Doc. No. TMDA/DMC/CTP/PMS/R/007

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

TMDA

Tanzania Medicines & Medical Devices Authority

POST MARKETING SURVEILLANCE (PMS) REPORT FOR SELECTED HUMAN AND VETERINARY MEDICINES CIRCULATING IN TANZANIA

2017/2018

Issue:8

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CONTENTS

Abbreviations

ADDO	Accredited Drug Dispensing Outlet.
FDC	Fixed Dose Combination.
MSD	Medical Store Department.
NCD	Non- Communicable Disease.
PIR	Product Information Review.
PMS	Post Marketing Surveillance.
TFDA	Tanzania Food and Drugs Authority.
TLC	Thin Layer Chromatography.
USP	United States Pharmacopeia
BP	British Pharmacopeia
UV	Ultra Violet Spectrophotometer.
WHO	World Health Organization.

Acknowledgements

The Post Marketing Surveillance (PMS) report of year 2017- 2018 presents the results of availability, distribution and quality of selected Human and Veterinary medicines circulating in the market. Preparation of this report would not have been possible without the commitment of TFDA staffs and various stakeholders at all levels of medicine distribution chain who worked closely to implement the two phases of the PMS program.

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Adam M. Fimbo
ACTING DIRECTOR GENERAL
TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

Executive summary

TMDA (previously known as TFDA) after a successful completion of previous PMS programs, is currently implementing another three (3) years PMS program (2017 to 2020) During the first year of implementation (2017/18), TFDA assessed the quality of selected human medicines namely Glimepiride tablets, Artemether Injection, Clotrimazole Vaginal Pessaries and veterinary medicines; Ivermectin Injection, Sulfadiazine and Trimethoprim , Trimethoprim and Sulfamethoxazole. Medicines were randomly sampled from ten (10) regions namely Dar es Salaam, Mwanza, Mbeya, Arusha, Morogoro, Mtwara, Pwani, Ruvuma, Tanga and Kilimanjaro.

Samples were systematically collected from both public and private hospitals, pharmacies, dispensaries, accredited drugs dispensing outlets (ADDOs), Medical Stores Department (MSD) and veterinary clinics.

A total of 102 samples of Human Medicines were collected from nine (9) regions where two (2) districts were randomly selected for each region. Out of 102 samples collected, 27.5 % (28/102) was Glimepiride tablets, 50% (51/102) was Clotrimazole V Pessaries and 22.5% (23/102) was Artemether injection. Most of human medicines samples were collected from Dar es Salaam region 25.5% (26/102) while fewest samples were collected from Kilimanjaro region 1.9% (2/102).

For Veterinary Medicines, samples were collected

from seven (7) regions namely Arusha, Dar es Salaam, Kilimanjaro, Morogoro, Pwani, Mwanza and Mbeya. Of all studied regions, Arusha was a leading region for collecting samples where 38% (26/68) of samples was collected followed by Kilimanjaro 27% (18/68) and Pwani was the least where only 4% (3/68) of samples was collected.

Collected samples (170) were subjected to product information review and showed that, most of samples had deficiencies relating to information on the label on the Primary, Secondary and Package insert. The main deficiency in human medicines was lack of Tanzania product registration number on the labels and package inserts (89.2%) (figure) followed by lack of date of publication on the package inserts (44.1%) (figure) and the least noted deficiency was storage condition on the label (1.0%). All samples had package insert.

A total of 102 (100%) collected samples [Glimepiride Tablets (28), Artemether Injection (23) and Clotrimazole Vaginal Pessaries (51)] were subjected to screening for disintegration, identification by UV and TLC tests and passed.

Subsequent laboratory analytical tests such as disintegration, assay and related impurities indicated compliance to the product specifications with exception of one (1) sample of Glimepiride tablets which did not conform to dissolution parameter and was subjected to regulatory action. These laboratory results are indicators of the existence of quality medicines in Tanzanian market which could be the outcome of the existing enforcement mechanism.

1. INTRODUCTION

The consistency of availability of good quality of medicines in the market has enhanced their rational use due to proper information to the patient as well as health professionals. Tanzania Food and Drugs Authority (TFDA) has three years (3) Post Marketing Surveillance (PMS) program of assessing and monitoring the quality of all medicines circulating in the market.

After successful completion of 2014-2017 PMS programs, TFDA implemented the first year (2017/18) of the fourth PMS program (2017/18 – 2019/20). The technique that are involved in the PMS process include; planning, training of sample collectors, sampling of the identified medicines as per the pre-arranged sampling plan, comprehensive review of the medicines information on the label and accompanied package inserts and laboratory quality control. The medicines which were included in the program were selected based on the established criteria which were monitored in phases. However, the previous PMS program has revealed that the techniques used are efficient and effective in identifying substandard and falsified medicine on the market.

The PMS program of year 2017-2018 was implemented through collection of samples of Human and Veterinary

Medicines. These samples were randomly collected from private and public hospitals, health centres and pharmaceutical outlets in two selected districts and municipal of ten (10) regions which included Dar es Salaam, Mwanza, Mbeya, Arusha, Morogoro, Mtwara, Pwani, Ruvuma, Tanga and Kilimanjaro.

Sampling was conducted by trained medicines inspectors in collaboration with local government pharmaceutical inspectors from respective districts and municipal councils of the aforementioned regions. After comprehensive product information review of the collected samples, laboratory analysis was done at TFDA - WHO prequalified laboratory. In this report, we have discussed results of the systematically assessed and monitored samples of the mentioned human and veterinary medicines.

2. OBJECTIVES

2.1 Broad Objective

To assess the quality of selected human and veterinary medicines circulating on the Tanzanian market for the period of July 2017 to June 2018

2.2 Specific Objectives

a) To assess the quality of collected samples of medicines
b) To disseminate information on the quality status of circulating medicines to all stakeholders.
c) To take relevant regulatory action(s) based on the outcome.
d) To identify areas of improvement in dossier review and inspection

3 METHODOLOGY

3.1 Medicine Selection

Selection of medicines monitored for quality was based on the following criteria

a) Medicines for treating non communicable diseases (NCDs);
b) Lifesaving medicines for women, children and

infants;

c) Medicines which have previously indicated poor quality and safety concern;

d) Veterinary medicines which are commonly used.

