Strengthening pharmacovigilance system to capture safety data from HIV clients on ART in Tanzania: Identification of gaps in safety reporting system

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I. EXECUTIVE SUMMARY

Background
In Tanzania, pharmacovigilance system is implemented by Tanzania Food and Drugs Authority (TFDA) that monitors drug use countrywide. TFDA is the main national custodian for recording, analyzing and disseminating safety information that is generated through conventional health care facilities. Since the introduction of Care and Treatment Centre (CTC) in the health care system, little has been achieved on translating safety information from these facilities to the TFDA.

Statement of the problem
Since the inception of national pharmacovigilance framework in 2003 there has been no systematic operational research to map the gaps in the existing pharmacovigilance system. Furthermore, it is not clear if there is adequate training and supervision. It is, therefore, important to strengthen antiretroviral therapy (ART) related adverse drug reactions (ADRs) reporting by mapping gaps in implementation of pharmacovigilance (PV) system. Information obtained will assist in addressing training needs to ensure effective reporting of ADRs through coordinated approach involving TFDA and National AIDS Control Program (NACP) in Tanzania.

Methodology
A cross-sectional study was conducted in four regions (Tanga, Singida, Dodoma and Mtwara) in two PV zones. Qualitative and quantitative data collection techniques with triangulation design were used. These included; desk document review of PV recording and reporting of drug safety information; in-depth interviews with various implementation stakeholders, exit interviews with patients, in-interviews with care takers and community based organizations (CBOs) involved in the provision of care and treatment of HIV/AIDS.

Results
A total of 801 respondents participated in the quantitative data component which included; 545 exit interviews to CTC clients, 177 health service providers, 62 in-depth interviews to CTC in-charges and 17 regional and district pharmacists. Ownership of these CTCs included 83.9% government, 12.9% faith based organizations and 3.2% co-owned by the government and faith based organizations. High proportions (97.2%) of the CTC health care providers had wide knowledge on ART related ADRs. However, more than half (53.4%) of the CTC service providers had not attended any training on ART related ADRs. Among the service providers, majority (67.8%) mentioned there was no guideline in place for reporting ART related ADRs. Only, 32.1% of health care providers indicated to be aware of the tool used for collection of ART related ADRs.
events. Of those, 37.5% mentioned that the forms were mainly obtained from district or regional pharmacists. The ADR reports were submitted to district and regional pharmacists 48.3%, TFDA 7.0%, and NACP 7.0%. Of those who indicated to have filled and submitted ADR form, only 7.4% received feedback. The proportion of ART clients who provided information was significantly different between urban and rural in Dodoma region (p=0.002). There was variation in proportions of ART clients who had mentioned seen/heard of ART related ADR by regions and difference was significant between rural and urban for all regions except Tanga (p<0.05). Majority (47.9%) of the ART clients reported ART related ADRs to the health provider for duration ranging from 3-7 days.

The qualitative results revealed that that most of the guidelines from TFDA were not known and unavailable according to most of the respondents at national level (NACP), regional, district, and at health facility level. It was surprising that one of the district pharmacists interviewed was unaware of existence of guidelines in place for ADR and PV for use in the districts. It was also found that Sometimes even when available at health facilities, there was inadequate knowledge on how to fill the ADR forms according to Key Informant at national level. Moreover, several health workers admitted that that they were not reporting ADR due to a lack of forms according to some CTC in-charges interviewed.

**Conclusion and recommendations**

This study has shown that despite the established PV system in Tanzania, the frequency of reporting of ART related ADRs to TFDA is low. This is due to inadequate training of health care providers on ADR reporting, shortage of staff, unavailability of TFDA ADR reporting forms and lack of regular supportive supervision. Based on these results therefore we recommend

i. TFDA should ensure that ADR reporting forms as well as guidelines are adequately supplied and utilized at CTC level

ii. NACP should ensure sharing of safety information with TFDA and recommend dedicated focal person liable for documenting and reporting ART related ADRs recorded in CTC II patient file.

iii. Regular training, supportive supervision and feedback on ART related ADR reporting system for health care providers is needed.

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We would like to acknowledge the District Executive Directors, Regional Medical Officers, District Medical Officers and staff of health facilities. TFDA, NACP and zonal pharmacovigilance centre are thanked for their co-operation. We would also like to sincerely thank the ART clients for their willingness to participate and co-operation. Research assistants are thanked for data collections. Sincere gratitude goes to NIMR Tanga Centre, NIMR Headquarters, Ifakara Health Institute (IHI) and TANHER Forum for logistical support. We would like to thank Global Fund Round 8 (GFR-8) and NIMR GF Secretariat for providing financial and technical support for this study.
### III. ACRONYMS

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADR</td>
<td>Adverse Drug Reaction</td>
</tr>
<tr>
<td>AEs</td>
<td>Adverse Events</td>
</tr>
<tr>
<td>AMOs</td>
<td>Assistant Medical Officers</td>
</tr>
<tr>
<td>ART</td>
<td>Antiretroviral Therapy</td>
</tr>
<tr>
<td>ARVs</td>
<td>Antiretrovirals</td>
</tr>
<tr>
<td>CBO</td>
<td>Community Based Organisations</td>
</tr>
<tr>
<td>COs</td>
<td>Clinical Officers</td>
</tr>
<tr>
<td>CTC</td>
<td>Care and Treatment Centre</td>
</tr>
<tr>
<td>DMOs</td>
<td>District Medical Officers</td>
</tr>
<tr>
<td>GFR8</td>
<td>Global Funds Round 8</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome</td>
</tr>
<tr>
<td>IDIs</td>
<td>In-depth Interviews</td>
</tr>
<tr>
<td>IHI</td>
<td>Ifakara Health Institute</td>
</tr>
<tr>
<td>MDs</td>
<td>Medical Doctors</td>
</tr>
<tr>
<td>MoHSW</td>
<td>Ministry of Health and Social Welfare</td>
</tr>
<tr>
<td>NACP</td>
<td>National AIDS Control Programme</td>
</tr>
<tr>
<td>NGO’s</td>
<td>Non-Governmental organisations</td>
</tr>
<tr>
<td>NIMR</td>
<td>National Institute of Medical Research</td>
</tr>
<tr>
<td>MRCC</td>
<td>Medical Research Coordination Committee</td>
</tr>
<tr>
<td>PMTCT</td>
<td>Prevention of Mother To Child Transmission</td>
</tr>
<tr>
<td>PV</td>
<td>Pharmacovigilance</td>
</tr>
<tr>
<td>RMOs</td>
<td>Regional Medical Officers</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>TANHER</td>
<td>Tanzania National Health Research Forum</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>TFDA</td>
<td>Tanzania Food and Drugs Authority</td>
</tr>
<tr>
<td>VCT</td>
<td>Voluntary counselling and testing</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
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</table>
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1. INTRODUCTION

