

# Quality of Selected Anti-Retroviral Medicines: Tanzania Mainland Market As A Case Study

**Sophia Mziray**

Tanzania Medicines and Medical devices Authority

**BETTY MAGANDA** (✉ [bettynjau7@gmail.com](mailto:bettynjau7@gmail.com))

Muhimbili University of Health and Allied Sciences School of Pharmacy <https://orcid.org/0000-0001-8932-3882>

**Kissa Mwamwitwa**

Tanzania Medicines and Medical Devices Authority

**Adam M. Fimbo**

Tanzania Medicines and Medical Devices Authority

**Seth Kisenge**

Tanzania Medicines and Medical Devices Authority

**Gerald Sambu**

Tanzania Medicines and Medical Devices Authority

**Yonah H. Mwalwisi**

Tanzania Medicines and Medical Devices Authority

**Adonis Bitegeko**

Tanzania Medicines and Medical Devices Authority

**Emmanuel Alphonse**

Tanzania Medicines and Medical Devices Authority

**Akida Khea**

Tanzania Medicines and Medical Devices Authority

**Danstan H. Shewiyo**

Tanzania Medicines and Medical Devices Authority

**Eliangiringa Kaale**

Muhimbili University of Health and Allied Sciences School of Pharmacy

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## Research article

**Keywords:** Medicines quality, Substandard, Falsified, Post market surveillance, antiretroviral medicines, Patient information leaflet

**Posted Date:** September 11th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-18179/v2>

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## Abstract

**Background:** Antiretroviral drugs (ARVs) have significantly reduced morbidity, mortality and improved the quality of life of people living with HIV infection. Poor quality ARVs may result in harmful consequences such as adverse drug reactions, treatment failure, and prolonged illness, development of drug resistant strains and sometimes death, which in turn may undermine the healthcare delivery system. Thus, to ensure optimal treatment outcomes, medicines quality control must be undertaken regularly. This study was aimed at evaluating the quality of ARVs circulating on the Tanzania Mainland market.

**Methods:** This was a survey study. ARVs samples were collected in 20 regions of Tanzania Mainland, between 2012 and 2018. All collected samples were subjected to screening testing using the Global Pharma Health Fund® Mini-Lab kits. Sampled ARV's that failed screening test or yielded doubtful results and ten percent (10%) of all that complied with the screening test requirements were selected for full quality control testing in the World Health Organisation prequalified laboratory at Tanzania Medicines and Medical Devices Authority (TMDA). Samples collected from the medicine distribution outlets were also subjected to product information review.

**Results:** A total of 2,630 samples were collected, of which 83.7% (2200/2630) were from port of entry (POEs). Of the 2200 samples screened, all conformed to the specifications, except of the fixed dose combination (FDC) lopinavir/ritonavir 0.27% (7/2630) and lamivudine/zidovudine/nevirapine 0.27% (7/2630) that failed the disintegration test. Also, of the 100 samples selected for full quality control testing, 3% of them failed to comply with the specifications, of which FDC stavudine/lamivudine/nevirapine failed disintegration and assay tests 2% (2/100) and 1% (1/100), respectively. Samples failing the assay test had low content of stavudine (86.6%) versus specification limits (90% -110%). Out of the 430 samples which were subjected to product information review, 25.6% (110/430) failed to comply with the packaging and labelling requirements.

**Conclusion:** The quality of majority of ARVs circulating on the Tanzania Mainland market was good but, significant deficiencies on labelling and packaging were observed. These results call for continuous monitoring of quality of medicines circulating on the Tanzania market.

## Background

Human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) are still major global health problem particularly in sub-Saharan Africa [1, 2]. Globally, HIV/AIDS has remained one of the leading causes of morbidity in the last three decade [3, 4, 5]. The prevalence of HIV/AIDS amongst Tanzanian aged between 15-64 years is 5% [1, 4]. According to UNAIDS and World Health Organization (WHO) reports, 21.7 million HIV-infected patients are currently, accessing antiretroviral therapy (ART) worldwide [1-3], with about 1.2 million of them residing in Tanzania [4]. The ART have significantly reduced morbidity and mortality, by preventing relapse and opportunistic infections and has lowered the risk of HIV transmission. [6, 7]. Specifications to measure the quality of medicines are defined by their manufacturers. Thus, medicines quality, are built into medicines during product development and production [8].

Even so, poor quality medicines are global problem, particularly in low and middle income countries. It is estimated that 10.5 to 50% of the medicines circulating on markets of low and middle income countries are either falsified or substandard, of which ARVs are of no exception [8-23]. Existence of a significant number of porous borders in these countries may accounts for their vulnerability to the infiltration of falsified and substandard medicines.

In 2003 and 2007, falsified ARVs were found circulating in the informal market of Democratic Republic of Congo and Zimbabwe, respectively [14, 24]. A falsified triple antiretroviral combination product, Ginovir 3D was also reported in Côte d'Ivoire in 2003 [14]. Kenya and Zimbabwe, in 2011 and 2013, respectively reported availability of falsified ARVs in their informal market [25, 26]. Again, in 2012 about 12,000 bottles of falsified ARVs were recalled from Tanzania market [27]. Report from a study conducted in Tanzania indicated that all of the tested Indinavir samples had high content (112.6% -118%) of the claimed active principle ingredient (API) compared to the official limit of 95-105% [24]. Also, one sample of Stavudine failed the dissolution test, releasing only 56% instead of the specified 80% of API [24]. In another study conducted by the WHO in seven African countries 1.8% of the tested ARVs samples failed to meet compendia specifications [21]. Poor quality ART poses a major public health threat such as treatment failure, drug toxicity, poor diseases prognosis and emergence of resistant strains; increased co-morbidity and healthcare cost to government and individual and sometimes may cause death [8, 21, 22, 28]. Of which in turn undermines and leads to loss of public confidence in the health care delivery system.

For this reason, continued monitoring of the quality of ART is of importance as can identify substandard and falsified medicines circulating on the market, thus, preventing them from causing harm to patients.

This study was aimed at evaluating the quality of selected ARVs circulating on the Tanzania Mainland market. The primary objective of this study was to determine the proportion of poor quality ART circulating on the market and secondary was to determine the quality of information on the primary and secondary packaging and availability of patient information leaflet.