3.2 Sampling Sites

The selection of sampling sites was based on the following criteria:

a) Regions with frequent reports of substandard and counterfeit medicines;

b) Regions bordering neighbouring countries;

c) Regions with very hot and humid climate; and

d) Regions where the selected medicines were likely to be available and highly consumed

The identified samples were collected from different pharmaceutical outlets to include MSD, public and private hospitals, health centres, wholesalers and retail pharmacies, ADDOs, and veterinary medicines outlets.

3.3 Sampling

3.3.1 Samples Collection

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

A "sample" is defined as a number of units (i.e. same product name, manufacturer, dosage form, package size, packaging material and strength) representing the same batch and collected at the same location/outlet.

Samples were collected according to Standard Operating Procedure by trained medicine inspectors from TFDA 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**.

3.3.2 Handling of Collected Samples and Shipment

Each collected sample was coded according to prescribed coding format. Coding was done to identify samples collected from different regions and thus helped to differentiate and avoid mix up. Coded samples with

respective sampling form were kept in the labeled sampling bag and sealed. Before and after transportation of the samples to TFDA Laboratory, measures were taken to ensure that samples were stored according to manufacturers' recommended storage conditions as prescribed in the product labels.

3.4 Sample Analysis

3.4.1 Screening Testing (Tier I)

Screening testing involved Product Information Review (PIR), physical/visual inspection, disintegration test and identification test by Thin Layer Chromatography (TLC) and UV Spectrophotometer.

3.4.1.1 Product Information Review (PIR)

All samples were subjected to product information review (PIR). This involved the review of information contained on the primary and secondary packaging, package inserts and label of each sample of medicine for conformity to the TFDA approved appearance of the product and labeling requirement.

Apart from appropriateness and legibility of the information on the label and associated insert, appropriateness of the type of container used, stickiness and printing on the label were also checked. Observation for each sample reviewed was recorded in the screening form attached as **Annex III.**

34.1.2 Physical/visual inspections

Visual inspections were conducted so as to give information about product quality prior to further laboratory testing of samples in comparison with registration information.

Injectable solutions were examined for leakage, particles, homogeneity, fill volume and colour change. For the case of oral solid dosage forms colour change, spots, moulds, abrasions, and odour were checked.

3.4.1.3 Simple disintegration Test

Disintegration test was used to test the possibility of solid dosage form to break into small particles that can dissolve and undergo dissolution to release active pharmaceutical ingredient. This was done by using disintegration test machine. The tablets which did not disintegrate within 30 minutes indicated dissolution problems necessitating confirmatory testing.

3.4.1.4 Identification Test by Thin layer Chromatography

TLC method was used for quantitative determination of active ingredients, related substances and impurities present in the dosage form. This method employs the principle of comparing spots obtained between test and

reference solutions. The principal spot obtained with the test solution must correspond with the chromatographic runs of the lower and higher standard solutions in terms of colour, shape, size, intensity and retardation factor (R_f) value.

3.4.1.5 Identification Test by UV Spectrophotometer

UV Spectrophotometry is an analytical method used for quantitative determination of drug substance in pharmaceutical dosage form. The method employs spectrophotometry principle whereby maxima absorption wave length of the sample (test solution) is compared with maxima absorption of the standard solution.

3.4.2 Laboratory Confirmatory Testing (Tier II)

All samples that failed screening test, all samples with doubtful screening results and 10% of all passed samples were selected for confirmatory testing. Confirmatory testing was performed by analyzing each product as per Pharmacopoeia monograph requirements. Among the parameters checked during confirmatory testing were appearance, identification, disintegration, assay, dissolution, pH, weight variation and sterility. Table 2 below shows method of analysis used for parameters tested in each medicine.

Table 2: Method of analysis used for parameters tested in each medicine			
Medicine Category	**Product**	**Parameters tested**	**Analytical Method**
Human Medicines	Glimepiride	Identification Dissolution Content of Uniformity Assay Related substances	Japanese Pharmacopoeia
	Artemether Injection	Identification Assay Physical examination	International Pharmacopoeia
	Clotrimazole V Pessaries	Identification Dissolution Assay	BP
Veterinary Medicines	Ivermectin Injection	Clarity of solution Identification, Related Substance/ impurities, clarity of solution and Assay	USP
	Sulfadiazine and Trimethoprim	Identification Assay Physical examination	USP
	Trimethoprim and Sulfamethoxazole	Identification Assay Physical examination	USP

4. RESULTS

4.1 Sample collection

Based on the criteria used for selection of human and veterinary medicines, the following medicines were selected as shown in Table 1 below

Table 1: Medicines selected for quality assessment

Medicine Category	Product	Selection criteria
Human Medicines	Glimepiride	Antidiabetics (for treating non communicable diseases)
	Artemether Injection	Lifesaving medicines for women, children and infants.
	Clotrimazole-V	Medicines which have indicated poor quality and safety concern on the market
Veterinary Medicines	Ivermectin Injection	Veterinary Medicines
	Trimethoprim and Sulfamethoxazole	Veterinary Medicines
	Sulfadiazine and Trimethoprim	Veterinary Medicines

4.1.1 Human Medicines sample collection

Total of 102 samples of Human Medicines were collected during the year 2017/18 (Phase I and II), from nine (9) regions in which two (2) districts were randomly selected in

each region. Out of 102 samples collected, 27.5 % (28/102) was Glimepiride tablets, 50% (51/102) were Clotrimazole V Pessaries and 22.5% (23/102) were Artemether injection as summarized in Table 2

Table 2 : Number of Human Medicines Collected in 2017 - 2018 (Phase I & II)

Region	PHASE 1 (July – Dec 2017)	PHASE II (Jan – June 2018)		Total
	Antidiabetics	Anti-fungal	Anti-Malaria	
	Glimepiride	Clotrimazole-V	Artemether Injection	
Arusha	16			16
Dar es Salaam	8	11	7	26
Kilimanjaro	2	-	-	2
Mbeya	2	-	-	2
Mwanza	0	-	-	0
Mtwara	-	5	3	8
Pwani	-	11	4	15
Ruvuma	-	13	5	18
Tanga	-	11	4	15
Total	**28**	**51**	**23**	**102**
Percentage (%)	**27.5**	**50**	**22.5**	**100**

4.1.2 Veterinary Medicines

Samples of Veterinary Medicines were collected in both phase I and phase II, from seven (7) regions namely Arusha, Dar es Salaam, Kilimanjaro, Morogoro, Pwani, Mwanza

and Mbeya. Of these regions, Arusha was a leading region where 38% (26/68) of samples were collected followed by Kilimanjaro 27% (18/68) and Pwani was the least region where only 4% (3/68) of samples were collected. This is shown on the 3 below.