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem (1). Post-marketing surveillance (PMS) is the practice of monitoring the safety of a pharmaceutical drug or medical device after it has been released on the market and is an important part of the science of pharmacovigilance. Adverse drug reactions (ADRs) is defined as harmful, unintended reactions to medicines that occur at doses normally used for treatment (2). Adverse events (AEs) is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment (3). Detailed data on AEs are collected during controlled clinical trials that are required for licensing. No matter how rigorous this process may be, the information collected cannot be regarded as entirely comprehensive due to the relatively restricted number of patients involved and the exclusion criteria that are frequently applied, for example to omit pregnant women, young children, severely ill patients or elderly patients (4;5). Accordingly, post-marketing surveillance, especially in the context of observational studies, can be a valuable source of additional safety data within a large patient population in a real-world setting.

Spontaneous reporting of suspected adverse drug reactions (ADRs) observed during drug therapy is not routinely done in many sub-Saharan Africa countries. Few PV activities implemented in African countries have been mainly focused on malaria medications (6-8). The main factors limiting the implementation of pharmacovigilance in these settings include limited access to healthcare facilities, availability of prescription drugs from the informal market, poor labelling of medications, high levels of illiteracy, poor record-keeping and shortage of qualified healthcare professionals. Lack of awareness of the importance of reporting ADRs among healthcare workers also affects the pharmacovigilance reporting system (7). Post-marketing surveillance, including monitoring of antiretroviral drugs (ARVs) is not currently undertaken in most sub-Saharan countries (8). Therefore, the benefits of pharmaco-epidemiological studies with planned protocol on collection of safety data may be particularly relevant in the early phase of enhancing the pharmacovigilance in the region.

In Tanzania, pharmacovigilance system is implemented by Tanzania Food and Drugs Authority (TFDA) that monitors drug use countrywide. However, there is no dedicated surveillance scheme to monitor safety of ART among HIV/AIDS clients. Like other HIV/AIDS burdened countries in sub-Saharan Africa, Tanzania has a comprehensive care and treatment infrastructure for most HIV/AIDS patients through which the provision of first line ART is conducted. In the care and treatment centers (CTCs) scanty safety information pertaining to ART use is informally generated and is mostly used to guide management of patient at local CTCs. The locally generated safety information is hardly relayed to National AIDS Control Programme (NACP),
the custodian of care and treatment services for HIV/AIDS in Tanzania. TFDA the main national custodian of safety information is actively involved in the recording, analyzing and disseminating safety information that is generated through conventional health care facilities. Since the introduction of CTC in the health care system around mid of the last decade, little has been achieved on translating safety information from these facilities to the TFDA.

1.1. **Rationale**

There is limited room for the generation of safety information during use of ART through CTC. This is because tools that are used to record safety information in the CTCs are not designed to address the question of information generation for use beyond local CTCs. These tools are also not designed for information sharing with other interfaces operating in the health system or those which are dealing solely with safety of medicinal products. At the national level in particular, there is no conventional interface through which NACP and TFDA share safety information generated through CTCs. Despite the sheer need for sharing safety information generated through CTC form II and TFDA-ADR reporting tools, for the benefit of patient and updating regulatory authorities’ database, there is neither a harmonized tool nor dedicated focal person to coordinate the recording, reporting and sharing of safety information between NACP and TFDA. Since the inception of national pharmacovigilance framework by TFDA in 2003 there has been no systematic operational research to map the gaps in the existing pharmacovigilance system. The passive nature of the reporting system makes it difficult to know if it has been implemented effectively and if there are any problems encountered. Furthermore, it is not clear if there is adequate training and supervision to ensure the system captures all required information. It is for these reasons, therefore, that the creation of a safety information interface between TFDA and CTC is essential.

Information obtained will assist in addressing training needs to ensure effective reporting of ADRs. This will also facilitate in devising strategies for engaging different stakeholders hence strengthening of the PV system.
1.2. Broad objective
To evaluate ART safety reporting mechanism through pharmacovigilance surveillance system in Tanzania

1.2.1. Specific Objectives
1. To map the gaps in the implementation of pharmacovigilance model in relation to ART safety reporting.
2. To assess the implementation strategy of pharmacovigilance system
3. To assess implementation knowledge gaps related to information sharing at different levels
4. To determine awareness about ADR reporting among HIV/AIDS clients receiving ART, their care takers and community based organization (CBOs) that assist care and treatment with ART.

2. Methodology
This was a cross-sectional study involving both qualitative and quantitative data collection techniques. It included desk review of pharmacovigilance recording and reporting of drug safety information; in-depth interviews with various implementation stakeholders, exit interviews with patients, in-depth interviews with care takers and CBOs involved in the provision of care and treatment of HIV/AIDS.

2.0. Study areas
The zonal centers for PV in Tanzania include Bugando hospital, Kilimanjaro Christian Medical Center (KCMC), Mbeya, Dodoma, Kigoma, Mtwara and Muhimbili National Hospital. This study was conducted in five regions with zonal centres in brackets including: Tanga (KCMC), Singida and Dodoma (Dodoma), Mtwara (Mtwara) and Muhimbili National Hospital (Muhimbili).

2.1 Sampling
This study attempted to achieve national coverage by working with a national representative sample of Regions (Primary Sampling Unit-PSUs) and Districts (Secondary Sampling Unit-SSUs) and CTCs & CBOs (Tertiary sampling Unit-TSUs) through multiple sampling techniques. Stratified random sampling technique was applied in selecting zones, regions and districts. CTCs and CBOs were conveniently selected to represent the rural and urban settings from each district visited. At each CTC, ten clients were conveniently selected for exit interviews. All CTC in-charges were included in the study for in-depth interview.
2.2. Data collection techniques

This study employed various approaches and data sources to address the objectives as given in annex 1.

2.2.1. Questionnaires

This included both open and close-ended questions. The questionnaire captured information regarding staffing at respective facility level, flow of the pharmacovigilance data, knowledge of workers on the importance and use of the pharmacovigilance data, constraints in collection and reporting of data, and available supervision mechanism. Open and close-ended questionnaire were used in the exit interview conducted to clients at the CTC exits. Information collected was on the knowledge of clients on adverse drug events, frequency of reporting such events, time and place they reported.

2.2.2. In-depth interviews

In-depth interviews were used to collect data from CTC, CBOs, and health managers responsible for ARV pharmacovigilance at district, Regional, zonal and national levels.

