Pharmacovigilance in the United Republic of Tanzania: a situational analysis at the end of the PAVIA project

29 August – 2 September 2022

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List of abbreviations

ADR	Adverse Drug Reaction
aDSM	active TB Drug-Safety Monitoring and Management
AE	Adverse Event
AEFI	Adverse Event Following Immunization
AMA	African Medicines Agency
ARRT	Adverse Reactions Reporting Tool
CEM	Cohort Event Monitoring
DR	Drug-Resistant
EAC	East African Community
GFATM	The Global Fund To Fight AIDS, Tuberculosis And Malaria
HCP	Health Care Professional
HCW	Health Care Worker
HIV	Human Immunodeficiency Virus
IEC	Information, Education And Communication
IVD	National Immunization and Vaccine Development (Programme)
KCMC	Kilimanjaro Christian Medical Centre
KCRI	Kilimanjaro Clinical Research Institute
MAH	Marketing Authorization Holder
MDR	Multidrug Resistant
MoH	Ministry of Health
NACP	National Aids Control Programme
NTLP	National Tuberculosis and Leprosy Programme
NMRA	National Medicines Regulatory Authority
PBRER	Periodic Benefit-Risk Evaluation Reports
PAVIA	Pharmacovigilance Africa
PHP	Public Health Program
PMS	Post Marketing Surveillance
PSUR	Period Safety Update Report
PV	Pharmacovigilance
SAE	Serious Adverse Event
SMS	Short Messaging Service
SOP	Standard Operating Procedures
SQRT	Safety and Quality Reporting Tool
SSA	Sub-Saharan Africa
TB	Tuberculosis
TFDA	Tanzania Food and Drugs Authority
TMDA	Tanzania Medicines and Medical Devices Authority
TWG	Technical Working Group
USSD	Unstructured Supplementary Service Data
WHO	World Health Organization
XDR	Extensively Drug-Resistant

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1. Introduction

1.1. PAVIA (Pharmacovigilance Africa)

PAVIA envisions to strengthen the pharmacovigilance (PV) systems in four Sub-Saharan Africa (SSA) countries: Ethiopia, Nigeria, Eswatini, and Tanzania, to have more effective drug safety reporting mechanisms for new products introduced and to gain a better understanding of their safety profiles. PAVIA's objectives are:

i. To strengthen governance of Pharmacovigilance (PV) systems, by strengthening regulatory and organizational structures and defining clear roles and responsibilities for all stakeholders
ii. To improve efficiency and effectiveness of national surveillance systems, by strengthening active (sentinel) surveillance of adverse drug reactions and implementation of tools and technologies for their detection, reporting, analysis, and dissemination
iii. To build capacity and skills to sufficiently conduct safety-monitoring activities throughout the country
iv. To improve readiness of health systems within SSA, by improving performance assessment of PV systems allowing identification of enablers and barriers for implementation

PAVIA's strategy is to strengthen national PV systems in a collaborative effort with Public Health Programs (PHPs), building up medicines safety surveillance activities in the context of the introduction of new drugs for (multi)drug-resistant ((M)DR) tuberculosis (TB). Capacity at the national PV Centre/ national medicines regulatory authority (NMRA) will be built gradually taking the PV activities for TB as the "building and training ground" for a generic PV system including data collection, database entry, data analysis, signal identification and causality assessment and risk management and communication. The results and lessons learned will be transferred by PAVIA to the PHP for HIV and malaria. Combined with identified enablers and barriers in addressing regional differences and needs, a blueprint will be developed that can guide other countries in strengthening their PV systems.

1.2. Pharmacovigilance

The World Health Organization (WHO) has defined PV as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other possible drug-related problems."[1] The aim of the PV system is to protect the public from medicines-related harm. Currently few low- and middle-income countries have a well-functioning PV system to support the timely identification, collection, and assessment of medicine-related adverse events.

1.3. TB / aDSM

Since 2013, after introduction of two new TB drugs (bedaquilline and delamanid), WHO recommends active TB-drug safety monitoring and management (aDSM) when using one of these drugs. aDSM is defined as the active and systematic clinical and laboratory assessment of patients on treatment with new TB drugs, novel MDR-TB regimens, or XDR-TB regimens to detect, manage, and report suspected or confirmed adverse drug reactions. The overall objectives of aDSM are to

[1] WHO 2009, The importance of pharmacovigilance. Safety monitoring of medicinal products. Geneva.

reduce risks from drug-related harms in patients on treatment for drug-resistant TB and to generate data to inform future policy updates on the use of such medicines.
In the lightest version, aDSM applies targeted reporting of serious adverse events, in the intermediate form adverse events of special interest are added. In its most rigorous form, aDSM is a cohort event monitoring (CEM) where all adverse events of a patient in a TB cohort are collected during treatment. This is not deemed feasible for routine monitoring. However, depending on the information and setting, CEM might be considered for a limited period.

1.4. Pharmacovigilance in Tanzania

Spontaneous reporting of adverse drug reactions started in Tanzania in 1989 as part of the activities of the Tanzania Drug and Toxicology Information Service, TADATIS, based at Muhimbili Medical Centre in Dar es Salaam. In 1993, the Tanzanian Ministry of Health (MoH) was officially admitted by WHO as a member of the WHO Program for International Drug Monitoring. In July 2003, by law, pharmacovigilance activities were transferred to the national centre for pharmacovigilance, the Tanzania Food and Drug Authorization (TFDA). This Authority was established in 2003 after the national Parliament enacted the Tanzania Food, Drugs and Cosmetics Act (Cap 219). The pharmacovigilance centre became an integral part of that organization. The remit of the pharmacovigilance centre covers mainland Tanzania and Zanzibar, having a separate entity responsible for regulation of medicines including pharmacovigilance activities. A change in legislative framework in 2019 (Finance Act, No. 8) led to a change of name to Tanzania Medicines and Medical Devices Authority (TMDA). The TMDA, acting as an Executive Agency, is responsible for regulation of the quality, safety and effectiveness of medicines, medical devices, diagnostics, biocidals, and tobacco products.

1.5 Summary of the outcomes of the baseline assessment

In 2018, a baseline assessment of the national PV system was conducted. The assessment concluded that the national PV programme in Tanzania has a robust support from legal instruments on different levels and a strong mandate to engage new stakeholders in the PV system through the Pharmacovigilance Regulations which were endorsed in April 2018. There was a specific budget line for PV allocated by the government. The PV centre had clear guidance documents and standard operating procedures (SOPs) in place. The staff at the centre was well-qualified and experienced and continued education of staff was taken care of.
Apart from healthcare professionals (HCPs), marketing authorization holders (MAHs), and PHPs, the general public could also submit adverse drug reaction (ADR) reports. Reporters received feedback. However, the number of reports received was very low, despite several sensitization activities and trainings. At baseline, the reasons were not fully investigated, but potential causes were resource limitations, inadequate infrastructure, other priorities, lack of understanding of the significance of PV or lack of commitment from the zonal and regional PV centres.
ADR reports were adequately validated and there was sufficient experience at the national centre to conduct active surveillance studies. There was a PV/adverse events following immunization (AEFI) Technical Committee with clear terms of reference to advise about safety of healthcare products. However, very few potential signals were received and investigated. Besides, new safety information generated outside Tanzania was not effectively considered and translated into up-to-date advice to prescribers and medicine users in the country. Several and diverse communication activities had been carried out to disseminate safety information to HCPs and the community.

In conclusion the assessors felt a need for a general mobilization of all stakeholders to bring the necessary raw material to the sophisticated PV machinery in place. Detailed results of the baseline assessment are summarized in baseline assessment reports[2,3].

2. Aim and objectives of the situational analysis

This report presents the situational analysis of the various aspects and needs of the PV systems in Tanzania in the last year of the PAVIA project (2022), including its strengths and gaps. The end-line assessment aimed to:

1. Asses the PV situation in Tanzania, as compared to the baseline situation, specifically to assess what progress has been achieved since the baseline assessment. We tried to make a distinction between progress that was (partly) achieved with support from PAVIA, and progress achieved through other sources
2. Collect success stories as well as lessons learned in Tanzania which are thought to be useful examples for NMRAs/PV centres wishing to strengthen their collaboration with (other) PHPs. These stories and lessons learned will be packaged in a practical blueprint for use in other SSA countries.

[2] The National Pharmacovigilance System in Tanzania: a situational analysis at the start of the PAVIA and Proforma projects. Part 1. National Medicines Regulatory Authority, Marketing Authorization Holders, Healthcare facilities. Internal report, PAVIA consortium partners: 2018. Available on request, EFDA, Addis Ababa, Ethiopia.

[3] The National Pharmacovigilance System in Tanzania: a situational analysis at the start of the PAVIA and Proforma projects. Part 1. National Medicines Regulatory Authority, Marketing Authorization Holders, Healthcare facilities. Internal report, PAVIA consortium partners: 2018. Available at https://static1.squarespace.com/static/61c1d6045fb033710879e4f1/t/61d840fdf43d3430368b44e4/1641562369922/BLA_report_Tanzania_Part_IIa_NTP_final.pdf (date accessed: 13 Sept 2022)

3. Methodology and team

3.1. Assessment strategy

In principle, the endline assessment followed the same methodology as the baseline assessment. To take most benefit of the in-country visit, however, this time the in-country visit was preceded by a preparatory phase.

3.1.1. Pre-visit data collection

In this phase, preceding the in-country visit, we gathered data and conducted interviews with relevant stakeholders to collect as much information on the status of the PV system as possible before the in-country visit. Parts of the PV indicators' tool were filled with the help of stakeholders and the PV coordinator, and relevant data and opinions were collected during distant stakeholder interviews. This work was done by an intern (Mohamed El Amrani) under supervision of Ineke Spruijt and Edine Tiemersma, who prepared short interview reports, pre-filled PV indicator tools and a list of documentation for the in-country assessors prior to the start of the in-country visit.

3.1.2. Data collection during the country visit

During the in-country visit, three assessors Linda Härmark, Liza de Groot, and Edine Tiemersma visited Tanzania to: verify the already collected data with key stakeholders and collect missing information in focus group discussions, by observations during on-site visits, and by additional in-depth interviews. The assessors also collected information to deepen our understanding of the project's successes and lessons learned. The findings from the in-country assessment were summarized in a PowerPoint presentation, which was discussed with key stakeholders on the last day of the in-country visit to check if assessors did represent all facts correctly. A program of the end-line assessment is provided in Annex 1.

3.2. Data collection tools

3.2.1. PV indicator assessment tool

PV indicators were assessed using a slightly modified questionnaire developed and already used by the East African Community (EAC) which is based on the Indicator-based Pharmacovigilance Assessment Tool[4] and the WHO PV indicators[5]. The following elements were addressed: health system, policies, laws and financing, PV processes, capacity and infrastructure including training needs, stakeholder environment and communication/ dissemination opportunities. The tool for assessment of the NMRA contains 58 indicators that address five PV components: i) policy, law, and regulation; ii) systems, structures, and stakeholder coordination; iii) signal generation and data management; iv) risk assessment and evaluation; and v) risk management and communication. The indicator list for the PHP consists of 20 indicators addressing components two to five. These tools had also been used during the baseline assessment for the PAVIA project. The indicator tools are attached as Annex 3 and 4.

[4] Strengthening Pharmaceutical Systems (SPS) Program. 2009. *Indicator-Based Pharmacovigilance Assessment Tool: Manual for Conducting Assessments in Developing Countries*. Submitted to the U.S. Agency for International Development by the SPS Program. Arlington, VA: Management Sciences for Health.
[5] WHO 2009: pharmacovigilance indicators: a practical manual for the assessment of pharmacovigilance systems.

3.2.2. Interviews

For the individual key stakeholder interviews, we prepared topic lists to guide the interviewer during the semi-structured interviews. There were different topic lists for different stakeholders, focusing on PV policies, PV practices, or programmatic aspects. Interviews were planned to take a maximum of one hour, and the interviewer asked for permission to go over the scheduled time if needed. Also, interviewees were asked for their informed consent to participate and for the interview to be audiotaped. Interviews with all key stakeholders were planned to be held online prior to the in-country visit. Interviews that could not be organized online or in time were conducted during the in-country visit. Interviewees did not receive an incentive. The pre-visit interviews were conducted by an intern MSc student of Management, Policy-Analysis and Entrepreneurship in Health and Life Sciences (Free University of Amsterdam, The Netherlands).
During the in-country visits, several group interviews with relevant stakeholders were organized. During these group interviews, missing information was collected and information already available was discussed, specifically regarding best practices and lessons learnt. Notes were taken during all group interviews, but most interviews were not audiotaped.

3.3. Assessment team

The assessment was conducted by Linda Härmark, pharmacist, epidemiologist and PV specialist, and leader of work package 3 of PAVIA, Liza de Groot, epidemiologist with experience in qualitative research, and Edine Tiemersma, epidemiologist and TB specialist, and leader of work package 4 of PAVIA.

3.4. Documents reviewed

A list of documents that were reviewed for this assessment is provided in Annex 5.

3.5. Sites assessed and stakeholders interviewed

The in-country work included visits to several health facilities (Annex 1). A list of stakeholders interviewed is provided in Annex 2.

3.6. Data compilation and analysis

Data collected during the semi-structured interviews, group interviews and observations was compiled and analysed. Interviews were transcribed verbatim using Otter software (https://otter.ai), and transcripts were cross-checked manually to identify and correct any errors in the transcription. The transcripts were analysed using ATLAS.ti (https://atlasti.com/), using a thematic approach, including both deductive and inductive coding strategies. For deductive coding, predefined codes and categories were based on the themes and subthemes of the interview topic guide. Inductive coding was guided by the data collected in the transcripts, thus allowing for new codes and categories to emerge. A separate report with more information about this qualitative data collection and analysis was prepared by the intern. For this report, we focused on lessons learned during PAVIA, comparing the data collected at endline to those collected at baseline (focusing on the gaps identified at baseline) and with the desired situation at the end of the

project as described in the country's PV Roadmap[6] .Results of the qualitative data analysis were triangulated with the quantitative data collected.