# Methods

## Study design

This was a survey study.

## Study settings

This study was conducted in 20 out of 26 regions of Tanzania mainland namely; Morogoro, Tanga, Dar es Salaam, Dodoma, Coast, Simiyu, Njombe, Arusha, Shinyanga, Kagera, Singida, Rukwa, Iringa, Geita, Kilimanjaro, Mara, Mbeya, Mtwara, Mwanza and Ruvuma. The regions were selected based on the pre-defined criteria including, highly populated regions, regions bordering other countries, regions with high prevalence of HIV infection and those reported to have medicine quality problems.

## Study duration

Antiretroviral drugs (ARVs) samples were collected from medicines distribution outlets in 20 regions of Tanzania Mainland, between 2012 and 2015 and port of entries between 2012 and 2018.

## ARVs sampling site and sample collection

Convenience sampling method was used in the collection of selected ARVs. Samples were collected from two distribution levels:-

- Level I: The highest distribution of the distribution system which covered the port of entries (POEs) and Medical Stores Department (MSD),
- Level II: This covered public and private hospitals, dispensaries, health centres, retail and wholesale pharmacies and Accredited Drug Distribution Outlets (ADDO).

Collection sample sites were selected in such a way to cover urban and sub urban areas and all distribution levels.

Samples were collected by trained drug inspectors according to the prepared sampling plan and Tanzania Medicines and Medical Devices Authority (TMDA) standard operating procedures. At the collection site, two batches were sampled per product and one brand per batch of the targeted dosage form and strength. All samples were collected in their original containers. Each collected sample was coded for traceability. Sample code included brand name, region, sampling site and sampling date. The following information were recorded for each sample in the Sample Information Collection Form: Brand and generic name, dosage form, strength, batch or lot number, date of manufacturing and expiration, name and address of the manufacturer, country of manufacturer, TMDA registration number, packaging and pack size, availability of package information leaflet, language and storage instruction, physical appearance of the primary and secondary package, site and date of sample collection.

Coded samples with their respective Sample Information Collection Forms were kept in the labelled sampling envelope and sealed.

Storage and handling of samples during collection, transportation and before analysis complied with the manufacturer's instructions and TMDA sample chain of custody procedures prior to screening.

All collected samples were subjected to screening test at TMDA zone laboratories and respective quality assurance (QA) centres. Those from medicine distribution outlets were further subjected to product information review (PIR).

Of the sampled ARVs, 100% of those that did not comply with screening testing requirements or yielded doubtful results and 10% of those that complied with screening test requirements were dispatched to TMDA-WHO prequalified laboratory for full quality control analysis.

## ARVs selection criteria

ARVs selected in this surveillance were those frequently prescribed for the management of HIV-infection with main focus on first line regimens as per National Guidelines for Management of HIV/AIDS [29] or those reported to have quality problem. These included the following monocomponent:

Efavirenz, nevirapine, lamivudine, zidovudine, abacavir sulphate, tenofovir disoproxil fumarate and fixed dose combination (FDC) containing tenofovir disoproxil fumarate /emtricitabine, lamivudine/zidovudine/nevirapine, lamivudine/stavudine/nevirapine, tenofovir/lamivudine/efavirenz, tenofovir/ emtricitabine/efavirenz and lopinavir/ritonavir.

## Site sampling techniques

A purposive sampling technique was used for the selection of medicine collection sites, from regions and district levels down to the distribution channels.

## **Quality evaluation**

### **Product information review**

Prior to further laboratory analysis, samples collected from medicine distribution outlets were subjected to PIR. Each sample was evaluated visually on physical appearance of primary and secondary packaging. Availability and information on package information leaflets (PIL) based on the TMDA labelling requirements and approved product information was also assessed.

Parameters checked during PIR included but not limited to appearance or description of the dosage forms, product's brand and generic name, dosage form and strength, name and address of the manufacturer, batch or lot number, date of manufacturing and expiration, TMDA registration number, packaging and pack size, PIL, language and storage instructions. The information was recorded on a designed form.

### **Tier I laboratory screening testing**

**All samples were subjected to screening test using Global Pharma Health Fund® (GPHF) Mini-Lab kits manual. The performed tests were simple visual inspection, disintegration for solid dosage forms and identification test using Thin Layer Chromatography (TLC) method**

## **Visual inspection**

All sampled solid dosage forms were checked for shape uniformity, physical damage (capping and chipping), altered surface (coating swelling), odor, discoloration and dirty marks.

### **Simple disintegration test**

A simple disintegration test was performed to assess the possibility of instant-release of oral solid dosage forms. This was done by using a 100mL wide neck glass bottle filled with water heated to 37°C. Tablets were shaken or stirred occasionally. Disintegration was required to occur within 30 minutes. The sample was considered failed if did not disintegrate within 30 minutes in three (3) consecutive independent tests.

### **Product identification by thin layer chromatograph**

TLC method was used for product identification and qualitative determination of active ingredients, related substances and impurities present in the dosage forms. This method employed the principle of comparing spots test sample and reference solutions according to GPHF Minilab. The principal spot obtained with the test sample was required to correspond with the chromatographic runs of the standard solution in terms of colour, shape, size, intensity and retardation factor ( $R_f$ ) value. The test sample was considered failed if the  $R_f$  value of the test sample was different by more than 10% from that of the standard sample. Also, the sample was considered failed if the intensity of the spot was less than that of a reference containing 80% of the stated amount of the API and if failure was observed in all three independent experiments.

### **Tier II laboratory confirmatory testing**

All samples collected from medicines distribution outlets that had failed screening test, 10% of those which had passed screening test, and those with doubtful results were subjected to confirmatory testing. Confirmatory testing was carried out at the TMDA-WHO prequalified laboratory as per USP pharmacopoeia monograph requirements [30] and/or in house specifications or manufacturer's methods where no official pharmacopoeia monograph existed.

Typical parameters tested were physical appearance, identification, disintegration, dissolution, assay, related substances and weight uniformity.

### **Data management and analysis**

The collected data were checked for any inconsistencies. The data was double-entered into a Microsoft Access database, verified and exported to SPSS (version 20) software for analysis. The SPSS was used only in the analysis of the dataset of PIR for the sampled ARVs. Descriptive statistics was used for the purpose. Frequencies of the analysed variables in the PIR dataset are presented in percentage.