2.2.3. Documentary reviews

At the national level, documentary review was conducted at both TFDA and NACP on pharmacovigilance recording, reporting and policy guidelines. Moreover, the review was used to track records that NACP is implementing in relation to documentation, reporting and dissemination of ART safety information.

2.2.4. Ethical Considerations

Ethical Clearance was obtained from the Medical Research Coordinating Committee MRCC) of the National Institute for Medical Research. Prior to data collection the study teams were trained to familiarize with the study protocol, and general conduct of the study. Study participants were consented using consent form written in Kiswahili language. For those who were not able to read and write they were asked to sign using a thumb-print.

2.3. Data Management and Analysis

Quantitative data generated by this study was double-entered by two independent data entrants and managed using Microsoft Access software. Analysis of data was carried out using Stata version 10. Chi-square test was used to assess association between categorical variables and student-t test was used to compare continuous variables as appropriate. Probability values (p-
values) were calculated, and variables was considered to have significant effect if p-values was <0.05.
Qualitative data was audio-recorded and transcribed for content coding. The analysis of the data collected was carried out by describing, summarising and interpretation guided by the research objectives. The emerging themes were underlined before the results were deployed to reach key conclusions pertaining to the research objectives of the study.
3. RESULTS

A total of 801 respondents participated in both quantitative and qualitative data collection through exit interviews with CTC clients (545), semi-structured interviews with health service providers (177), in-depth interviews to CTC in-charges (62) and regional and district pharmacists (17).

3.1. PART I: QUANTITATIVE RESULTS

3.1.1. Characteristics of study sites and population

The quantitative part of the study covered a total number of 722 respondents which included 545 exit interviews to CTC clients and 177 semi-structured interviews to health service providers. Distribution of interviews by region and setting is as shown in Table 1 below.

Table 1: Type and number of interviews conducted by regions and location

<table>
<thead>
<tr>
<th>Exit interview to CTC clients</th>
<th>CTC Service providers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban</td>
<td>Rural</td>
</tr>
<tr>
<td>Dodoma</td>
<td>74</td>
</tr>
<tr>
<td>Tanga</td>
<td>81</td>
</tr>
<tr>
<td>Singida</td>
<td>80</td>
</tr>
<tr>
<td>Mtwara</td>
<td>75</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>310</strong></td>
</tr>
</tbody>
</table>

3.1.2. Social-demographic characteristics of clients Interviewed at CTCs

The mean age of all CTC clients interviewed was 40.8 years (Standard deviation [SD] =11.1) and range was 16 to 81. Proportion of female interviewees was significantly higher (69.8%) than that of male (p=0.017). Most interviewees were married (42.8%). These results have shown that a relatively high proportion of clients interviewed at CTCs were widows in Tanga (28.4%) and in Dodoma (24.2%) as compared to Singida and Mtwara (p<0.001) (Table 2). In terms of education, results showed majority 391/523 (74.8%) of the clients interviewed had primary education, while 85/523(16.3%) had not attained any formal education (p<0.001). However, a low proportion had secondary and post-secondary education as shown in Table 2.
Table 2: Socio-demographic characteristics of clients participating in exit interviews

<table>
<thead>
<tr>
<th>Variables</th>
<th>Dodoma</th>
<th>Mtwara</th>
<th>Singida</th>
<th>Tanga</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex- Male</td>
<td>31(24.2)</td>
<td>36(27.9)</td>
<td>37(27.0)</td>
<td>62(40.0)</td>
<td>166(30.2)</td>
</tr>
<tr>
<td>Female</td>
<td>97(75.8)</td>
<td>93(72.1)</td>
<td>100(73.0)</td>
<td>93(60.0)</td>
<td>383(69.8)</td>
</tr>
<tr>
<td>Mean age in yr (SD)</td>
<td>41.8(10.8)</td>
<td>36.4(10.6)</td>
<td>40.9(10.6)</td>
<td>43.5(11.0)</td>
<td>40.8(11.1)</td>
</tr>
<tr>
<td>Education- Primary</td>
<td>87(68.0)</td>
<td>92(71.3)</td>
<td>105(82.0)</td>
<td>107(77.5)</td>
<td>391(74.8)</td>
</tr>
<tr>
<td>Secondary</td>
<td>10(7.8)</td>
<td>12(9.3)</td>
<td>11(8.6)</td>
<td>9(6.5)</td>
<td>42(8.0)</td>
</tr>
<tr>
<td>Post-secondary</td>
<td>0(0)</td>
<td>2(1.6)</td>
<td>1(0.8)</td>
<td>2(1.5)</td>
<td>5(1.0)</td>
</tr>
<tr>
<td>None</td>
<td>31(24.2)</td>
<td>23(17.8)</td>
<td>11(8.6)</td>
<td>20(14.5)</td>
<td>85(16.3)</td>
</tr>
<tr>
<td>Marital status- Single</td>
<td>15(11.7)</td>
<td>32(24.8)</td>
<td>38(27.7)</td>
<td>21(13.6)</td>
<td>106(19.3)</td>
</tr>
<tr>
<td>Married</td>
<td>63(49.2)</td>
<td>51(39.5)</td>
<td>58(42.3)</td>
<td>63(40.7)</td>
<td>235(42.8)</td>
</tr>
<tr>
<td>Divorced</td>
<td>19(14.8)</td>
<td>28(21.7)</td>
<td>10(7.3)</td>
<td>27(17.4)</td>
<td>84(15.3)</td>
</tr>
<tr>
<td>Widow/Widower</td>
<td>31(24.2)</td>
<td>18(14.0)</td>
<td>31(22.6)</td>
<td>44(28.4)</td>
<td>124(22.6)</td>
</tr>
</tbody>
</table>

A total of 177 health service providers from 62 CTCs were surveyed from 16 districts in the 4 study regions; and their distribution by facility type as shown in Figure 1.

![Figure 1: Distribution of health providers by type of facility](image)

A total of 31 out of 62 (50.0%) CTCs were situated in urban areas and the rest in rural settings. Ownership of these CTCs was 52(83.9%) government, 8(12.9%) faith based organisations and 2(3.2%) were co-owned by the government and faith based organisations. Among the service
providers interviewed, out of 177; 42(23.7%) had primary education, 65(36.7%) had secondary education and 70(39.6%) post-secondary education. Among the service providers, 11(6.4%) were: assistant medical officers, 26(15.03%) clinical officers, 88(50.88%) nurses, 6(3.5%) counsellors while 42(24.3%) were categorized as others.