3.7 Presentation of results

In this report, we present the results of this endline assessment as follows. We have compared the situation in the country during the endline assessment to the *situation at baseline* (described in the baseline assessment reports (see footnotes 2 and 3 for reference)) and the *planned situation at endline*, as provided in the country's *roadmap*[6]. We have used colour coding to provide a quick overview of where the country stands per topic, in which green indicates that the planned situation has been fully reached (and/or that there is marked improvement since the baseline assessment), yellow means that there is improvement since baseline and/or steps have been taken for improvement, but that the anticipated endline is not yet reached; and orange means that there are no improvements from baseline and/or no steps have been taken yet to reach the anticipated situation at endline.
Per area, we provide a short summary of the situation at endline, discussing lessons learned. Further, we present case reports of best practices in text boxes.

3.8. Limitations

This assessment report contains qualitative data collected during in-depth private and group interviews, observations, and quantitative data collected from VigiFlow. During this exercise, the assessors and the intern could only speak to a limited number of stakeholders and visit a limited number of health care facilities.
No in-depth interviews could be organized with senior TMDA management. Therefore, this assessment does not include information about the vision of the management about the place of PV within TMDA, financial prospects for PV, government official's opinions, and plans to further strengthen PV in the country.
As the focus of the country visit was to work out leads for success stories, health facilities with a relatively poor performance with respect to pharmacovigilance were not prioritized and are therefore underrepresented in this assessment. Still, the assessment team does believe that sufficient information was collected to get a broad understanding of the issues regarding PV in Tanzania.

[6] The National Pharmacovigilance Roadmap 2019-2023. TMDA: 2019. Available at: https://static1.squarespace.com/static/61c1d6045fb033710879e4f1/t/61d7faa61b91704f92ef0ad4/1641544362938/The+National+Pharmacovigilance+++Plan_22JAN2020+no+2.pdf (date accessed: 13 Sept 2022).

4. Results, compared to situation at PAVIA baseline and anticipated endline

4.1. Policy, law, and regulations

Twelve indicators were collected for this area (see Annex 3).

4.1.1. Summary of the situation at endline

Hereunder, the main gaps identified during the baseline assessment are listed against the (anticipated) situation at endline:

Gap identified at baseline*	Situation at endline	Anticipated situation at endline**
No high-level national PV policy document (which may increase engagement of stakeholders)	• PV regulations approved in 2018 • EAC harmonized compendium on safety and vigilance of medical products and health technologies (March 2019) used as the PV guideline	3.1.5 Develop, print and disseminate PV tools (Regulations, Guidelines)
	• SOPs in place at TMDA • Several stakeholders have access to electronic PV register (VigiFlow) • Two safety bulletins published between 2018 and 2021	3.1.5 Develop, print and disseminate PV tools (…, SOPs, Registers, Bulletins)
	PV regulations were shared with zonal TMDA offices and regional PV coordinators. Further dissemination is ongoing.	3.1.2. Orient and disseminate new PV regulations to all PV stakeholders

*See baseline assessment reports for Tanzania (footnotes 2 and 3); **See National Pharmacovigilance Roadmap 2019-2023 (footnote 6).

Acts, Regulations and Guidelines

The legal provisions for pharmacovigilance or medicine safety are described in the "Tanzania Food, Drugs and Cosmetics Act" (2003). Subsequently in 2003, the TMDA was established. The TMDA is the successor of the TFDA and functions as Tanzania's drug regulatory authority. The function of the TMDA is described in this document in Section 5 subsection 1: "The authority shall ensure that evidence of existing and new adverse events, interactions and information about pharmacovigilance of products monitored globally, and are analysed and acted upon".

The functions and mandates of TMDA are legally provided for in this Act, the Tanzania Medicines and Medical Devices Act (2019, revised in 2021) and in "The Tanzania Food, Drug, and Cosmetics (Pharmacovigilance) Regulation (2018).

The Regulation requires manufacturers and MAHs to establish a pharmacovigilance system (Part II, 8(1)), and health facilities and pharmaceutical outlets to establish a system for collecting, managing and reporting adverse events (AEs) to TMDA and appoint a PV focal person (Part III, 25). Also, PHPs should appoint a PV focal person (Part III, 27). The Regulations also encourage distributors, importers, exporters, healthcare institutions, other stakeholders, and consumers to report ADRs and AEs to the TMDA. Moreover, manufacturers are required to do investigations as part of the safety and quality issues.

> *District Medical Officer: "…in that Regulation, basically it is stipulated and it's explained in terms of how the pharmacovigilance system should be, from the national level, pharmacovigilance centres, but also the roles in terms of our zone office and the regional level. So that's one of the strengths that we have, having in place the*

instrument, that's one. But secondly, a platform [supporting] *the Regulation that we have in place. Also, we have various guidelines and SOPs, which can guide the service provider at all levels, to be able to report the adverse event."*

There is a national policy on pharmacovigilance available in Tanzania, which is called "The National Health Policy". In this policy, it is stated that the government will 1) ensure quality and safety of traditional and alternative medicines in use; 2) strengthen basic and scientific research on traditional medicine practice, traditional medicines, and medicinal plans for improvement of traditional health services; and 3) promote industrial manufacturing of materia medica (traditional medicines). The policy was last reviewed in 2017.
The TMDA website (https://www.tmda.go.tz/) presents all relevant acts, regulations and guidelines related to PV. Furthermore, and in addition to the government gazette, the website functions as the official source of information on medicinal products that are licensed for use in the country.

National Essential Medicines List

The Standard Treatment Guidelines and National Essential Medicine List Tanzania Mainland was last reviewed in 2021. The document is available at the pharmaceutical section of the Ministry of Health. The experts in the essential medicines list selection committee are from different institutions, including TMDA, and consult medicine safety information. This process was earlier described in a scientific paper[7], though at that time, consultation of and reliance on scientific evidence was judged to be minimal at that time. The 2018 version was therefore developed in a series of workshops building capacity of the committee members in evidence-based medicine (see https://www.idsihealth.org/blog/new-treatment-guidelines-launched-in-tanzania/).

Developments since 2018

Although the enabling legal environment already existed in 2018, new documents became available or were updated. Also, in the past few years, the Regulations and Guidelines have been actively shared with zonal and regional PV focal persons during trainings and sensitization meetings.
Despite these encouraging developments, interviewees expressed that there is a lack of putting the regulations and guidelines into practice, which may be due to insufficient law enforcement.

4.1.2. Best practices

Decentralisation to strengthen PV at the Health care facility level

Tanzania is a large country, both in terms of area and population. To promote the importance of pharmacovigilance in general and the reporting of adverse drug reaction in particular, it is important for TMDA to reach the individual health care professionals, health care workers and patients at the local health facility level. To be able to do this, TMDA has introduced a decentralized PV system. In this system, the TMDA headquarters are responsible for coordinating all PV related activities nationwide. The TMDA is also responsible for sharing Tanzanian ADR reports with the global database. The TMDA zones have a zonal PV coordinator who is responsible for the coordination of the PV activities in the zone. At a zonal level ADR reports are also collected, and the zonal staff are also able to enter reports into the Tanzanian database VigiFlow. Each zonal office is responsible for a number of regional PV centres. The regional offices are not part of the TMDA structure, they are usually located in the regional referral hospitals. Each regional centre has a regional PV coordinator, often this is the regional pharmacist who is employed by the regional referral hospital. All health facilities at the district and community level should have a PV focal person, who is responsible for promoting pharmacovigilance and collecting reports at a local level. Although not all facilities have implemented this full yet, some examples such as at Muhimbili and Dodoma facilities, see success story on data collection and management,

[7] Mori et al. The role of evidence in the decision-making process of selecting essential medicines in developing countries: the case of Tanzania. PLoS One 2014; 9:e84824. https://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0084824&type=printable. Date accessed: 7 Sept 2022.

show how powerful such a system with PV focal persons can be if implemented well. The system with PV focal persons in all facilities is made possible because the regulation stipulates that each health facility should have a PV focal person (article 25.2).

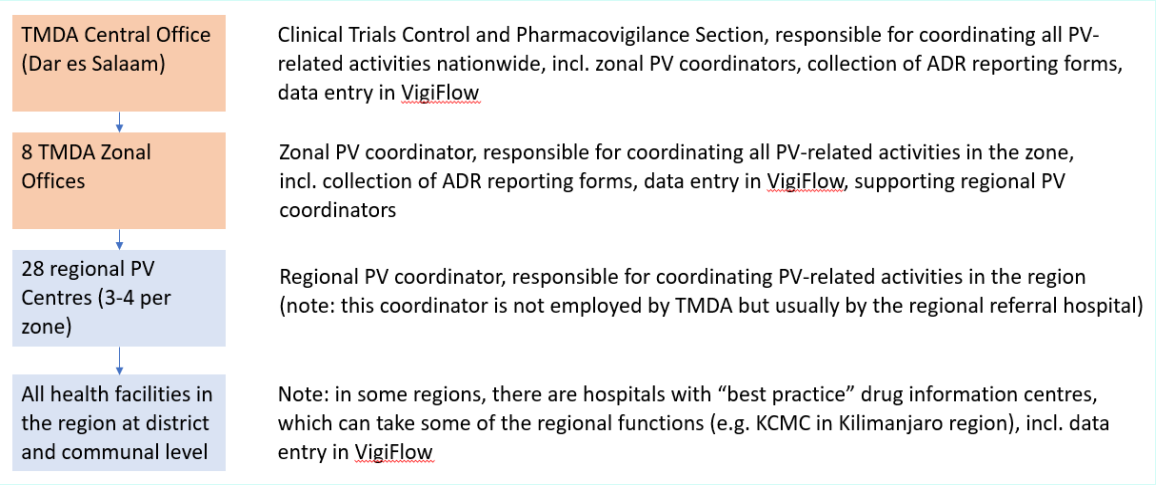

Figure. Schematic presentation of decentralisation of PV system from national to health facility level.

4.2. Systems, structure, and stakeholder coordination

In this area, fifteen indicators were assessed at the level of the NMRA (Annex 3), and six indicators at the level of the PHPs (Annex 4).

4.2.1. Summary of the situation at endline

The situation at endline is summarized in the following table:

Gap identified at baseline*	**Situation at endline**	**Anticipated situation at endline****
Funding		
Budget allocation at various levels is too low for implementation of new PV guidelines	The Regulation prescribes that all PHPs and health facilities should conduct PV. PHPs should incorporate PV in their strategic plans and budgets. The NTLP and NACP have done this though the budget of NTLP is minimal. According to the Medicines and Therapeutic Committee Guideline, health facilities are required to budget for accommodation of monitoring of medicine safety.	3.5.3 Sensitize Health facility and PHPs to plan and budget for PV activities
Staffing		
No internal competence and capacity for a pharmacovigilance inspectorate able to supervise and guide development of pharmacovigilance systems in the private sector	• NACP and NTLP have a PV focal person trained by TMDA • Public Regional referral hospitals have PV focal persons, training ongoing • Private health facilities have PV focal persons on their own initiative • MAHs received training and letters requiring the appointment of	3.5.1 Appoint PV focal person in all health facilities, PHP, Medical Stores Department, MAH and community pharmacies.

Gap identified at baseline*	Situation at endline	Anticipated situation at endline**
	qualified PV focal persons • No PV focal persons in Medical Stores Department or community pharmacies yet	
	So far, very few inspections were done. This is planned for Q4 2022; Good Manufacturing Practice inspection will incorporate PV.	3.1.4 Conduct PV inspection as per the PV regulations
PV structures at subnational level		
• Limited engagement and commitment from the zonal representatives of the TFDA • No PV focal persons at all regional and district centres	• TMDA has appointed a PV focal person in all 8 zonal TMDA offices; all staff of these offices was trained on PV • 28 regional PV-centres were installed and part of these equipped with computers and printers	3.5.4 Establish 24 and revive seven (7) PV regional centres by providing working tools for PV activities in the existing infrastructure of referral regional hospitals.
	PV Regulation requires all hospitals to establish a PV system, but this is not yet checked or enforced by TMDA. Currently, not all private hospitals have a PV system	3.5.2 Establish PV task force in all public and private hospitals
• Staff of regional PV centres is not trained for assigned tasks and operate in isolation • No regular communication about PV-relevant matters between national and subnational levels	• 12 of the regional PV focal persons received training; training is planned for more regional PV focal persons • VigiFlow training planned once per year (physical or via Zoom) – so far, two trainings were held for 175 PV focal persons (70 in 2021 via Zoom, 105 in 2022 face-to-face) • Biannual progress workshops for PV centres performed	3.7.4 Conduct biannual PV centres workshops to discuss progress and sharing experiences from the best performers
Training		
No plan for competence development of new staff in the PV system	There is a 3-year staff development plan. PROFORMA project includes MSc and PhD training.	3.6.1 Establish training plan for existing PV staff, including short course, MSc and PhD training.
Additional resources needed for capacity building and competence development both internally and among the new stakeholders	• 150 HCWs were trained in aDSM through blended-training. • 62 HCWs were trained in PV	3.6.2 Identify and conduct PV training and sensitization to Health Care Workers at all levels
	• Council and District Health Management Teams trained by TMDA on PV.	
No mechanism in place to monitor transfer of knowledge from trained personnel to other staff who are not trained	Blended learning program implemented using Training-of-Trainers approach. Different trainees have trained other HCWs. However, no clear system is in place to keep track of this and keep it rolling.	Not formulated
Little capacity in Drugs and Therapeutic Committees at regional and health facility level (if at all available)	Medicine and Therapeutic committees trained on the use of the PV guideline. Community Advisory boards: community leaders and community	3.6.3 Train and sensitize Medicine and Therapeutic Committee members and Community Advisory Boards on

Gap identified at baseline*	Situation at endline	Anticipated situation at endline**
	health workers have been sensitized about PV.	PV activities.
--	Reporting via SMS installed. All trainings and sensitization meetings include training on all ADR reporting methods, including via SMS.	3.6.4 Train and emphasize on the use of m-Health in reporting ADR by the HCWs
No standard undergraduate basic PV curriculum for HCPs	PV curriculum developed with MUHAS for pharmacy, medicine and nursing undergraduates. (PROFORMA project) MUHAS has incorporated this curriculum in the pharmacy, but not yet in the medicine and nursing curricula.	3.6.5 Mapping of the Health Training Institutions for inclusion for PV module in their Curriculum 3.6.6 Develop and introduce PV modules in the medical curricula at Health Training Institutions
Stakeholder coordination		
Little international collaboration and participation in international meetings	TMDA has been participating in different regional activities (see text for examples) organized by AMA and EAC.	3.8.1 Attend Regional and International meetings on PV 3.8.2 Harmonize on PV activities within EAC region
No collaboration between National PV Centre and PHPs	PHPs are required to incorporate PV in their strategic plans and budget; this is done by NTLP and NACP. However, structural links are not yet existing (in the form of SOPs or ToRs).	3.2.1 Establish a structural link between the National PV Centre and PHPs
	ADRs are to be collected on aDSM paper forms, which are to be entered in SQRT. However, the procedures are not entirely clear and different health facilities use different procedures (see text for more information).	3.2.2 Establish standardized procedures for collecting information on adverse drug reactions (ADRs) from PHPs and sharing this information with the national PV Centre
	TWG established. Quarterly meetings conducted.	3.2.3 Establish national PV Technical Working Group (TWG)
Few of the domestic pharmaceutical corporations are equipped in terms of structures, processes and competence to comply with the new pharmacovigilance regulations	PV Regulations in place which prescribe having a PV system in place. TMDA conducts inspections to MAHs, manufacturers and health facilities, which include PV sensitization.	3.1.7 Conduct annual stakeholders meeting to sensitize and create awareness on safety monitoring of medicines
Other structure-related issues		
No system for estimating the level of medicine use in major segments of the Tanzanian healthcare system	No progress	3.1.3 Establish system to capture medicines utilization in the country in order strength PV system.