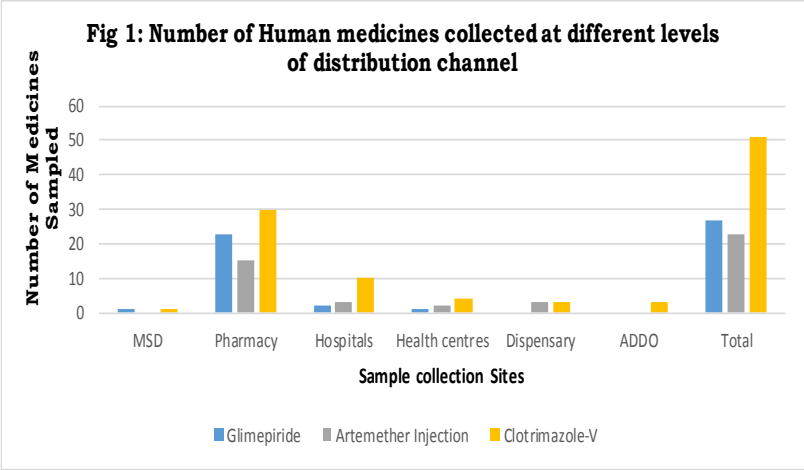
Table 3: Number of collected Veterinary Medicines samples

Region	Phase I (July – Dec 2017)	Phase II (Jan - Jun 2018)		Total (%)
	Ivermectin Injection	FDC of Trimethoprim/ Sulfamethoxazole	FDC of Sulfadiazine/ Trimethoprim	
Arusha	22	1	3	26 (38)
Dar es Salaam	3	0	3	6 (9)
Kilimanjaro	18	-	-	18 (27)
Mbeya	5	-	-	5 (7.4)
Morogoro	-	0	5	5 (7.4)
Mwanza	-	2	3	5(7.4)
Pwani	-	0	3	3 (4)
Total (%)	**48 (70)**	**3 (5)**	**17 (25)**	**68(100)**

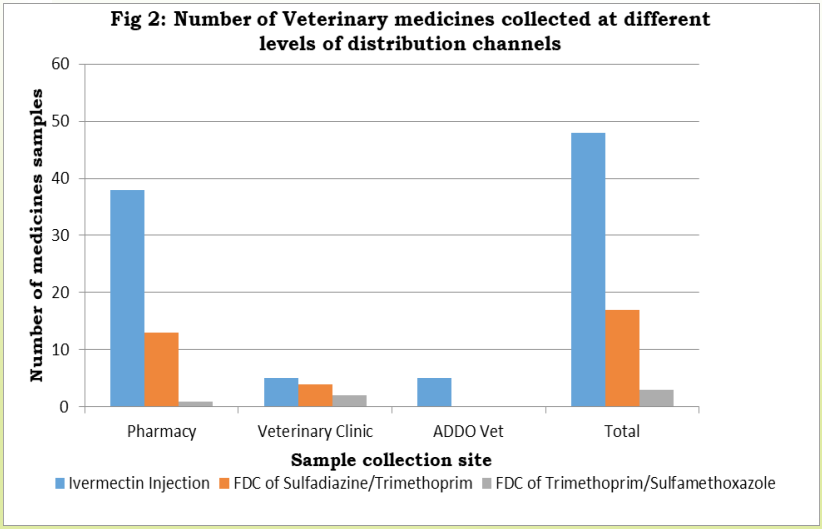
4.2 Samples Collection Sites

Figure 1 below shows, a total of 102 samples of Human Medicines which were sampled from different medicines distribution channel namely; MSD, Pharmacies, ADDOs, Dispensaries, Health Centres and Hospitals. The results show that, the high number of Human Medicines samples were collected from Pharmacies 66.7% (68/102) and the

least were sampled from ADDOs 2.9% (3/102).



Also, 68 samples of Veterinary Medicines were sampled from Veterinary Pharmacies, Veterinary Clinics and ADDOs Veterinary, and the majority of sampled medicines were collected from Veterinary Pharmacies 76.5% (52/68) while the least were sampled from ADDOs Veterinary 7.3% (5/68).



Majority of collected Samples of Human Medicines (Glimepiride, Artemether Injection and Clotrimazole Vaginal pessaries) and Veterinary Medicines (Ivermectin Injection, FDC of Sulfadiazine / Trimethoprim Injection) were imported from different manufacturers as shown in Table 4 below. Few samples were collected from domestic manufacturers.

Table 4: Human Medicines and Veterinary Medicines sampled with respective Manufacturer(s)

Product	Manufacturer	Country of origin
Glimepiride	Sanofi-Aventis South Africa (Pty) Ltd	South Africa
	CCL Pharmaceuticals (Pvt.) Ltd	Pakistan
	Micro Labs Ltd	India
	Sun Pharmaceutical Ind. Ltd	India
	Denk Pharma GmbH & Co	Germany
	Aurochem Pharmaceuticals (I) Pvt.Ltd	India
	Shin Poong Pharm Co.Ltd	Korea
	Cadila Pharmaceutical Ltd	India

Artemether Injection	Lincoln Pharmaceutical Ltd.	India
	KPC Pharmaceutical Inc.	China
	IPCA laboratories Ltd.	India
	Rotexmedica GmbH	Germany
	Dafra Pharma GmbH	Switzerland
	Kunming Pharmaceutical Ltd.	China
	Plethico Pharmaceuticals Ltd.	India
Clotrimazole-V	Astra Life Care (India) Pvt, Ltd.	India
	Aurochem Pharmaceuticals Ltd.	India
	Elys Chemical Industries Ltd.	Kenya
	Glenmark Pharmaceuticals Ltd.	India
	Laboratory&allied ltd.	Kenya
	Universal Corporation Ltd.	Kenya
Sulfadiazine and Trimethoprim	Laprovet BP. 67562 Tours Ltd.	France
	Laprovet BP. 37075 Cedex Ltd.	France
	Under Licenced Vetcare Africa Ltd.	Kenya
	Inter Chemie Werken B.V Ltd.	Holland
	Kulpersweg Ltd.	Holland
	Fabrication Kela Ltd.	Belgium
	Ashish Life Science Pvt Ltd.	India
	Kepro B.V Devernter Ltd.	Holland
	Farmers Center Ltd.	Tanzania
	Kela N.V Ltd.	Belgium
Trimethoprim and Sulfamethoxazole	Nerix Pharma Ltd.	Kenya
	Laprovet BP. 67562 Tours Ltd.	France