These results have shown that the mean experience of health providers at CTCs by regions were as follows: Dodoma 3.3 years (SD=2.2), Mtwara 4.0(SD=2.4), Singida 2.7(2.0) and Tanga 3.4(SD=2.1). The overall mean duration in the current service position was 3.3 years (SD=2.2) ranging from 5 months to 12 years in the 4 regions. The monthly average numbers of clients attended in the four regions were: 336, 178, 124 and 744 for Dodoma, Singida, Mtwara and Tanga respectively. Number of health providers had varying work load which increased with the type of health facility. Those working at the dispensary attended a median of 55 patients per month, while the providers working at the regional hospital CTCs reported the high number of patients. It was also observed that providers at non-public hospital CTCs had slightly lower number of patients, Figure 2.

![Figure 2](image_url)

**Figure 2:** Distribution of median (solid line) and interquartile range (dotted lines) of number of clients attended by health providers at different facilities

### 3.1.3. Health provider’s awareness on ART related ADRs

Table 3 shows that high proportion of the HIV/AIDS service providers was aware on ART related ADR. However, in terms of training, almost half (53.4%) of the CTC service providers had not attended any training on ART related ADRs. For those that had attended training, the mean duration of the training was 10 days ranging from 3 to 90 days. There was statistical difference in the training duration among the regions ($\chi^2=68.6$, p<0.001). Only a few 38/176 (21.6%) of the HIV/AIDS service providers mentioned to have not attended a client with ART
related ADR. Furthermore, there was no significant difference in duration of training between service providers from urban and rural facilities (p=0.445).

Table 3: Awareness of HIV/AIDS service providers on Adverse Drug Reactions

<table>
<thead>
<tr>
<th></th>
<th>Dodoma (n=50)</th>
<th>Mtwara (n=28)</th>
<th>Singida (n=48)</th>
<th>Tanga (n=51)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awareness of ADR</td>
<td>50(100%)</td>
<td>28 (100%)</td>
<td>45(93.8%)</td>
<td>49(96.1%)</td>
<td>172(97.2%)</td>
</tr>
<tr>
<td>Mean training (days)</td>
<td>7.1</td>
<td>11.8</td>
<td>12.3</td>
<td>11.5</td>
<td>10</td>
</tr>
<tr>
<td>Attend client with ADR</td>
<td>44(89.8%)</td>
<td>21(75.0%)</td>
<td>30(62.5%)</td>
<td>43(84.3%)</td>
<td>138(78.4%)</td>
</tr>
</tbody>
</table>

Although awareness of health service providers on ART related to ADR were higher in rural than in the urban, there was no significant difference (P=0.873), Figure 3.

![Figure 3: Proportion of health service providers attended training on ART related ADR by region and location](image)

Among the interviewed service providers, majority 120/177(67.8%) mentioned there was no guideline in place for reporting ART related ADRs. Of those who mentioned to have the guideline in place, 40/52(77%) showed the guideline to the investigator. Mostly, the guideline shown was the National Guideline for the Management of HIV/AIDS (MoHSW). Dodoma region had the lowest proportion of health providers who mentioned to have the guidelines and
there was no difference between urban and rural location with exception of Tanga region (Figure 4).

Figure 4: Availability of any guidelines for reporting ART related ADR

Distribution by type of health facility of proportion of providers who mentioned to be aware of any ADR reporting tools is presented in Figure 5. None of health providers at dispensary level CTCs were aware of availability of any ADR reporting tools. A total of 52/162 (32.1%) indicated they were aware of tool for collection of ART related ADRs events. There was no significant difference between urban (27/96=28.2%) and rural (25/66=37.9%) locations, $\chi^2=1.71$, $p=0.191$. Interestingly, 18/48 (37.5%) indicated they were aware of ADR reporting form supplied by TFDA (yellow/blue forms). The forms were obtained from district/regional pharmacist 25/45 (55.6%). There was slightly higher degree of awareness on the ADRs reporting among the providers in the facilities owned by public. However, only eight facilities were non-public.
Figure 5: Availability of any ADR reporting tools by type of health facility
Case documentation of ART related ADR revealed that majority were reported in the CTC form II, Figure 6.

Figure 6: Documentation of ART related ADRs at CTCs

3.1.4. Information Sharing Among Stakeholders (CTC, Zonal pharmacovigilance centres, TFDA and NACP)
Among the CTC service providers interviewed mentioned that they submit their ADR report to DP or RP 14/29(48.3%), TFDA 2(7.0%), NACP 2(7.0%) and others 11(38.0%), respectively. Promptness of reporting ART was: within 24hours 14/22 (64.0%), within 48hours 4/22(18.2%) and more than 2 days was 4/22(18.26%). The common communication channel for submission of ADR report forms were by physical submission 12/20(60%) and ordinary mail 4/20(20%). Of those who indicated to have filled and submitted ADR form, only 2/27(7.4%) received feedback.

3.1.5. Shortcomings of ADR reporting
Of the CTC HIV health providers interviewed 25/37(68.0%) mentioned that current ADR reporting form does not adequately capture the required ART related ADR information; with only 12/37(32.0%) mentioning yes it does capture the required information. Some of the shortfalls identified by the service providers include: absence of focal person, inadequate knowledge, no reliable and quick means of reporting for CTCs in the peripheral areas, lack/inadequate supply of the ADR reporting forms, ADRs are reported in the patient file and CTC form II and not the required TFDA tool. Among HIV/AIDS service providers at CTCs 75/92 (81.5%) mentioned to have encountered problems in reporting ADRs while only 17/92(18.5%) did not. Some of mentioned problems in reporting include: type of the ADRs (systemic or local, severity etc), unavailability of forms, lack of training on ADR reporting, no
feedback mechanism from national to local settings, the tool does not allow the backup of information at the CTC level after submission.

### 3.1.6. ART Client’s awareness on adverse drug reactions

In this study, it was observed that high proportion of clients in CTC in Tanga region (95.5%) were aware on ART related ADRs, while Singida had the lowest awareness (74.4%), Table 4.