## Results

### Antiretroviral samples collected

A total of 2,630 ARVs samples were collected between 2012 and 2018 from POEs and medicine distribution outlets in Tanzania Mainland. Large quantity of samples 83.7% (2,200/2,630) were collected from POEs as depicted in Figure 1.

ARVs samples from POEs were collected in large quantity in the years 2014, 2015, 2016 and 2017, 77% (1,695/2,200) compared to other years, as shown in Figure 2.

Regarding, the number of samples from different medicine distribution outlets, hospitals ranked highest amounting to 61% (262/430) as portrayed in Figure 3. Regional wise, 30% (129/430) were sampled from Dar es Salaam, Mwanza and Iringa and least quantity 1.4% (6/430) was collected from Kagera.

Thirteen generic brands (6 API and 7 fixed dose combinations) contributed to the 430 samples collected from the medicine distribution outlets. The FDC of lamivudine/zidovudine/nevirapine tablets was collected in large quantity 17% (73/430) followed by lamivudine/zidovudine tablets combination 16.3% (70/430) as compared to other ARVs. The proportions are summarized in Table 1 below:

#### Quality evaluation

##### Product information review

In this study only samples collected from medicine distribution outlets were subjected to PIR and the results are summarized in Figure 4. Of the examined samples, 25.6% (110/430) did not comply with the packaging information requirements. The highest failure rate was found in the samples collected in the year 2012, 53% (44/83). Interesting observation was found in the year 2013, whereas, all samples passed the PIR assessment. Inappropriate or lack of storage condition, lack of the name and address of the manufacturer, discrepancy of address of the manufacturer on the primary and secondary packaging and lack of package insert were the common deficiencies. On the other hand, all sampled medicines were found to be registered in Tanzania, but some of labels did not indicate the Tanzania registration numbers. The trend is comparable to recent studies conducted on antimalarial and antihypertensive drugs [9, 10].

### Laboratory tier I screening testing

All ARVs, sampled from POEs conformed to tier I screening test requirements. All sampled ARVs from medicine distribution outlets conformed to visual appearance and identification test requirements. However, 3.3% (14/430) of the samples from the medicines distribution outlets, failed disintegration test; these were FDC of lopinavir/ritonavir tablets (7/430) and lamivudine/zidovudine/nevirapine tablets (7/430).

### Laboratory tier II confirmatory testing

Of the 430 ARVs samples collected from medicine distribution outlets and subjected to tier I screening testing, 100 of them were subjected to tier II confirmatory test. These samples included all those failed screening tests, 10% of those which passed screening test and those whose results were doubtful as depicted in Table 2.

Majority of samples 94% (94/100) complied with confirmatory test requirements. However, 3% (3/100) failed confirmatory test and 3% (3/100) samples were beyond the expiration dates at the time of analysis, hence, were not analyzed. The failed samples were of FDC of stavudine/lamivudine/nevirapine 3% (3/100) which failed disintegration test 2% (2/100) and assay test 1% (1/100), having low content of stavudine (86.6%) of the specified amount (limit 90% -110%). This necessitated more samples from the same manufacturer to be subjected to confirmatory test as described in the USP. The additional samples also failed assay test with results ranging between 86.4 and 87.1%. This confirmed the non conformity of Stavudine against the specified requirements. These results are summarized in Figure 5.

## Discussion

Quality medicines are essential to promote public health and disease management. However, various studies conducted worldwide have reported availability of poor quality medicines in the market including ARVs, mostly in developing countries such as Tanzania [8-23].

This survey assessed the quality of 2,630 ARVs samples, collected from medicine distribution outlets and POEs. A total of twenty (20) regions representing more than 76% of the regions of Tanzania Mainland were selected for the purpose. The selection of the regions to be surveyed included some regions bordering other countries; frequency of inspection by the regulatory bodies; areas previously reported to have medicines quality problems and HIV prevalence patterns as indicated in HIV/AIDS and malaria indicator survey of 2011/12 and HIV impact survey of 2016/17 [28,29]. In this survey, 30% (129/430) of samples from medicine distribution outlets were collected in three regions namely Mwanza, Dar es Salaam and Iringa matching with high prevalence of HIV infection [4,29].

It is clear from our results that, majority 83.7% (2200/2630) of the samples were collected from POEs showing the dependence of the country on imported medicines. This observation is in agreement with TMDA data of 2017 [32] and well supported with results from this study that among of the collected samples none were locally produced.

A significant increase of ARVs sampled from the POEs in the year 2014, 2015, 2016 and 2017 compared to 2012/13 can be associated with the scaling up of ARVs access in low and middle income countries through the WHO and Global Fund initiatives [33]. Improved access to ARVs has accounted to the levelling off of new HIV infections cases, deaths and life longevity amongst HIV-infected patients [1- 3].

Despite the inclusion of ADDO and pharmacies among the medicine distribution outlets, no sample was obtained from these sources. This is an interesting finding on compliance to requirements on availability of ARVs in specialized HIV-clinics, hospitals, health centres and dispensaries [33].

Among the collected FDC samples, oral solid dosage forms were the majority (99.8%). 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 [7]. The FDC of lamivudine/zidovudine/nevirapine ranked highest (17%) amongst other ARVs. This was a default regimen during the survey period which is reflected by its wide collection [29].

Samples collected from the POEs were not subjected to PIR. This is because, they were being collected on daily basis within the framework of medicines quality assurance system in which the first step is laboratory screening. On the other hand, 25.6% (110/430) of the sampled ARVs from medicines distribution outlets, subjected to PIR failed to comply with requirements. The failure rate was highest in 2012, but decreased significantly in subsequent years, as shown in Figure 3. Adherence to regulatory requirements of individual countries as well as harmonization efforts on technical requirements across the regions could explain the continuing improvement. Compared with PIR results for other medicine categories in the implementation of PMS programs, these results are far much better [9,10,34]. Even so, results obtained from a study conducted in Cameroon are much far better compared to PIR results of this survey [35]. All pharmaceutical products must be stored under conditions provided by manufacturers to ensure that their potency and qualities are not compromised during the distribution process and storage. In this study it was observed that some of the manufacturers did not indicate proper storage conditions while some provided conditions that are not achievable in tropical set up, such as "store below 25°C". In country like Tanzania which fall under ICH zone IVb climatic condition it is not easy to achieve/maintain the aforementioned storage condition [36]. Improper storage of pharmaceutical products could negatively impact on their potency, quality, efficacy, safety and subsequently compromising the quality of life of the end users [37, 38].