Ivermectin Injection	Chongqing Fangtong Animal Pharm Co.Ltd	China
	Ceva Sante Animale, La Ballastie're	France
	Alfasan Woerden	Holland
	Hebei Yuanzhung Pharmaceutical Company Ltd	China
	Anguin Nutrition Product Company	United Kingdom
	Kela N.V. sint-lenaartseweg	Belgium
	Anupco Anglian Nutrition Product Co.	United Kingdom

None of sampled human medicines were domestically manufactured while 4.4% of Veterinary medicines (FDC of Sulfadiazine/Trimethoprim Injection) were domestically manufactured. Most of Human Medicines sampled were imported from India 41.2% (42/102) and 44.0%

(30/68) of Veterinary Medicines sampled were imported from China as shown on the Table 5 below.

Table 5: Percentage of sampled Human Medicines and Veterinary Medicines that were imported and Domestically Manufactured

Type of product	Total	Domestically manufactured	Percentage (%)	Imported	Foreign manufactured (Country of origin)	Percentage (%)
Human Medicines						
Glimepiride	28	0	0	18	India	17.6
				4	Germany	3.9
				3	Pakistan	2.9
				2	Korea	2.0
				1	South Africa	1.0
Clotrimazole-V	51			36	Kenya	35.3
				15	India	14.7
Artemether Injection	23			9	India	8.8
				2	Germany	2.0
				10	China	9.8
				2	Switzerland	2.0
Total	**102**	**0**	**0**	**102**		**100**

Veterinary Medicines						
Ivermectin Injection	48	0	0	30	China	44.0
				10	France	15.0
				2	U.K	3.0
				2	Belgium	3.0
				4	Holland	6.0
Sulfadiazine and Trimethoprim	17	3	4.4	2	India	3.0
				6	France	9.0
				4	Belgium	6.0
				5	Holland	7.0
Trimethoprim and Sulfamethoxazole	3	0	0	3	Kenya	4.0
Total	**68**	**3**	**4.4**	**68**		**100.0**

4.3 Screening Results

4.3.1 Product Information Review Results

A total of 170 collected samples (102 for human medicines and 68 for veterinary medicines) were subjected to Product Information Review (PIR) in terms of required information on the label in the Primary and Secondary containers, and Package insert.

The results showed that, most of samples reviewed had deficiencies on the label on the Primary and Secondary

container as well as the Package insert.

The main deficiency observed in human medicines was lack of Tanzania Registration Number on the label and package insert (89.2%) followed by lack of date of publication on the package insert (44.1%) and the least noted deficiency was storage condition on the label (1.0%). All samples were observed to have package inserts. The outcome/results of PIR is summarized in Table 6 below:

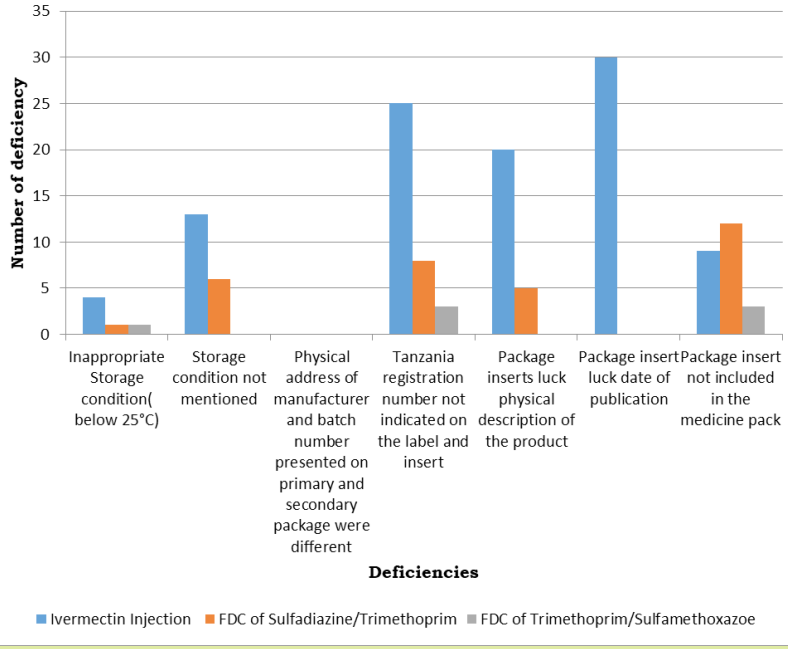
Table 6: PIR Results for Samples of Human Medicines

Problems/deficiency	Glimepiride	Artemether Injection	Clotrimazole-V	Total	% Based on total number of samples (102)
Inappropriate Storage condition (below 25°C)	0	0	1	1	1.0
Storage condition not mentioned	12	4	2	18	17.6
Physical address of manufacturer & batch number presented on primary and secondary package were different	2	0	0	2	1.9
Tanzania registration number not indicated on the label and insert	25	22	44	91	89.2
Package inserts lack physical description of the product	13	7	22	42	41.2
Package insert lack date of publication	22	10	13	45	44.1

Package insert not included in Medicine pack	0	0	0	0	

Out of 68 samples of the veterinary medicines reviewed for their information on the label and associated package insert, majority 52.9% (36/68) failed to indicate Tanzanian registration number on the label and package insert and 44.1% (30/68) lacked date of publication on the insert. All collected samples of veterinary medicines were found to have consistence information on the physical address of the manufacturer and batch number in the primary, secondary and package inserts. This is shown in Figure 3 below.

Fig 3: PIR Results for samples of Veterinary Medicines



4.3.2 Results for Physical description

All collected samples of Human Medicines (102) and Veterinary Medicines (68) which were subjected for screening by visual inspection passed the test.

4.3.3 Results of Disintegration and Identification Test

Collected Samples of Ivermectin Injection (48), FDC of Trimethoprim/Sulfamethoxazole (3) and FDC of Sulfadiazine/Trimethoprim (17) passed the screening test for identification by Thin Layer Chromatograph (TLC).