#### Table 4: Response of ART clients on questions on awareness of ART related ADR

<table>
<thead>
<tr>
<th>Variable</th>
<th>Dodoma (n=128)</th>
<th>Mtwara (n=129)</th>
<th>Singida (n=137)</th>
<th>Tanga (n=155)</th>
<th>Total (N=549)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awareness on ADR</td>
<td>117(91.4%)</td>
<td>109(84.5%)</td>
<td>106(77.4%)</td>
<td>148(95.5%)</td>
<td>480(87.4%)</td>
</tr>
<tr>
<td>Information on possible ADR given to clients</td>
<td>107(83.6%)</td>
<td>94(72.9%)*</td>
<td>107(78.1%)*†</td>
<td>138(89.0%)*‡</td>
<td>446(81.2%)*††</td>
</tr>
<tr>
<td>Ever experienced ADR</td>
<td>79(61.7%)</td>
<td>33(25.8%)</td>
<td>32(23.4%)</td>
<td>57(36.8%)</td>
<td>201(36.6%)</td>
</tr>
<tr>
<td>Seen/heard ADR case</td>
<td>103(80.5%)</td>
<td>61(47.3%)</td>
<td>79(57.7%)</td>
<td>99(63.9%)</td>
<td>342(62.3%)</td>
</tr>
</tbody>
</table>

* n=127, † n=133, ‡ n=153, †† n=541

There was significant difference in the level of awareness between the regions ($\chi^2=28.8$, $p<0.001$). However, the difference was not significant between rural and urban locations ($p=0.686$). On average ART clients were well informed on where to report whenever they experience ADR, with Tanga having the highest proportion, Table 4. Detailed analysis showed that the proportion of ART clients given information by health service providers on where to report ART related ADR was significantly different between urban and rural in Dodoma region ($p=0.002$), Figure 7.
Clients on ART in Dodoma region reported highest proportion of having experienced ART related ADR, whereas Singida had the lowest, Table 4. Majority of clients who mentioned to have experienced ART related ADR, were from rural areas in Dodoma, Mtwara and Singida except Tanga where there was no statistical difference between urban and rural (p=0.570) as shown in Figure 8.

![Figure 8: Distribution of responses of ART clients whether had experienced ADR stratified by location](image)

Majority of ART clients interviewed mentioned to have seen/heard of case of ART related ADR in their areas, with Mtwara having relatively low proportion, Table 4. There was variation in proportions of ART clients who had mentioned seen/heard of ART related ADR by regions and the difference was significant between rural and urban in all of the 4 regions except Tanga (P<0.05), Figure 9. Contrary to other regions, Singida region had higher proportion in rural compared to urban.

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Across all study sites, it was observed that 178/201 (87.1%) of the clients reported to service provider. However, 10 (6.5%) said they did not take any action while 10 (5.0%) stopped taking ART (Table 5).

<table>
<thead>
<tr>
<th>Action taken by ART client</th>
<th>Dodoma</th>
<th>Mtwara</th>
<th>Singida</th>
<th>Tanga</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stopped ART</td>
<td>2 (2.5%)</td>
<td>5 (15.2%)</td>
<td>2 (6.3%)</td>
<td>1 (1.8%)</td>
<td>10 (5.0%)</td>
</tr>
<tr>
<td>Report to health provider</td>
<td>76 (96.2%)</td>
<td>27 (81.8%)</td>
<td>21 (62.6%)</td>
<td>54 (94.7%)</td>
<td>178 (88.6%)</td>
</tr>
<tr>
<td>Did nothing</td>
<td>1 (1.2%)</td>
<td>1 (3.0%)</td>
<td>9 (28.1%)</td>
<td>2 (3.5%)</td>
<td>13 (6.5%)</td>
</tr>
<tr>
<td>Total</td>
<td>79</td>
<td>33</td>
<td>32</td>
<td>57</td>
<td>201</td>
</tr>
</tbody>
</table>

In this study it was observed that, majority (47.9%) of the clients interviewed reported their ART related ADRs to the health providers in a period of more than a week, followed by a period ranging from 3-7 days (28.1%), Figure 10. It was also observed that a high proportion 160/190 (84.2%) of clients mentioned that they were provided with explanation when presenting a case of ART related ADRs. Only a small proportion (15.8%) mentioned that they were not given explanation when reporting ART related ADRs.
Majority 179/297 (51.0%) of the clients interviewed suggested that emphasis on immediately reporting of ART related ADR should be given priority, followed by regular health education of ART clients 105/297 (44.0%) on ART related ADR (Figure 11).

Figure 10: Length of time taken by client to report ADR

Figure 11: ART Client’s suggestion on improving ART related ADR reporting
3.2. PART II: QUALITATIVE RESULTS

Qualitative data were collected through in-depth interviews at national level (2), zonal level (2), regional and district pharmacists (17) and CTCs in-charges (62). This information was complemented with a thorough review of documents of PV related to ART.

Policy and guidelines in implementation of PV activities
Pharmacovigilance activities are guided by the National Medicine Policy. The policy clearly states the need for raising awareness on reporting adverse drug reactions (ADRs) at all levels of health service delivery. In the policy the role of Tanzania Food and Drugs Authority (TFDA) is stipulated as the leading institution in coordinating activities related to monitoring and reporting of existing and new adverse events associated with the use of medicinal products as stipulated under section 5(1) of the Tanzania Food and Cosmetics Act, 2003. The activities include detection, assessment, understanding and prevention of ADRs. Among the systems for reporting and monitoring adverse events and/or reactions, include spontaneous reporting systems, active surveillance system (e.g. cohort monitoring, pregnancy register, case control studies, drug registrants and manufacturers in the country. The 2nd edition of National Guidelines for monitoring Medicines Safety (2010) stipulates roles of various parties in ADR monitoring and reporting. These include Marketing and Authorization Holder (MAH), patients or consumers, health facilities, Council Health Management Teams (CHMTs), Regional Health Management Teams (RHMTs), Zonal Pharmacovigilance Centers, TFDA zone offices and TFDA headquarter office. The guidelines also value the role of development partners, public health programs such as The National Aids Control Programme (NACP), National Malaria Control Programme (NMCP) National Tuberculosis and Leprosy Control Programme (NTLP) and the Ministry’s Expanded Programme for immunization (EPI), etc, and Ministry of Health and Social and Welfare (MoHSW).

Views of informants at TFDA on existing system on ART safety reporting
All Key Informants at national level and zonal pharmacovigilance centres were of same views that pharmacovigilance aspects are necessary, not only on ARVs but also all medicines used by human populations. They concurred that TFDA has the mandate to spearhead safety monitoring for all medicines in Tanzania using various guidelines, standard operating procedures (SOP’s), and different tools such as forms for collecting safety data on medicines. According to respondent at TFDA, the relevant available guidelines relating to ADR reporting include:
1. National Guidelines for Monitoring Medicine Safety (2010). The guidelines describe various tools for collection of safety information. The tools include:

- Green Forms in Swahili language: Designed for patients to fill in when they encounter a drug reaction.
- Patient ADR Alert Card (pink): these are small cards which are given to patients indicating if a patient has a reaction to a certain drug presented during prescription and dispensing of medicines.
- Poor Quality Defect Program (blue): this is a form to be filled by a pharmacist for reporting poor quality product.
- Yellow form: improved version with sections V & VI on Therapeutic failure, Medication Errors and over dosage.


