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TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

TMDA

Tanzania Medicines & Medical Devices Authority

POST MARKETING SURVEILLANCE (PMS) REPORT FOR SELECTED HUMAN MEDICINES (ANTI-MALARIA, ANTI TUBERCULOSIS AND ANTIRETROVIRAL) CIRCULATING IN TANZANIA

2020

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Abbreviations

ADDOs	Accredited drugs dispensing outlets
ALU	Artemether/Lumefantrine
EDQM	European Directorate for Quality of Medicines
ICRS	International Chemical Reference Substance
MAH	Marketing Authorization Holders
MSD	Medical store department
PMS	The Post Marketing Surveillance
PIR	Product information review
POEs	Port of entries
TLC	Thin Layer Chromatography test

Acknowledgement

The Post Marketing Surveillance (PMS) report of year 2020 presents the results of the quality of selected three (3) categories of human medicines (anti-malarial, anti-retroviral and anti-TB) circulating in the market. Preparation of this report would not have been possible without the commitment of Tanzania Medicines and Medical Devices Authority (TMDA) staffs and various stakeholders at all levels of medicine distribution chain who worked closely to implement the PMS program.

On behalf of TMDA Management, I would like to thank those who brought in their contributions during the preparation of this document. Special thanks are extended to the following: Kissa Mwamwitwa, Dr Bety Maganda, Sunday Kisoma, Nellin Shiletiwa, Dr Goodluck Gotora, Dorine Nyaki and Mosses Nandonde who worked tirelessly in the development of this report.

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Ultimately, I appreciate the contribution of Global fund for their financial support as well as the TMDA management for their support and leadership which facilitated the successful implementation of the activities

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FOREWORD

Monitoring the quality, safety and efficacy of medicines circulating in the market is fundamental in protecting public health. Routine surveillance of medicines after registration (Post Marketing Surveillance - PMS) is one of the key responsibilities of a functional national medicine's regulatory authority. PMS helps medicines users, especially patients, who are key stakeholders in the pharmaceutical industry, to build confidence in the medicines they use that they will meet the expected standards for quality, safety and ultimately treat the intended diseases.

PMS involves sampling of medicines from the market using a pre-arranged sampling plan, physical collection of samples, product information review and quality control testing in the laboratory. It helps timely detect and removal of falsified and substandard medicines from the market thus protecting the public against the possible hazards associated with their use.

A total of 919 samples were collected. About 36% (332/919) of the collected samples were from different distribution outlets while 64% (587/919) were collected from port of entries (POEs) and domestic manufacturers. After collection, product information review (PIR) was performed and later on laboratory screening and testing on selected critical parameters was carried out. The whole exercise was conducted by the qualified personnel who were well versed with the PMS protocol.

All samples collected from distribution outlets were subjected to Product Information Review (PIR) and the results revealed that 179 samples out of 332 (54%) did not meet the requirements. All the samples which were subjected to confirmatory laboratory testing complied with the test requirements.

In this report we present methodology and detailed results for PMS of selected categories of medicines (anti-malarial, anti-retroviral and anti-TB).

Overall, the PMS exercise was excellently planned and the execution was well coordinated. Implementation was carried out by various dedicated stakeholders within and outside TMDA. Key lessons learned from the PMS exercise will be used to improve the quality, safety and ultimately efficacy of medicines circulating in Tanzanian market. Moreover, it will assist TMDA to improve the subsequent PMS programs and ultimately protect public health.

I would like to extol all esteemed stakeholders involved including our collaborators and partners for making the 2020/2021 PMS program a success.

Adam M Fimbo
ACTING DIRECTOR GENERAL
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EXECUTIVE SUMMARY

Tanzania Medicines and Medical Devices Authority (TMDA) after successful completion of previous PMS programs, is currently implementing another one (1) years PMS program (2020) of Anti-Malaria, Anti Tuberculosis and Antiretroviral Medicines under support from global fund.

During the financial year of implementation (2020/2021), TMDA assessed the quality of selected three (3) categories of human medicines namely the anti-malarial(Artesunate injection, Quinine tablets and syrup, Artemether/Lumefantrine (ALU) tablets for adults and dispersible for children), anti-retroviral (Dolutegravir tablets, Tenofovir/Lamivudine/Dolutegravir, Abacavir sulfate/Lamivudine) and anti-TB(Isoniazid, Ethambutol, Rifampicin/Isoniazid, Rifampicin/Isoniazid/Pyrazinamide, Rifampicin/Isoniazid/Pyrazinamide/ Ethambutol and Levofloxacin tablets).

Medicines were systematically sampled from ten (10) regions namely Dar es Salaam, Tanga, Coastal Region, Mwanza, Kagera, Mbeya, Kilimanjaro, Morogoro, Dodoma and Mtwara. Samples were collected at port of entries (POEs), local manufacturers, public and private hospitals, dispensaries, health centres and pharmaceutical premises as per developed sampling plan.

A total of 919 samples were collected in which 36.0% (332/919) were collected from different distribution outlets and 64% (587/919) were collected from POEs and domestic manufacturers. Out of 919 collected samples, 47.99% (441/919) were antimalarial, 16.54% (152/919) anti-TB and 35.47% (326/919) were ARVs.

The collected samples from medicines distribution outlets were subjected to Product Information Review (PIR). Results of PIR revealed that 179 samples out of 332 (54%) did not meet the requirements. The remarkable deficiencies observed during PIR included improper storage condition, lack of the name and physical address of the product's manufacturer, different shelf lives from the approved ones, lack physical description of the product on the package insert, in appropriate language used in labelling and package insert, unregistered medicines, inappropriate primary package material, incomplete leaflet, artwork and unit package deviations.

All samples from medicines distribution outlets passed the laboratory screening tests consisting of visual inspection, disintegration test and TLC identification. The confirmatory test was conducted to 10% of samples from medicine distribution outlets. All the selected samples complied with the confirmatory test.

Generally, laboratory test results of the selected medicines are indicators of the

existence of quality medicines in Tanzanian market which could be the outcome of the existing enforcement mechanism in the country.

1 INTRODUCTION

Post Marketing Surveillance (PMS) entails gathering information on the product(s) after its approval. It is a methodology designed to monitor the quality of registered medicines circulating in the market. The PMS technique involves sampling of medicines from the market using a pre-arranged sampling plan, physical collection of samples, product information review and laboratory quality control testing.

The core function of Tanzania Medicines and Medical Devices Authority (TMDA) is to ensure that, medicines circulating in the Tanzanian market are of good quality, safe and efficacious. The assessment of product quality and compliance of Good Manufacturing Practice (GMP) is verified by TMDA through evaluation of technical production documents and inspection of the manufacturing facilities before issuing marketing authorization. Additional quality assurance is achieved by different schemes of sampling and testing of registered medicines either sampled from the market or at different entry points to the country. Through PMS, a number of substandard and falsified medicines have been detected in the market.

In previous years, TMDA through PMS programme has been able to monitor the quality of imported anti-retroviral (ARVs), anti-tuberculosis (anti-TB) and anti-malarial medicines. These medicines were sampled from different pharmaceutical outlets. Also, locally produced medicines including antimalarials which are circulating in the market were surveyed. The three (3) categories of medicines are for diseases of public health importance which are consumed by majority of Tanzanians. Hence, continued monitoring the quality of these medicines is essential in achieving the desired goal of managing these threatening diseases and mitigating morbidity and mortality.

In the current PMS similar group of medicines were surveyed. The samples were collected from port of entries, local manufacturers and public and private hospitals, dispensaries, health centres and community pharmacy premises as per pre-arranged sampling plan. The samples were analysed at WHO prequalified TMDA laboratory. Product information review, physical/visual examination, screening and confirmatory testing were conducted to verify compliance with quality standards.

Therefore, TMDA is reporting the findings of PMS and the regulatory actions taken to involve the three (3) categories of registered medicines namely; anti-malarial, anti-retroviral and anti-TB. The PMS was conducted for the period of July 2020 to

December, 2020 with the financial support from development partner, the Global Fund.

2 OBJECTIVES

2.1 Broad objective

The broad objective of the survey was to protect and promote public health by monitoring the quality of selected anti-malarial, antiretroviral and anti-tuberculosis medicines in Tanzanian market.

2.2 Specific objectives

The specific objectives of the survey of anti-malarial, anti-retroviral and anti-tuberculosis medicines are:

a) To collect samples of selected medicines from the market;
b) To conduct product information review of collected samples;
c) To conduct quality testing of collected samples and take relevant regulatory action(s) of failed sample; and
d) To assure the public on the quality status of medicines.

3 METHODOLOGY

3.1 Selection of Medicines

Criteria for selection of the surveyed medicines were based on the following:

(i) Priority medicines for specific population groups (i.e people with TB, HIV)
(ii) New molecule for treatment of HIV infection
(iii) Experience gained in previous PMS survey on Anti-Malaria, Anti-Tuberculosis and Anti-retroviral medicines,
(iv) Reports on substandard medicines received by TMDA from various sources;

Medicines surveyed in this programme include;

(i) Antimalarial: Artesunate injection, Quinine tablets and syrup, Artemether/Lumefantrine (ALU) tablets for adults and dispersible for children

(ii) Antiretrovirals: Dolutegravir tablets, Tenofovir/Lamivudine/Dolutegravir, Abacavir sulfate/Lamivudine and

(iii) Anti-Tuberculosis: Isoniazid, Ethambutol, Rifampicin/Isoniazid, Rifampicin/Isoniazid/Pyrazinamide, Rifampicin/Isoniazid/Pyrazinamide/ Ethambutol and Levofloxacin tablets.

3.2 Selection of regions

Selection of sampling regions were based on the regions with increased number of patients with TB, HIV and Malarial and those regions bordering the neighbouring countries, regions with very hot & humid climate and regions where the selected medicines were likely to be available and highly consumed.

3.3 Sampling sites

During the survey, convenience sampling method was used for selection of sampling sites. Sampling sites were selected depending on the medicines to be sampled. The collection of sample at various levels of distribution channel was based on the developed sampling plans (Annex I). The pharmaceutical site selection per region covered the entire medicines distribution chain including referral/ regional hospitals, district hospitals, faith-based hospitals, private hospitals, wholesale pharmacies, retail pharmacies and ADDOs.

3.4 Sampling of medicines

Sampling encompasses the operations designed to collect samples of different dosage forms in representative manner for testing of agreed quality parameters against acceptable standards. Sampling plan was prepared and approved before sample collection considering the logistics and availability of resources. The approved sampling plan was made available to all zones and inspectors who were involved in sample collection.

3.4.1 Sample collection

Collections of samples at various levels of distributions channels were based on the developed sampling plans. Sampling plans were prepared and contained detailed information on sampling sites at regional and district level, product name, number of brands to be collected, dosage forms, strength and pack size Sampling plans are attached as Annex I.