A total number of 102 (100%) samples of Glimepiride Tablets (28), Artemether Injection (23) and Clotrimazole Vaginal Pessaries (51) samples which were subjected to screening for disintegration and identification by UV and TLC passed the tests.

4.4 Confirmatory Testing Results

Based on selection criteria, a total of 18 samples (10 from Human Medicines and 8 from Veterinary Medicines) were taken for confirmatory testing as shown in the table 7a below.

Table 7a: Number of Samples Selected for Confirmatory Testing

Category of medicine	Product name	Samples Collected	Samples Screened		Samples selected
			Passed	10% of the passed	
Human medicines	Glimepiride	28	28	2.8	3
	Artemether Injection	23	23	2.3	2
	Clotrimazole-V	51	51	5.1	5
	Total	**102**	**102**	**10.2**	**10**
Veterinary medicines	Ivermectin Injection	48	48	4.8	5
	Sulfadiazine and Trimethoprim	17	17	1.7	2
	Trimethoprim and Sulfamethoxazole	3	3	0.3	1
Total		**68**	**68**	**6.8**	**8**

Table 7b: Laboratory confirmatory Test Results for Human and veterinary Medicines										
(i) Human Medicines										
Types of medicines	**Identification**		**Physical Examination**		**Dissolution**		**Assay**		**Related substance**	
	P	**F**	**P**	**F**	**P**	**F**	**P**	**F**	**P**	**F**
Artemether injection	2	0	2	0	2	0	2	0	2	0
Clotrimazole -V	5	0	5	0	5	0	5	0	5	0
Glimepiride	3	0	3	0	2	1	3	0	3	0
(ii) Veterinary Medicines										
Ivermectin Injection	5	0	5	0	5	0	5	0	5	0
Sulfadiazine and Trimethoprim	2	0	2	0	2	0	2	0	2	0
Trimethoprim and Sulfamethoxazole	1	0	1	0	1	0	1	0	1	0

NB: P= Passed, F= Failed

All samples of human and veterinary medicines passed the confirmatory test parameters with exception of Glimepiride tablets in which 33% (1/3) failed dissolution testing parameter by having dissolution rate of 49.7% (Limit NLT 70%±5% and mean NLT 55%).

Plan includes collection of samples for Telmisartan/HTZ. However, samples were not collected and not discussed.

5. DISCUSSION

The 2017/2018 results of PMS from both human and veterinary medicines surveys showed that less number of human medicines 26.50% (102/385) and veterinary medicines 37.8% (68/180) of targeted sample were collected. This was due to unavailability of selected medicines from sampled and studied pharmaceutical outlets. Similar findings were observed in the previous studies and PMS programme reports [1, 2].

Human medicines sampled were prescription only medicine and large quantity of medicines were sampled in Pharmacies while the least were from ADDO shops. Survey results also indicate private sites such as pharmacies located in cities were more stocked with many medicines including those for management of non-communicable disease as compared to rural areas. Similar findings were reported in previous surveys conducted in Kenya and

Tanzania [2, 3, 4, 5]. Similarly, all veterinary medicines were from private pharmaceutical outlets since currently there is no public supply mechanism for veterinary medicines.

In both Phase I and II, the majority of human medicines samples were collected from Dar es Salaam 25.5% (26/102) followed by Ruvuma region 17.6% (18/102) and Mbeya and Kilimanjaro regions contributed only 1.9% each (2/102). Most of Veterinary Medicines were collected from Arusha region 38% (26/68) followed by Kilimanjaro region 27% (18/68) while Pwani region contributed the least 4% (3/68). Dar es Salaam region has high business volume of pharmaceuticals while Arusha and Kilimanjaro regions located in northern Tanzania are famous in livestock keeping which contributes to high availability of veterinary medicines in these regions [1].

Of all samples of human, clotrimazole vaginal pessaries were mostly collected to form half (50%) medicines collected. This medicine is readily available, with high demand and categorized as Over the Counter (OTC) which enables the product to be available in all pharmaceutical outlets. This could be due to scheduling regulations of selected medicines to be dispensed in pharmacy only [2].

Noncompliance of human medicines samples to the labeling requirements was on the higher side 89.2% while majority of samples are veterinary medicines 52.9% (36/68)

lacked Tanzanian registration number on the label and of package insert 44.1% (30/68) lacked date of publication on the insert. Significant failure to adhere with labeling requirements and information presented on the package insert observed in this survey could result into irrational use and poor storage conditions which may cause treatment failure [6, 7]. This may increase the burden of diseases as well as healthcare budget in Tanzania due to use of ineffective medicines [8].

As noted earlier in the previous PMS surveys, large quantity of the surveyed samples for human (100%) and veterinary medicines (95.6%) were imported. Majority of human medicines were imported from India 41.2% (42/102) followed by Kenya 35.3% (36/102)), while veterinary medicines were from China 44% (30/68) followed by France 24% (15/68). This is justified by the fact that domestic manufacturing facilities in Tanzania still have low capacity (20-30%) to serve the country's medicines demand [9,10]. Poor compliance to labelling requirements may be attributed by the fact that majority of these products are imported and some foreign manufacturers are reluctant to abide to labeling requirements. Some of the possible reasons being provided are that during production phase, batches are non country specific and that manufacturers tend to produce large batches for regional market because demand per country is usually small [11].

Evaluation of physical description of all collected samples depicts the critical role done by inspectors in quick identification of the presumptive counterfeit product especially at the official ports of entry. In this study, 100% compliance to the visual screening indicates existence of proper control mechanism in the import's inspection control for all imported products.

In addition, subsequent laboratory analytical tests such as disintegration tests, assay and related impurities indicate compliance to the product specifications. One (1) sample which did not conform to dissolution parameter was subjected to regulatory action. Such situation clearly proves the existence of quality medicines in Tanzanian market which could be the outcome of the existing enforcement mechanism and robust medicines regulatory system.

6. REGULATORY ACTION TAKEN

The following regulatory actions were taken by TFDA:

6.1 Identified poor quality batches of Glimepride tablets were withdrawn from the market. In addition, the manufacturer was directed to conduct thorough investigation on the batches which failed confirmatory reports.

6.2 Importation of future batches of the identified poor-quality product was suspended until after

manufacturer has submitted investigation report.

6.3 All manufactures whom their medicines failed product information review (PIR) were directed to rectify the anomalies identified during the PIR evaluation.