Information on package inserts is necessary since it is associated with drug safety, adherence to treatment, rational drug use and reporting adverse drug reactions [39]. Our findings revealed absence of package inserts from majority of the collected samples.

All ARVs sampled in this study were registered in Tanzania but the registration number which is a prerequisite was not indicated on the labels to some packages. The Tanzania registration number enables easy identification of pharmaceutical products authorized by TMDA to be in the market and prevents availability of falsified products on the market. These results are consistent with PIR results from previous survey study conducted in Tanzania for other categories of medicines [9, 10].

All sampled ARVs, conformed to tier I screening test specifications except of FDC of lamivudine/zidovudine/nevirapine and lopinavir/ritonavir tablets 0.53% (14/ 2630) which disintegration test. Similar results have been reported by the WHO in a study conducted in seven African countries [20]. Passing Tier II confirmatory test for the aforementioned samples provided evidence that were of good quality. The situation which stresses on the need for confirmatory tests before conclusion can be made on quality of medicines.

In confirmatory testing by full monograph, all samples tested met the specifications except two (2) samples of FDC of stavudine/lamivudine/nevirapine which failed disintegration test and one (1) sample of the same which failed assay test. A sample which failed the assay specifications had stavudine content below the acceptance criteria. This was confirmed by the consistency of results obtained from repeated analysis done in triplicate. The cause of failure in the screening test for only products sampled from medicine distribution outlets may be due to poor storage conditions. Improper storage of pharmaceutical products is known to decrease their potency and quality [37, 38, 40].

As a point of information, the stavudine concentration is no longer an issue of discussion since ARVs regimen containing stavudine has been phased out in the country due to its severe toxicity [41-43].

Disintegration of tablets within 30 minutes predicts dissolution within the required time *in vivo* [44], and is a precondition to drug absorption process. Poor absorption of the medicine is associated with poor therapeutic outcomes and development of resistant strains. Disintegration failure rate in this survey was only 2%. This finding is comparable to previous finding reported by the WHO conducted in seven African countries, of the tested samples only 0.6% failed disintegration test [20]. Still, this cannot be ignored because presence of substandard drugs in the market at any percentage poses threats to society. These threats include but not limited to drug toxicity, poor treatment outcomes and disease prognosis, drug resistance and death but also in terms of economic implications and effects on global pandemics [37, 38].

Results for assay test in this study are consistent with reports from various studies worldwide, which have shown that failure rates for ARVs, is very low [ 2, 20, 21, 35 45]. Only 0.25% of ARVs, sampled in seven African countries failed the assay test and none of them failed in the study conducted in Cameroon [20, 35]. This can be explained by the fact that most of ARVs 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 and so, low failure rates [20, 46]. These findings are also, supported by a previous study conducted in seven African countries assessing the quality of ARVs; Tanzania was the first country (76%) using pre-qualified drugs compared to other the studied countries [20].

Of importance is that for all sampled medicines that were deemed to have deficiencies during PIR, the TMDA directed manufacturers to bring requests for amendments for all deficiencies observed. Also, the manufacturers and local agents were informed to recall all batches that failed the confirmatory test from the market. The manufacturers were further directed to halt importation of such products and to conduct thorough investigations to identify possible causes of the failure.

## Conclusion

The quality of the majority of ARVs surveyed was good, however, significant deficiencies on labelling and packaging were observed. These results indicates that the efforts made by the WHO and other organizations on prequalification and purchase policies on ARVs have a positive effect.. As well as these results call for continuous monitoring of quality of medicines circulating on the Tanzanian market with much emphasis on the adequate information on labeling and packaging

## Abbreviations

ADDO: Accredited Drug Dispensing Outlet; MSD: Medical Stores Department;

TMDA : Tanzania Medicines and Medical Devices Authority; TLC: Thin Layer Chromatography; ARVs: Antiretroviral drugs; WHO: World Health Organization; POEs: Port of entries.

## Declarations

### Ethics and consent to participate

Not applicable

### Consent for publication

Not applicable

### Availability of data and materials

All relevant data generated and analyzed during this study are available from the Director General of TMDA on reasonable request.

### Competing interests

The Authors declared that no competing interest.

### Funding

We declare that the study was funded by Global Funds (GF) and TMDA government funds.

### Authors' contributions

SM and KM contributed in study conception and design, data collection, analysis and manuscript writing, SK contributed in data collection, analysis and manuscript writing. BAM contributed in data analysis and manuscript writing and proof reading. GS, YHM and DHS contributed in laboratory and data analysis and manuscript writing, whereas AB and EA contributed in data collection and manuscript writing. Lastly, AF, AK and EK contributed in writing and proof reading the manuscript. All authors participated in reading and approving the final manuscript.

## Acknowledgements

We wish to express our heartfelt appreciation to all parties involved in this activity particularly; Department of Pharmacovigilance and Clinical Trial at TMDA which coordinates post market surveillance activities. Drug inspectors who took part in sample collection, evaluator's who reviewed the product information and analysts who carried out laboratory testing are highly thanked.