*See baseline assessment reports for Tanzania (footnotes 2 and 3); **See National Pharmacovigilance Roadmap 2019-2023 (footnote 6).

The National PV Centre

PV is the responsibility of the Clinical Trials Control and Pharmacovigilance Section at TMDA (hereafter referred to as *(national) PV centre* for brevity). The section has 7 full time employees who are responsible for regulation of clinical trials, PV and post marketing surveillance. The mandate and organizational structure of the section is described in "The Tanzania Food, Drug, and

Cosmetics (Pharmacovigilance) Regulation" (2018) and in "The National Guideline for Monitoring Medicines Safety" (2020). It should be noted that the TMDA PV staff can involve TMDA staff working in other sections whenever needed. Likewise, the PV staff also provides assistance to other tasks of TMDA if needed.

The PV staff implement and coordinate activities related to PV, safety in clinical trials and post marketing surveillance (PMS), provide sensitization and education about the importance of ADR reporting to the general population and healthcare workers, and respond to customer inquiries regarding PV and PMS. They also review Periodic Safety Update Reports (PSURs), Periodic Benefit Risk Evaluation Reports (PBRERs) and Risk Management Plans required from MAHs and communicate with these about safety matters. Also the Clinical Trials Control and Pharmacovigilance Section coordinates Zonal and regional PV offices, provides for the secretariat of different entities (PMS task force, national PV TWG), and collaborates with different stakeholders (universities and research institutes, PHPs) in strengthening the PV system. For the received ADR and AEFI reports from HCPs and the community, the section conducts causality assessment. Of note, causality assessment of serious adverse events (SAEs) is conducted by the national PV TWG (now called the Pharmacovigilance Technical Committee).

The TMDA conducts PV inspections at all hospitals. During these inspections, they validate that the drugs sold are registered and of quality. During these inspections, information about PV (aims, duties of HCPs) is provided.

Although, after making an official request, the PV section can involve staff from other TMDA sections, the current staffing is barely sufficient to conduct all main tasks concerning PV. The PV section has a constant supply of intern pharmacists (n=3) who mainly enter ADR reports into VigiFlow. However, also this is not enough staff to clear backlogs in report validation and entry. Staff turnover is low, but well-trained staff may leave or is seconded to serve as consultants in other organizations.

TMDA has developed and is funding a 3-year development plan for its own staff, which is reviewed annually.

Funding

In the last fiscal year, 29,342,320 Tanzanian Shilling (TZS, equivalent to 12,584 US dollars) were allocated for PV activities by the government and 1,026,194,496 TZS (equivalent to 445,784 US dollars) were allocated by donors. The total budget available for PV increased from 447,967,500 TZS in 2018 to 1,055,536,816 TZS in 2022, but it is unclear if the allocation of budget from government (29,342,320 TZS) has increased over these years. Moreover, only 3% of the total funding allocation in 2022 was made available by the government. Thus, the sustainability of the current system is still at stake.

The Tanzania Food, Drug, and Cosmetics (Pharmacovigilance) Regulation and the Medicine and Therapeutic Committee Guideline specify the need to budget for and conduct drug safety monitoring in health facilities, there is no specific budget allocation to PV. The budget is used for regular meetings in which, amongst other things, PV issues are discussed.

Government funding is based on TMDA projections per section and relies on Parliamentary approval of Ministerial budgets. The MoH subsequently approves TMDA budget and the management team of TMDA decides how the total budget is divided, following advice from TMDA's planning section.

Subnational structures

During the PAVIA project period, one additional zonal TMDA office in Geita was established, bringing the total to eight zonal centres. Also, 20 regional PV-centres were installed, one of these being in Geita Regional Hospital. The zonal PV coordinators are employed by TMDA in the zonal TMDA offices (one per office). They support the staff of the Clinical Trials Control and Pharmacovigilance Section in their zone, and coordinate all PV-related activities in their zone. The regional PV coordinators are employed by the regional hospitals in which they are located

(following the Regulation). Usually, these are pharmacists or pharmacist technicians. Sometimes, they are supported by other hospital staff. With support of the PAVIA project, 20 of the regional PV (or drug information) centres were supplied with computers and printers to facilitate AE reporting. Training of the zonal PV coordinators has been conducted, while training of the regional PV coordinators is ongoing. The Clinical Trials Control and Pharmacovigilance Section is planning further roll-out to district and local levels.
While the Regulation stipulates that all health facilities and community pharmacies should have a PV system, not all have a PV focal person as the Regulation is not enforced.

> *Staff of Clinical Trials Control and Pharmacovigilance Section at TMDA: "We have so much pharmacists in the country, PV is not clear to them. (…) Maybe we should start with* [training] *hospital pharmacists* [as PV focal persons]*: they have their responsibilities clear outlined. The private pharmacists are more difficult"*

Twenty regional PV coordinators and all PV focal persons at the 8 TMDA zonal offices have been trained on VigiFlow and can directly enter ADR reports into VigiFlow. In addition, staff from specialized hospitals and regional pharmacists were trained.

Training

In-service training

The TMDA organized different trainings on PV for PV-focal persons at healthcare facilities using its PV training manual and guide. A practical session on filling the yellow and/or aDSM forms and data entry in VigiFlow was part of the training. Several interviewees indicated that continuous training is needed to keep the reporting rates high:

> *DR-TB nurse: "Train more people, transferring knowledge is not an easy task."*

> *Pharmacist Drug Information Centre: "Through my experience, we need to do awareness every three months, so that they* [healthcare providers] *know the importance of reporting ADRs."*

The COVID-19 pandemic has hindered the continuity of trainings, as some staff members were not trained due to time-constraints or because of sickness from COVID-19. The pandemic also caused several in-person trainings to be less efficient than face-to-face trainings due to sickness and for safety measures. Lack of funding is a risk to continued trainings, as many trainings between 2018 and 2020 were organized using PAVIA budget, which will not be available after 2022.
Under the PAVIA project, a blended learning training was coordinated and organized by TMDA with support of the University of Verona for a limited group of trainees, who were supposed to act as trainers in step-down trainings. Several trainees have indeed provided step-down trainings to staff in their own facility. For example, at Kilimanjaro Christian Medical Centre (KCMC), step-down trainings were organized for 62 HCWs. An important barrier for the training was the lack of designated training time for HCWs: all training participants had to prepare and study the training materials in their spare time. In the monitoring system, the staff of the Kilimanjaro Clinical Research Institute (KCRI) could see that only part of the trainees had responded to the outstanding questions on time. As the second course (focusing on TB) was less relevant to some staff, less staff completed the second than the first course. Still, the blended learning training was perceived to be very useful by interviewees:

> *Pharmacist Drug Information Centre: "The champions are the ones who have been trained, and we keep following them up."*

Previously, the Elisabeth Glaser Pediatric AIDS Foundation (EGPAF) provided training on PV in collaboration with TMDA, particularly for HIV drugs. Currently, such trainings are not provided.
Through the ASCEND project, Muhimbili University of Health and Allied Sciences provides short training programmes on PV in clinical trials.

Pre-service training

At MUHAS, although new curricula on PV are available for the studies of pharmacy, medicine and nursing, the curriculum is only incorporated in the pharmacy degree programme.
At KCMC, currently, clinicians are trained on PV after being employed at the hospital. Therefore, there is the plan to introduce PV as a topic in the curricula for medical students. Nurses do not receive PV training.

Within TMDA

For its own staff, TMDA also organizes trainings, both according to a standard 3-year training programme and by short-term programmes, which are tailored to the workers' needs. TMDA staff can also follow BSc and MSc trainings. Two staff members from TMDA's management are currently receiving PhD training through the PROFORMA project.

Stakeholder coordination

Since 2018, TMDA is collaborating with an increasing number of international partners in PV. Apart from the EAC, there are also collaborations with the African Vaccine Regulatory Forum (AVAREF), the Southern African Development Community (SADC), and the African Medicines Agency (AMA). Examples of international collaboration are participation in approval of new medicines and joint inspections. Besides, TMDA is providing technical assistance, training and mentorship to the NMRA of Burundi.
Several PHPs have started or intensified their collaboration with TMDA since 2018: the National Tuberculosis and Leprosy Programme (NTLP), the National AIDS Control Programme (NACP), and the National Immunization and Vaccine Development (IVD) Programme. There are three pharmacists employed at the NTLP, one of whom serves as PV focal persons to TMDA. Also the NACP, the National Malaria Control Programme and the IVD Programme each have a PV focal person.
Prior to the PAVIA project, collaboration between the TMDA and NTLP (and other institutions) was facilitated by the fact that the institutions are all linked to the MoH. For example, research units of hospitals would need to report their clinical trials to the MoH. The PAVIA project provided infrastructure through the PAVIA triangle. Regular PAVIA triangle meetings have helped to strengthen the collaboration through building personal relationships. The improved collaboration between the two institutions was further facilitated by the fact that the directors of the TMDA, the NTLP, and the KCRI were willing to join the PAVIA triangle meetings.
The improved relationships have also helped in PHPs involving TMDA staff in new studies. For example a study protocol is being developed for new TB preventive treatment regimens for persons with TB/HIV co-infection by NTLP and NACP jointly. They have reached out to TMDA for technical support in development of the PV section of this protocol.

PAVIA triangle

The PAVIA triangle was seen as a successful model to strengthen collaboration between TMDA and PHPs. At the time of the assessment, TMDA was considering to add the NACP to the Triangle.
Triangle meetings used to be held face-to-face, but Zoom was adopted as a meeting platform during the COVID-19 pandemic. Barriers to the triangle meetings are unclarity about who is responsible (formally, this responsibility is with the PV coordinator of TMDA, but KCRI is often asked to assist with setting time slots and inviting Triangle members), absence due to illness, lack of reliable internet access in several facilities, and lack of funding to organize face-to-face meetings.

4.2.2. Best practices

Involving all levels starts with training

Multiple trainings on pharmacovigilance (PV) were developed by TMDA and provided to different target groups. Also, PAVIA developed a blended learning training.

- All eight zonal PV focal persons (appointed by TMDA) were trained on PV during a training at national level in Dar es Salaam.
- Subsequently, these zonal PV focal persons trained twelve out of 28 regional PV focal persons.
- The most enthusiastic and engaged trainees receive additional on-the-job training from the central TMDA office, by involving them in tasks that the central office conducts in their region (e.g. inspections following a potential signal).
- At Kilimanjaro Christian Medical Center (KCMC) a 5-day training was given to train 20 trainees, using a training of trainers approach. These trained people were seen as champions from their health facility: after receiving the training on PV, they became trainers themselves, and trained their colleagues in health centres and hospitals. Unfortunately, no clear system is in place to keep track of this and keep it rolling.
- In total 62 Health Care Workers (HCWs) were trained at KCMC. All HCWs successfully completed the first course. Not all of these completed the second course on tuberculosis (TB), because for some of them, this subject was less relevant.
- 150 HCWs were trained in using aDSM through blended training.
- It is planned to provide annual training on data entry in VigiFlow: via Zoom or physical.

Dr. Eva Muro, PV coordinator at KCMC

Eva Muro gave trainings on PV and tutored trainees (once they are giving trainings to their colleagues). She explains the importance of educating HCWs on PV:

> *"People should be made aware about the law, it is part of their duty to report".*

Currently, a lot of HCWs do not see reporting as their responsibility, are in stress of time, experience administration burden, or are afraid of punishment:

> *"We need to do sensitization, because nurses and clinicians sometimes say: if we report, we are getting punished. So, we told them nothing will happen, we just want to know."*

Furthermore, she stressed the value of practicing the use of yellow forms and aDSM forms:

> *"Now they have so many forms to fill in, aDSM is not popular, but it is important that they know how to use them in a correct way."*

At KCMC, the drug information and pharmacovigilance (DIP) department – a collaboration of pharmacists and pharmacist-volunteers – are eagerly reporting Adverse Drug Reactions (ADRs). All employees at the DIP followed a training on PV, which was received well, as Deogratius explains:

> *"The e-course is a very good start for someone who wants to know about PV"*.

However, he also emphasizes that

"The training is quite difficult, because you have the test at the end of the day, there is no time for studying".

Pharmacists of the KCMC DIP are discussing an ADR report. F.l.t.r: Deogratius, Mercy, Rahim and Ismail

Also, DIP staff is involved in continuous on-the-job training, as is shown on the photograph.