Samples were collected according to standard Operating procedure by trained medicines inspectors from TMDA and Local Government Authorities. Samples were collected in their original containers and/or packages and details of the collected samples were recorded in the sample collection form attached as Annex II. Each collected sample was coded for its traceability. Coded samples with their respective samples collection forms were kept in the labeled sampling envelope/plastic bags and sealed. The units collected depended on the type of formulation i.e.

i. Tablets & capsules – 100 tablets per brand per batch
ii. Injections - 40 vials per brand per batch
iii. Suspension & syrups - 10 bottles per brand per batch

3.4.2 Handling of collected Sample and Shipment

The collected samples were stored and transported according to manufacture recommended storage instructions for each respective medicine. The samples were transported to relevant zone offices where data entry into RIMS software was carried out. Physical samples were transported by courier to Dar es Salaam sub-office and corresponding information was submitted to responsible Manager in RIMS software.

3.4.3 Quality control analysis

The quality of the samples was evaluated using three stage testing approach which included Product information review, screening and full quality control analysis.

3.4.4 Product Information Review

Prior to further laboratory analysis sample collected from medicines distribution outlets were subjected to product information review (PIR). Each collected sample was checked for information contained on the primary and secondary packages. Availability and information on package information leaflet against TMDA labeling guidelines and approved product information captured in RIMS. Parameters checked during PIR included but not limited to product brand and generic name, dosage form and strength, name and address of manufacturer, batch number, physical appearance, manufacturing and expiry date, language, indication and storage instruction.

3.4.5 Screening

Screening of samples was carried out at the TMDA WHO prequalified medicines testing laboratory. Samples were subjected to visual inspection, disintegration test (for solid dosage forms) and Thin Layer Chromatography test (TLC) as shown in table 1 below. Methods that were used include pharmacopial, manufacturer and GPHF minilab manual.

Visual inspections were conducted by comparing the appearance of the dosage form against that of the registered product. Tablets were checked for shape, size, brittleness, physical damage (capping and chipping), mottling, odour, altered surface (coating and swelling) colour, embossing and debossing. Injectable solutions were checked for clarity, particulates, turbidity and colour.

Disintegration testing was performed to assess the possibility of instant release of solid dosage forms (e.g. tablets, capsules) as described in pharmacopoeia general chapter. Disintegration times were recorded and compared against reference monographs/product specification.

Thin layer chromatography (TLC) was used for product identification and for semi-quantitative determination of active ingredients and possibly presence of degradants in the dosage form. The method employs the principle of comparing chromatogram obtained between test and reference sample. The standards used were primary reference standard obtained from European Directorate for Quality of Medicines (EDQM), International Chemical Reference Substance (ICRS) and Manufacturers. Interpretation of results was done by observing principal spots on the chromatogram and calculation of retardation value (R_f) values.
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Table 1: Screening test performed in each medicine

	NAME OF PRODUCT	SCREENING TEST
ANTI MALARIALS		
	Artesunate injection	Thin Layer Chromatography test (TLC),
	Quinine tablets	Thin Layer Chromatography test (TLC) and disintegration
	Quinine syrup	Thin Layer Chromatography test (TLC)
	Artemether/Lumefantrine (ALU) Tablets	Thin Layer Chromatography test (TLC) and disintegration
ANTIRETROVIRALS		
	Dolutegravir tablets	Thin Layer Chromatography test (TLC) and disintegration
	Tenofovir/Lamivudine/Dolutegravir tablets	Thin Layer Chromatography test (TLC) and disintegration
	Abacavir sulfate/Lamivudine tablets	Thin Layer Chromatography test (TLC) and disintegration
ANTI-TUBERCULOSIS		
	Isoniazid tablets	Thin Layer Chromatography test (TLC) and

		disintegration
	Ethambutol tablets	Thin Layer Chromatography test (TLC) and disintegration
	Rifampicin/Isoniazid tablets	Thin Layer Chromatography test (TLC) and disintegration
	Rifampicin/Isoniazid/Pyrazinamide tablets	Thin Layer Chromatography test (TLC) and disintegration
	Rifampicin/Isoniazid/Pyrazinamide/Ethambutol tablets	Thin Layer Chromatography test (TLC) and disintegration
	Levofloxacin tablets	Thin Layer Chromatography test (TLC) and disintegration

3.4.6 Confirmatory testing

All samples that failed/or with doubtful and 10% of that passed screening tests (visual inspection, disintegration and identification) were subjected to confirmatory testing. Samples were analyzed according to pharmacopeial monographs, in house methods and manufacturer's own methods as indicated in Table 2 below.The remaining units of tested samples will be retained for at least one year after completion of the analysis and stored according to manufacturer's recommended storage conditions.

Provide table no and legend.

Table 2: Parameter investigated during confimatory testing of selected samples

	NAME OF PRODUCT	**MONOGRAPH**	**TESTED PARAMETERS**	**ACCEPTANCE CRITERIA**
ANTI MALARIALS				

	NAME OF PRODUCT	MONOGRAPH	TESTED PARAMETERS	ACCEPTANCE CRITERIA
	Artesunate injection	International Pharmacopeia 9th Edition (1)	Assay Sterility	90.0 – 110.0% Should be sterile
	Quinine tablets	In House/BP (2)	Assay	95.0 – 105.0%
	Quinine syrup	In House/BP (2)	Assay	95.0 – 105.0%
	Artemether/Lumefantrine (ALU) Tablets	In House/International Pharmacopoeia 9th Edition (1)	Assay Related substances	90.0 – 110.0% TLC Spot obtained from the sample solution should be similar in shape, size, colour, intensity and distance travelled to that obtained from the standard.
ANTIRETROVIRALS				
	Dolutegravir tablets (Aurobindo &Lauras)	Manufacturer (3, 4)	Assay Dissolution	95.0 – 105.0% NLT 80% (Q) labeled amount of Dolutegravir within 30 minutes.
	Tenofovir/Lamivudine/Dolutegravir tablets (Mylan)	Manufacturer (5)	Assay Dissolution	95.0 – 105.0% NLT 75% (Q) of tenofovir,

	NAME OF PRODUCT	MONOGRAPH	TESTED PARAMETERS	ACCEPTANCE CRITERIA
				lamivudine and dolutegravir within 45 minutes
	Tenofovir/Lamivudine/Dolutegravir tablets(Aurobindo)	Manufacturer (3)	Assay Dissolution	95.0 – 105.0% NLT 80% (Q) of Tenofovir/Lamivudine/Dolutegravir within 30 minutes
	Tenofovir/Lamivudine/Dolutegravir tablets (Lauras)	Manufacturer (4)	Assay Dissolution	95.0 – 105.0% NLT 75% (Q) of Tenofovir/Lamivudine/Dolutegravir within 45 minutes
	Abacavir sulfate/Lamivudine tablets (Hetero)	Manufacturer (6)/USP 43 NF 38 (7)	Assay Dissolution	90.0 – 110.0% NLT 75% (Q) within 30 minutes for abacavir/lamivudine.
	Abacavir sulfate/Lamivudine tablets (Mylan)	Manufacturer (5)/USP 43 NF 38 (7)	Assay Dissolution	90.0 – 110.0% NLT 75% (Q) of Abacavir Sulfate/Lamivudine within 45 minutes

	NAME OF PRODUCT	MONOGRAPH	TESTED PARAMETERS	ACCEPTANCE CRITERIA
ANTI-TUBERCULOSIS				
	Isoniazid tablets	International Pharmacopeia 9th Edition (1)	Assay	90.0 – 110.0%
			Related Substance (TLC)	Spot obtained from the sample solution should be similar in shape, size, color, intensity and distance traveled to that obtained from the standard solution.
	Ethambutol tablets	International Pharmacopeia 9th Edition (1)	Assay	90.0 – 110.0%
	Rifampicin/Isoniazid tablets	International Pharmacopeia 9th Edition (1)	Assay	90.0 – 110.0%
			Related Substance	Hydrazone Impurity NMT 5.0%
				Rifampicin Quinone NMT 4.0%
				Any Other Peak NMT 1.5%
				The Sum of All Peak NMT

	NAME OF PRODUCT	MONOGRAPH	TESTED PARAMETERS	ACCEPTANCE CRITERIA
				10.0%
	Rifampicin/Isoniazid /Pyrazinamide tablets	International Pharmacopeia 9th Edition (1)	Assay	90.0 – 110.0%
			Related Substance	Hydrazone Impurity NMT 5.0%
				Rifampicin Quinone NMT 4.0%
				Any Other Peak NMT 1.5%
				The Sum of All Peak NMT 10.0%
	Rifampicin/Isoniazid /Pyrazinamide/ Ethambutol tablets	International Pharmacopeia 9th Edition (1)	Assay	90.0 – 110.0%
			Related Substance	Hydrazone Impurity NMT 5.0%
				Rifampicin Quinone NMT 4.0%
				Any Other Peak NMT 1.5%
				The Sum of All Peak NMT 10.0%
	Levofloxacin tablets	USP 43 NF 38 (7)	Assay	90.0 – 110.0%

4 RESULTS

4.1 Samples collected

During the period of July to December, 2020 a total number of 919 samples were collected for quality verification in which 36% (332/919) were collected from different distribution outlets and 64% (587/919) were sampled from POEs and domestic manufacturers under routine quality assurance programme. Data are summarized in figure 1 below.

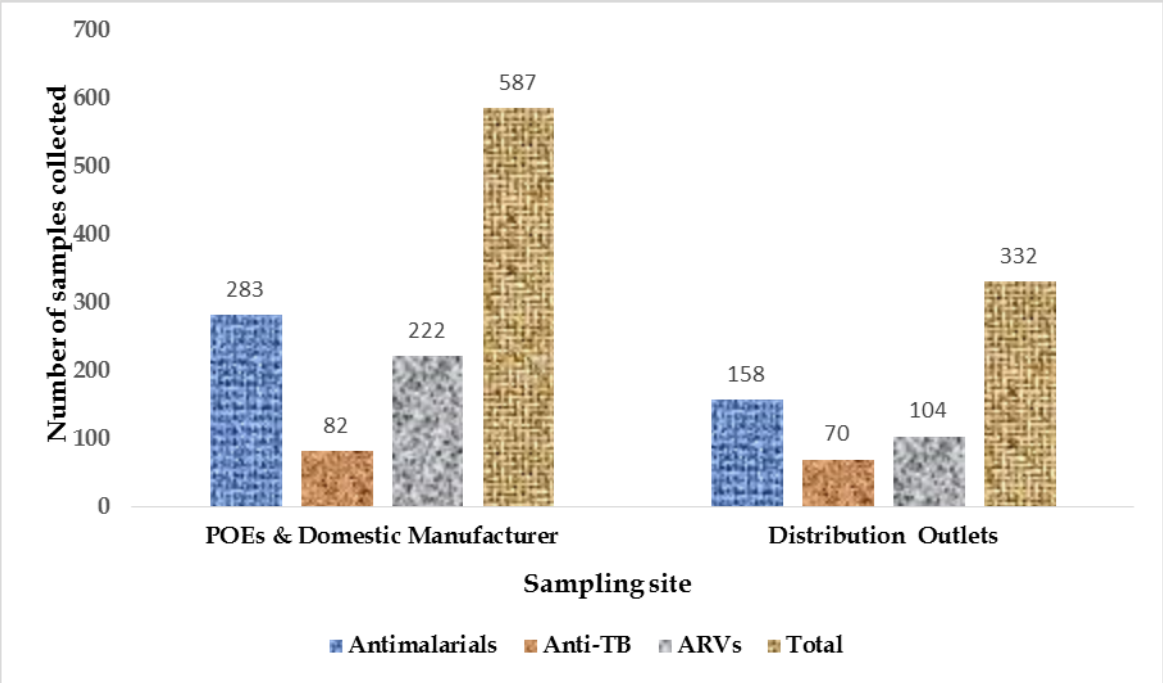

Figure 1: Type and number of samples collected from the POEs, domestic manufacturers and distribution outlets Samples collected from distribution outlets

A total of 332 samples of antimalarial 47.6% (158/332), anti-TB 21.1% (70/332) and ARVs 31.3% (104/332) were collected from ten (10) different regions and two (2) districts per region. As per sampling plan, the expected samples to be collected were 470, however, only 70.6% (332/470) samples were collected as shown in Figure 2.