3. Standard Operating Procedures such as Receiving and Processing ADR report; Review and Annotation of ADR Report; Development and Approval of TFDA ADR bulletin and Organizing and Conducting of PV Committee meetings

3.2.1 Gaps in the implementation of pharmacovigilance model in relation to ART safety reporting in Tanzania.

Shortage of guidelines

Most of the guidelines from TFDA were neither known nor available to most respondents at national level (NACP) and Zonal pharmacovigilance centre, regional, district and health facility levels. Some of the few written materials known beyond TFDA including the Yellow Form were unavailable to respondents during data collection at these levels. With exception of Mtwara region where the regional pharmacist acknowledged presence of PV supervisory guidelines and for ADR reporting, the rest of pharmacists in Singida and Tanga regions had no such supplies. Although the regional pharmacist in Tanga region reported that yellow cards for ADR reporting were previously available it was not possible to demonstrate if there was any available stock. Such information was not obtained from Dodoma region due to unavailability of the regional pharmacist for interview. The health facilities were even more disadvantaged in terms of supplies for ADR reporting. The following quote illustrates similar concerns from national to district level on situation of SOPs and guidelines.

“Surely there are various guidelines and SOPs but currently we don’t have any. You might find them at TFDA” (KI at NACP).
“There are no guidelines in place for ADR reporting and there are also no PV Supervisory guidelines in place” (District pharmacist Kondoa district).

“We have not seen any one; we are using only national guideline for management of HIV patients” (CTC in-charge Manyoni district).

3.2.2. Assessment of the implementation strategy of pharmacovigilance system

Awareness about roles of different stakeholders

The Key Informants at TFDA, NACP and zonal pharmacovigilance centre centers were asked several questions on reporting system for adverse drug events in line with the implementation strategy of pharmacovigilance system in the country. All respondents expressed common understanding that, once detected at health facilities, information regarding adverse drug events for ARVs and other medicines should be sent to TFDA by pharmacovigilance focal persons, who are normally hospital/district or regional pharmacists. The respondents mentioned possibilities of cooperation between TFDA and NACP in conducting training to health workers about ADR for ART.

“There is close cooperation in implementation of sensitization strategy to clients who develop adverse reactions. TFDA will surely inform us whenever there is a plan for training on ADR to health facility staff particularly if it will involve those dealing with ARVs” (KI- National level).

Key Informants at national, zone, regional and district levels reported low awareness and knowledge on ADR reporting among health workers. Some health workers are not aware of the existence of reporting forms “yellow forms”, inadequate capacity in recognition or diagnosis of ADR was another major problem despite reported trainings.

“I have been visiting health facilities. Sometimes you may find challenges on availability of ADR forms sometimes knowledge gaps on how to fill those forms and sensitization on use of those forms” (Key informant- NACP).

Moreover, there was an assumption from one side that information about ADR for ART was rarely available due to likelihood of few episodes. The respondent associated such assumption with the fact that Tanzania procures WHO prequalified drugs.

“It is possible that we don’t get information often because challenges on this side [ADR associated with ART] are few. Most drugs that are brought in the country are from WHO prequalified manufacturers, governed by good quality assurance and monitoring system” (Key informant- National level).
Likewise, results also show that the roles of different stakeholders on PV system are not known particularly among district and CTC staff in most of surveyed health facilities. There was better awareness among regional staff. For example, Mtwara regional pharmacist mentioned that commitment was missing although the role of stakeholders including TFDA and NACP were very clear. In Dodoma region, TFDA was recognized as an overall in charge of the safety and efficacy of the drugs. The NACP’s role was to ensure that guidelines are put into place and used by all implementers while CTCs had a direct link with clients. Its primary objective was to ensure availability of information from the clients. The role of Zonal level was not known even after probing, among CTC staff. District Pharmacist acted as a link between CTCs and higher levels. Client’s role was reporting ADR to the health facility or care taker. However, some of them pointed out lack of guidelines which stipulates the roles and responsibilities of actors as one of the reasons.

“I am not aware of the roles and responsibilities of NACP and TFDA in ADR reporting...” (KI Mtwara rural district official)

“I don’t know the roles of different actors, because I don’t know the ADR related to ART reporting system” (CTC in-charge, Mtwara Urban).

3.2.3. Gaps on information sharing

With regard to the link between knowledge on ADR reporting and information sharing at different levels, some of the respondents reported the existence of a gap in information sharing between NACP, TFDA and the lower levels. This was attributed to limited communication between different stakeholders working at different levels of recording and reporting ADR from the district level to national level. There was no record if NACP and TFDA had been regularly exchanging information about ADR to TFDA, in case of obtaining such data during routine activities. This was due to lack of shared commitments among these national level stakeholders on how both could complement each other’s roles, including tracking and sharing/exchange of information on ADR, through a network of staff including hospital staff, district pharmacists, DAC, RAC and zonal pharmacovigilance centre. Likewise, CTC in-charges complained that there are no feedbacks even for the cases that have been reported. In general, there were hardly any dedicated sessions on information exchange between TFDA and NACP.

There is no any agreed standard guideline for conducting regular meetings or exchanging information about ADR. If needed, we can request data and obtain data on ADR through official correspondence with TFDA. That might be why we don’t have such data now, (KI- National level)
Responses from the zonal level, district and CTC in-charges indicated that information about PV system and corresponding activities had not been adequately shared to them. Some of them did not know about existence of the system at all. Some of the respondents among the CTC staff who knew about the system argued that it was weak.

Most of providers at CTC level consider only the severe cases of ADRs (KI- Arusha TFDA zonal)

“Basically many people have little or no knowledge of ADR related to ART reporting.” (Key informant, Newala district)

“Information sharing is not being practiced among the stakeholders, most of the ADR reporting ends at the level of the health facility” (CTC In-charge Kondoa).

**Time and frequency of reporting ADRs**

Interviews with National level, Zone and CTC in-charges reveal that there are very few reports submitted to TFDA from hospitals and health centers, contrary to expectations. There was an impression that some health workers do not report ADRs because symptoms are perceived as not serious and subside spontaneously. Key Informants at National and Zonal PV centre concurred as they cited misconception on financial incentives as a barrier to timely ADR reporting among health workers even if they had been trained. Other reasons contributing to underreporting include shortage of health workers and limited knowledge on ADR reporting among those available.