7. CONCLUSION

The survey has revealed significant number of samples of both human and veterinary 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 TFDA in the year 2014-2017. Though TFDA is taking action for the specific products identified, more efforts are required to enforce labelling and product information requirements. Proper and regular inspection at ports of entry is of paramount important to identify medicines which are not adhering with labelling requirements before being allowed into the country.

Moreover, presence of some substandard medicines on the market as evidenced in this survey call for 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.

8.1 Marketing authorization holder should be reminded to comply with labelling requirements.

8.2 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.

8.3 Laboratory consumables and reagents should be purchased and in time so that implementation plans is not affected.

8.4 Reviewer of product information should be trained so as to avoid improper recording of deficiencies observed during product information review.

9. LIMITATIONS

Limitations encountered during planning, implementation, analysis and writing up of the report include;

a) Difficult in tracing some dossiers and registration samples for comparison during product information review;

b) Limited capacity of TFDA Quality Control Laboratory

which caused delay of analytical results

c) Lack of some laboratory consumables and/or reagents for testing collected samples.

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11. Guidelines for Good Manufacturing Practices (GMP - 2008)

Annex I: Sampling Plan

SAMPLING PLAN FOR YEAR 2017/18 (PHASE I & II)

1.1a: SAMPLING PLAN FOR CONDUCTING PMS OF TELMISARTAN/HYDROCHLORTHIAZIDE AND GLIMEPIRIDE IN ARUSHA, KILIMANJARO, MBEYA, MWANZA AND AND DAR-ES-SALAAM REGIONS

Sampling sites	Product Category	Product	Dosage Form	Strength	Number of brand to be collected	Number of batch per brand to be collected	Unit Pack	Number of unit pack per batch to be collected	Total number of samples to be collected	Unit cost	Total cost
Level 1: Regional											
MSD Retail Pharmacy	Antihypertensive	Telmisartan/ hydrochlorothiazide	Tablets	80mg/ 12.5mg	2	1	P/30	5	10	40,000	400,000
	Antidiabetics	Glimepiride	Tablets	2mg	2	1	P/30	5	10	10,000	100,000
Importer	Antihypertensive	Telmisartan/ hydrochlorothiazide	Tablets	80mg/ 12.5mg	2	1	P/30	5	10	40,000	400,000
	Antidiabetics	Glimepiride	Tablets	2mg	2	1	P/30	5	10	10,000	100,000

Wholesaler	Antihypertensive	Telmisartan/ hydrochlorothiazide	Tablets	80mg/ 12.5mg	2	1	P/30	5	10	40,000	400,000
	Antidiabetics	Glimepiride	Tablets	2mg	2	1	P/30	5	10	10,000	100,000
Retail Pharmacy	Antihypertensive	Telmisartan/ hydrochlorothiazide	Tablets	80mg/ 12.5mg	2	1	P/30	5	10	40,000	400,000
	Antidiabetics	Glimepiride	Tablets	2mg	2	1	P/30	5	10	10,000	100,000
Private hospital	Antihypertensive	Telmisartan/ hydrochlorothiazide	Tablets	80mg/ 12.5mg	2	1	P/30	5	10	40,000	400,000
	Antidiabetics	Glimepiride	Tablets	2mg	2	1	P/30	5	10	10,000	100,000
Sub total					**20**						**2,500,000**

Level 2: Districts

District 1

Wholesaler Pharmacy	Antihypertensive	Telmisartan/ hydrochlorothiazide	Tablets	80mg/12.5mg	2	1	P/30	5	10	40,000	400,000
	Antidiabetics	Glimepiride	Tablets	2mg	2	1	P/30	5	10	10,000	100,000

Retail Pharmacy	Antihypertensive	Telmisartan/ hydrochlorothiazide	Tablets	80mg/12.5mg	2	1	P/30	5	10	40,000	400,000
	Antidiabetics	Glimepiride	Tablets	2mg	2	1	P/30	5	10	10,000	100,000
Private hospital	Antihypertensive	Telmisartan/ hydrochlorothiazide	Tablets	80mg/12.5mg	2	1	P/30	5	10	40,000	400,000
	Antidiabetics	Glimepiride	Tablets	2mg	2	1	P/30	5	10	10,000	100,000
Sub total					**12**						**1,500,000**
District 2											
Wholesaler Pharmacy	Antihypertensive	Telmisartan/ hydrochlorothiazide	Tablets	80mg/12.5mg	2	1	P/30	5	10	40,000	400,000
	Antidiabetics	Glimepiride	Tablets	2mg	2	1	P/30	5	10	10,000	100,000
Retail Pharmacy	Antihypertensive	Telmisartan/ hydrochlorothiazide	Tablets	80mg/12.5mg	2	1	P/30	5	10	40,000	400,000
	Antidiabetics	Glimepiride	Tablets	2mg	2	1	P/30	5	10	10,000	100,000
Private hospital	Antihypertensive	Telmisartan/ hydrochlorothiazide	Tablets	80mg/12.5mg	2	1	P/30	5	10	40,000	400,000
	Antidiabetics	Glimepiride	Tablets	2mg	2	1	P/30	5	10	10,000	100,000

Sub total	**12**						**1,500,000**
Grand Total per region							**5,500,000**
Grand Total per region 4 regions							**22,000,000**
Expected number of batches/samples to be collected from districts and region level	**44**						
Expected number of samples to be collected from 4 regions (i.e 44 x 5)	**220**						
*** depends on the availability of MSD zone in respective region*							

1.1b: SAMPLING PLAN FOR CONDUCTING PMS OF IVERMECTIN 1% INJECTION IN ARUSHA, MBEYA, KILIMANJARO AND DAR ES SALAAM REGIONS

Sampling sites	Product Category	Product	Dosage Form	Strength	Number of brand to be collected	Number of batch per brand to be collected	Unit Pack	Number of unit pack per batch to be collected	Total number of samples to be collected	Unit cost	Cost
Level 1: Regional											
Importer/ Wholesale pharmacy	Tripanocide	Ivermectin	injection	10mg/ml	2	1	20ml/ bottle	15	30	6,000	180,000
Retail pharmacy/ Veterinary Shops	Tripanocide	Ivermectin	injection	10mg/ml	2	1	20ml/ bottle	15	30	6,000	180,000
Private Veterinary Clinic	Tripanocide	Ivermectin	injection	10mg/ml	2	1	20ml/ bottle	15	30	6,000	180,000