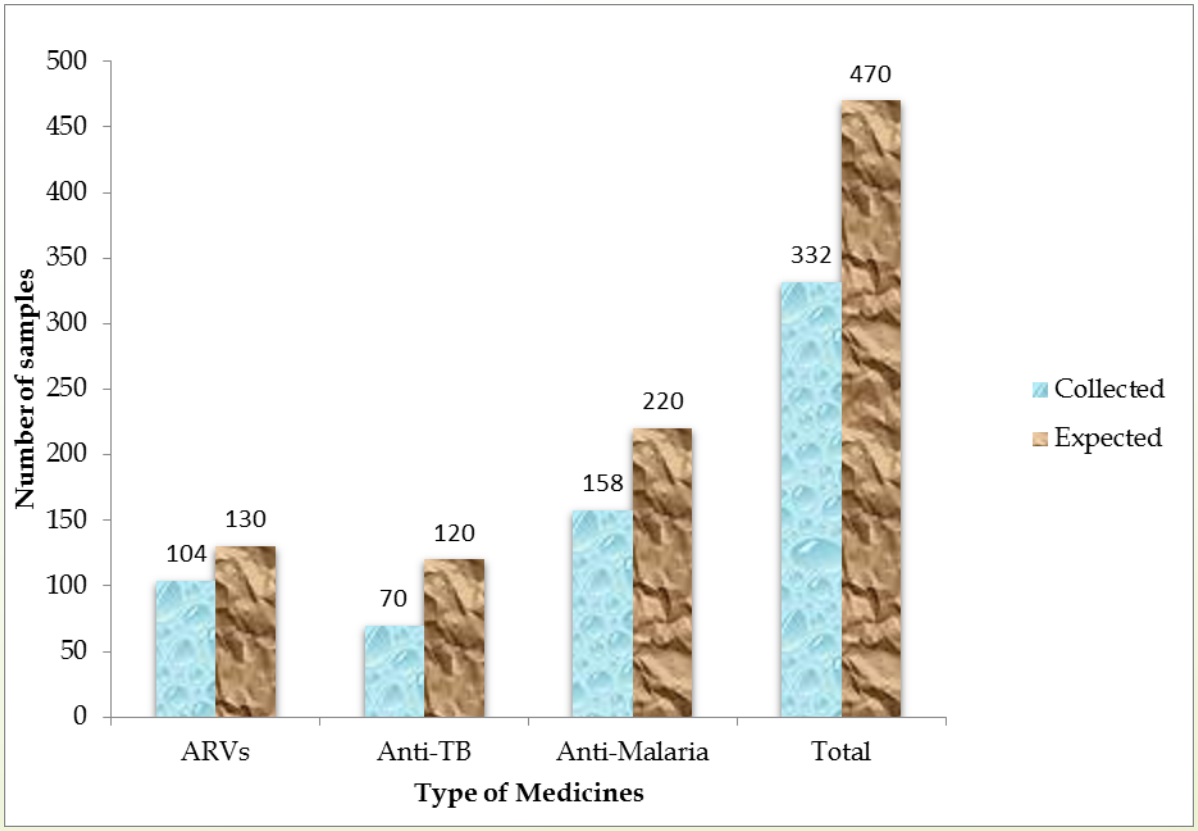

Figure 2: Number of medicines samples expected to be collected and collected samples

4.1.1 Antimalarials

A total of 158 samples of anti-malarias were collected. Out of the 158 samples collected, 53.2% (84/158) were ALU 20mg/120mg tablets, 28.4% (45/158) quinine (300mg tablets & 50mg/5ml syrup) and 18.4% (29/158) artesunate 120mg injection as summarized in Table 3.

4.1.2 Anti-Tuberculous medicines

A total of 70 samples of anti-TB medicines were collected. Out of the 70 samples collected, of FDC were 41.4% (29/70) rifampicin/ isoniazid/ pyrazinamide/ ethambutol (150mg/75mg/400mg/275mg) tablets, 1.4% (1/70) rifampicin/ isoniazid/pyrazinamide (150mg/75mg/400mg) tablets, 40% (28/70) rifampicin/ isoniazid (150mg/75mg) tablets, and of mono-component were 4.7% (4/70) isoniazid 75mg, 4.3% (3/70) ethambutol 400mg and 7.1% (5/70) for levofloxacin 500mg tablets as summarized in Table 3.

4.1.3 Antiretrovirals (ARVs)

A total of 104 samples of ARVs medicines were collected. Out of 104 samples collected, of FDC were 36.5% (38/110) dolutegravir/ lamivudine/tenofovir disoproxil fumarate (50mg/300mg/) tablets 33.7% (35/110) abacavir/lamivudine (120mg/60mg) tablets, and of mono-component was 29.8% (31/110) dolutegravir 50mg tablets as shown in Table 3 below.

Table 3: Number of Antimalarials, Anti-TB and ARVs Medicines samples collected

Region	Anti-malarials		Anti-TB		ARVs	
	No.	Type	No.	Type	No.	Type
		QUI/ALU/ART		RH/RHZE/RHE/H/E/LEV		DTG/AL/TLD
Dar es Salaam	12	5/5/2	7	4/3/0/0/0/0	11	3/3/5
Tanga	33	8/20/5	5	2/2/0/0/0/1	13	4/5/4
Coast Region	12	1/8/3	4	2/2/0/0/0/0	10	3/4/3
Mwanza	15	4/6/5	9	3/4/1/0/0/1	9	3/3/3
Kagera	11	2/7/2	6	3/3/0/0/0/0	7	2/1/4
Mbeya	19	8/9/2	8	3/4/0/0/0/1	14	3/7/4
Kilimanjaro	4	0/3/1	3	2/1/0/0/0/0	8	3/2/3
Morogoro	16	6/8/2	4	2/2/0/0/0/0	8	3/2/3
Dodoma	18	6/9/3	13	4/4/0/4/0/1	12	3/4/5
Mtwara	18	5/9/4	11	3/4/0/0/3/1	12	4/4/4
Total	**158**	**45/84/29**	**70**	**28/29/1/4/3/5**	**104**	**31/35/38**
Percentage (%)	**48**	**29/53/18**	**21**	**40/42/1/6/4/7**	**31**	**30/34/36**

NOTE:

QUI/ALU/ART = Quinine/ Artemether + Lumefantrine/Artesunate

RH/RHZE/RHE/H/E/LEV = Rifampicin + Isoniazid/ Rifampicin + Isoniazid + Pyrazinamide + Ethambutol/ Isoniazid/Ethambutol/Levofloxacin

DTG/AL/TLD = Dolutegravir/Abacavir+Lamivudine/Tenofovir+Lamivudine+Dolutegravir

4.1.4 Samples collection sites

In this survey, a total of 332 samples of antimalarials, anti-TB and ARVs medicines were sampled from different medicines distribution outlets namely; MSD, hospitals, retail and wholesale pharmacies, healthcare centres, dispensaries and ADDOs as depicted in Figure 3. Findings indicate that large quantity 41.3% (137/332) of sampled medicines, ARVs-58, Anti-TB – 41 and antimalarial-38 were collected from hospitals (public facilities), followed by antimalarials 22.6% (75/332) collected from pharmacies (54) and ADDOs (21). There was no any anti-TB or ARVs which were sampled from pharmacies or ADDOs. These findings are summarized in Figure 3.

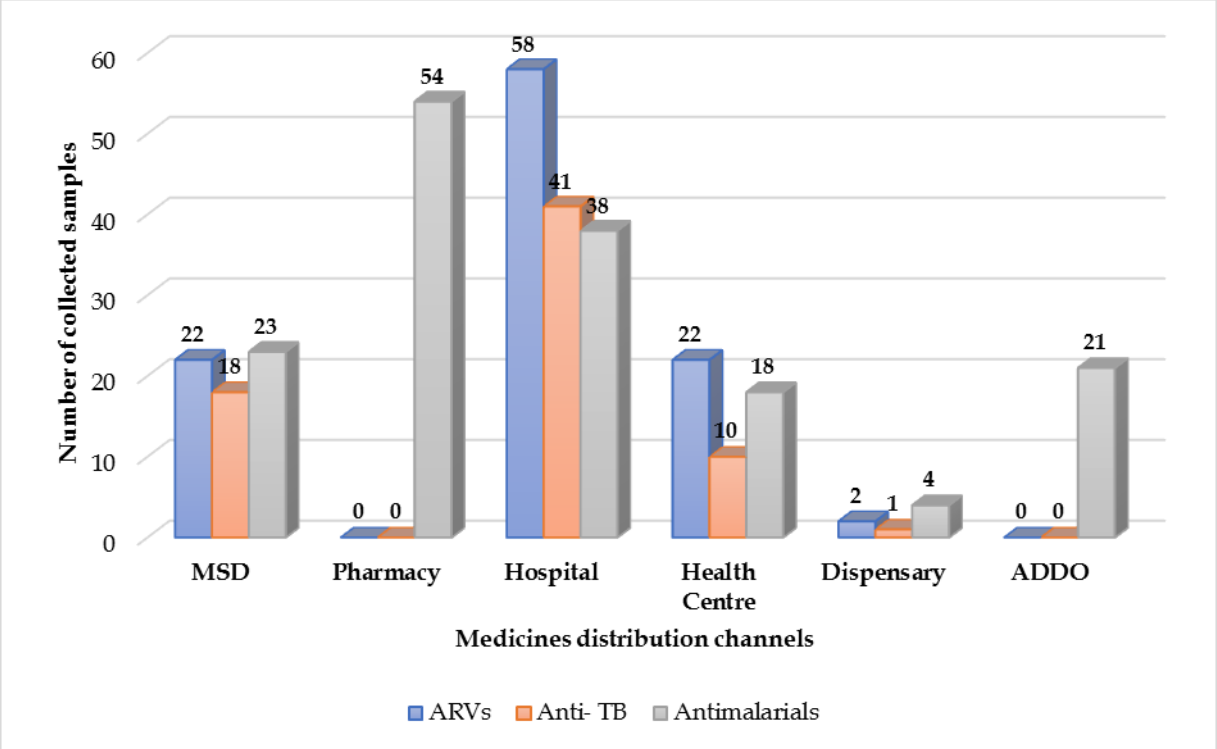

Figure 3: Number of antimalarial, anti-TB and ARVs medicines sampled at different levels of distribution outlets

Majority of collected samples of Anti-malarials, Anti -TB and ARVs medicines were imported from different manufacturers 97.4% (895/919). Of collected antimalarial samples, only 15.2% (24/158) were domestic manufactured as shown in Table 4 below.