Engaging PHPs by setting up personal relationships

Historically, PHPs have worked with TMDA. The fact that TMDA and the PHPs are all situated within the Ministry of Health simplifies this collaboration. Representatives of the National AIDS Control Programme (NACP) and the NTLP mentioned to collaborate with TMDA for the approval of the importation of (new) medicines, medical devices and diagnostic equipment, and to ensure that high-quality drugs are being used by the PHPs via regular inspections.

The PAVIA project has further improved this collaboration with regards to pharmacovigilance. Pharm. Jumanne Mkumbo, PV focal person at the NTLP, explains that the PAVIA project facilitated in setting up regular meetings between the NTLP, TMDA and KCRI and that this helped to strengthen personal relationships, create partnership and mutual understanding of the issues. These strong relationships make it also easier to meet each other on ad-hoc basis, e.g., to solve any challenge that may occur. Such meetings are either initiated by TMDA or NTLP.
Improved collaboration led to providing more training and on-the-job training to TB staff in health facilities. This way, the awareness among healthcare providers about the importance of PV increased and this in turn led to increased numbers of TB-related ADR reports being received by TMDA.

"I think if you don't have that spirit of reporting, you will fail. So the only thing is to ensure that we mobilize our people, we make sure that we sensitize our people see the importance of reporting, because reporting of adverse drug reactions saves some lives, some people's lives. So if they realize that, I think they will be automatically continue reporting without hesitating."

Pharm. Jumanne Mkumbo, PV focal person at the NTLP

TMDA helped in setting up VigiFlow in several health facilities including facilities where DR-TB patients are treated. This helped to improve the data flow from the facilities to TMDA and beyond.
There is also a clear understanding of the roles and responsibilities of both partners:

> *DR-TB focal person: "What we* (NTLP) *are doing here is just identifying the adverse events from the treatment sites, and then record the events and report to the TMDA, which are the ones who are supposed to do the signaling and causality assessment." […] "I think the TMDA needs to provide this feedback, so that, because the policy allows them to do that, and we are supposed to follow their advice regarding the safety of the patient. So I think that the TMDA needs to provide those feedbacks. If there is a need to change the treatment modality or policy, we will do that. But we cannot do that without having evidence or recommendation from the PV unit of the TMDA."*

Based on this encouraging example, NACP, which is located in the same building as the NTLP, intensified and broadened its contacts with TMDA. Supported by TMDA, NACP is currently conducting a study on possible side effects of dolutegravir. NACP and NTLP have jointly prepared a pilot study for introducing a TB preventive treatment regimen containing rifapentin (3HP) for persons living with HIV. The PV focal person of the TMDA branch office in Dodoma assisted in development of training materials for technical committee members and healthcare providers involved in following up on the safety of this new 3HP regimen.

Pharm. Seraphina Cleophas from the TMDA Dodoma branch office, who provided training to NACP staff on patient safety monitoring.

4.3. Signal generation and data management

In this area, six indicators were assessed at the level of the NMRA (Annex 3) and one indicator at the level of the PHPs (Annex 4).

4.3.1. Summary of the situation at endline

The following gaps were identified at baseline, and these were addressed as follows:

Gap identified at baseline*	Situation at endline	Anticipated situation at endline**
Necessary equipment for patient monitoring to prevent and/or detect AE early is not available in all DR-TB centres	The hospitals visited during the assessment (Muhimbili, Kibong'oto, KCMC and Dodoma General Hospital) reportedly all had equipment in place. ECG machines were provided by the MoH to all bigger hospitals with referral functions. However, NTLP staff admitted that not all hospitals caring for DR-TB patients have (working) equipment in place (see quote).	Not formulated
Separate reporting routines within NTP and PV system lead to scattered availability of data, with SAE being sent to both systems, but other AE only to the aDSM system	• TMDA was engaged in setting up the aDSM reporting system. aDSM reports can be entered in SQRT. • Reporting is still scattered, as some health facilities report on both the aDSM form and the yellow form, whereas others only report on the aDSM form. aDSM and yellow paper reports still follow separate routes. Because of this double reporting, TMDA in principle does not take aDSM reports into account.	3.3.1 Establish a process for including active surveillance data from PHPs in data used by regulatory authorities for decision-making. 3.3.2 Engage in active surveillance for safety monitoring of medicines including DR-TB medicines in collaboration with PHPs
No copies of reports sent by HCPs to TFDA available in health facilities (no tracking possible)	Visited health facilities all keep copies of reports sent to TMDA and/or NTLP.	Not formulated
Separate electronic reporting systems for TB-related ADRs via the aDSM system and other ADRs	A link between SQRT and VigiFlow has not yet been established. Instead, data reported in SQRT is hand-copied from SQRT in VigiFlow.	3.4.1 Create a link between TFDA electronic reporting system and electronic aDSM system for NTLP.
Infrastructure (e.g. offices, computers, internet) is lacking within the national PV network	There is no linkage to the electronic patient registers. SQRT provides for electronic reporting of ADRs through the website, a mobile phone app, and SMS. ARRT, the predecessor of SQRT, is still available for reporting. It is not clear were reports submitted to ARRT end up.	3.4.2 Create a link between DHIS2/ETL Register and TFDA electronic reporting system 3.4.3. Harmonize current health management information systems and electronic ADR reporting systems
Reporting rate has not reached a level that is likely to reflect the frequency of medicine related problems happening in the healthcare system	Reporting rate has increased from 4.8/100,000 population in 2018 to 150.0/100,000 population in 2020. This is still below the expected reporting rate.	
Lack of engagement from healthcare system	All health facility inspections conducted by TMDA include a component on PV sensitization.	Not formulated

Gap identified at baseline*	Situation at endline	Anticipated situation at endline**
No PV focal persons in healthcare facilities	According to the PV Regulations, all health facilities should implement a PV system. TMDA has supported this process in regional referral hospitals, providing for computers and printers for 20 regional PV centres, and training of regional PV coordinators and their assistants in 27 centres. TMDA is planning to further support this roll-out to district and local levels	Not formulated

*See baseline assessment reports for Tanzania (footnotes 2 and 3); **See National Pharmacovigilance Roadmap 2019-2023 (footnote 6).

Detection of AE

Detection of (laboratory-based) adverse events in DR-TB patients remains a challenge, according to NTLP staff:

> *NTLP PV focal person: "… there are barriers in identifying the adverse events themselves, especially those who are based on laboratory testing. Because, you know, sometimes we don't have access to the laboratory testing. For example, in the MDR TB, we do biochemistry, where we have to check the liver function, renal and electrolytes, also have to check the heart if it's working well using the ECG machine. So, you'll find that some of the facilities have not the ma… equipments which are used to do this test. Or if they have, they have no reagents or something, there is breakdown of the machines. Or sometimes they have to send the specimen to another lab for testing, and there they would need money to pay for the consult testing in another facility. So, there are challenges in identifying the adverse events themselves."*

Collection of PV data, AE reporting

According to Section 26 of the Tanzania Food, Drug, and Cosmetics Regulation (2018), the regional and council health management teams must plan, budget and supervise the implementation of PV activities within their regions and councils and ensure reports to be submitted to the TMDA on a quarterly basis. With support from TMDA, regional PV coordinators were trained on reporting and data entry in VigiFlow. The strengthening of regional and zonal levels has led to a huge increase in the number of reports received (in 2022, the number of reports was almost 33-fold higher than in 2018), while these reports are mostly entered in the regional levels.

However, in 2022, in most of the 4 hospitals visited, for DR-TB patients experiencing an AE, still two forms are filled: the aDSM form, which is sent to the regional aDSM coordinator who submits it to NTLP where it is entered into the Safety and Quality Reporting Tool (SQRT) developed by and for TMDA and in an Excel line list; and the yellow form, which can be sent to the regional PV coordinator, the zonal or the national TMDA office for data entry into VigiFlow. Some regional PV coordinators have access to VigiFlow and enter these yellow forms themselves.

Since last summer, the TMDA has advised against double reporting, meaning that for some of the facilities reporting AE experienced by DR-TB patients, only the aDSM form is filled, while in other facilities, both forms are filled. Because of the previous double reporting structure, TMDA does currently not take aDSM reports into account. In Figure 2A, the current reporting flow is provided.

Apart from the double reporting, several barriers were mentioned by healthcare providers and coordinators: firstly, some clinicians and nurses feel that AE reporting is not their responsibility; secondly, lack of time especially for reporting AE among DR-TB patients, where the paper workload is already heavy; thirdly, fear of being held liable for reported AE (although it is clearly mentioned on the yellow form that all information regarding the reported event will be treated confidentially); fourthly, lack of airtime (which was previously provided to DR-TB staff involved in aDSM); and lastly, the lack of stable internet access in several PV centres (Box 1).

Pharmacist Drug Information Centre: "Some of the healthcare providers think that it's only the pharmacists who are supposed to report the adverse drug reactions, we have tried to do awareness, we are struggling, it is coming up bit by piece by piece."

Regional PV coordinator: "It's not active, we are doing voluntary reporting. So sometimes, if a clinician is very busy, they might also forget to report but also changing the shift: Maybe in the morning, someone was there and then in the evening, if you misplace now the form someone might not see them and things of that kind."

Pharmacist Drug Information Centre: "… some of them are a bit reluctant. And think that if they report an adverse drug reaction, especially when they have administered a preparation, they think that they're going to be sued for doing something wrong while administering. But we have tried to console them, telling them that nothing is going to happen."

Regional PV coordinator: "Once the network is down, that's a barrier to our reporting system."

Box 1. Reporting barriers mentioned by several interviewees.

Observations in one hospital also learned that incomplete yellow forms are not entered in VigiFlow, even though most of these forms had all important data fields filled.

Enablers for reporting mentioned were making reporting mandatory, provide incentives or feedback, and training and sensitization:

> *DR-TB advisor: "Actually, the* [reporting] *process…, because it is spontaneous and is voluntary, it is not a mandatory. It is now because some people may decide not to report and there is no measures which have been taken to rectify that. So I think they need to design a better system which can remind the healthcare workers that you have to identify any events and this need to be reported. Because right now, it is just you decide: should I report or not, there is no enforcement on that. (…) So I think maybe come with law enforcement or any other means to motivate people to report every event they encounter."*
>
> *NTLP PV focal person: "I think if you don't have that spirit of reporting, you will fail. So the only thing is to ensure that we mobilize our people, we make sure that we sensitize our people see the importance of reporting, because reporting for the Adverse Drug Reactions saves some lives, some people's lives. So if they realize that, I think they will be automatically continue reporting without hesitating."*

Reporting tools, data flow and management

TMDA has the following paper forms: a yellow form for reporting of AE and AEFI by healthcare providers, a green form for reporting of AE by patients, and a blue form for reporting issues with medical devices. The aDSM paper forms have been developed by NTLP with support from TMDA, and are being managed by NTLP.
Currently, most providers use paper forms; electronic forms are available but not frequently used.

Regional PV coordinator: "Yeah, yellow forms are done, which are distributed by TMDA. We have three kinds of forms to fill the pharmacovigilance and these have been distributed. The yellow forms are there for clinicians, nurses, pharmacists to fill in adverse events, which has been seen or reported. But we also have the green form, where a patient is given, especially for a patient who is treated for the drugs, which we know that some of the adverse events might come like those who are taking ARVs and TB. So they are given the green form, they will fill, and then they will come to report to the nurse or clinician who is attending them. But we also have the blue form. A blue form is for the store managers. Wherever they see that the product itself is not, as I said, in the shelf life. (…) So those are the forms, which were given by the TMDA, but the pharmacovigilance one for the adverse events is the yellow form."

Also, TMDA has a toll-free SMS number (*152*00#), which can be used for the reporting of adverse events (Figure 1). This number is advertised on TMDA's website. Reports through this system are automatically uploaded to SQRT.

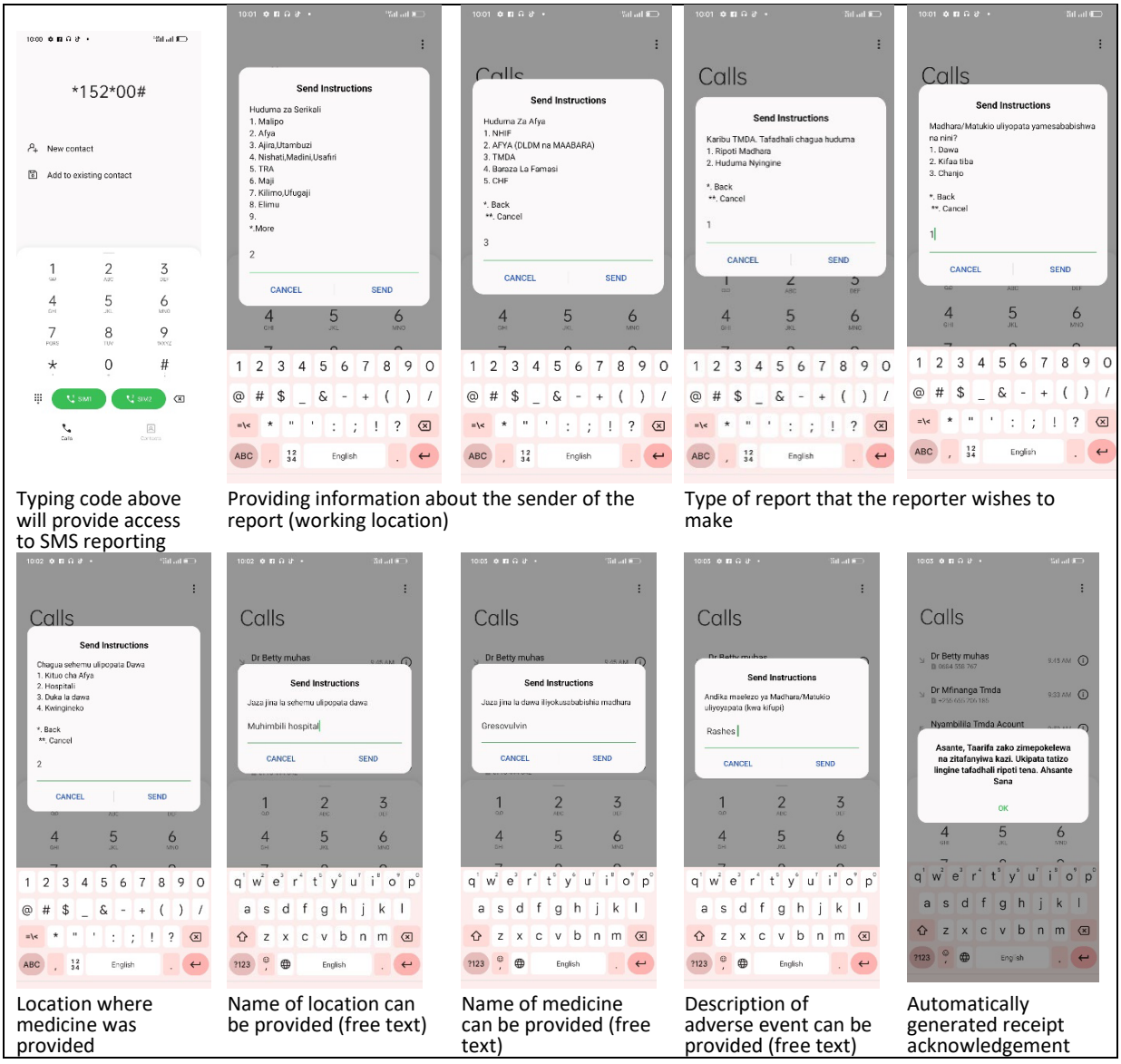

Figure 1. Screenshots from the SMS AE reporting tool.