There is a challenge in filling those forms because even some staff at a Consultant Hospital believe that zonal officers are paid for that and should therefore do it. (KI-zonal level)

Certainly some information on ADR is not reported. The magnitude is not known, unless someone conducts research about that. (KI- NACP)

“My understanding is that District Pharmacist from the Government is the one who should report (CTC in-charge Dodoma urban – Chamwino).

**Capability of staff involved in ADR reporting for ART**

Majority of the CTC in-charges reported that they had inadequate knowledge of capturing and reporting of ADR related to ART because they had not received corresponding training.
Consequently, some cases had been referred to the district or regional hospitals for management without reporting ADR. The limited capability for ADR reporting is not only common to health facility personnel but also among CBO staff.

“One of the major constraints to effective ADR reporting is inadequate training to health service providers” (CTC in-charge Singida)

“There is lack of regular training to service providers as well as lack of incentive especially for peripheral health facilities.” (KI Singida region).

“There are no training opportunities which could help us identify and capture ADR (CBO staff Mtwara)

“Regarding safety reporting of ADR I am not so conversant with the guideline” (CTC In-charge, Madimba, Mtwara Rural).

**Supervisory visits**

Responses from respondents at different levels indicated that supervisory visits were not taking place as required due to limited financial resources. Such visits could provide opportunities to assess and improve health worker’s knowledge and practices about ADR reporting.

“Supervisory visits are there theoretically. As a focal person I am supposed to visit colleagues or rather conduct meetings on ADR with health care providers at all facilities in my zone. However, it becomes difficult; you can’t call a person from [X region or Y district] without resources to reimburse allowance or even a fare and drinking water. Ideally we were supposed to visit those centers and hospitals so that we could see as a group and sensitize them so that it can be active” (KI- zonal pharmacovigilance centre)

“TFDA did come and sensitize people on ADR reporting in the region and issued the ADR reporting forms. Since then, no follow-up or supervision has ever been made” (KI Mtwara).

**3.2.4. Awareness of PV among HIV/AIDS Community Based Organisations (CBOs)**

Staff from Community based organisation (CBO) involved in home based care (HBC) commented that there was generally low knowledge among them on how to detect and report ADR related to ARTs because they had not yet received such training. However, HBC providers
would often refer any health complication to CTC.

“We have not engaged ourselves in ADR reporting. What we do in case of any client’s health complication is that we advise them to go back to respective CTC for further assistance” (CBO staff Mtwara Rural).

“There is no training on reporting ADR related to ART” (CBO staff Newala).

“Normally all cases of ART related ADRs are referred to District Hospital CTC where patient management is done and no documentation is done at our CBO level” (CBO staff Tanga)

3.2.5. Comments/opinions the stakeholders on effective ADR reporting on ART

Key informants from different levels were asked their opinion on how to improve and strengthen ART safety reporting. There were views that information on ADR should be disseminated at all levels, explaining the roles of different stakeholders in ADR reporting. In addition, ADR data collection and reporting forms used by TFDA and NACP should be harmonised and made available at all health facilities. There was also a need for training of service providers in ADR reporting. Supportive supervision was also recommended as an important aspect in improving ADR reporting. Clear roles and responsibilities among actors need to be taken into account. It was recommended to strengthen communication at all levels including provision of internet connectivity.

“Roles and responsibilities between the DAC and the District Pharmacist need to be clearly known.” (KI Mtwara rural)

“Harmonisation of papers used by TFDA and NACP to a single ADR reporting tool can reduce workload and motivate the reporting of ADR. There is also a need to provide regular training to staff working with clients on ART at the CTC facilities” (CTC in-charge Singida Urban).

“It is important to introduce PV concepts and practice in training curriculum for nursing and medical schools because very few graduates from these students know at least about yellow” (KI- Zonal level)
4. DISCUSSION

General view
The quantitative and qualitative results presented in this report have demonstrated gaps, strengths and opportunities of existing mechanisms in view of generating evidence for strengthening ADR reporting system for ART through coordinated approach involving TFDA and NACP in Tanzania. Generally, ADR reporting was not optimal according to information triangulated from different sources in this study. This is not a unique situation for Tanzania as reporting of suspected ADRs observed during drug therapy is not routinely done in many sub-Saharan Africa countries (4,7); and the few PV activities in some African countries have mainly focused on antimalarials (8). Consistent with reported higher prevalence of HIV among females compared to males in Tanzania and other sub-Saharan Africa (9; 10), the majority of CTC clients in this study were females.

Strategy for implementation of pharmacovigilance system
Both quantitative and qualitative results have shown that TFDA plays a central role in all activities related to monitoring and reporting of ADR in Tanzania. There was no doubt that TFDA provides the ADR reporting forms to health facilities. Likewise, many health workers recognise the importance of reporting ADR to TFDA. This is in line with National Medicine Policy and section 5(1) of the Tanzania Food and Cosmetics Act, 2003. (11) [REF] which clearly states the need for raising awareness on reporting adverse drug reactions (ADRs) of existing and new adverse events associated with the use of medicinal product at all levels of health service delivery.

In accomplishment of ADR monitoring and reporting TFDA engages various parties including Marketing and Authorization Holder (MAH), patients or consumers, health facilities, Council Health Management Teams (CHMTs), Regional Health Management Teams (RHMTs), Zonal Pharmacovigilance Centers and TFDA zone offices. The guidelines also value the role of development partners, public health programs such as the National Aids Control Programme (NACP), National Malaria Control Programme (NMCP), National Tuberculosis and Leprosy Control Programme (NTLP) and the Ministry’s Expanded Programme for immunization (EPI), etc and Ministry of Health and Social and Welfare (MoHSW). Despite the joint efforts in developing guidelines, the study could not establish evidence of clear coordination mechanisms among the main stakeholders including TFDA and NACP in terms sharing information on adverse drug reactions (ADRs) on ART. This calls for urgency to set strategies for joint mechanisms for enhancing pharmacovigilance system and sharing of ART related ADRs. This
should include harmonized strategies and tools on reporting ART related ADRs and ensure the resources required are in place at all responsible levels.

**Gap in implementation of pharmacovigilance model in relation to ART safety reporting**

Contrary to the National Guidelines for monitoring medicine safety (2010), results have also shown that CHMTs and RMHTs were not conducting PV supervision visits. Likewise, Zonal centres are incapable of carrying out monitoring and evaluation of PV activities in their zones.