	Table 4: Type of medicines sampled with respective Manufacturer(s)

Product Name	No./ product	No. of samples	Manufacturer	Country of origin
Quinine tablets / Syrup	43	16	Shelys Pharmaceuticals Limited	Tanzania
		11	S-Kant Healthcare Limited	India
		5	Prince Pharmaceuticals Company Ltd	Tanzania
		3	Zenufa Laboratories Ltd	Tanzania
		2	Universal Corporation Ltd	Kenya
		4	Remedica Limited	India
		2	Lincoln Pharmaceuticals Ltd	India
Artesunate injection	29	23	Guilin Pharmaceutical Ltd	India
		6	Lincoln Parenterals Ltd	India
ALU tablets	84	11	Ajanta Pharma Limited	India
		15	IPCA Laboratories Limited	India
		15	Macleods Pharmaceuticals Limited	India
		14	Mylan Laboratories Limited	India
		7	Cipla Limited	India
		7	Cipla Quality Chemical Industries Ltd (QCIL)	Uganda
		3	S-Kant Healthcare Ltd	India
		9	Lincoln Pharmaceuticals Ltd	India
		2	Strides Arcolab Limited	India
		1	Strides Shasun Limited	India
Anti-malarial medicines samples - Total	**156**	**156**		
Rifampicin + Isoniazid	28	17	Lupin Limited	India
		6	Svizera Laboratories	India

		3	Macleods Pharmaceuticals Ltd	India
		1	Aurobindo Pharma Limited	India
		1	Oxalis Lab	India
Rifampicin + Isoniazid + Ethambutol	1	1	Macleods Pharmaceuticals Ltd	India
Rifampicin + Isoniazid + Pyrazinamide + Ethambutol	29	18	Lupin Limited	India
		8	Svizera Laboratories	India
		3	Macleods Pharmaceuticals Ltd	India
Ethambutol	3	2	Macleods Pharmaceuticals Ltd	India
		1	Svizera Laboratories	India
Isoniazid	4	4	Macleods Pharmaceuticals Ltd	India
Levofloxacin	5	5	Medochemie Ltd	India
Anti-TB medicines samples - Total	**70**	**70**		
Dolutegravir	31	16	Aurobindo Pharma Ltd	India
		14	Laurus Labs Limited	India
		1	Hetero Laboratories Limited	India
Abacavir + Lamivudine	35	18	Hetero Laboratories Limited	India
		11	Cipla Limited	India
		5	Mylan Laboratories Ltd	India
		1	Guilin Pharmaceuticals Company Ltd	India
Tenofovir + Lamivudine + Dolutegravir	38	17	Aurobindo Pharma Limited	India
		14	Mylan Laboratories Limited	India
		7	Laurus Labs Limited	India

Antiretroviral medicines samples - Total	**104**	**104**		

Of the imported medicine large quantity were from India 90% (297/330) followed by Uganda 2.1 (7/330) and Kenya 0.6% (2/330). These results are shown in Figure 4.

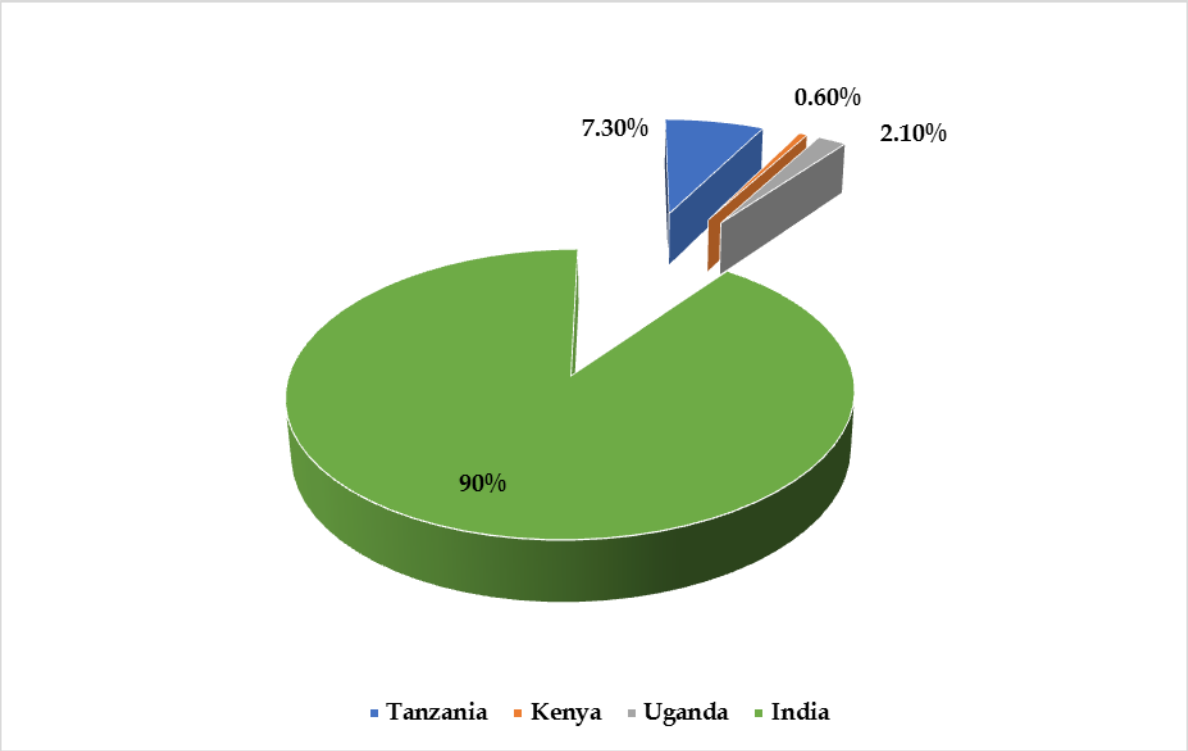

Figure 4: Percentage of sampled medicines manufactured in different countries

4.1.5 Samples collected from Port of Entry and domestic manufacturers

Apart from the survey conducted at the distribution outlets to verify the quality of anti-malarial, Anti-TB and ARVs, also, the routine quality assurance was conducted by collecting samples of the aforesaid medicines from the POEs and domestic manufacturers. A total of 587 samples were sampled, this included: - 48% (283/587) of anti-malarial, 14% (82/587), anti-TB and 38% (222/587) ARVs as shown in Table 5 and figure 5 below.

Table 5: Type of medicines sampled at the POEs and domestic manufacturers with respective country of origin

Product	No. of samp	No. of samples	Manufacturer	Country of origin

	le/product			
ALU tablets	200	36	Oxalis Labs	India
		30	Lincoln Pharmaceuticals Ltd	India
		23	Macleods Pharmaceuticals Limited	India
		21	Ajanta Pharma Limited	India
		19	IPCA Laboratories Limited	India
		17	Strides Shasun Limited	India
		17	Mylan Laboratories Limited	India
		11	Blis EVS Pharma	India
		8	Shelys Pharmaceuticals Limited	Tanzania
		9	S-Kant Healthcare Limited	India
		4	Dafra Pharma	Switzerland
		3	Norvatis	Switzerland
		2	Cipla Ltd	India
Artemether injection	8	3	Lincoln Parenterals Ltd	India
		3	KPC Pharmaceutical Ltd	India
		1	Surge Laboratories	India
		1	IPCA Laboratories	India
Artesunate injection	45	29	Guilin Pharmaceuticals	India
		7	Fosun Pharma	India
		6	Lincoln Pharmaceuticals	India
		3	IPCA Laboratories	India
Dihydroartemisinin + Piperaquine	14	5	Fosun Pharma	India
		4	KBM Zhejiang Pharmaceutical Co. Ltd	China
		3	Guilin Pharmaceuticals	India
		2	Ajanta Pharma Limited	India
Quinine tablets	7	4	S-Kant Healthcare Ltd	India
		2	Shelys Pharmaceuticals Limited	Tanzania

		1	Lincoln Pharmaceuticals Ltd	India
Artesunate + Mefloquine	1	1	Acino Pharma	Germany
Sulfadoxine + Pyrimethamine	3	3	Shelys Pharmaceuticals Limited	Tanzania
Sulfamethoxypyrazine + Pyrimethamine	5	5	Shelys Pharmaceuticals Limited	Tanzania
Anti-malarial medicines samples -Total	**283**	**283**		
Rifampicin + Isoniazid	11	11	Oxalis Labs	India
Pyrazinamide	3	3	Oxalis Labs	India
Rifampicin + Isoniazid + Pyrazinamide	5	5	Oxalis Labs	India
Linezolid	1	1	Macleods Pharmaceuticals Ltd	India
Levofloxacin	1	1	Medochemie Ltd	India
Isoniazid	49	3	Lupin Limited	India
		18	Cadila Pharmaceuticals Ltd	India
		28	Oxalis Labs	India
Delamanid	2	2	Otsuka Novel	Germany
Clofazimine	3	3	Novartis Pharma	Germany
Ethambutol	7	7	Oxalis Labs	India
Anti-TB medicines samples -Total	**82**	**82**		
Abacavir + Lamivudine		25	Cipla Ltd	India
	30	4	Hetero Laboratories Limited	India
		1	Mylan Laboratories	India

Atazavir + Ritonavir	15	15	Mylan Laboratories Limited	India
Tenofovir + Lamivudine + Dolutegravir	114	39	Laurus Labs Limited	India
		35	Hetero Laboratories Limited	India
		20	Mylan Laboratories Limited	India
		20	Aurobindo Pharma Limited	India
Emtricitabine + Tenofovir	12	7	Mylan Laboratories	India
		5	Hetero Labs Ltd	India
Lamivudine + Zidovudine	5	4	Hetero Laboratories Limited	India
		1	Cipla Ltd	India
Lopinavir + Ritonavir	41	29	Mylan Laboratories	India
		9	Aesica Pharmaceuticals Ltd	India
		3	Abbvie	Germany
Raltegravir	1	1	Merck Sharp	USA
Ritonavir	1	1	Abbvie	Germany
Darunavir	1	1	Hetero Laboratories Limited	India
Lamivudine	1	1	Hetero Laboratories Limited	India
Zidovudine	1	1	Hetero Laboratories Limited	India
Antiretroviral medicines samples -Total	**222**	**222**		

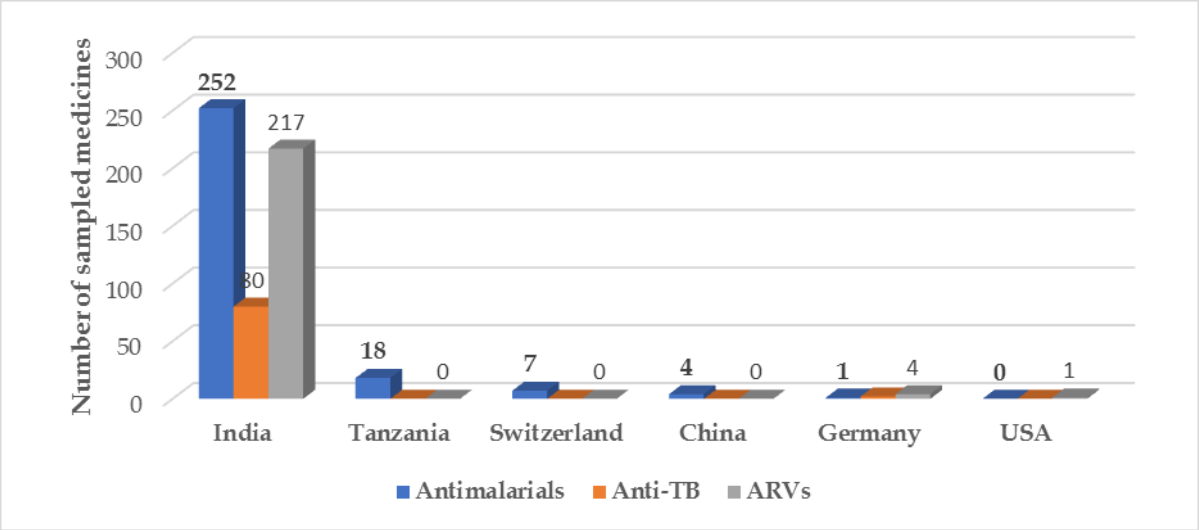

Figure 5: Sample collected at POEs per country including domestic manufacturers

4.2 Product Information Review

All collected samples from medicines distribution outlets were subjected to PIR by comparing the information accompanying commercial packs of the surveyed products against approved product information and TMDA product information requirements.