Open Market/ Auctions	Tripanocide	Ivermectin	injection	10mg/ml	2	1	20ml/ bottle	15	30	6,000	180,000
Sub total											**720,000**
level 2: Districts											
District 1											
Retail pharmacy	Tripanocide	Ivermectin	injection	10mg/ml	2	1	20ml/ bottle	15	30	6,000	180,000
ADDO Veterinary Shop	Tripanocide	Ivermectin	injection	10mg/ml	2	1	20ml/ bottle	15	30	6,000	180,000
Open Market/ Auctions	Tripanocide	Ivermectin	injection	10mg/ml	2	1	20ml/ bottle	15	30	6,000	180,000
Sub total											**540,000**
District 2											
Retail pharmacy	Tripanocide	Ivermectin	injection	10mg/ml	2	1	20ml/ bottle	15	30	6,000	180,000
ADDO Veterinary Shop	Tripanocide	Ivermectin	injection	10mg/ml	2	1	20ml/ bottle	15	30	6,000	180,000
Open Market/ Auctions	Tripanocide	Ivermectin	injection	10mg/ml	2	1	20ml/ bottle	15	30	6,000	180,000
Sub total											**540,000**
Grand Total per region											**1,800,000**
Grand Total per 4 regions											**7,200,000**
	Expected number of batches to be collected from Regional and District Level)				**20**						
	Total number of samples to be collected from 4 regions (i.e 20 x 4)				**80**						

1.2a: SAMPLING PLAN FOR CONDUCTING PMS OF ARTEMETHER INJECTION AND CLOTRIMAZOLE VAGINAL PESSARIES IN TANGA, COAST, MTWARA, RUVUMA AND DAR-ES-SALAAM REGIONS

Sampling sites	Product Category	Product	Dosage Form	Strength	No. of brand to be collected	No of batch per brand to be collected	Unit Pack	No. of unit pack per batch to be collected	Total No. of samples to be collected	Unit cost	Total cost
Level 1: Regional											
**MSD Retail Pharmacy	Antimalarial	Artemether	injection	40mg/2ml	2	1	vial	40	80	7,000	560,000
	Antifungal	Clotrimazole vaginal pessaries	tablets	100mg	2	1	P/6 tabs	25	50	6,000	300,000
Importer / Wholesaler	Antimalarial	Artemether	injection	40mg/2ml	2	1	vial	40	80	7,000	560,000
	Antifungal	Clotrimazole	vaginal pessaries	100mg	2	1	P/6 tabs	25	50	6,000	300,000
Regional/ Referal hospital	Antimalarial	Artemether	injection	40mg/2ml	2	1	vial	40	80		
	Antifungal	Clotrimazole vaginal pessaries	vaginal pessaries	100mg	2	1	P/6 tabs	25	50		-
Retail Pharmacy	Antimalarial	Artemether	injection	40mg/2ml	2	1	vial	40	80	7,000	560,000
	Antifungal	Clotrimazole	vaginal pessaries	100mg	2	1	P/6 tabs	25	50	6,000	300,000

Private hospital	Antimalaria	Artemether	injection	40mg/2ml	2	1	vial	40	80	7,000	560,000
	Antifungal	Clotrimazole	vaginal pessaries	100mg	2	1	P/6 tabs	25	50	6,000	300,000
Sub total					**20**						**3,440,000**
Level 2: Districts											
District 1											
District hospital	Antimalarial	Artemether	injection	40mg/2ml	2	1	vial	40	80		
	Antifungal	Clotrimazole	vaginal pessaries	100mg	2	1	P/6 tabs	25	50		

Retail Pharmacy	Antimalarial	Artemether	injection	40mg/2ml	2	1	vial	40	80	7,000	560,000
	Antifungal	Clotrimazole	vaginal pessaries	100mg	2	1	P/6 tabs	25	50	6,000	300,000
Private hospital/ Faith based organisation	Antimalarial	Artemether	injection	40mg/2ml	2	1	vial	40	80	7,000	560,000
	Antifungal	Clotrimazole	vaginal pessaries	100mg	2	1	P/6 tabs	25	50	6,000	300,000
Sub total					**12**						**1,720,000**
District 2											

District hospital	Antimalarial	Artemether	injection	40mg/2ml	2	1	vial	40	80		
	Antifungal	Clotrimazole	vaginal pessaries	100mg	2	1	P/6 tabs	25	50		
Retail Pharmacy	Antimalarial	Artemether	injection	40mg/2ml	2	1	vial	40	80	7,000	560,000
	Antifungal	Clotrimazole	vaginal pessaries	100mg	2	1	P/6 tabs	25	50	6,000	300,000
Private hospital/ Faith based organisation	Antimalarial	Artemether	injection	40mg/2ml	2	1	vial	40	80	7,000	560,000
	Antifungal	Clotrimazole	vaginal pessaries	100mg	2	1	P/6 tabs	25	50	6,000	300,000
Sub total					**12**						**1,720,000**
Grand Total per region											**6,880,000**
Grand Total per region 4 regions											**27,520,000**
	Expected number of batches/samples to be collected from districts and region level				**44**						
	Expected number of samples to be collected from 5 regions (i.e 44 x 5)				**220**						
*** depends on the availability of MSD zone in respective region*											

1.2b: SAMPLING PLAN FOR CONDUCTING PMS OF SULFAMETHOXAZOLE/TRIMETHOPRIM ORAL POWDER IN ARUSHA, COAST, MWANZA, MOROGORO AND DAR ES SALAAM REGIONS

Sampling sites	Product Category	Product	Dosage Form	Strength	Number of brand to be collected	Number of batch per brand to be collected	Unit Pack	Number of unit pack per batch to be collected	Total number of samples to be collected	Unit cost	Cost
Level 1: Regional											
Importer/ Wholesale pharmacy	Tripanocide	Sulfamethoxazole/ trimethoprim 40 + 200 mg/ml	Powder for oral use	10mg/ml	2	2	Sachets of 100g	10	20	10,000	200,000
Retail pharmacy/ Veterinary Shops	Tripanocide	Sulfamethoxazole/ trimethoprim 40 + 200 mg/ml	Powder for oral use	10mg/ml	2	2	Sachets of 100g	10	20	10,000	200,000
Private Veterinary Clinic	Tripanocide	Sulfamethoxazole/ trimethoprim 40 + 200 mg/ml	Powder for oral use	10mg/ml	2	2	Sachets of 100g	10	20	10,000	200,000
Open Market/ Auctions	Tripanocide	Sulfamethoxazole/ trimethoprim 40 + 200 mg/ml	Powder for oral use	10mg/ml	2	2	Sachets of 100g	10	20	10,000	200,000
Sub total											**800,000**
level 2: Districts											
District 1											