The most critical challenge for implementing supervisory visits was limited financial resources. Lack of such visits denies opportunities to assess and improve health worker’s knowledge about ADR reporting. TFDA has developed several documents such as training manuals, guidelines/SOPs and ADR reporting forms. Surprisingly, with exception of yellow forms, this study did not find most of these materials starting from Zonal level to health facilities. Yet, low awareness and knowledge among health facility staff on the existence of reporting forms “yellow forms”, inadequate capacity in recognition or diagnosis of ADR could as well be linked to inadequate enabling mechanisms for TFDA, NACP and relevant stakeholders to match policy and guidelines on ADR reporting with practice.

**Knowledge gap related to information sharing about pharmacovigilance activities at different levels**

Both qualitative and results have demonstrated a great knowledge gap associated with information sharing on ADR as shown by this study. Respondents from national to health facility levels concurred on inadequate knowledge in ADR reporting especially among health care providers, clients and caretakers. Besides limited training opportunities among health workers, lack of supervisory visits and unavailability of relevant guidelines contributed to observed knowledge gaps, such as inadequate awareness about ADR reporting and unsatisfactory completion of ADR forms. Moreover, there were no forums dedicated to sharing information about ADR reporting and feedback among stakeholders, namely TFDA, NACP, Zonal PV centres, RHMTs, CHMTs, health care providers and clients. The training on ADR reporting is necessary at all levels. If at all, the little communication channel that exists is one way, from health facilities to higher levels without receiving any feedback, which might lead to low morale and confidence among those affected.
**Awareness about ADR reporting among HIV/AIDS clients receiving ART, their care takers and community based organization (CBOs) that assist care and treatment with ART.**

The findings from different sources used in this study clearly depict inadequate awareness about ADR reporting among HIV/AIDS clients receiving ART, their care takers and community based organization (CBOs). This mirrors claims raised by health workers who lack opportunities to training and information sharing on reporting ADR related to ART. One of the consequences is inability of such workers to disseminate information about ADR related to ART to community home based care providers, clients, care takers and community at large. If well equipped, health workers could play vital role in awareness creation to clients, general population and CBOs on ADR and importance of reporting. Paying attention to service providers at primary health care facilities is vital since they are health gatekeepers to the community. Among others, they should be motivated, skilled and supported through supportive supervision, career development and recognition of services they provide (12).

**CONCLUSION**

Structures for conducting PV activities including indentifying and reporting ART related ADRs in Tanzania exist under coordination of TFDA. However, the system does not perform optimally, leading to inadequate reporting. Efficiency of PV system in this country is constrained by a lack of well trained personnel at health facilities, inadequate financial resources to facilitate on the job training on ADR reporting and unrealistic supportive supervisions from zonal, regional and district levels to health facilities as well as shortage of ADR reporting forms. Interestingly, there are prospects to improve PV system in Tanzania under coordination of TFDA, by engaging other stakeholders in exploiting opportunities for enhancing joint mechanisms to improve surveillance and reporting of ADRs in the country.
RECOMMENDATIONS

i. There is urgency for National level stakeholders including TFDA, NACP and other stakeholders to explore opportunities for devising joint mechanisms to enhance PV system in the country and sharing of information on ART related ADRs. This may include developing harmonised mechanisms to capture and report ADRs during routine activities.

ii. There is a need to improve dissemination and ensure constant availability of TFDA guidelines, reporting forms (yellow/blue) and other necessary supplies at all health facilities

iii. There is a need to equip TFDA and other stakeholders with adequate financial resources to facilitate planned training, supportive supervision and reporting of information about ADR coupled with timely feedback to health facility personnel.
REFERENCES


## APPENDIX

### Annex 1: Objectives operational structure

<table>
<thead>
<tr>
<th>Objective</th>
<th>Activity</th>
<th>Execution</th>
<th>Information to be documented</th>
</tr>
</thead>
<tbody>
<tr>
<td>To map the gaps in the implementation of pharmacovigilance model in relation to ART safety reporting.</td>
<td>1. Desk review process&lt;br&gt;2. In-depth interview with national pharmacovigilance implementers</td>
<td>Review of literatures, guidelines and policy documents on pharmacovigilance implementation&lt;br&gt;2a. Interview with TFDA, NACP at national level</td>
<td>Assessment of supervisory mechanism and its implementation&lt;br&gt;Availability of resources to synthesize information, availability of drug profiles&lt;br&gt;Flow of information from TFDA to other stakeholders e.g (NACP)&lt;br&gt;Flow of information between high/low levels of ARV providers (TFDA/NACP, Zone, regional, district and CTC), and timeframe, feedback mechanism&lt;br&gt;Distribution of AE by CTC sites&lt;br&gt;Feedback mechanism to low levels&lt;br&gt;Roles of zonal, regional &amp; districts on reporting of ADR to TFDA</td>
</tr>
<tr>
<td>2. To assess the implementation strategy of pharmacovigilance system</td>
<td>In-depth interview with pharmacovigilance implementers at national level</td>
<td>2b. Interview with TFDA, NACP</td>
<td>Assessment of the mechanism, of ADR reporting from CTC to higher levels&lt;br&gt;Feedback to lower levels&lt;br&gt;Information flow from TFDA and NACP to lower levels&lt;br&gt;Available facilities ( telephone, computers and internet )&lt;br&gt;System of coordination and supervision of ADR reporting</td>
</tr>
<tr>
<td>3. To assess implementation knowledge gaps related to information sharing at different levels</td>
<td>1. In-depth interview with pharmacovigilance implementers&lt;br&gt;2. Mapping of knowledge gaps among health care providers</td>
<td>Cross Cutting: Interview with pharmacological implementers at national to CTC levels&lt;br&gt;3. Questionnaire to CTC staff</td>
<td>Frequency and timely of ADR reports from TFDA to NACP and WHO&lt;br&gt;Assessing CTC awareness on ADR reporting Instruction to clients on ART intake and possibility of unwanted effects&lt;br&gt;Shortcoming of ADR data reporting form&lt;br&gt;Information sharing from TFDA and NACP to lower levels&lt;br&gt;Assessment of the mechanism, of ADR reporting from CTC to higher levels&lt;br&gt;Available facilities ( telephone, computers and internet )&lt;br&gt;System of coordination and supervision of ADR reporting</td>
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</tbody>
</table>
4 To determine awareness about ADR reporting among HIV/AIDS clients receiving ART, their care takers and community based organization (CBOs) that assist care and treatment with ART

2. In-depth interviews with care takers and CBOs undertaking care and treatment activities

4. Interview with clients/care taker

5. In-depth interviews with CBOs

<table>
<thead>
<tr>
<th>Awareness of ADR</th>
<th>Frequency of reporting ADR</th>
<th>Time of reporting such ADR</th>
<th>Where does s/he report to?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exit interview with ART clients at CTCs</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>