Out of the 332 samples subjected to PIR, 54% (179/332) did not meet the requirements. Of the failed samples 58.1% (104/179) were Antimalarials, 4.5% (8/179) ARVs and 37.4% (67/179) Anti-tuberculous medicines as shown in Figure 6 below.

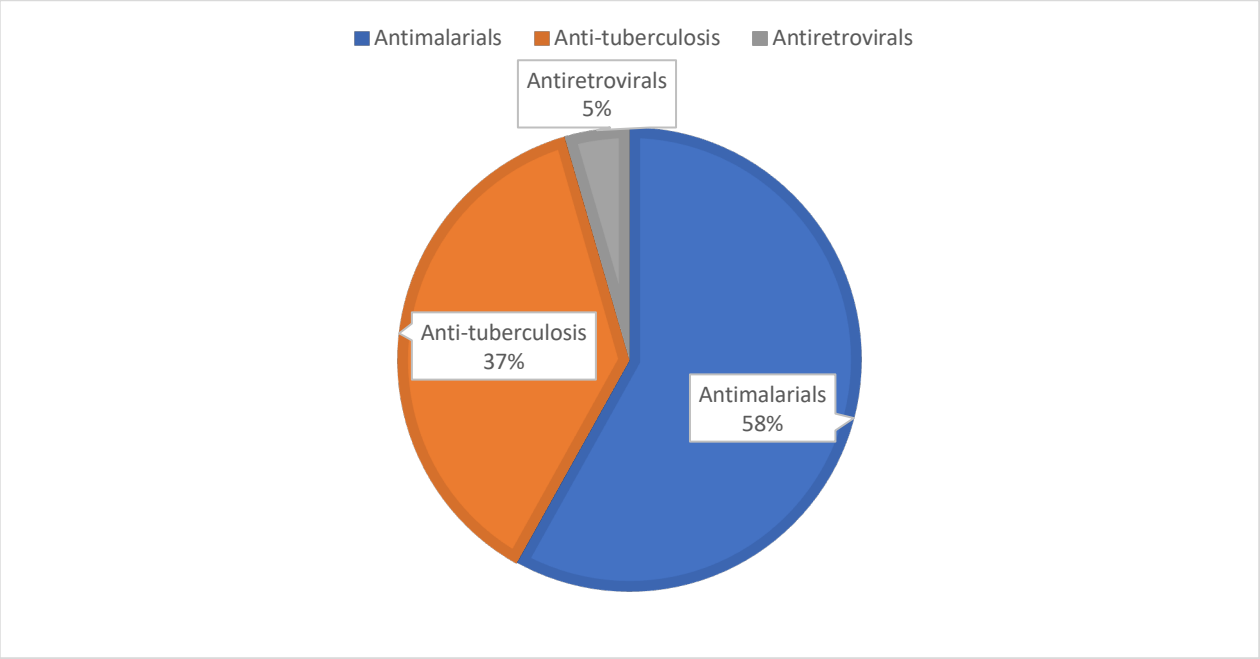

Figure 6: Distribution of samples that failed PIR among the sampled groups of medicines

Among the 67 failed samples of Anti-TB, 7.4% (5/67) were for levofloxacin tablets, 4.5% (3/67) ethambutol tablets, 40.3% (27/67) rifampicin + isoniazid tablets, 41.8% (28/67) rifampicin/isoniazid/ethambutol/pyrazinamide and 1.5% (1/67) rifampicin/isoniazid/ethambutol tablets. Among the 104 samples of anti-malarial which failed PIR, 29.8% (31/104) of the samples were for quinine tablets, 47.1% (49/104) artemether/lumefantrine tablets and while 24 samples (23.1%) artesunate injection. Furthermore, out of 8 samples of ARVs which failed PIR, majority of failed samples 75% (6/8) were for abacavir/lamivudine tablets while 25% (2/8) tenofovir/lamivudine/dolutegravir tablets. Figure 7 below shows percentage distribution of failed products in each category of medicines.

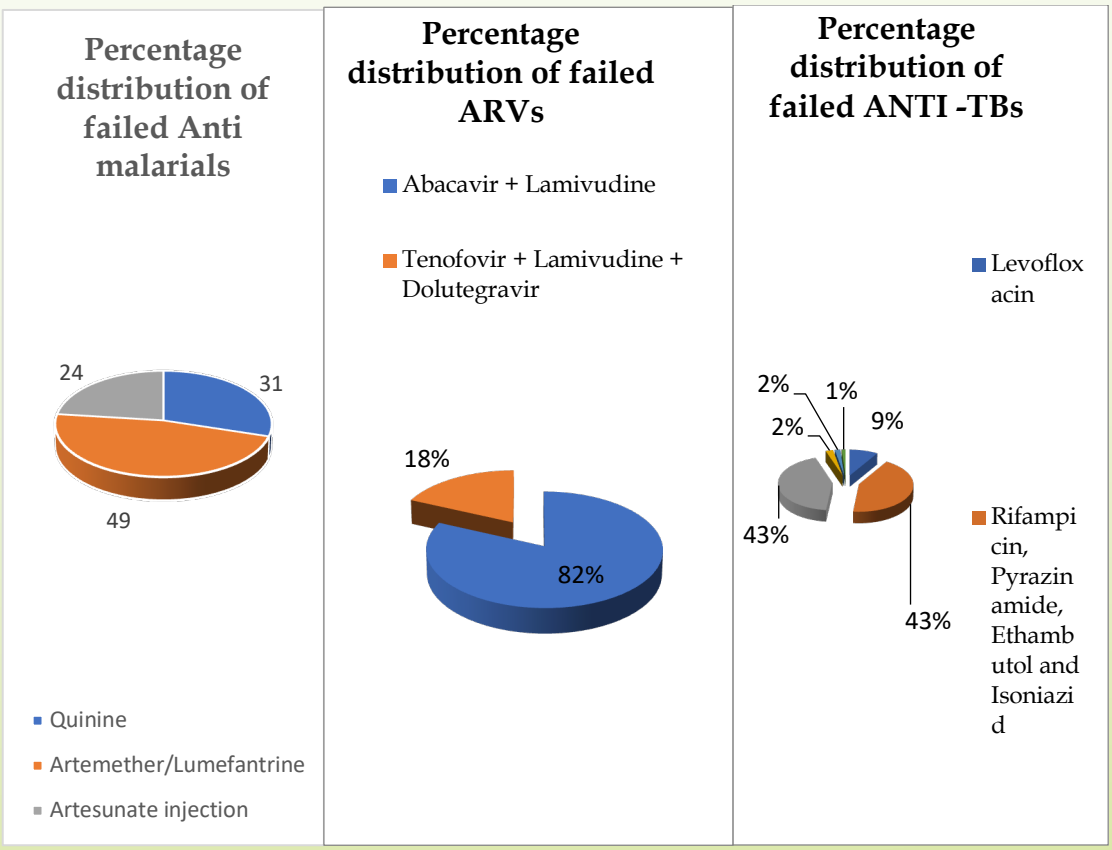

Figure 7: Distribution of failed products in each category of medicines

The major deficiency observed in the evaluated samples of medicines was incomplete leaflet which contributed to 29.6% (101/341) of the observed deficiencies. This was followed by in appropriate storage condition 12.3 % (18/149 followed by deviations on shelf life specified on the pack versus the approved shelf life which contributed 9.7% (33/341) of the observed discrepancies. Deviations in physical appearance of the product primary pack as compared to the approved pack contributed to 9.4% (32/341) of the observed deficiencies. Fewer deficiencies were observed from the product inserts which were lacking physical description of product 0.5% (2/341). Notably that other

uncategorized minor deficiencies and discrepancies contributed to as high as 13.8% (47/341) of the observed deficiencies. The results of observed deficiencies across the types of reviewed medicines and the total deficiencies are summarized in Table 6 below:

Table 6: Observed PIR deficiencies across the types of reviewed medicines and the total deficiencies

Discrepancies	**ARVs**	**Anti TB**	**Anti-malari**	**Total**	**%**
Lack of manufacturer name and address on secondary, primary and package insert	0	6	8	14	**4.1**
In appropriate storage conditio	0	42	0	42	**12.3**
Un registered medicines	0	31	1	32	**9.4**
Use of inappropriate p package material	0	28	0	28	**8.2**
Incomplete leaflet	0	32	69	101	**29.6**
Shelf-life deviation	1	4	28	33	**9.7**
In appropriate Language used in labelling and package insert	6	0	1	7	**2.1**
Product insert lack physical description of the product	0	0	2	2	**0.5**
Artwork deviations	4	2	26	32	**9.4**
Unit package deviation	0	0	3	3	**0.9**
Others	0	27	20	47	**13.8**
Total	**11**	**172**	**158**	**341**	**100**

As seen in table 6 above, among deficiencies observed in Anti-TBs majority were related to inappropriate storage conditions 24% (42/172), followed by incomplete leaflet 18.6% (32/172), it was also observed that 18% (31/172) were unregistered medicines. Other issues include use of in appropriate package material which contributed 16.3 % (28/172) and other

issues which contributed to up to 16% (27/172). The percentage distribution of deficiencies among Anti TBs is also shown in Figure 8 below.