In the web-based SQRT system, also yellow, green, blue and aDSM forms can be entered.
On the TMDA website, also an electronic reporting form is offered through a link on the web page about electronic submission of ADRs (see https://www.tmda.go.tz/pages/electronic-submission-of-adverse-drug-reactions). The link leads to a web address suggesting that this electronic form would be uploaded in the Adverse Reactions Reporting Tool (ARRT), the predecessor of SQRT, but that site is currently not working (5 September 2022). The ARRT mobile phone application is still downloadable for Android and Apple smartphones. It is unclear where reports entered in the application are sent to, and if they are received at TMDA.
Paper reports from healthcare facilities tend to arrive delayed at TMDA. Having to cross-check reports with NTLP costs additional time. Lack of internet access may lead to more delays, as cross-checking reports will then take more time due to the longer delays.
As there is no automatic export function from SQRT to VigiFlow yet, the information collected in SQRT still needs to be hand-copied to VigiFlow (Figure 2). This also causes delays.
Not all reports stored in VigiFlow are submitted to VigiBase, as some reports are incomplete.

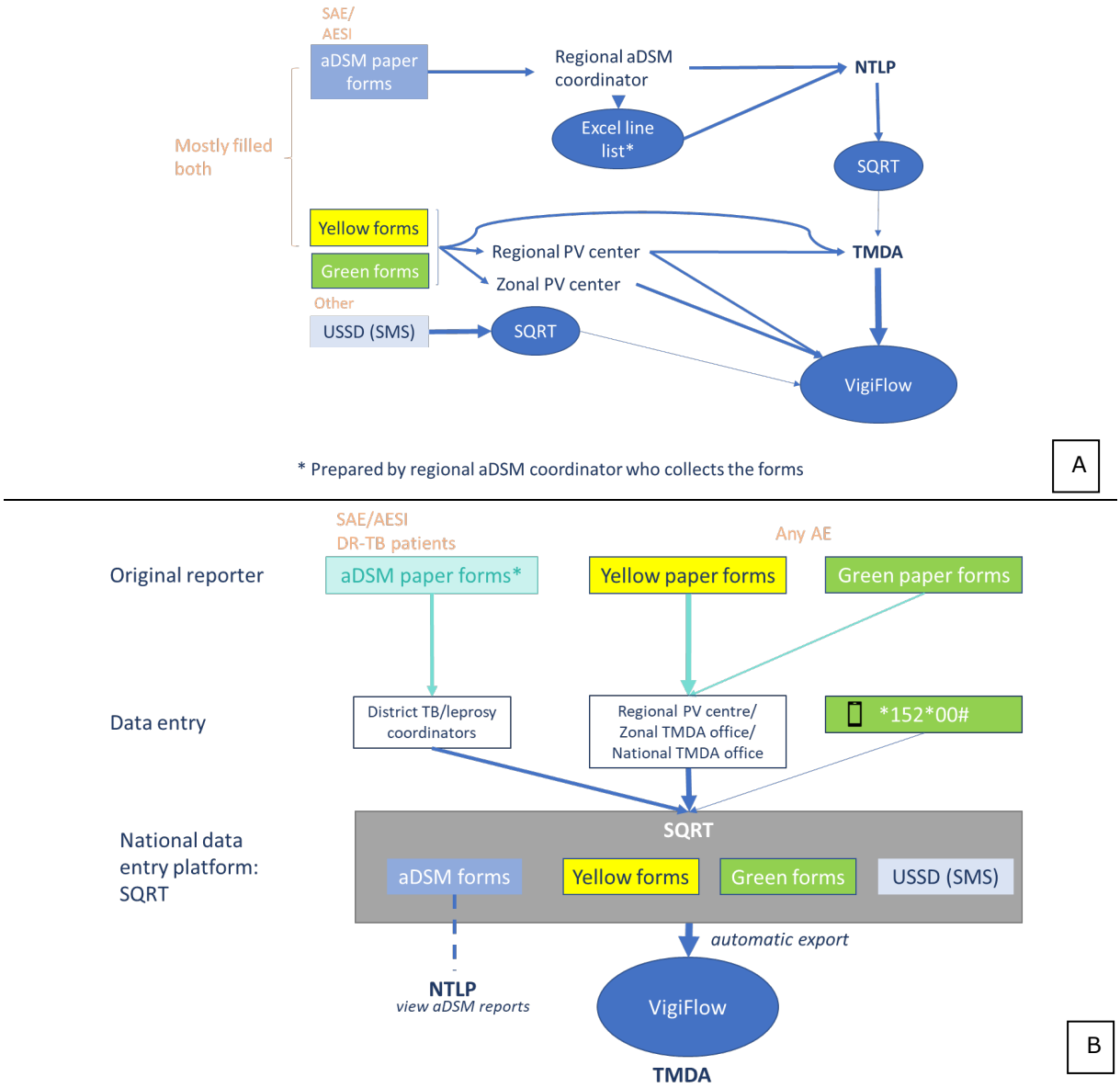

Figure 2. Current (A) and recommended (B) ADR reporting flow. In the recommended flow, SQRT takes the central place as the national data entry platform. From here, reports are automatically exported to VigiFlow.

Issues with low quality of received reports were also mentioned by an informant from the NTLP:

> *PV focal person, NTLP: "… the data that was filled in the forms had also,… we say, low quality, whereby some of the important information were missing. So when you want to conduct assessment you need to start calling the person who filled the reports. If not calling but you need also to invite them and come with a clinical file, the patient file, whereby you can follow up."*

Low quality of reports also hinder causality assessment and signal generation.
Only the paper forms sent to TMDA receive acknowledgement of receipt.

Importantly, the number of reports received at TMDA and entered into VigiFlow has hugely increased between 2018 and 2021 (Figure 3). It should be noted however, that 86% of the reports received in 2021 was coming from a single hospital, which is a large tertiary hospital in Dar Es Salaam with a very strong internal PV system (see section 4.3.2 for more information). A few more hospitals are also contributing disproportionally, while most hospitals in the country are not or rarely contributing reports. Thus, continued education, taking the best reporters as an example, is needed.

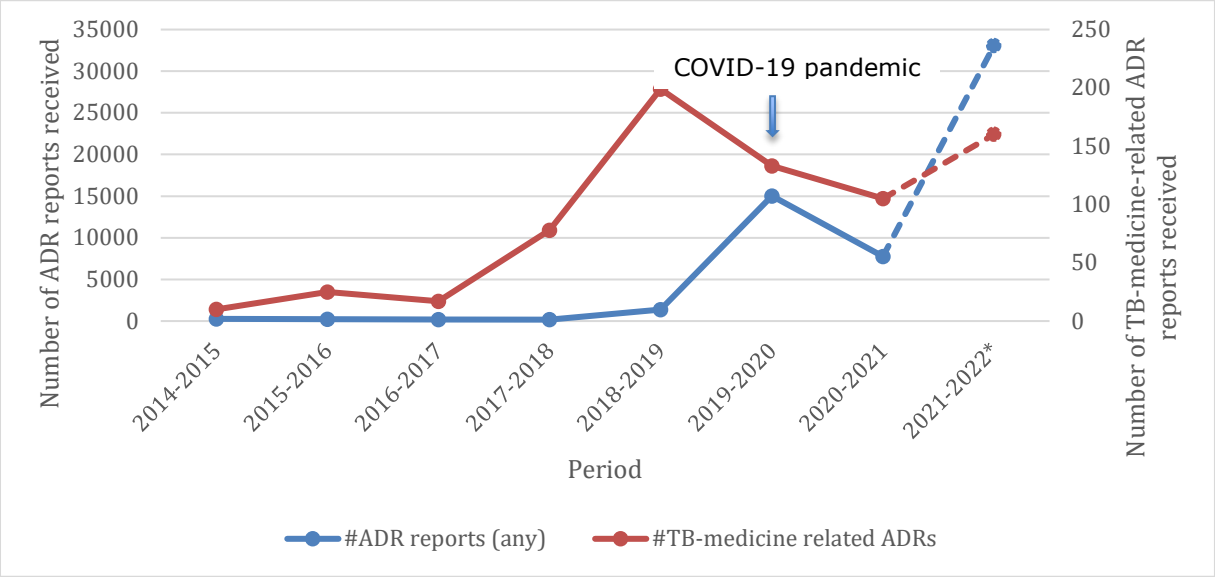

Figure 3. Number of ADR reports and number of TB-medicine related ADR reports per year, 2014-2022. * Extrapolated based on the number of reports received in the first quarter of 2022.

4.3.2. Best practices

Champions in ADR reporting

Muhimbili National Referral Hospital, pharmacy Out-patient Department & Drug Information Center (DIC)

Pharmacists actively counsel patients (new and continuing) on how they are feeling, regarding medication intake. DIC has given a training on what relevant information to abstract from the patients.

> *"We tend to take key points in this register* (shows hard copy notebook)*, when we come here* (office) *and have time, we fill in the yellow forms".*

Pharmacist Fredrick Mathube giving out medication to a patient and counseling her on potential ADRs and the importance of reporting those

Fredrick Mathube stresses the importance of creating a safe environment:

> *"We make a friendly environment, so they* (patients) *can talk freely …*
> *if they see someone that they don't feel comfortable with* (colleague, neighbour, etc.)*, we take them here* (office next to pharmacy)*… this is more private"*.

The challenge is when patients are not giving (the right) information:

> *"Then we put a star* (in electronic system)*, to remember next time we still need to ask them"*.

Pharmacovigilance is intertwined in the whole organization. People at all levels of the organization are involved. This all started with Dr. Deus Buma, head of the pharmacy department, who did his PhD on PV for HIV medication. Ever since, he is very motivated to let Muhimbili hospital succeed in reporting ADRs. He is very successful in engaging others, like Fredrick Mathube says:

> *"DIC portraits it to us, now it is a way of live".*

Dr. Deus Buma is happy with the progress Muhimbili hospital is making:

> *"Phase one is get them reporting, don't care about the quality. But now we go to the phase of quality reporting".*

Dominique Migi shows numbers on reporting. In 2021, Muhimbili hospital submitted 8675 ADR reports to VigiFlow, which is a disproportionally big contribution to the total numbers of ADR reports in Tanzania. His advice to other hospitals who want to improve their PV:

> *"You don't have to wait for computers and printers, you can just start (with PV)"*

Dodoma Regional Referral Hospital, Drug Information & Production (DIP)

Next to the clinical meetings which take place every morning, pharmacists also educate the patients – on a daily basis – in the waiting room on ADRs and the importance of reporting. In 2021, 234 yellow forms were uploaded into VigiFlow, 98 blue forms, and 20 green forms. It might not seem much, but those 20 reports mean that there were 20 patients who reported an ADR on behalf of themselves. Yet, this is where Musa and Jihad see possibilities for improvement:

> *"The user, consumer needs to be more involved in the reporting"*.

Both are trained in PV, and Musa is also providing trainings. They both acknowledge the positive effect of trainings on the number of reports:

> *"From three years past and now, there is a big difference in number of reports and accuracy … because of the training"*.

However, Jihad does think *"More training is required for nurses and clinicians ... for new ones and the ones that are already there"*.

According to Jihad and Musa, PAVIA contributed to PV awareness in the hospital, delegation of tasks, and improvement of (S)AE reporting.

Musa Halinginoti (regional PV focal person, right) and Jihad Juma (assistant) standing in front of the DIP

4.4. Risk assessment and evaluation

In this area, twelve indicators were assessed at the level of the NMRA (Annex 3), and eight indicators at the level of the PHPs (Annex 4).