## References

1. UNAIDS data. 2017. [http://www.unaids.org/sites/default/files/media\\_asset/20170720\\_Data\\_book\\_2017\\_en.pdf](http://www.unaids.org/sites/default/files/media_asset/20170720_Data_book_2017_en.pdf). Accessed 25 June 2019.
2. World Health Organization. HIV/AIDS key facts. 2019. <http://www.who.int/news-room/fact-sheets/detail/hiv-aids>. Accessed 25 June 2019.
3. Global HIV & AIDS statistics-fact sheet. 2018. [www.unaids.org/en/resources/fact-sheet](http://www.unaids.org/en/resources/fact-sheet). Accessed 18 January 2019.
4. Ministry of Health Tanzania. Tanzania HIV impact survey (THIS) 2016-2017. 2017. [http://phia.icap.columbia.edu/wp-content/uploads/2017/11/Tanzania\\_SummarySheet\\_A4.English.v19.pdf](http://phia.icap.columbia.edu/wp-content/uploads/2017/11/Tanzania_SummarySheet_A4.English.v19.pdf). Accessed 2 June 2019.
5. The United Republic of Tanzania: Global AIDS response country progress report. 2014. [http://www.unaids.org/sites/default/files/country/documents/TZA\\_narrative\\_report\\_2014](http://www.unaids.org/sites/default/files/country/documents/TZA_narrative_report_2014). Accessed 30 August 2019
6. United State of America Food and drug administration (FDA). Antiretroviral drugs used in the treatment of HIV infection. <http://www.fda.gov/ForPatients/Illness/HIVAIDS/Treatment/ucm118915.htm>. Accessed 4 September 2019
7. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach. Second edition. 2016. [https://apps.who.int/iris/bitstream/handle/10665/208825/9789241549684\\_eng.pdf;jsessionid=B3C358E06E50A996385D3778BB625263?sequence=1](https://apps.who.int/iris/bitstream/handle/10665/208825/9789241549684_eng.pdf;jsessionid=B3C358E06E50A996385D3778BB625263?sequence=1). Accessed 20 June 2019.
8. Survey of the quality of selected antimalarial medicines circulating in six countries of Sub-Sahara Africa. 2011. <http://apps.who.int/medicinedocs/documents/s17835en/s17835en.pdf>. Accessed 28 August 2019.
9. Mziray S, Mwamwitwa K, Kisoma S, Augustine S, Fimbo A. Post Marketing Surveillance of Anti-malarial Medicines in Tanzania. *Pharm Regul Aff.* 2017; 6(191):2.
10. Mwamwitwa K, Fimbo A, Mziray S, Nandonde M, Hipolite D, Kijo AS, Njau B and Kaale E. Post Marketing Surveillance of Antihypertensive Medicines in Tanzania. *Pharmaceut Drug Regul Affair J.* 2018; 1: 1-10.
11. Counterfeit Medicines: an update on estimate. 2006. <http://www.who.int/medicines/services/counterfeit/impact/TheNewEstimatesCounterfeit.pdf> Accessed 22 June 2019.
12. Primo-Carpenter J, McGinnis M. Matrix of Drug Quality Reports in USAID-assisted Countries by the U.S. Pharmacopeia Drug Quality and Information Program. 2006. [https://pdf.usaid.gov/pdf\\_docs/Pnadh099.pdf](https://pdf.usaid.gov/pdf_docs/Pnadh099.pdf). Accessed 20 June 2019.
13. Hajjou M, Krech L, Lane-Barlow C, Roth L, Pribluda VS, Phanouvong S et al. Monitoring of Quality of medicines – results from Africa, Asia and South America. *Am J Trop Med Hyg.* 2015; 92 (6): 68-74.
14. Almuzaini T, Choonara I, Sammons H. Substandard and counterfeit medicines: a systematic review of the literature. *BMJ Open.* 2013; 3: e002923.
15. Chikowe I, Osei-Safo D, Harrison J, Konadu D, Ivan Addae-Mensah I. Post-marketing surveillance of anti-malarial medicines used in Malawi. *Malaria Journal.* 2015; 14:127.
16. Osei-Safo D, Agbonon A, Konadu DY, Harrison JJ, Edoh M, Gordon A et al. Evaluation of the Quality of Artemisinin-Based Anti-malarial Medicines Distributed in Ghana and Togo. *Malar Res Treat.* 2014; 2014: 806416.
17. Lalani M, Kaur H, Mohammed N, Mailk N, Wyk AV, Jan S et al. Substandard Anti-malarials Available in Afghanistan: A Case for Assessing the Quality of Drugs in Resource Poor Settings. *Am J Trop Med Hyg.* 2015; 92 (6): 51–8.
18. Jande M, Ngassapa O, Kibwage I. Quality of sulfadoxine/ pyrimethamine tablets marketed in Dar es Salaam, Tanzania. *East Cent Afr J Pharm Sci.* 2000; 3: 20–4.
19. Minzi OM, Moshi MJ, Hipolite D, Masseur AY, Tomson G, Ericsson O et al. Evaluation of the quality of amodiaquine and sulphadoxine/pyrimethamine tablets sold by private wholesale pharmacies in Dar Es Salaam, Tanzania. *J Clin Pharm Ther.* 2003; 28: 117–22.