Retail pharmacy	Tripanocide	Sulfamethoxazole/ trimethoprim 40 + 200 mg/ml	Powder for oral use	10mg/ml	2	2	Sachets of 100g	10	20	10,000	200,000
ADDO Veterinary Shop	Tripanocide	Sulfamethoxazole/ trimethoprim 40 + 200 mg/ml	Powder for oral use	10mg/ml	2	2	Sachets of 100g	10	20	10,000	200,000
Open Market/ Auctions	Tripanocide	Sulfamethoxazole/ trimethoprim 40 + 200 mg/ml	Powder for oral use	10mg/ml	2	2	Sachets of 100g	10	20	10,000	200,000
Sub total											**600,000**
District 2											
Retail pharmacy	Tripanocide	Sulfamethoxazole/ trimethoprim 40 + 200 mg/ml	Powder for oral use	10mg/ml	2	2	Sachets of 100g	10	20	10,000	200,000
ADDO Veterinary Shop	Tripanocide	Sulfamethoxazole/ trimethoprim 40 + 200 mg/ml	Powder for oral use	10mg/ml	2	2	Sachets of 100g	10	20	10,000	200,000
Open Market/ Auctions	Tripanocide	Sulfamethoxazole/ trimethoprim 40 + 200 mg/ml	Powder for oral use	10mg/ml	2	2	Sachets of 100g	10	20	10,000	200,000
Sub total											**600,000**
Grand Total per region											**2,000,000**
Grand Total per 5 regions											**8,000,000**
	Expected number of batches to be collected from Regional and District Level)				**20**						
	Total number of samples to be collected from 5 regions (i.e 20 x 5)				**100**						

Annex II: Sample Collection Form

TFDA Tanzania Food & Drugs Authority	**MEDICINES POST MARKETING SURVEILLANCE SAMPLE COLLECTION FORM**	**TFDA/DMC/ CTP/F/002 Rev #:0**

1. Sample code: .....

   (Region/product/sequence number/sampling date ddmmyy)***

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.No	Name	Organization	Signature	Date

Note: Samples collected must remain in their original containers.

Annex III: Screening Form

TANZANIA FOOD AND DRUGS AUTHORITY DIRECTORATE OF LABORATORY SERVICES MEDICINES QUALITY ASSURANCE CENTERS

Compliance with the basic requirements for information accompanying the product and report on Minilab testing

Product name:_____

INNs:_____

1- External packaging	**Information present on the label**
Product name	YES NO
INN	YES NO
Strength	YES NO
Batch number	YES NO
Expiry date	YES NO
Manufacturer Name & Physical address	....
Storage conditions	.....

2- Primary packaging	**Information present on the label**
Product name	YES NO
Strength	YES NO
Unit dose per blister or container stated	YES NO

Batch number	YES NO
Expiry date	YES NO
Manufacturer name (specify only if different from the external packaging under point 1)	 YES NO .....

3- Package leaflet	
Presence of the leaflet	YES NO
Language(s) of the leaflet	.....
Composition	YES NO
Manufacturer name & physical address (specify only if different from the external packaging under point 1)	YES NO ....
Storage conditions (specify only if different from the external packaging under point 1)	YES NO ....

4- Observation on any discrepancy between the above points 1, 2 or 3 or non-compliance, if any

5- Report on Minilab testing:

PHYSICAL/VISUAL INSPECTION TEST	
Description of dosage form	
Shape (circular, oval, flat sides, other)	
Uniformity of shape	
Uniformity of color	
No physical damage (cracks, breaks, erosion, abrasion, sticky)	
Other observations (no foreign contaminant, dirty marks, proper seal - for capsule)	
DISINTEGRATION TEST	
Time of complete Time in minute of complete Did the drug pass Disintegration expected disintegration observed disintegration test? (30 minutes for uncoated tablet) ---------- Yes No	
RESULT OF TLC TEST (see Appendix 2 for TLC result interpretation)	

Rf Standard (---): ---------- Rf Standard (---): ---------- Rf Standard (---): ---------- Rf Standard (---): ---------- Rf Sample (1): ---------- Rf Sample (2): ---------- Rf Sample (3): ---------- Rf Sample (4): ----------	Did the drug and the standard Spots have the same intensity? ---------- Was there any contaminant spot on TLC? ----------	Did The sample pass quality by using the TLC Test? Yes No

FINAL COMMENTS

The sample conformed with basic testing specifications

The sample not-conformed with basic quality testing

(Reason:.....)

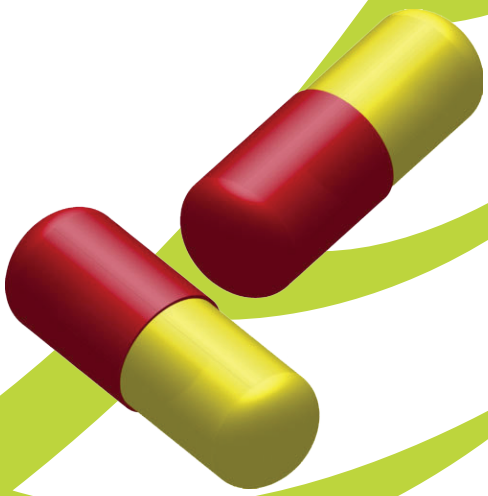
The sample is doubtful for its basic quality testing

(Reason:.....)

REPORT PREPARED BY:	REPORT REVIEWED BY:
Date:	Date: .....
Name:	Name: .....
Signature:	Signature:.....
ACTION TO BE TAKEN BY THE SUPERVISOR OF MEDICINES QUALITY ASSURANCE CENTER1	
Report the result to TFDA Date of report ..... Signature.....	Send the remaining sample units together with this Form to the TFDA QC lab for further testing Date..... Signature.....
Reasons given for the chosen action: --- --- ---	

(Footnotes)

1 Action to be taken and communication between should be dependent on country's rules and regulations.



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