4.4.1. Summary of the situation at endline

The following table describes the situation at baseline and endline:

Gap identified at baseline*	**Situation at endline**	**Anticipated situation at endline****
Little awareness about causality assessment, signal analysis and benefit-harm assessment among members of the National PV/AEFI Technical Committee	The national PV TWG was revived and includes scientists from different universities and disciplines, and some clinicians. The secretariat is at TMDA. The aim for the committee is to meet quarterly. The last meeting was held on 24 May 2022. The TWG was trained on the conduct of causality assessment for AEFI by WHO.	Not formulated
No causality assessment conducted for TB-drugs related ADRs	The technical committee conducts causality assessment if it concerns SAE which are reported and end up in VigiFlow. Other AE are undergoing in-house causality assessment at TMDA by 1-2 employees.	Not formulated
Signal analysis process, which is the backbone of pharmacovigilance, receives very few hypotheses to analyse	Still, there are few hypotheses investigated. At the time of the country visit, a potential signal related to bupivacaine was being investigated	Not formulated
TFDA does not currently have	PSUR/PBRER assessors are positioned at	Not formulated

Gap identified at baseline*	Situation at endline	Anticipated situation at endline**
routines or capacity to analyse aggregated safety information submitted from MAH as Periodic Safety Update Reports (PSUR or PBRER)	TMDA's Medicines Inspection and Enforcement Section. Additional assessors from universities were appointed and trained by TMDA. 70% of PSUR/PBRER is being evaluated on annual basis.	
--	No progress	3.7.1 Develop a monitoring and evaluation tool for Pharmacovigilance at all levels (from National level, Regional, District to the facility level)
--	No progress; planning for inspections to MAHs in Q4 of 2022	3.7.2 Quarterly monitoring of implementation of Pharmacovigilance at selected PV stakeholders (MAH, PHPs)

*See baseline assessment reports for Tanzania (footnotes 2 and 3); **See National Pharmacovigilance Roadmap 2019-2023 (footnote 6).

Data analysis and causality assessment

At the national PV centre, only one staff member masters VigiLyze, the signal detection and management tool developed by the Uppsala Monitoring Centre.

Causality assessment is done on regular basis by TMDA staff for non-SAEs. The PV technical committee assesses all SAEs and meets quarterly. The last meeting was held in May 2022. The committee is existing of scientists from different disciplines and universities, clinicians from several tertiary care hospitals, and MoH staff. TMDA staff serves as the secretariat. TMDA staff prepares short reports for clusters of SAEs and presents these during the meeting, after which the experts do the assessment. TMDA makes minutes of these meetings. However, the result of these causality assessments seems not to reach all key stakeholders:

> *DR-TB advisor: "Tanzania medicines and medical device authority (…) are the ones who are supposed to do the signaling and causality assessment. And for the MDR TB drugs, we haven't yet received a report on the causality assessment since we have started reporting. But for other medicines, like there was a report which was given out to stop the usage of some of the medicines which are used to reduce pain from patients, which seem to cause some labour and other issues and they were stopped by the TMDA. So for the TB, we haven't yet received any reports on the signaling or causality assessment."*

4.4.2. Best practices

Signals lead to investigations

From the spontaneous reporting system, TMDA has started several investigations (Table). Investigations are done when serious ADR/AEFI are received or when a fast and unexpected increase in the frequency of a known ADR/AEFI is observed. Investigations aim to:

- Confirm the diagnosis made by the healthcare providers
- Confirm the seriousness of the ADR/AEFI
- Investigate how the product were administered and who administered it
- Investigate if there were no other factors that contributed to that ADR/AEFI
- Investigate if there were other patients who used the same products in the visited facility, and if these developed ADRs/AEFIs that were not reported
- Check if the same health complaints also occurred in the community, among those not exposed to the suspected product

Investigations are usually done by the zonal TMDA branch offices, with support from the central

office. During such investigations, TMDA may also make use of trained staff in health facilities. For example, they involved Musa Halinginoti, pharmacist at Dodoma General Hospital (see paragraph 4.3.2) in several recent investigations, thus providing on-the-job training.

For each investigation, the following preparations are made by the national PV centre:

1. compose an investigation team (members depending on the product to be investigated)
2. decide on the places and/or facilities to be visited
3. prepare specific investigation forms (see Annex 6 for an example)
4. send a letter to the relevant District and Regional Administration offices to introduce the TMDA and request for the participation in the investigation of practicing pharmacists in the area
5. conduct a sensitization visit to the administration and the regional and district staff
6. visit facilities from where the ADRs/AEFIs were reported and check in the registers if the reported patients indeed received the suspected medication from the facility
7. call the patients who received the suspected medication and ask if they agree to participate in the investigation
8. patients who agree are given the option to be visited at home, or to meet at another place
9. interrogate the patients using the investigation form
10. analyse the collected data
11. prepare an investigation report, containing information about how the investigation was conducted, findings and recommends and actions to be taken (if needed)

Several investigations have led to actions (Table). For the ongoing investigations into bupivacaine, the PAVIA PV coordinator has also made use of the PAVIA network, by asking other PV coordinators if they saw similar issues in their respective countries.

Table. Signals identified and (being) investigated by TMDA since 2019.

Product	Signal	Source	Decision
Chloramphenicol Inj.	Palpitation	Spontaneous RS	Withdraw of product
Ceftriaxone injection	Difficulty in breathing	Spontaneous RS	Specific batch detained Investigation on-going
Ceftriaxone injection	Difficulty in breathing	Spontaneous RS	Specific batch detained Investigation on-going
Oxytocin injection	Lack of effectiveness	Spontaneous RS	Investigation On-going
Vancomycin inj.	Palpitation sweating	Spontaneous RS	Advice on the appropriate administration
Bupivacaine	Convulsion	Spontaneous RS	Investigation On-going

4.5 Risk management and communication

In this area, ten indicators were assessed at the level of the NMRA (Annex 1), and five indicators at the level of the PHPs (Annex 2).

4.5.1. Summary of the situation at endline

The following table describes the situation at baseline and endline:

Gap identified at baseline*	Situation at endline	Anticipated situation at endline**
Little awareness and engagement of all stakeholders	TMDA has invested a lot in raising public awareness on PV. There were several community outreach activities, television and radio broadcasts, and TMDA has developed IEC materials. Also, TMDA owns cars with PV messages	3.1.6 Raise awareness on PV to the public through different media

Gap identified at baseline*	Situation at endline	Anticipated situation at endline**
	(see paragraph 4.5.2).	
Little dissemination of information, education and counselling materials re. PV and drug safety issues	This aim is partly met. While TMDA has invested in raising public and health care worker's awareness about PV in several trainings, it has not published any Safety Bulletins in the last two calendar years. Other PV tools are published on TMDA's website.	3.1.5 Develop, print and disseminate PV tools (Regulations, Guidelines, SOPs, ADR Registers, Bulletins)
No publicly available phone lines to receive and provide PV information in health facilities and regional PV centres	A publicly available phone line is available and published at TMDA's website (0800110084). This number is also provided in IEC materials. Also, a free reporting tool through SMS is available (*152*00#) (see Figure 2).	3.4.4 Ensure availability and public displaying of a toll free phone number for reporting ADR
New safety information generated outside Tanzania is not effectively considered and translated into up-to-date advice to prescribers and medicine users in the country.	Information on signals that do not require withdrawal of certain drugs does not effectively reach HCWs.	Not formulated
No detailed PV communication plan	TMDA is using the EAC compendium as this includes detailed information about communication. This communication plan still needs to be tailored to the Tanzanian situation. The TMDA PV and AEFI guidelines include a section about communication.	Not formulated

*See baseline assessment reports for Tanzania (footnotes 2 and 3); **See National Pharmacovigilance Roadmap 2019-2023 (footnote 6).

Signal detection and risk management

According to key informants, no signals were investigated or acted upon in the previous calendar year, although currently, a potential signal involving bupivacaine used as anaesthesia mainly for caesarean sections, is being investigated. In 2019, TMDA was responsible for removing losartan and valsartan from the market after the international signal was received. Another interviewee mentioned a signal shared and subsequent action taken by TMDA (see section 4.4.1).

A few barriers, including lack of human capacity and budget, were mentioned by TMDA staff regarding signal detection and risk management:

> *Staff of Clinical Trials Control and PV section: "TMDA was responsible, but before PAVIA we didn't have a good template to help guideline…, to guide us during assessment. So, we have never looked at things like templates, things to guide us on how to assess this… assess the risk and identify their signals. And we have learned what is signals and how to identify signals." (…) "…many, many funds are needed to do a field investigation after receiving a report. So, identify a signal. Because sometimes when we receive the ADR because of fund, we cannot do a field investigation. So, if you want to get what is supposed to be done, is to go to the field to assess the cause of that ADR, to collect the samples which were taken by that, maybe patient sent sample to laboratory for screening. So, screening of the samples require many reagent which need money to buy that reagent, much variety of reagent because every medicine have its reagent for testing the quality so, human resource, fund for buying reagents and funding for further investigation."*

Communication

In recent years, TMDA has shared messages about ADR reporting to the public in several different ways: through radio and television broadcasts, community outreach activities, production of information, education and consultation (IEC) materials.

> *Pharmacist Drug Information Centre: "Yeah, but something else which has increased the reporting: (…) they had a session at the TV station. I think it was twice a week, something of that time. And then for someone who is also at home or someone who has been treated at the private hospital, they were also able to report directly.*

Key messages are also shared as cartoons on TMDA buildings and cars (Section 4.5.2, Figure). Also, TMDA has actively communicated with HCWs during health facility visits which included sensitization about PV, and by providing trainings to HCWs (see above). Relevant PV tools are published on the website. On the other hand, the Drug Safety Bulletin, intended to be published at least twice per year, was last published in October 2020.

4.5.2 Best practices

Public health message sharing through cartoons on TMDA cars. The text in the cartoon reads: Patient: "I got this rash after taking the medicine you gave me". Clinician replies: "I'm very sorry for those side effects, I will provide you with treatment and I will also send a report about it to TMDA"

Raising public awareness

TMDA has invested a lot in raising public awareness on pharmacovigilance (PV). There were several outreach activities: radio and television broadcasts, TMDA has developed Information, Education, and Communication (IEC) materials, and TMDA also owns cars with PV messages. The cars are decorated with cartoons on drug safety. Moreover, TMDA's toll free phone number is pasted on the back. The public can use this number to report on drug safety issues. Next to this phone number, a free reporting tool for the public is available. By sending a text message to *152*00# a person is guided through the reporting tool. Last, TMDA has invested in raising public by several trainings.

Communication with other stakeholders

Whenever TMDA did a site visit for investigation, sensitization of people present was included. This took also place in both the public and the private sector. Next to this, trainings of health care workers took place. A news magazine was published until 2019 (two times a year); however, it did not include a Safety Bulletin. TMDA is using the EAC compendium as this includes detailed information about communication. The TMDA PV and AEFI guidelines include a section about communication.

5. Conclusions and recommendations

5.1. Conclusions

Policy, law and regulations

The Acts, Regulations, Policies and Guidelines provide a strong and up-to-date legal framework. A strength is that TMDA has increased its collaboration at supranational level, within the EAC, NEPAD and AMA. An example is the adoption of the EAC harmonized compendium on safety and vigilance of medical products and health technologies (March 2019) as the PV guideline. The enforcement of the policies, however, remains a point of consideration.

Systems, structures and stakeholder coordination

TMDA has been very successful in strengthening national PV by training regional and zonal PV coordinators. These are also trained on the job, by enabling them to join inspections in their region.

The Clinical Trial Control and PV Section of TMDA receives some domestic funding. However, this is only a very small part (<5%) of its total income. Activities such as trainings are usually paid from donor funding and are thus prone to changes in funding. Also, the equipment of regional PV centres with computers and printers, done so far in 14 centres, may not be continued due to lack of funding.

The blended learning program was judged to be very helpful, and several trainees have organized step-down trainings to involve more staff.

The collaboration with PHPs currently seems to dwell mainly on strong personal relationships, which were built during the regular PAVIA triangle meetings. More formal structures, such as Terms of References, SOPs or guidelines for collaboration do not seem to be in place.

Methodology of data collection

The number of ADR reports received has much increased since 2018, although >80% of the reports is coming from one big teaching hospital (Muhimbili). There are still issues with reporting, such as lack of time or interest to report, feeling it is not part of clinicians' and nurses' responsibilities, and fear of liability. For DR-TB, the detection of adverse events measured from laboratory values is still challenging, as equipment or consumables are not always available or working, and then need to be purchased from other sites.

The current reporting flow is complex and leads to duplicate and scattered data. Duplicate because aDSM data are both requested on aDSM forms (which are entered in Excel line lists and in SQRT) and on yellow forms (which are entered in VigiFlow), and scattered because DR-TB sites are now transitioning from double reporting to only filling in aDSM forms, while TMDA is not yet considering SQRT for aDSM reports.

Another issue is that the previous data platform, ARRT, has been replaced by SQRT, but that the ARRT mobile phone application is still available and that yellow, blue, and green forms can still be entered and sent through that application. It is unknown where these reports end up.

Data from SQRT is hand-copied into VigiFlow, which is not efficient and prone to copy errors.

A strength of the current data collection system is that it is organized in such way that data can be entered into digital databases at all levels (district, regional, zonal), wherever there are people trained for this job.

The SMS reporting system provides a nice, accessible and low-cost tool for AE reporting, and may be of interest to other countries with low internet network and/or smartphone coverage but good telephone services.

Data management and causality assessment

Causality assessment is now done routinely at TMDA, and the SAE are routinely assessed by the PV TWG. This TWG received training on causality assessment for AEFI from WHO. This is an important improvement from baseline, when only some adverse events were subjected to causality assessment. Still, there are issues hindering the causality assessment process. First,

Risk assessment and evaluation

While the number of reports has increased, the number of signals has not increased. TMDA has processes in place to investigate potential signals and is currently assessing a signal for bupivacaine. However, if the collected data would be more intensively analysed, likely, more potential signals for further verification would come up. Thus, data validation and analysis processes could be further improved.

Risk management and communication

While the reporting rate for adverse events has gone up markedly, especially during and due to the COVID-19 pandemic and associated vaccination campaigns, it still is lower than the anticipated level of 200 per million population. Some health facilities have experimented with obligate reporting by interns, but this has reportedly lead to low-quality reports and may also lead to reports just for the sake of reporting. TMDA has invested in reaching the general population, by accepting patient reports on the so-called green forms, publishing its SMS-reporting system, and mass campaigns on television and radio. Also, it has been visible at events where MAHs meet, and by continuous sensitization of healthcare providers. TMDA could further improve its visibility in the latter group by making sure that all reports receive acknowledgement, and that regular statistics about the data are shared in Newsletters and possibly in a dashboard e.g. on the TMDA website. This may improve their motivation, as this way, TMDA is showing that the data is actually being used.