20. Quality assurance and safety medicines policy and standards. Survey of the quality of antiretroviral medicines circulating in selected African Countries. 2007. <http://apps.who.int/medicinedocs/documents/s14230e/s14230e.pdf>. Accessed 8 September 2019.
21. Mcginnis MA. Media Reports on Medicine Quality: Focusing on USAID-assisted Countries. By the Promoting the Quality of Medicines program. 2013. <http://www.globalforumljd.org/sites/default/files/docs/library/USAID%20PQM%202013%20-%20Media%20Reports%20on%20Medicines%20Quality.pdf>. Accessed 21 June 2019.
22. Kelesidis T, Falagas ME. Substandard/counterfeit antimicrobial drugs. *Clin Microbiol Rev.* 2015; 28(2):443-63.
23. Quality of antiretroviral drugs, stavudine and indinavir capsules available in the Tanzanian market. *Tanzania Med J.* 2006;21:8–12.
24. Zimbabwe: Fake ART Flood Country, *Financial Gazette.* 2007. <https://allafrica.com/stories/200707260858.html> Accessed 28 August 2020
25. 2011. Kenya: government grapples with counterfeit ARVs. <http://www.irinnews.org/report/94012/kenya-government-grapples-with-counterfeit-arvs> Accessed 02 September 2020.
26. Anonymous. Counterfeit drugs flood Zim market. *The Zimbabwe Independent.* 2013. <http://www.theindependent.co.zw/2013/10/25/counterfeit-drugs-flood-zim-market/>. Accessed 1 September 2020.
27. Tanzania investigates fake HIV drugs. 2012. <https://www.bbc.com/news/world-africa-19914662> Accessed 02 September 2020.
28. Renschler PJ, Walters KM, Newton PN, Laxminarayan R. Estimated Under-Five Deaths Associated with Poor-Quality Anti-malarials in Sub-Saharan Africa. *Am J Trop Med Hyg.* 2015; 92 (6): 119–126.
29. National guidelines for the management of HIV and AIDS. National AIDS Control Programme. 2012. [https://aidsfree.usaid.gov/sites/default/files/hts\\_policy\\_tanzania.pdf](https://aidsfree.usaid.gov/sites/default/files/hts_policy_tanzania.pdf). Accessed 6 July 2018.
30. United State Pharmacopeia (USP) NF 32 Rockville, MD, USA 2012-2014
31. Ministry of Health of Tanzania. HIV/AIDS and malaria indicator survey of 2011/12. 2012. <https://dhsprogram.com/pubs/pdf/AIS11/AIS11.pdf>. Accessed 20 June 2019
32. Tanzania Food and Drugs Authority Registration Data Base, 2017.
33. The importance of HIV care and support services. 2016. [http://www.unaids.org/en/resources/presscentre/featurestories/2016/december/20161202\\_HIV-care](http://www.unaids.org/en/resources/presscentre/featurestories/2016/december/20161202_HIV-care) Accessed 08 July 2019
34. Post Marketing Surveillance Report of the Quality of Selected Medicines under phase III- IX of 2011-2013 PMS Program. 2016. Tanzania Food and Drugs Authority, Dar-es-Salaam, Tanzania
35. Djobet MP, Singhe D, Lohoue J, Kuaban C, Ngogang J, Tambo E. Antiretroviral therapy supply chain quality control and assurance in improving people living with HIV therapeutic outcomes in Cameroon. *AIDS Res Ther* (2017) 14:19.
36. Climatic Zones for Stability Studies, <http://www.pharmaguideline.com/2010/12/different-climatic-zones-for-stability.html>. Assessed on 09 March 2019.
37. Ansari FAA. Study of various storage conditions on the pharmaceutical products and its implementation at retail store. *The Pharma Innovation Journal.* 2017; 6(9): 475-78.
38. Shafaat K, Hussain A, Kumar B, Ul Hasan R, Prabhat P, Kumar VY. An overview: storage of pharmaceutical products. *World journal of pharmacy and pharmaceutical sciences.* 2013; 2:2499-515
39. Sillo HB, Masota NE, Kisoma S, Rago L, Mgozela V, Kaale EA (2018) Conformity of package inserts information to regulatory requirements among selected branded and generic medicinal products circulating on the East African market. *PLoS ONE* 13(5): e0197490.
40. Shakoore O, Taylor RB, Behrens RH. Assessment of the incidence of substandard drugs in developing countries. *Trop Med Int Health.* 1997; 2(9):839-45.
41. Minzi O.M.S., Irunde H, Moshiro C. HIV patients presenting common adverse drug events caused by highly active antiretroviral therapy in Tanzania. *Tanzania Journal of Health Research.* 2009; 11 (1): 5-10.
42. Franzeck FC, Letang E, Mwaigomole G, Jullu B, Glass TR, Nyogea D, Hatz C, Tanner M, Battegay M. cART prescription trends in a prospective HIV cohort in rural Tanzania from 2007 to 2011. *BMC Infect Dis.* 2014; 14:90.
43. Palmer M, Chersich M, Moultrie H, Kuhn L, Fairlie L, Meyers T. Frequency of stavudine substitution due to toxicity in children receiving antiretroviral treatment in sub-Saharan Africa. 2013; 27(5):781–85.
44. Marton S, Szentmiklósi P, Rácz I. Correlation between disintegration, dissolution and in vivo absorption rate in the case of compounds with benzyl-isoquinoline structures and its pharmacokinetic aspects. *Pol J Pharmacol Pharm.* 1984; 36(4):385-95.
45. Ministry of Public Health and Sanitation Ministry of Medical Services. Post market survey of antiretroviral medicines in Kenya. 2012. <http://apps.who.int/medicinedocs/documents/s21944en/s21944en.pdf>. Accessed 20 June 2019.
46. Ozawa S, Evans DR, Bessias S, Haynie DG, Yemeke TT, Laing SK, Herrington JE. Prevalence and Estimated Economic Burden of Substandard and Falsified Medicines in Low- and Middle-Income Countries: A Systematic Review and Meta-analysis. *JAMA Netw Open.* 2018; 1(4):e181662.

# Tables

Table 1: Proportions of anti-retroviral medicines sampled from medicine distribution outlets between 2012 and 2015

S/N	Name of active (s) ingredient(s)	Number of samples	Percentage
1	Efavirenz tablets	66	15.3
2	Nevirapine tablets	23	5.4
3	Nevirapine oral suspension	11	2.6
4	Lamivudine tablets	10	2.3
5	Zidovudine tablets	2	0.5
6	Tenofovir Disoproxil Fumarate tablets	5	1.2
7	Lamivudine/Zidovudine tablets	70	16.3
8	Abacavir Sulphate tablets	16	3.7
9	Lopinavir/Ritonavir tablets	18	4.2
10	Tenofovir Disoproxil Fumarate /Emtricitabine tablets	14	3.2
11	Tenofovir Disoproxil Fumarate/Lamivudine/Efavirenz tablets	29	6.7
12	Lamivudine/Zidovudine/Nevirapine tablets	73	17
13	Lamivudine/Stavudine/Nevirapine tablets	66	15.3
14	Tenofovir Disoproxil Fumarate /Efavirenz/Emtricitabine tablets	27	6.3
<b>TOTAL</b>		<b>430</b>	<b>100</b>

Table 2: Number of samples selected and tested for confirmatory testing

## Figures

Product name	Samples collected and screened			Confirmatory test	
	Samples collected	Samples screened and passed	Samples Failed	Samples eligible for confirmatory	Samples selected and tested
Efavirenz	66	66	0	7	14
Nevirapine tablets	34	34	0	4	7
Lamivudine tablets	10	10	0	1	10
Zidovudine tablets	2	2	0	1	2
Tenofovir Disoproxil Fumarate tablets	5	5	0	1	5
Lamivudine/Zidovudine tablets	70	70	0	7	7
Abacavir Sulphate tablets	16	16	0	2	4
Lopinavir/Ritonavir tablets	18	12	7	9	9
Tenofovir Disoproxil Fumarate /Emtricitabine tablets	14	14	0	2	4
Tenofovir Disoproxil Fumarate /Lamivudine/Efavirenz tablets	29	29	0	3	6
Lamivudine/Zidovudine/Nevirapine tablets	73	73	7	14	14
Lamivudine/Stavudine/Nevirapine tablets	66	59	0	10	10
Tenofovir Disoproxil Fumarate /Efavirenz/Emtricitabine tablets	27	27	0	3	8
<b>Total</b>	<b>430</b>	<b>416</b>	<b>14</b>	<b>61</b>	<b>100</b>