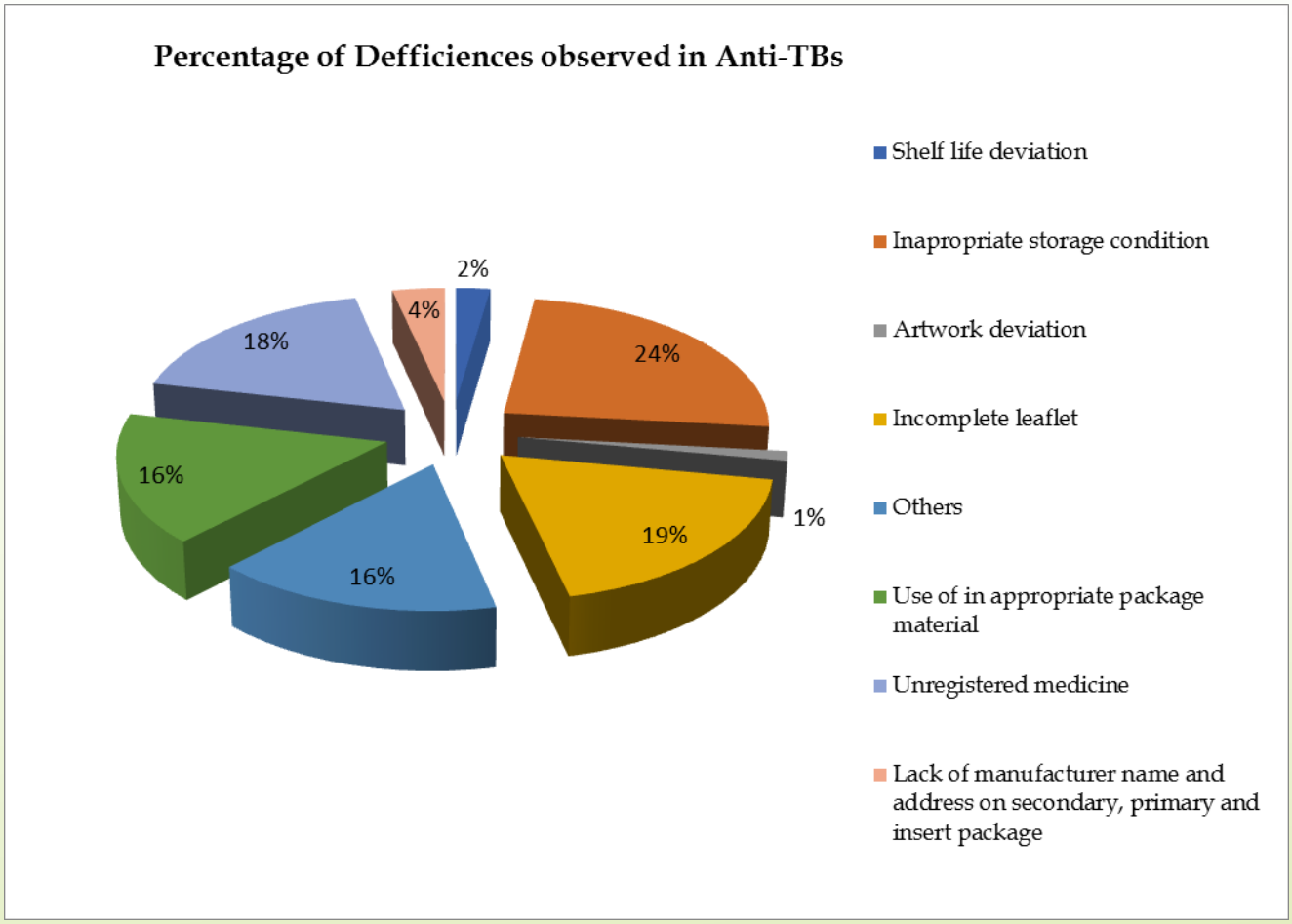

Figure: 8: Distribution of deficiencies among Anti TBs

Of the surveyed antimalarial incomplete package information leaflets attributed to 43.7% (69/158), followed by shelf-life deviation 17.7% (28/158) and product artwork 16.5% (26/158). These results are summarized in Figure 9

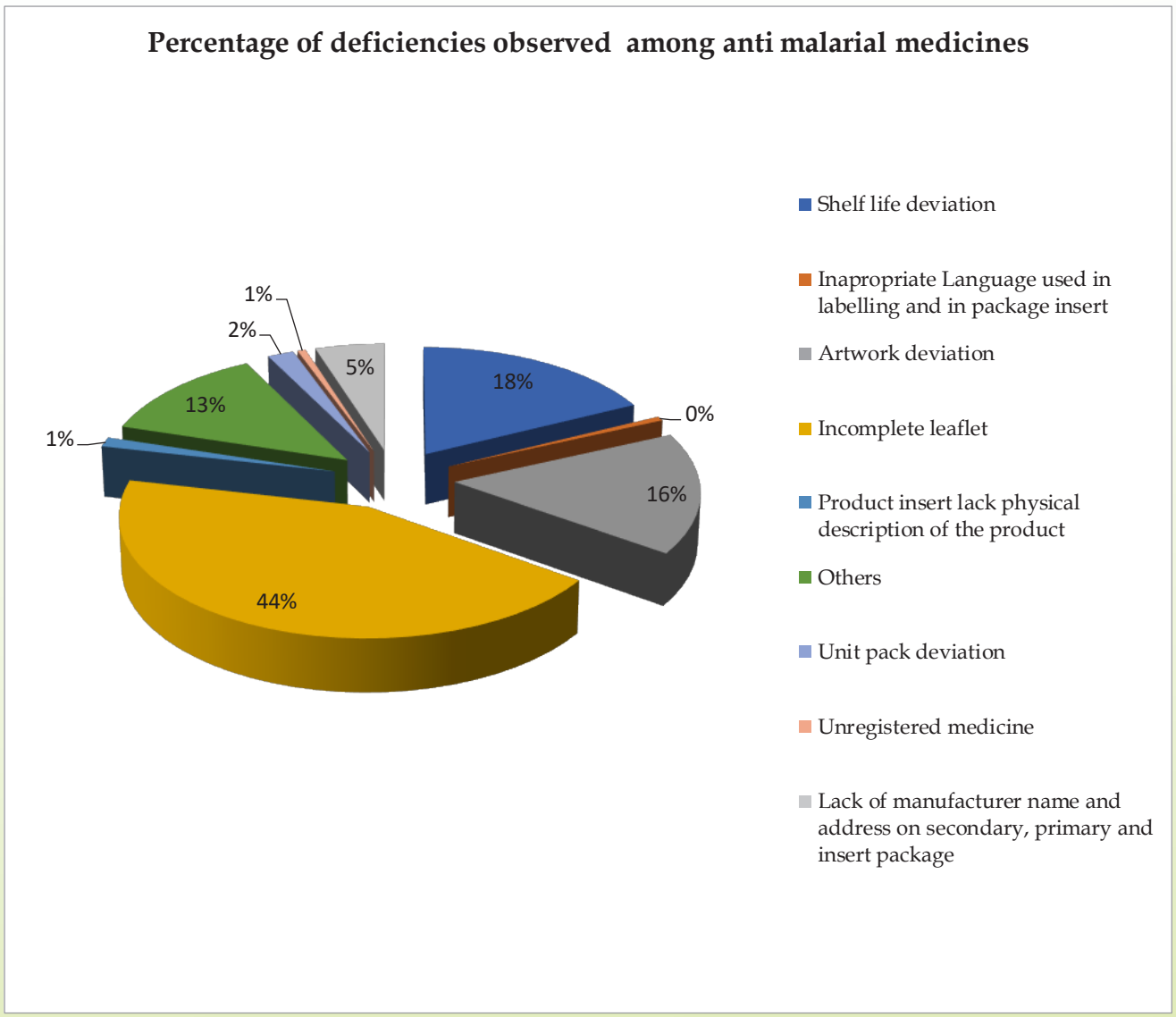

Figure 9: Distribution of deficiencies among antimalarials

Among the discrepancies observed from the sampled ARVs, majority 54.5% (6/11) were inappropriate language on the label and package information leaflet, followed by 36.4% (4/11) attributed to product artwork deviation. Lastly only 9% (1/11) observation was made with respect to different shelf-life compared to the approved shelf life. Figure 10 below shows percentage distribution of deficiencies observed among ARVs surveyed.

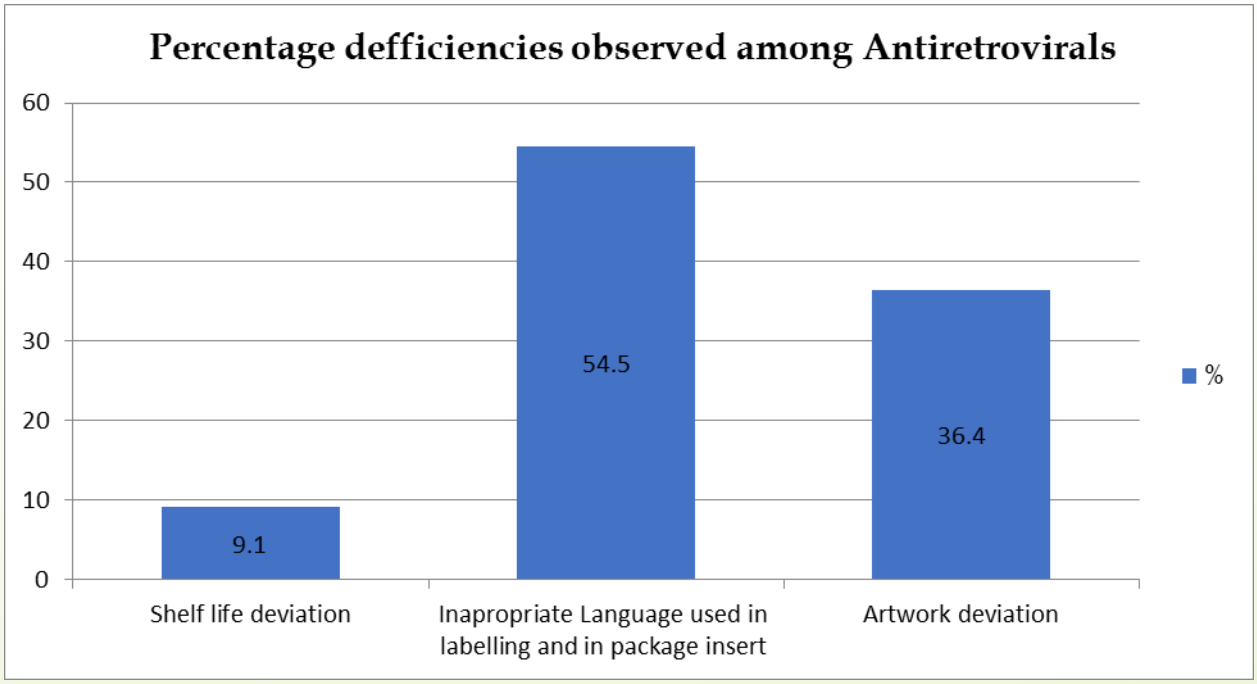

Figure 10: Percent of Deficiencies observed among surveyed antiretrovirals

4.3 Laboratory Screening Test

The laboratory screening test consisted of visual inspection, TLC identification and disintegration test.

4.3.1 Visual Inspection Test

All ARVs, Anti-TB and anti-malarials sampled from POEs and medicines distribution outlets (919) conformed to visual appearance requirements.

4.3.2 Disintegration Test

For all sampled oral solid dosage forms from POEs and medicines distribution outlets of artemether/lumefantrine tablets, quinine sulphate tablet, dolutegravir tablets, abacavir/lamivudine, dolutegravir/lamivudine/tenofovir tablets, levofloxacin tablet, Isoniazid tablets ethambutol tablets, rifampicin/isoniazid tablets, rifampicin/isoniazid/pyrazinamide tablets and rifampicin/isoniazid/pyrazinamide/ethambutol tablets and subjected to disintegration testing, disintegrated within 30 minutes at 37°C (between 1-6 minutes).

