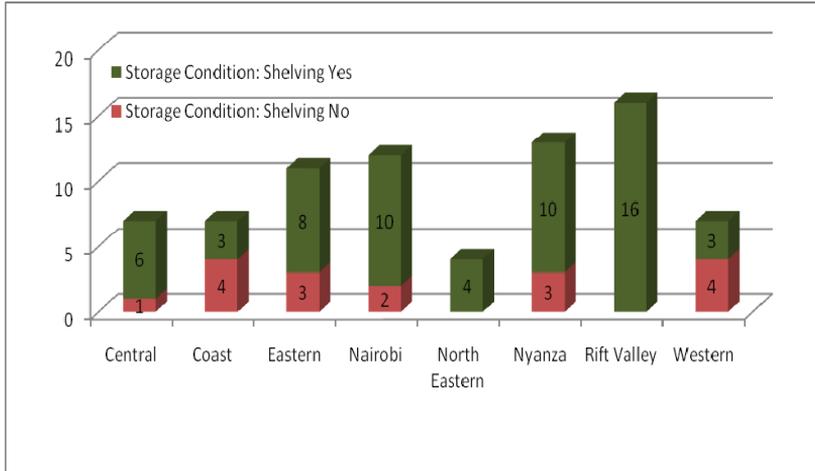


Storage condition: Ventilation per province





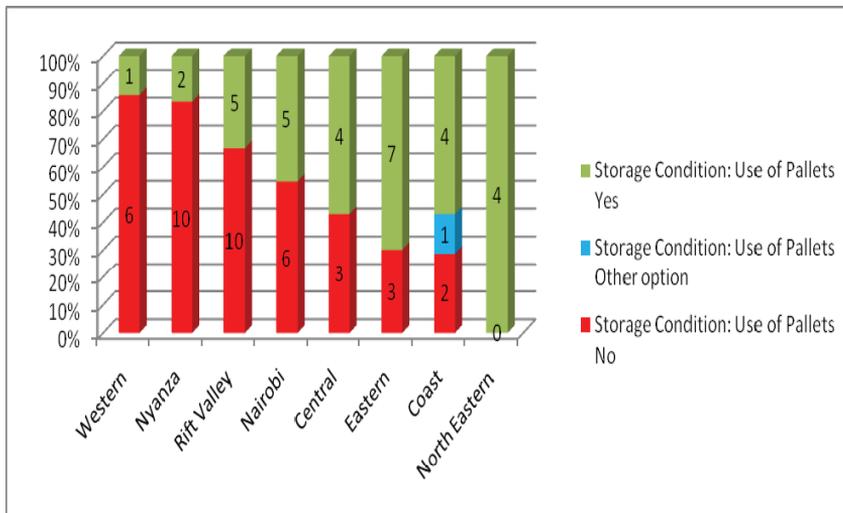
## Summary of shelving



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## Use of pallets





## Analysis results for 2 component FDC (Rifampicin/Isoniazid) tablets



S/ No	Brand name	Formulation	No. Of samples submitte d	Results		Test failed	Registration status
				Samples failed	Samples passed		
1.	RIFINAH – 300 TABLETS	RH (300/150mg)	2	2 (100%)	0	Assay	Registered
2.	RIHIDE-P PAEDIATRIC DISPERSIBLE TABLETS	RH (60/30mg)	11	6 (55%)	5	Assay	Registered
3.	RIHIDE FILM COATED TABLETS	RH (150/75mg)	2	0	2	-	Registered
4.	AKURIT TABLETS	RH (150/75 mg)	3	0	3	-	Registered
5.	RIFAMPICIN / ISONIAZID TABLETS	RH (150/75mg)	8	0	8	-	Registered