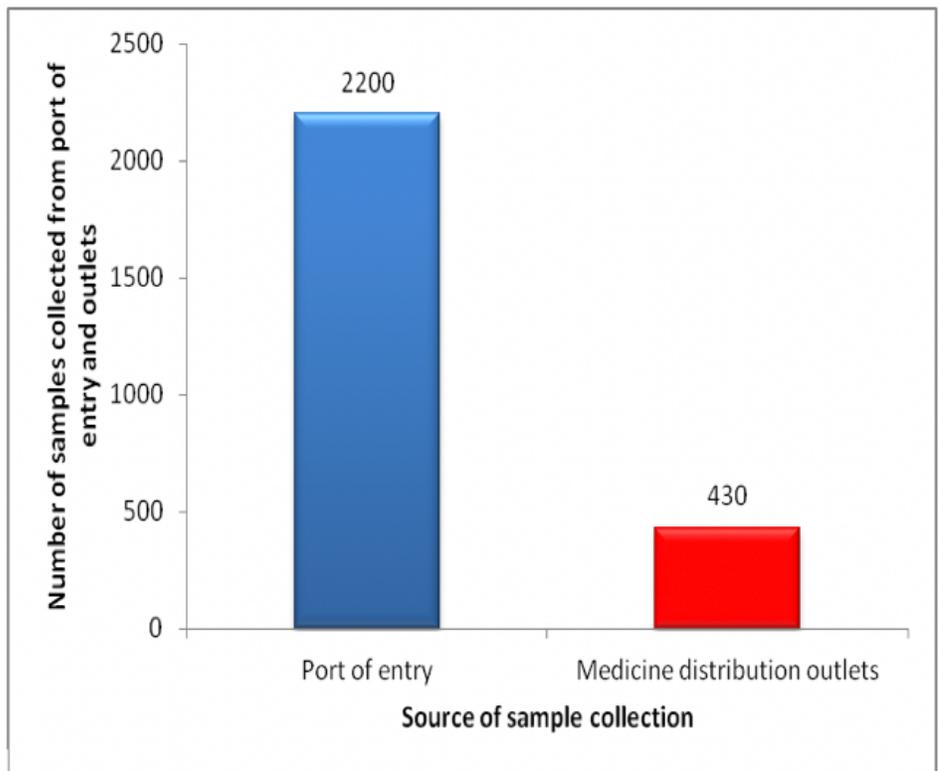


Figure 1

Proportion of antiretroviral drug samples collected from port of entry and medicine distribution outlets

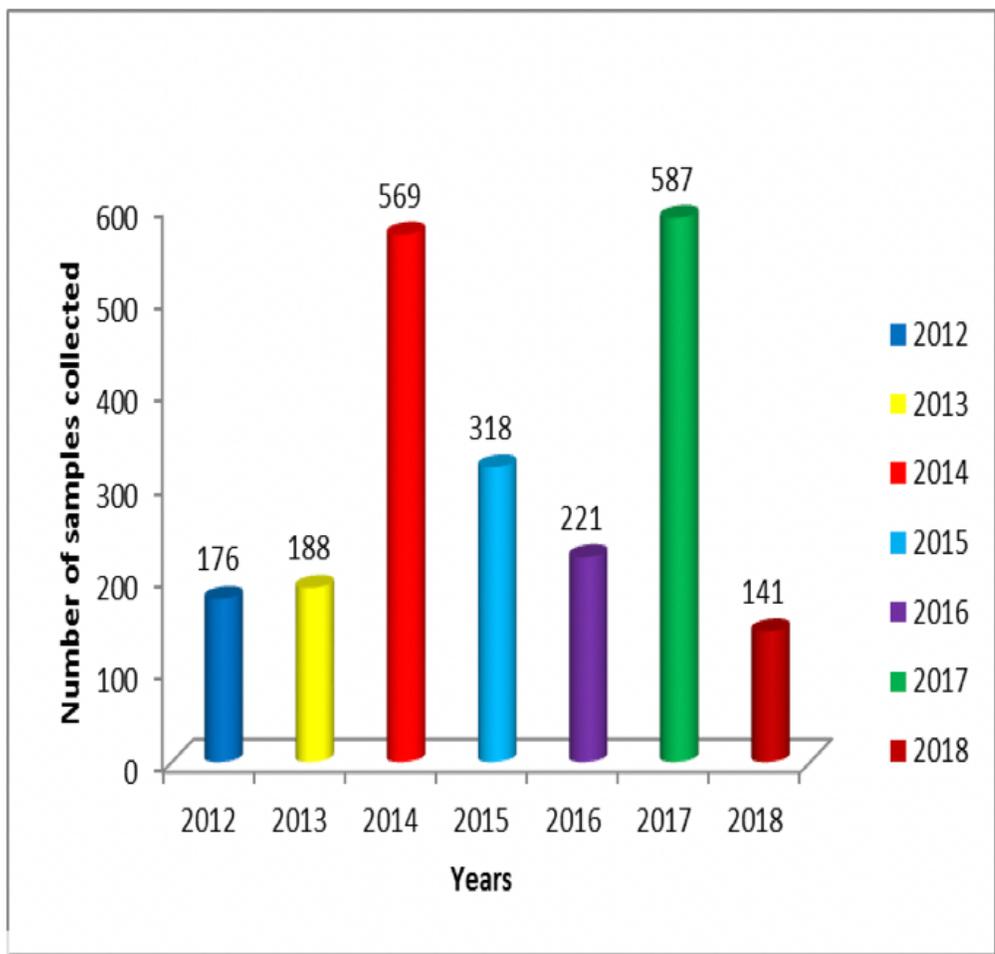


Figure 2

Number of antiretroviral drug samples collected at the port of entry annually (2012 - 2018)