4.3.3 Identification Test

Identification of active principle (API) was performed using TLC. All collected samples of artemether/lumefantrine tablets, artesunate powder for injection, quinine sulphate tablets, quinine sulphate syrup, dolutegravir tablets, dolutegravir/lamivudine/tenofovir tablets, abacavir/lamivudine tablets, levofloxacin tablets, ethambutol tablets, Isoniazid tablets, rifampicin/isoniazid tablets, rifampicin/isoniazid/pyrazinamide tablets and

rifampicin/isoniazid/pyrazinamide/ethambutol tablets from POEs and medicines distribution outlets and subjected to TLC passed the identification test.

4.3.4 Laboratory Confirmatory Testing

All 33 samples selected for confirmatory testing which accounts to 10% of those passed screening test from medicine distribution outlets as depicted in Table 7 below complied with the evaluated parameters as per Pharmacopoeial monograph, in house method and/manufacturer own method requirements [1-7].

The assay content of ARVs for mono-component of dolutegravir was in the following range (99.2-101.5%) and for FDC of dolutegravir (99.8-102.0%), lamivudine (97.8-103.1%), tenofovir (98.4-101.8%) and abacavir (96.1-99.2%). As well for anti-TB the assay content for the FDC of rifampicin was in the following range (90.8-100.3%), isoniazid (93.1-108.6%), pyrazinamide (98.1-102.7%) and ethambutol (97.0-102.1%). The range of dosage of active principle of mono-component of artesunate was (98.0%) and for quinine sulphate (97.3-100.8%) and for FDC of artemether (90.8 - 105.7%) and for lumefantrine (94.2-96.6%).

Table 7: Sampled antiretroviral, anti-tuberculosis and anti-malarial medicines from medicine distribution outlets and number of samples selected and tested for confirmatory test

Product name	Samples collected and screened			Confirmatory test	
	Samples collected	Samples screened and passed	Samples Failed	Samples eligible for confirmatory	Samples selected and tested
Artesunate injection	29	29	0	3	3
Quinine tablets	23	23	0	3	3
Quinine syrup	20	20	0	2	2
Artemether/Lumefantrine (ALU) Tablets	84	84	0	8*	5
Dolutegravir tablets	31	31	0	3	3
Tenofovir/Lamivudine/Dolutegravir tablets	38	38	0	3	3
Abacavir sulfate/Lamivudine tablets	35	35	0	3	3
Levofloxacin tablet	5	15	0	2	2
Isoniazid tablets	4	4	0	1	1
Ethambutol tablets	3	3	0	1	1
Rifampicin/Isoniazid tablets	28	28	0	3	3
Rifampicin/Isoniazid/Pyrazinamide tablets	1	1	0	1	1
Rifampicin/Isoniazid/Pyrazinamide/ Ethambutol tablets	29	29	0	3	3
Total	**332**	**332**	**0**	**36**	**33**

5 DISCUSSION

Quality assurance of anti-malarial, anti-TB and ARVs is of crucial importance for the protection of public health (1). Accordingly, to ensure the medicines circulating on Tanzania market are of good quality, the regulatory authority conducted the survey and routine quality assurance by collecting samples from different levels of the distribution outlets starting from national, regional and district levels, and POEs.

The samples and regions were selected using criteria set in the PMS programme for Antimalarials, Anti-TB and ARVs (1). Samples were collected from two districts in ten (10) regions as per plan. However, numbers of samples collected were 70.6% (332/470) which was below the target set in the plan (2). This was due to unavailability of some of the medicines at the time of collection. This is a common problem during sample collection especially in peripheral areas where the medicines supply is still low. This has been a repetitive challenge as reported in previous PMS programme (3,4).

Of the sampled medicines large quantity 97.4% (895/919) were imported showing the dependence of the country on imported medicines from abroad. This is justified by the fact that domestic manufacturing facilities in Tanzania still have low capacity to manufacture antimalarials, anti-TB and ARVs. The manufacturing capacity of domestic manufacturers are 20 -30% which can not suffice the country's medicines demand (5). Zero capacity of ARVs and Anti-TB. Similar observation has been reported in various PMS programmes and TMDA data of 2017 and a previous study conducted in Tanzania (5). Such situation is likely to make the country vulnerable in case of public health emergences such as it was observed during first phase of COVID-19 pandemic (6).

Findings from this surveillance also revealed that, antimalarials were the most collected drugs, 48% (441/919), followed by ARVs 35.5% (326/919) and then Anti-TB 16.6% (152/919). This trend was observed for samples collected from distribution outlets and those collected from the POEs and domestic manufacturers. For anti-TB, Rifampicin/Isoniazid/Pyrazinamide/Ethambutol tablets were sampled more compared to other anti-TB medicines. For ARVs, TLD was sampled more compared to other ARVs. The same trend was observed for samples collected under routine quality assurance at the POEs and domestic manufacturers. Currently, ALU and TLD are recommended first line treatment of malaria and HIV infection could account for the observed trend in number of samples collected (7,8). Furthermore, the observed trend could be explained by prevalence of respective disease condition in the country (9,10). Likewise, among of the collected samples, FDC samples were the majority 664/919 (72.3%). FDCs are desirable and recommended by the WHO,

as it simplify treatment, ideally resulting in improved medication concordance, clinical outcomes and quality of life of patients(11).

Additionally, routine quality assurance was conducted by collecting the aforesaid medicines from POEs and domestic manufacturers. Samples collected from the POEs and domestic manufacturers were higher by 63.9% (587/919) to those collected from the market in different distribution channels. This is attributed by the fact that all incoming batches of the respective medicines are sampled and tested.

Notably, none of anti-TB and ARVs were found in the distribution outlets compared to antimalarial whereas about 22% (75/332), of the samples were collected in the former. Similar findings were observed in previous PMS studies conducted in Kenya and Tanzania (2,4,5). In Tanzania, all ARVs and Anti TB are currently procured by the government and available at public supply chain. This is of an interest for law enforcement and adequate regulatory control on availability of ant-TB and ARVs in specialized outlets as per TMDA requirements.

A medicine's product information is regulated, scientifically validated information that assists healthcare professionals in prescribing and dispensing of medicines and informs patients and consumers about their medicines, safe use and storage of the respective medicines. The dangers associated with the use of improperly labelled medicines may result into medication errors, which often have serious consequences to health of the patients (12).

The observed higher percentage of failure contributed by antimalarials (58%) is attributed by the fact that amongst the types of surveyed, antimalarial are the most commonly consumed products due to relatively higher prevalence of malaria in Tanzania as compared to tuberculosis and HIV/AIDS (13). This is also attributed by the fact that large proportion of the collected samples was antimalarial together with widespread use of these medicines in the country which could in turn drive the demand and fewer adherences among the manufacturers.

Among the sampled Anti-TB highest failures were contributed by Rifampicin + Isoniazid tablets (40.3%) and Rifampicin/Isoniazid/Ethambutol/Pyrazinamide (41.8%). Furthermore, out of this group of medicines, majority of the failures were attributed by the inappropriate storage conditions and use of inappropriate primary package material compared to the approved pack of the product. Studies have shown that inappropriate storage of rifampicin based fixed dose combination anti tuberculous medicines is likely to result into quality defects of the products due to hygroscopic nature of the Rifampicin component of the product (14). It has also been noted in the current International Pharmacopoeia monograph that Rifampicin is prescribed for stored in tightly closed containers (15). Furthermore, Ethambutol has also been

generally characterized as a highly hygroscopic molecule (14). In view of this, inappropriate storage conditions on the labels of the respective products are likely to result into quality defects as a result of absorption of moisture which may cause deterioration in quality and performance characteristics of the dosage forms, such as molding, hardening and degradation of the active moieties.

From the reviewed samples of anti-malarial medicines subjected to PIR, majority of failed samples were noted to be those of Artemether + Lumefantrine tablets which contributed to 31.4% of the failed samples. Specific discrepancies were mainly on incompleteness of information contained in the package leaflets followed by shelf-life deviation and artwork deviation from approved labelling orientations of the respective products. Lack of adequate information on package information leaflets is likely to impact proper prescription and dispensing of the medicine to the patient as well as improper use and adherence among the patients.

Furthermore, from within the failed samples of Antiretrovirals, majority of failed samples (6) equaling to 75% were for Abacavir tablets while only 2 samples (25%) were for Tenofovir/Lamivudine/Dolutegravir tablets. With majority of observed discrepancies attributed by inappropriate language on the label and leaflet as well as artwork deviations from approved product labels. The latter is considered critical with respect to rational prescribing and dispensing of the ARVs as well as use by the patients.

All sampled ARVs, anti-TB and anti-malarial from POEs and medicines distribution outlets (919) conformed to screening and confirmatory tests requirements. This continues improvement in quality of sampled medicines over years of implementation of the PMS program could account for adherence to regulatory requirements by market authorization holders and medicine distribution outlets (1,5). This also, can be explained by the fact that most of ARVs, anti-TB and anti-malarial in the market are procured by government agencies with donor funding. The funding agencies impose stringent procurement condition such as requirements for the WHO pre-qualification for all suppliers (16,17). Low failure rate has been observed in countries such as Tanzania using the WHO-prequalified products as reported in a previous study (18). These results are much far better compared to previous PMS program results for similar medicines (2012-2015) (1,5) .

6 REGULATORY ACTIONS TAKEN

TMDA issued directive letters to MAH whose product failed to comply with TMDA labeling and package insert requirement to rectify and submit application for variation.

7 CONCLUSION

The survey has unveiled significant number of samples of medicines which did not meet labelling and product information requirements. This still is an alarming situation since similar findings were observed for other medicines surveyed by TMDA in previous investigations.

Therefore, more effort is required to enforce Marketing Authorization Holder (MAH) to ensure that their products meet product information requirements before being imported and allowed to be on the market. In addition, inspection activities need to be strengthened especially at ports of entry to identify medicines which are not labelled in the manner that conform to the labelling requirements before being allowed into the country.

Results from screening and confirmatory testing showed that all samples of medicines tested met the specifications. This shows adequate execution and enforcement of post- registration phase of medicinal product cycle. Yet, it is recommended continuous monitoring of quality of medicines circulating on the market and reminding distributors and sellers of medicines on the importance of adhering to good distribution practices, storage, labelling and proper handling of medicines.

8 RECOMMENDATIONS

The following are recommendations from the experience gained in this survey.

a. Marketing authorization holders should be reminded to comply with labelling requirements.

b. Before embarking into sample collection sample collectors should be trained on how to conduct sampling as well as pros and cons for adhering and not adhering to the sampling standard operating procedures.

c. Stake holders who are directly receiving complains with regard to product quality and safety should be involved in sampling plan preparation and implementation of PMS programme.

d. Training to the sample collectors on the proper data entry by using RIMS before sample collection process start.

e. Reviewers of product information should be trained so as to improve the recording of deficiencies observed during product information review.

9 LIMITATIONS

Limitations encountered during planning, implementation, analysis and writing up of the report include insufficient samples collected from the planned sampling sites compared to the targeted number due to unavailability of products.