5.2. Changes from baseline attributable to PAVIA

PAVIA has contributed to the baseline assessment, which showed the gaps and areas where PV programme could be strengthened in 2018, and has supported subsequent national PV roadmap development. One of the aims outlined in the roadmap was to revitalize the zonal TMDA offices and regional PV centres. Strengthening of the zonal offices with emphasis on zonal PV coordinators increased the total number of TMDA staff members focusing on PV to 15, while at the same time, in the central TMDA office staff in the PV section has decreased from 10 to 7. Also, 28 regional PV coordinators are in function and 12 of these have received training from TMDA as well as computers and printers. The trainings and hardware were financially supported by PAVIA. Some regional PV coordinators are actively engaging in PV activities of TMDA. For example, if TMDA conducts inspections in Dodoma region, they frequently invite the regional PV coordinator to join them. This way, the coordinator is further trained on PV on the job.

PAVIA also helped in printing and distributing IEC and other materials, such as the Regulations and Guidelines to zonal and regional PV focal persons.

The blended learning programme developed by PAVIA has led to multiple step down trainings, further increasing the number of persons trained.

Collaboration with several PHPs has improved in the past years through joint development of the PV roadmap initiated through the PAVIA project, the organization of joint trainings and PAVIA triangle meetings, although formal structures to sustain these collaborations are not yet in place.

Continuous sensitization and trainings, in part supported by PAVIA, also helped to increase ADR reporting, notably also for TB drug-related ADRs.

The PAVIA-project helped with integrating VigiFlow in TMDA's digital AE-reporting system. The PAVIA blended learning course helped to train multiple healthcare providers in the country, and, allegedly this training and subsequent stepdown trainings helped to increase AE reporting.

Pharmacist Drug Information Centre: "The e-blended course was done by PAVIA. It was very useful."

DR-TB advisor: "I think PAVIA played a bigger role in strengthening the TMDA pharmacovigilance system per se. So it has some impact in the general pharmacovigilance in the country, not only the TB aspect. So, I think PAVIA has contributed to something big in the pharmacovigilance activities."

Through providing advanced and practical trainings, PAVIA further strengthened TMDA's capacity in the conduct of causality assessment and assessing potential signals. This has led to the revitalization of the PV technical committee which conducts causality assessment for SAE.

5.3. Recommendations to further strengthen PV in Tanzania

Policy, law and regulations

- The Acts, Regulations, Policies and Guidelines provide a strong and up-to-date legal framework. TMDA should explore means of enforcing the Regulation.

Systems, structures and stakeholder coordination

- TMDA has successfully involved zonal and regional level staff to improve PV reporting and structures. This process of involving lower level staff by trainings, sensitization visits and on-the-job training should be continued and, as TMDA is planning, also be rolled out at district and lower levels.
- The PAVIA blended learning programme has been quite successful and this programme of training all levels should be continued.
- The collaboration with the NTLP has been successful, but largely depends on personal relationships and interest in PV. Therefore, we recommend to continue building such relationships with PHPs, but also suggest to install a more formal structure, by e.g. developing Terms of References and/or Memoranda of Understanding with PHPs, in which roles and responsibilities are clearly outlined.

Methodology of data collection

- The continuous training of reporters and those supporting reporting by collection and data entry of paper forms works well and should be continued. During the trainings, it would be good to emphasize the trainees that they, in turn, should train other potential reporters in their health facility.
- The training ideally should stress that reporting is a responsibility of all health care providers, and that there is no reason to be afraid of liability issues.
- Think of small incentives for "top"-reporters. These incentives do not necessarily have to be monetary, but can also consist of honorable mention (e.g., being the best reporter over a certain period).
- Upon data entry into VigiFlow/SQRT, the contact details of the original reporter should be mentioned, not those of the one entering the data. This way, TMDA can get back to the reporter should additional information on the report be required.
- Duplicate reporting of adverse events for DR-TB patients on both the aDSM and the yellow forms should be stopped. Instead, reporters should be informed that only the aDSM form needs to be filled. This prevents collation of duplicate and scattered data at TMDA.
- aDSM forms are sometimes stored in the patient files and not sent to the NTLP. To train healthcare providers to submit these forms, during supportive supervision, it should be checked if forms are kept in patient files and healthcare providers should be retrained to submit the forms.

Data flow and management

- Develop and implement a strategy for reporting that is simple and streamlined taking into account using SQRT and VigiFlow (see Figure 2B)
- The National PV centre is encouraged to check all reports for completeness and consistency at regular basis
- SQRT offers a great potential for serving as the central platform for data collection, provided that automated data transfer from SQRT to VigiFlow is possible. It could also be considered to see if the DHIS system/ETL can be used for the collection of PV data in future.
- As ARRT is no longer used and looked at at TMDA, remove ARRT from the mobile phone app stores and make sure that apps that have already been downloaded are made unavailable. The national PV centre should also check if there are remaining reports stuck in this ARRT system and upload these in VigiFlow.

Risk assessment and evaluation

- To detect more potential signals, the processes for detection of potential signals in the database should be intensified.

Risk management and communication

- The communication with stakeholders could be further improved by the publication of regular Newsletters containing statistics about the reports received (e.g. number of reports received in the last quarter, number of serious adverse events reported, number of actions taken, diseases/conditions most commonly occurring in reports, etc.), also, feedback on reports other than (only) acknowledgement of receipt may increase their motivation to report adverse events.

Annex 1. Program of the in-country endline assessment

Day and time	Activity	Involved	Location
Mon 29 August, 2022			
AM	Discuss and check final programme with key staff	Key team*	Dar es Salaam
PM	Interviews **TMDA** (management level): - Mr Adam Fimbo - Head Clinical Trial Control & PV Section With staff of Clinical Trial Control & PV Section: - Collect missing indicators - Interviews, photos, collect documentation for success stories: o Increases in reporting (by type) o Blended e-learning, other trainings o PAVIA Triangle	Key team*, TMDA management	Dar es Salaam
Tue 30 August, 2022			
AM – 2 PM	Visit **Muhimbili hospital** - Interviews, photos, collect documentation for success stories: o Increases in reporting (by type): enablers/barriers o Trainings received	Key team*, key staff of hospital	Dar es Salaam
PM	*Travel to Dodoma*	*Key team**	
Wed 31 August, 2022			
AM	Visit **NTLP** in Dodoma - Interviews, photos, collect documentation for success stories: o Electronic reporting of aDSM data to TMDA o Increases in reporting (by type) o PAVIA Triangle After introductions, split into 2 teams. Team 1 stays at NTLP/MoH; Team 2 visits **Dodoma General Hospital** - Interviews, photos, collect documentation for success stories: o Increases in reporting (by type): enablers/barriers o Trainings received	Key team*, key staff NTLP (PV focal person, national coordinator) Key team*, key staff of Dodoma General hospital	Dodoma
PM	Visit **TMDA zonal office Dodoma** - Interviews, photos, collect documentation for success stories: o Electronic reporting to TMDA o Increases in reporting (by type)	Key team*, zonal PV coordinator, key staff	Dodoma
Evening	*Travel to Kilimanjaro*	*Key team**	
Thu 1 September, 2022			
AM	Visit **Kilimanjaro Clinical Research Institute** - PAVIA Triangle Visit **Kilimanjaro regional PV center** at Kilimanjaro Christian Medical Center - Interviews, photos, collect documentation for success stories: o Electronic reporting to TMDA o Increases in reporting (by type) o Blended e-learning, other trainings	Key team*, Kissa, key staff KCRI Key team*, Eva, other relevant staff of Kibong'oto hospital	Moshi
PM	Visit **Kibong'oto Infectious Diseases hospital**: - Interviews, photos, collect documentation for success stories: o Electronic reporting of aDSM data to TMDA and NTLP o Increases in reporting (by type): enablers/barriers o Blended e-learning, other trainings	Key team*, PV focal person, other key staff	Sanya Juu
Evening	*Travel to Dar es Salaam*	Key team*	
Fri 2 September, 2022			
AM	Visit to **TMDA PV unit** - Discuss remaining issues and gaps - Visit data entry unit	Key team*	Dar es Salaam, TMDA
Tbd			
	Closure meeting: - Discuss findings of assessors, check if these match with true situation - Compare end-line to baseline assessment results to assess progress - Compare end-line assessment results to roadmap to assess progress - Discuss examples to be included in the PAVIA blueprint document - Agree about time lines and roles and responsibilities for finalizing the endline assessment and preparing stories for blueprint	All key stakeholders in country	

* The key team consisted of Seth Heri Kisenge and Nellin Shiletiwa of TMDA, Linda Härmark from the Netherlands Pharmacovigilance Center Lareb and Edine Tiemersma and Liza de Groot from KNCV Tuberculosis Foundation, the Netherlands.

Annex 2. List of key stakeholders interviewed

Affiliation	Name	Type of interview
TMDA Clinical Trial Control and Pharmacovigilance section	Pharm. Seth Heri Kisenge	On-site group interview by assessors
	Pharm. Nellin Shiletiwa	Online one-on-one interview by intern, on-site group interview by assessors
	Dr. Elirehema Mfinanga	Online one-on-one interview by intern, on-site interview by assessors
	Mtani Njegere (acting head of section)	On-site group interview by assessors
TMDA management	Pharm. Adam Fimbo	Short face-to-face courtesy meetings by assessors
	Pharm. Kissa Mwamwitwa	
	Yonah Hebron	
Muhimbili National Referral Hospital	Dr. Deus Buma	On-site group interview by assessors
	Pharm. Dominick J. Mfoi	On-site group interview by assessors
	Pharm. Fredrick Mathube	On-site group interview by assessors
	Pharm. Mtoke Ahmadi Uledi	On-site group interview by assessors
	Nuru Daniel Msanga	On-site group interview by assessors
NTLP, Dodoma	Dr. Aifello Wedson Sichalwe	On-site group interview by assessors
	Pharm. Crispin Mamkinga	On-site group interview by assessors
	Pharm. Jumanne Mkumbo	Online one-on-one interview by intern
	Dr. Isack Lekule	Online one-on-one interview by intern
	Pharm. Riziki Kisonga	Online one-on-one interview by intern
Dodoma Regional Referral Hospital	Jihad Medallah Juma	On-site group interview by assessors
	Musa Halinginoti	On-site group interview by assessors
	Sister Matilda Peter	On-site group interview by assessors
Dodoma TMDA Zonal Office	Pharm. Seraphina Cleophace	On-site group interview by assessors
	Pharm. Elizabeth Mollel	On-site group interview by assessors
Kilimanjaro Clinical Research Institute	Prof. Blandina Mmbaga	Online one-on-one interview by intern, on-site interview by assessors
	Prof. Eva Muro	Online one-on-one interview by intern, on-site interview by assessors
	Rehema Fumbwe	Online one-on-one interview by intern
	Dr. Marion Sumari-de Boer	Online one-on-one interview by intern
Kilimanjaro Christian Medical Center	Charles Michael	On-site group interview by assessors
	Deogratius Lyimo	On-site group interview by assessors
	Mercy Naftal Laizer	On-site group interview by assessors
	Rahim Senkondo Msangi	Online one-on-one interview by intern, on-site interview by assessors
	Ismail Gelle	On-site group interview by assessors
	Dr. Khadija Semvua	Online one-on-one interview by intern
Kibong'oto National Infectious Diseases Hospital	Athumani Mohamed Ngoma	On-site group interview by assessors
	Yolanda Jacob Mlacha	On-site group interview by assessors
	Asnath Bashiri	On-site group interview by assessors
	Atanasia Tarimo Karoli	On-site group interview by assessors
Moshi Brand Creators	Timothy Vivian Wonanji	Online one-on-one interview by intern

Annex 3. NMRA assessment tool

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
Component 1. Policy, Law, and Regulation					
1.1	Existence of a policy document that contains essential statements on pharmacovigilance or safety of medicines, health products and technologies (stand alone or as a part of some other policy document)	Is there a national policy on pharmacovigilance or medicine safety, or a more general medicines policy that contains essential statements?	Yes	The National Health Policy (2007): *5.17.2. Policy objective Safety, quality traditional healing and alternative medicine services* *5.17.3. Policy statements (page 33-34) The Government will:* *1. Ensure quality and safety of traditional and alternative medicines in use;* *2. Strengthen basic and scientific research on traditional medicine practice, traditional medicines and medicinal plants for improvement of traditional health services;* *3. Promote industrial manufacturing of materia medica (Traditional Medicines)*	MoH Website https://www.africanchildforum.org/clr/policy%20per%20country/2018%20Update/Tanzania/tanzania_nationalhealthpolicy_2017_en.pdf
		When was the policy last reviewed?	2017		
1.2	Existence of specific legal provisions for pharmacovigilance in the national medicine's legislation or similar legislation	Are there legal provisions for pharmacovigilance or medicine safety in the medicines act or law?	Yes	The Tanzania Food, Drugs and Cosmetics Act, Cap 219 (2003) and The Tanzania Medicines and Medical Devices Act, Cap 219 (2019, revised 2021): *Function of the Authority Section 5 subsection (1) c;* *The Authority shall ensure that evidence of existing and new adverse events, interactions, and information about pharmacovigilance of products being monitored globally, are analysed and acted upon*	https://www.tmda.go.tz/uploads/publications/en1623838708-TFDA%20ACT%202003.pdf https://www.tmda.go.tz/uploads/1630838474-CHAPTER%20219%20THE%20TANZANIA%20FOOD,%20DRUGS%20AND%20COSMETICS%20ACT.pdf
1.3	Legal provisions for Marketing Authorization Holders to monitor and report the safety and quality of their products	Is it mandatory by law or regulations for MAHs to:		Tanzania Food, Drug and Cosmetics (Pharmacovigilance) Regulation section 40 subsection (1) and (2): *Requirements for Periodic safety update reports and periodic benefit-risk evaluation. Every marketing authorization holder shall submit to the Authority periodic safety update and Benefit-Risk Evaluation Reports. The reports shall be submitted to the Authority immediately upon request or in accordance with the following-(a) where a product has not yet been placed on the market, at least every 6 months following authorization and until the placing on the market; (b) where a product has been placed on the market, at least every six months during the first two years following the initial placing on the market, once a year for the following two years and at three yearly intervals thereafter*	https://www.tmda.go.tz/uploads/publications/en1545477373-Control%20of%20Medical%20Devices%20Regulations,%202015.pdf
		- conduct post marketing safety activities?	Yes		
		- report adverse drug reactions/medicine safety related issues?	Yes		
		- regularly submit periodic safety update reports (PSUR) or periodic benefit-risk evaluation reports (PBRER)?	Yes		
1.4	Existence of legal provisions empowering the national regulatory authority to require Marketing Authorization Holders to submit proof of their proactive pharmacovigilance planning as	Does the national regulatory authority have the power to require MAH to submit any of the following documents prior to product licensing?	Yes	Tanzania Food, Drug and Cosmetics (Pharmacovigilance) Regulation section 23 (1): *The holders of marketing authorizations and manufacturers shall be proactively responsible for on-going safety monitoring of the products they place on the market. MAHs shall submit to the Authority the name and contact details of the focal person responsible for pharmacovigilance, summary of the pharmacovigilance system, Risk*	https://www.tmda.go.tz/uploads/publications/en1545477373-Control%20of%20Medical%20Devices%20Regulations,%202015.pdf