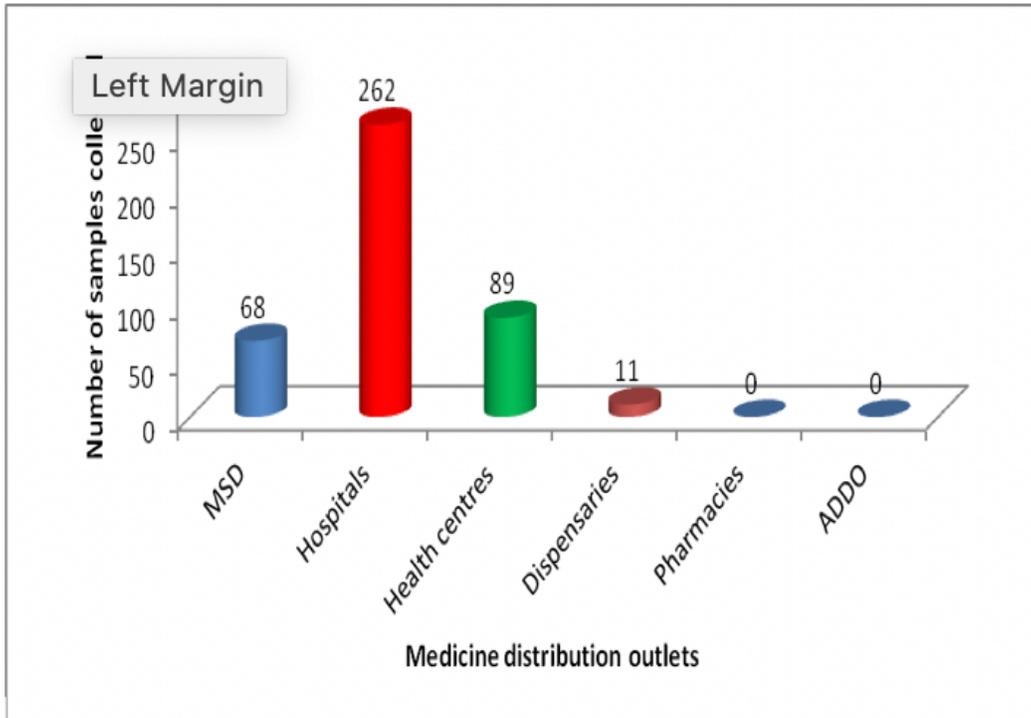


Figure 3

Samples of antiretroviral drugs collected from different medicine distribution outlets

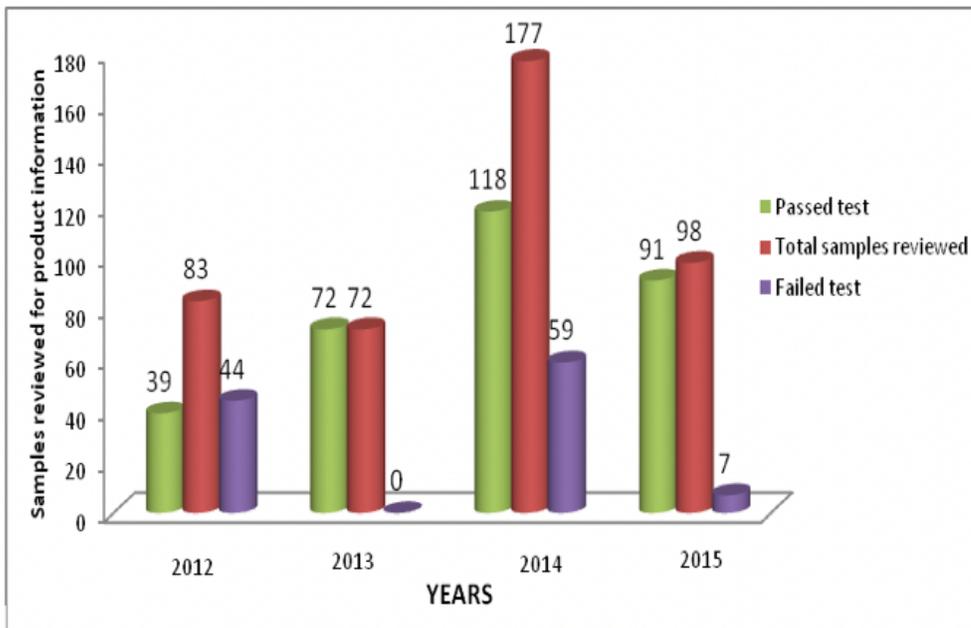
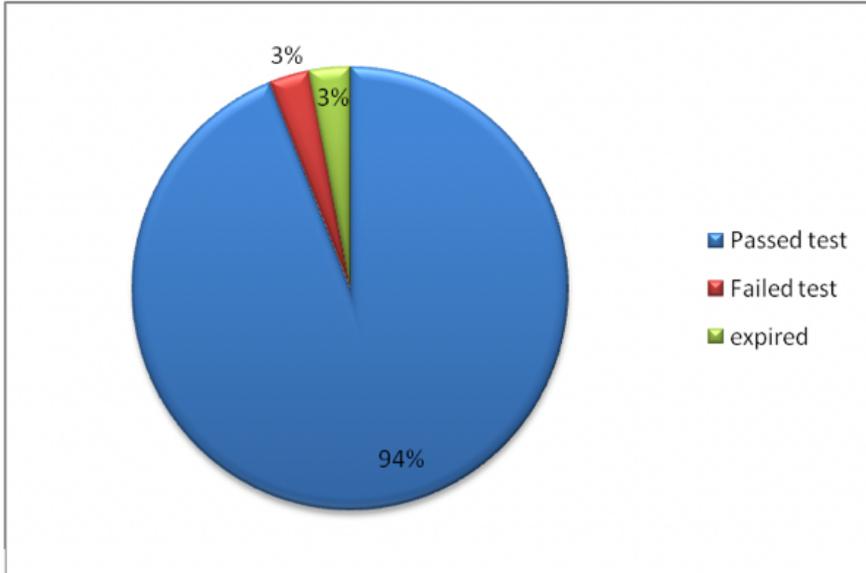


Figure 4

Results of product information review per year



**Figure 5**

Proportion of samples passed laboratory tier II confirmatory testing

## Supplementary Files

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- [STROBEchecklistcrosssectionalqualityofARVs.doc](#)