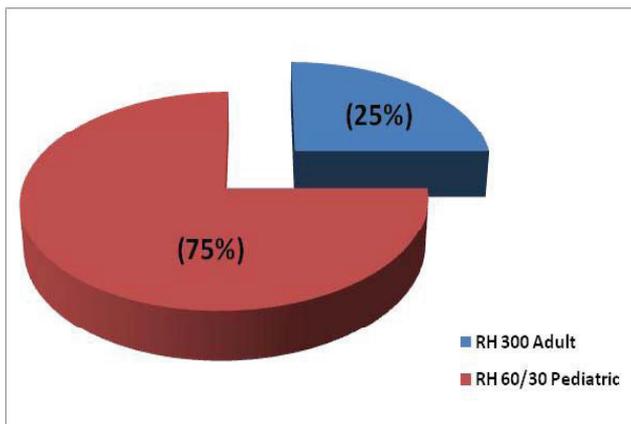
## Analysis results for 2 component FDC (Ethambutol/Isoniazid) tablets



S/NO	BRAND NAME	FORMULATION	NO. OF SAMPLES SUBMITTED	RESULTS		TEST FAILED	REGISTR ATION STATUS
				SAMPLES FAILED	SAMPLES PASSED		
1.	ECONEX-400 TABLETS	EH (400/150 mg)	9	0	9	-	Registered
2.	ETHAMBUTOL / ISONIAZID TABLETS	EH (400/150mg)	15	2 (13%)	13	Dissoluti on	*Not Registered at the time of survey



## Distribution of RH samples that failed assay tests (n=8)



## Registration status of first line anti-TB drugs in Kenya



- 13 out of 14 different brands of anti-TB medicines found in the market had current registration status.
- The unregistered product was EH 400/150mg



## Summary of Findings

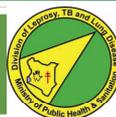


- The recommended first line medicines and formulations for the treatment of TB are available in Kenyan healthcare facilities.
- Temperature control in medication storage areas was inadequate in some facilities
- The relative humidity levels in medication storage areas countrywide are within acceptable limits and thus humidity is not expected to contribute to affecting the quality of anti-TB medicines in Kenya.

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## Cont...



- Poor ventilation is common in many medication storage areas in Kenya.
- Use of pallets and shelving for medicines is not up to desired standards in Kenya.
- The failure rate in laboratory analysis for anti-TB medicines in Kenya is 8.3% and mainly related to paediatric formulations (6/26).
- All anti-TB medicines sampled during the survey have current registration with PPB

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## Recommendations to PPB



- Regularly monitor the quality of pharmaceuticals in the market and support all PMS activities
- Develop and disseminate SOPs for corrective and regulatory actions following a PMS (to key stakeholders)
- To develop guidelines on effective execution of PMS exercises.
- PMS results should be used to inform policies regarding drug regulation in Kenya.

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## Recommendations to NQCL



- Review the cost of analyses for post-marketing surveillance samples
- Reduce the turn-around time to ensure that the results are relevant at the time of dissemination
- Invest in state of the art equipment that would result in greater efficiency
- Increase capacity to cope with service demand

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## Recommendations to DLTL



- PMS dissemination should be done immediately after survey.
- PMS should be a regular exercise (every 2 years)
- Establishing sentinel sites to monitor quality, safety and efficacy of anti-TB medicines
- Second-line anti-TB drugs should be incorporated in subsequent PMS activities.
- To increase budgetary allocation for purchase of PMS samples from the private sector.

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## Recommendations to DLTL



- Should involve pharmaceutical personnel in the management of commodities at the health facilities.
- Should improve on support supervision to facilities from the national level.
- Advocate for a multi-country survey quality of anti-TB medicines in the region.

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## Recommendations DoP



- To provide resources for rehabilitation and construction of medical stores within health facilities.
- To advocate for management of TB medicines by pharmaceutical personnel at all levels of care
- To advocate for regular joint PMS among programmes to guide policy.
- To integrate the PMS activities within the two ministries to reduce the cost.

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## Recommendations to Partners



- To continually provide technical and financial support for post marketing surveillance activities.
- To provide support for operational research in quality control and assurance of medicines.
- Commitment to provision of drugs with appropriate quality

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## Recommendations to Consumers



- Should communicate any quality issue regarding medicines to the relevant authorities

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## Corrective and Regulatory Actions: Progress



- Countrywide recall of failed products
- SOP on corrective and regulatory actions to be taken following PMS- currently under development
- Mandate of pharmaceutical personnel expanded to include management of anti-TB medicines
- PMS included in current DLTLD strategic plan

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## Acknowledgements

- Head DLTD and staff members
- CDC
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