10 AREA FOR IMPROVEMENT

a. Training of sample collectors

b. Increasing the sentinel sites in rural areas to enable representation samples from rural areas or hard to reach areas. This will enable to easily reach the targeted sample size. Since the supply of medicines in these areas is limited, the planned sample size should be representative enough to improve the strength of evidence generated by data from these areas.

c. Changing the sampling technique from convenient to random sampling such as stratified or systematic sampling. The later to methods have advantage of reducing biasness in selecting the facility from which the samples are to be collected.

11 REFERENCES

1. Tanzania Food and Drugs Authority. Post Marketing Surveillance (Pms) Report for Selected Human and Veterinary Medicines Circulating in Tanzania 2015/2016. 2016.
2. Petersen A, Held N, Heide L. Surveillance for falsified and substandard medicines in Africa and Asia by local organizations using the low-cost GPHF

Minilab. PLoS One. 2017;12(9):1–22.
3. Tanzania Food and Drugs Authority Registration Data Base. 2017.
4. Wande DP, Sangeda RZ, Tibalinda P, Mutta IK, Mkumbwa S, Bitegeko A, et al. Pharmaceuticals imports in Tanzania: Overview of private sector market size, share, growth and projected trends to 2021. PLoS One. 2019;14(8):1–17.
5. Mziray S, Mwamwitwa K, Kisoma S, Augustine S, Fimbo A, Hipolite D, et al. Post Marketing Surveillance of Anti-malarial Medicines in Tanzania. Pharm Regul Aff Open Access. 2017;06(01).
6. Kangwerema A, Thomas H, Knovicks S, Safari J, Diluxe M, Madadi S, et al. The challenge of dearth of information in Tanzania's COVID-19 response. J Glob Heal Sci. 2021;3(2):2–5.
7. Tanzania Ministry of Health. NATIONAL GUIDELINES FOR THE MANAGEMENT OF HIV AND AIDS. Natl Guidel Manag HIV AIDS. 2020;(April):266–7.
8. Marealle AI, Mbwambo DP, Mikomangwa WP, Kilonzi M, Mlyuka HJ, Mutagonda RF. A decade since sulfonamide-based anti-malarial medicines were limited for intermittent preventive treatment of malaria among pregnant women in Tanzania. Malar J. 2018;17(1).
9. Mboera LEG, Rumisha SF, Lyimo EP, Chiduo MG, Mangu CD, Mremi IR, et al. Cause-specific mortality patterns among hospital deaths in Tanzania, 2006-2015. PLoS One. 2018;13(10).
10. Mangu CD, Rumisha SF, Lyimo EP, Mremi IR, Massawe IS, Bwana VM, et al. Trends, patterns and cause-specific neonatal mortality in Tanzania: A hospital-based retrospective survey. Int Health. 2021;13(4).
11. Panchagnula R, Agrawal S, Kaur KJ, Singh I, Kaul CL. Evaluation of rifampicin bioequivalence in fixed-dose combinations using the WHO/IUATLD recommended protocol. Int J Tuberc Lung Dis. 2000;4(12).
12. Fortescue EB, Kaushal R, Landrigan CP, McKenna KJ, Clapp MD, Federico F, et al. Prioritizing strategies for preventing medication errors and adverse drug events in pediatric inpatients. Pediatrics. 2003;111(4).
13. Tanzania ministry of health. Tanzania Hiv Impact Survey (This) a Population-Based Hiv Impact Assessment. Phia [Internet]. 2018;(December 2018):1–6. Available from: https://phia.icap.columbia.edu/wp-content/uploads/2017/11/Tanzania_SummarySheet_A4.English.v19.pdf
14. Diniz LF, Carvalho PS, De Melo CC, Ellena J. Reducing the Hygroscopicity of the Anti-Tuberculosis Drug (S,S)-Ethambutol Using Multicomponent Crystal Forms. Cryst Growth Des. 2017;17(5).
15. WHO Library. The International Pharmacopoeia 9th Edition. WHO Libr. 2019;1–28.
16. World Health Organization. Survey of the quality of selected antimalarial medicines circulating in six countries of sub-Saharan Africa. World Heal Organ. 2011;
17. Beargie SM, Higgins CR, Evans DR, Laing SK, Erim D, Ozawa S. The economic impact of substandard and falsified antimalarial medications in Nigeria. PLoS One. 2019;14(8):1–16.
18. Post Marketing Surveillance Report of the Quality of Antimalarial, Anti-Retroviral and Anti-Tuberculous Medicines Circulating in Tanzania for the

year 2012-2015. Tanzania Food and Drugs Authority, Dar-es-Salaam, Tanzania. TMDA. 2016;67(5).

Annex I – Sample collection form

TMDA	MEDICINES POST MARKETING SURVEILLANCE SAMPLE COLLECTION FORM	*TMDA/DMC/CTP/F/002 Rev #:1*

1. Sample code: .....
(Region/product/sequence number/sampling date dd/mm/yy)***

2. Name of Premises where sample was taken: .....

3. Physical Address.....Postal address.....
Telephone No..... Fax No.....
Email address..... (If applicable)

4. Product name of the sample: .....

5. Name of active pharmaceutical ingredient(s) (INN) with strength: .....
.....

6. Dosage form (tablet, oral powder, etc): .....

7. Package size & type: .....

8. Batch/lot number: ..... Date of manufacture: .....
Expiry date: .....

9. Name and physical address of the manufacturer: .....
.....

10. Number of units collected: .....

11. Is the product registered in Tanzania? Yes/ No. If Yes, indicate the registration number:
.....

12. Comment on storage condition of product at the premises:
.....
.....

13. Name and signature of the Representative of the premise where sample was collected:

Name: ..... Signature: ..... Date: .....

14. Name of Drug Inspector (s)/Sampling officer

S/n	Name	Organization	Signature	Date

Note: Samples collected must remain in their original containers.

Approved by MCTP (Signature) _____ Effective Date: 25/03/2020

ORIGINAL COPY

Annex II-SAMPLING PLAN

SAMPLING PLAN FOR COLLECTION OF SELECTED ANT TB, ARVS AND ANTIMALARIA MEDICINES FROM PUBLIC AND PRIVATE FACILIES IN TEN (10) REGIONS (KILIMANJARO, DAR ES SALAAM, DODOMA, MWANZA, GEITA, MTWARA, MBEYA, PWANI, MOROGORO, KAGERA)						
Sampling levels	**Product Category**	**Product**	**Dosage Form**	**Strength**	**Number of Batches per Product**	**Number of Brand to be collected**
Level 1.	**PUBLIC SECTOR**					
	REGIONAL REFERAL HOSPITAL					
	Antimalaria	Alu- Adult	Tablet	20/120mg	1	1
		Alu-Paediatrics	Tablet	20/120mg	1	1
		Quinine	Tablet	300mg	1	1
		Quinine	Syrup	50mg/5ml	1	1
		Artesunate	Injection	120mg	1	1
						5
	ARVs	Zidovudine + Lamivudine	Tablet	300/150mg	1	1
		Lopinavir + Ritonavir	Tablet	100/25mg	1	1
		Efavirenz (EFV)	Tablet	60mg	1	1
		Tenofovir + Lamivudine + Dolutegravir	Tablet	300mg/150mg/50mg	1	1
		Tenofovir+Emtricitabine+ Efaverenz	Tablet	300mg/200mg/600mg	1	1
						5
	Anti-TB	Rifampicin + Isoniazid, Pyrazinamide + Ethambutol (RHZE)	Tablet	150/75/400/275mg	1	1
		Rifampicin + Isoniazid (RH)	Tablet	150/75mg	1	1
		Rifampicin + Isoniazid + Ethambutol (RHE)	Tablet	150/75/275mg	1	1
		Levofloxacin	Tablet	500mg	1	1
		Rifampicin + Clofazimine + Dapson	Tablet	300/100/100mg	1	1
						5
		Expected number of batches/samples to be collected at Regional Hospital				**15**
	DISTRICT HOSPITAL					
	Antimalaria	Alu- Adult	Tablet	20/120mg	1	1
		Alu-Paediatrics	Tablet	20/120mg	1	1
		Quinine	Tablet	300mg	1	1
		Quinine	Syrup	50mg/5ml	1	1
		Artesunate	Injection	120mg	1	1

						5
	ARVs					
		Zidovudine + Lamivudine	Tablet	300/150mg	1	1
		Lopinavir + Ritonavir	Tablet	100/25mg	1	1
		Efavirenz (EFV)	Tablet	60mg	1	1
		Tenofovir + Lamivudine + Dolutegravir	Tablet	300mg/150mg/50mg	1	1
		Tenofovir+Emtricitabine+ Efaverenz	Tablet	300mg/200mg/600mg	1	1
						5
	Anti-TB					
		Rifampicin + Isoniazid, Pyrazinamide + Ethambutol (RHZE)	Tablet	150/75/400/275mg	1	1
		Rifampicin + Isoniazid (RH)	Tablet	150/75mg	1	1
		Rifampicin + Isoniazid + Ethambutol (RHE)	Tablet	150/75/275mg	1	1
		Levofloxacin	Tablet	500mg	1	1
		Rifampicin + Clofazimine + Dapson	Tablet	300/100/100mg	1	1
						5
		Expected number of batches/samples to be colected at district hospital				**15**
Level 2.	**PRIVATE SECTOR**					
	PRIVATE HOSPITAL REGIONAL					
	Antimalaria					
		Alu- Adult	Tablet	20/120mg	1	1
		Alu-Paediatrics	Tablet	20/120mg	1	1
		Quinine	Tablet	300mg	1	1
		Quinine	Syrup	50mg/5ml	1	1
		Artesunate	Injection	120mg	1	1
						5
	ARVs					
		Zidovudine + Lamivudine	Tablet	300/150mg	1	1
		Lopinavir + Ritonavir	Tablet	100/25mg	1	1
		Efavirenz (EFV)	Tablet	60mg	1	1
		Tenofovir + Lamivudine + Dolutegravir	Tablet	300mg/150mg/50mg	1	1
		Tenofovir+Emtricitabine+ Efaverenz	Tablet	300mg/200mg/600mg	1	1
						5
	Anti-TB					

		Rifampicin + Isoniazid, Pyrazinamide + Ethambutol (RHZE)	Tablet	150/75/400/275mg	1	1
		Rifampicin + Isoniazid (RH)	Tablet	150/75mg	1	1
		Rifampicin + Isoniazid + Ethambutol (RHE)	Tablet	150/75/275mg	1	1
		Levofloxacin	Tablet	500mg	1	1
		Rifampicin + Clofazimine + Dapson	Tablet	300/100/100mg	1	1
						5
		Expected number of batches/samples to be colected at district hospital				**15**
	PRIVATE PHARMACY AT REGION					
	Antimalaria					
		Alu- Adult	Tablet	20/120mg	1	1
		Alu-Paediatrics	Tablet	20/120mg	1	1
		Quinine	Tablet	300mg	1	1
		Quinine	Syrup	50mg/5ml	1	1
		Artesunate	Injection	120mg	1	1
		Expected number of batches/samples to be colected from Private Pharmcy				**5**
	DLDM AT DISTRICT					
	Antimalaria	Alu- Adult	Tablet	20/120mg	1	1
		Alu-Paediatrics	Tablet	20/120mg	1	1
		Quinine	Tablet	300mg	1	1
		Quinine	Syrup	50mg/5ml	1	1
		Artesunate	Injection	120mg	1	1
	Expected number of batches/samples to be colected from DLDM					**5**