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
	part of an application for product licensing			*Management Plans, Periodic Safety Update Reports, Risk-benefit assessment reports and reports on adverse reactions and events occurring within and outside*	
		I. Pharmacovigilance plan	Yes	Tanzania Food, Drug and Cosmetics (Pharmacovigilance) Regulation section 16 (1): *Every manufacturer and marketing authorization holder shall have Pharmacovigilance master plan that includes safety specifications and pharmacovigilance Plan.*	
		II. Risk management plan	Yes		
		III. Risk minimization/mitigation plan	Yes		
		Are MAHs required to adapt the plans to the particular risk situation of the population in the country?	Yes	Tanzania Food, Drug and Cosmetics (Pharmacovigilance) Regulation section 8 (1) & (2): *Marketing Authorization holders shall establish a pharmacovigilance system. The system shall be comprised of structures, processes, and outcomes which shall be adaptable to public health emergencies or development plans.*	
1.5	Existence of national pharmacovigilance guidelines developed or reviewed within the past 5 years	Does a national guideline for PV (or a related document) exist?	Yes	The EAC Harmonized Compendium On Safety and Vigilance of Medical Products and Health Technologies is used as the PV guideline. This compendium is currently being customized for the Tanzanian situation. A first draft is under review. Apart from this, there is the National Guidelines for Monitoring Medicines Safety (2018)	https://www.tmda.go.tz/uploads/publications/en1594202820-PV%20COMPENDIUM%20VALIDATED%2018%2003%202019.pdf https://www.tmda.go.tz/uploads/documents/en1628143300-en1554375724-16.%20REVISED%20%20NATIONAL%20PV%20GUIDELINES%20%20%20%20JUNE%202018(1)-2.pdf
		Has the national PV guideline been developed or reviewed within the past 5 years?	Yes		
		When were the guidelines last reviewed?	2019 (Comp) 2018 (Natl guidel)		
1.6	Regulations and guidelines encourage distributors, importers exporters, health-care institutions, other stakeholders and consumers to report ADR and/or AE to the MAH and/or NRA	Do regulations and guidelines encourage distributors, importers exporters, health-care institutions, other stakeholders and consumers to report ADR and/or AE to the MAH and/or NRA	Yes	The Tanzania Food, Drug and Cosmetics (Pharmacovigilance) Regulation The EAC Harmonized Compendium On Safety and Vigilance of Medical Products and Health Technologies National Medicine and Therapeutic Committee Guidelines (MoH, 2021)	See above for references https://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0084824&type=printable
1.7	The legal provisions and/or regulations allow NMRA to require manufacturers and/or MAHs to conduct specific studies on safety and effectiveness under specific conditions	Does the national regulatory authority have the mandate to require manufacturers and/or marketing authorization holders to conduct and present results from specific studies addressing identified safety concerns?	Yes	They are informed to do investigations as part of the safety quality issues Tanzania Food, Drug and Cosmetics (Pharmacovigilance) Regulation (2018), section 43 (1): *The Authority may impose on the marketing authorization holder the obligation to conduct post-authorization studies on safety and on efficacy as a condition at the time of the granting of the marketing authorization or later.*	See above for references

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
1.8	Legal provisions, regulations and/or guidelines require manufacturers and/or marketing authorization holders to designate a Qualified Person responsible for vigilance.	Do legal provisions, regulations and/or guidelines require manufacturers and/or marketing authorization holders to designate a Qualified Person responsible for vigilance?	Yes	During regular MAH inspections, it is checked if a qualified PV focal person is in function and their qualifications are checked. Enforcement through the Regulations is possible by withdrawing the drugs from the Tanzanian market, but TMDA prefers a dialogue about the requirements instead.	PV coordinator
1.9	Existence of updated National Essential Medicines List that was reviewed with consideration of medicine safety information	Is there an essential medicines list in use?	Yes	Available at the pharmaceutical section of the MoH	Standard Treatment Guidelines and National Essential Medicine List Tanzania Mainland, 2021
		Does the essential medicines list selection committee consult medicine safety information?	Yes	The experts are from different institutions, including TMDA. The selection process is described in a scientific paper: Mori et al., PLoS One 2014;9:e84824 (https://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0084824&type=printable)	
		When was the list last reviewed?		2021	
1.10	Existence of a medicines regulatory authority or agency	Is there a drug regulatory authority or agency?	Yes	TMDA (successor of TFDA which was established in 2003)	https://www.tmda.go.tz/
1.11	Existence of official records of licensed medicinal products	Is there an official source of information on medicinal products that are licensed for use in the country?	Yes	TMDA website & the government gazette. The tool for reporting ADRs also has this	Government's Official Gazette and https://www.tmda.go.tz/
1.12	Accreditation of private health facilities includes requirements for the existence of a pharmacovigilance system	Does the public authority responsible for accreditation of private health facilities require that a pharmacovigilance system is in place?	No	Healthcare facilities are registered with the MoH, which requires that all facilities shall have a PV system in place. However, the enforcement of this requirement is not in TMDA's hands. TMDA can inform the MoH about failure to comply with the requirement, but only the MoH can remove accreditation.	PV coordinator
Component 2. Systems, Structures and Stakeholder Coordination					
2.1	Existence of a national pharmacovigilance centre with a clear mandate and structure	Is there a National PV centre or any other body assigned the responsibility of monitoring safety of medicines?	Yes	Documents describing the mandate and organizational structure: 1. The Tanzania Food, Drug and Cosmetics (Pharmacovigilance) Regulation. (2018) https://www.tmda.go.tz/uploads/publications/en1597132154-PHARMACOVIGILANCE.pdf Section 4 subsection (1) & (2) of this regulation states; *The Authority shall establish and maintain, a National Pharmacovigilance Centre, which is also known by its acronym "NPC". Subject to sub-section (1), the Authority may establish pharmacovigilance zone centers for the appropriate coordination of pharmacovigilance activities in the zones.* 2. National Guidelines for Monitoring Medicines Safety (2020) https://www.tmda.go.tz/uploads/publications/en1599223225-TFDA-National-Guidelines-for-Monitoring.pdf	TMDA WEBSITE: https://www.tmda.go.tz/
		Is there a clear mandate and organizational structure for the pharmacovigilance centre?	Yes		

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
2.2	The pharmacovigilance centre has designated, qualified human resources to carry-out its functions	How many staff members (full-time equivalent) does the PV centre or system have who are specifically responsible for carrying out its functions (technical and administrative)?	16 (see comments)	The Clinical Trials Control and PV unit at TMDA headquarters has 8 full-time employees. The 8 zonal TMDA offices all have one PV focal person who is responsible for the coordination of all PV activities in the zone. However, for any activity needing staff other staff of the zonal office will be included.	PV coordinator, head of TMDA zonal office Dodoma
2.3	Existence of a dedicated financial provision or statutory budget for the pharmacovigilance centre	Is there an annual budgetary allocation for PV activities or for the PV Centre?	Yes	Section 26 of the Tanzania Food, Drug and Cosmetics (Pharmacovigilance) Regulation (2018) states: *Regional and Council Health Management Teams shall plan, budget and supervise the implementation of pharmacovigilance activities within their regions and councils and ensure reports are submitted to Authority on quarterly basis.* See report for more details.	Annual work Plan and budget
		In the last fiscal year, how many funds were allocated by the government and donors for pharmacovigilance activities? *Please specify the amount & currency*		Government: ▪ 29,342,320 TZS ▪ 12,584 USD (equivalent) Donors: ▪ 1,026,194,496 TZS ▪ 445,784 USD (equivalent)	
2.4	Existence of a functional national medicine safety advisory committee	Does a national medicine safety advisory committee exist with the responsibility to provide technical advice on the safety of medicines to the regulatory authority?	Yes	National medicine safety advisory committee consists of: ▪ Staff from Ministry of health, ▪ healthy programs, ▪ public and government health care providers ▪ high learning institution ▪ research institution The Chairman, elected among the committee members, leads the activities of the national medicine safety advisory committee. The TMDA hosts the secretariat. The committee meets quarterly in principle; the last meeting held on 24 May 2022.	Minutes of National Medicine Safety Advisory Committee
		Has the national medicine safety advisory committee met at least twice in the previous calendar year?	Yes		
2.5	Existence of standard operating procedures (SOPs) for conducting pharmacovigilance activities	Does the NMRA / PV centre have SOPs for pharmacovigilance activities?	Yes	Several SOPs are available, e.g. • Procedure for enforcement of pharmacovigilance activities • Procedure for conducting active PV surveillance on safety of medicines • Procedure for reviewing and annotating ADR reports • Procedure for development and approval of TMDR ADRs bulletin • Process flowchart for ADR assessment	List of SOPs, Clinical Trials Control and PV unit TMDA
		When were the SOPs last reviewed?	March 2022		
2.6	Existence of a source of data on consumption and prescription of medicines	Are there any sources of information on sales or consumption of medicines on a national, regional or local level?	No	Only the list of registered medicines is found on the TMDA website, but no information about sales or consumption of these medicines	

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
		Are they publicly available?	NA		
2.7	Existence of a library or other reference source for drug safety information	Does the PV centre have access to a library or electronic sources providing up-to-date information on medicine safety and the progress of scientific knowledge in the domain?	Yes	Yes, several, including WHO Vigibase, EMDEX, British National Formulary, SPCs, scientific publications, and the TMDA library. One trained librarian.	
2.8	Existence of a mechanism to disseminate pharmacovigilance information (including one or more of the following: newsletters, information bulletin, website or phone line for dissemination of pharmacovigilance information)	Is there a communication plan in place to disseminate PV information?	Yes	TMDA is using the EAC compendium as this includes detailed information about communication. The TMDA PV and AEFI guidelines include a section about communication.	
		Is there a newsletter or information bulletin for dissemination of PV information?	Yes	The Drug Safety Bulletin. The TMDA also publishes a newsletter, but this covers all activities of TMDA. The last version (2021) did not contain any PV information.	https://www.tmda.go.tz/uploads/publications/en1661782920-DRUG%20SAFETY%20A5%20.pdf
		How many issues of the medicine safety bulletin are supposed to be published per year	2		
		How many issues of the medicine safety bulletin were published in the previous calendar year?	0	The last Drug Safety Bulletin (issue 4) was published in October 2020, the fore last in January 2020.	
		Is there a website for dissemination of PV information?	Yes		TMDA | CLINICAL TRIALS CONTROL AND PHARMACOVIGILANCE – SECTION PROFILE
		Is there a publicly advertised phone line to receive and provide medicine safety and PV information?	Yes	A number for toll-free support is published on TMDA's website: 0800-110084 but it is a general number which is re-directed to the responsible person in PV office. There is also a free SMS service to report ADR: *152*00#.	TMDA website
		Are findings published in national/international journals?	Yes	Between 2020 and 2022 (August), 5 papers were published: • Fimbo AM, et al. Prevalence and Correlates of Lymphatic Filariasis Infection and Its Morbidity Following Mass Ivermectin and Albendazole Administration in Mkinga District, North-Eastern Tanzania. J Clin Med. 2020 May 21;9(5):1550. doi: 10.3390/jcm9051550. • Mwamwitwa KW, et al. A retrospective cross-sectional study to determine chirality status of registered medicines in Tanzania. Sci Rep. 2020 Oct 20;10(1):17834. doi: 10.1038/s41598-020-74932-x. • Mziray S, et al. Quality of selected anti-retroviral medicines: Tanzania Mainland market as a case study. BMC Pharmacol Toxicol. 2021 Aug 26;22(1):46. doi: 10.1186/s40360-021-00514-w. • Fimbo AM, et al. Safety and Tolerability of Ivermectin and Albendazole Mass Drug Administration in Lymphatic Filariasis	See papers.

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
				Endemic Communities of Tanzania: A Cohort Event Monitoring Study. Pharmaceuticals (Basel). 2022 May 12;15(5):594. doi: 10.3390/ph15050594. • Fimbo AM, et al. Post marketing surveillance of selected veterinary medicines in Tanzania mainland. BMC Vet Res. 2022 Jun 9;18(1):216. doi: 0.1186/s12917-022-03329-x.	
		Is there another mechanism for dissemination of PV information?	Yes	Through meetings, but no documentation available	
2.9	Existence of harmonized pharmacovigilance curricula for key healthcare workers - **Pre-Service**	Is PV incorporated into the national **pre-service** curricula of **doctors?**	No	Curriculum developed by MUHAS but not yet incorporated	
		Is PV incorporated into the national **pre-service** curricula of **nurses?**	No	Curriculum developed by MUHAS but not yet incorporated	
		Is PV incorporated into the national **pre-service** curricula of **pharmacists?**	Yes		
2.10	Existence of harmonized pharmacovigilance curricula for key healthcare workers - **In-Service**	Is there a pharmacovigilance training module, manual, or curriculum for **in-service** training of health care workers?	Yes		PV training manual and Training guide for healthcare workers
2.11	Number of healthcare workers trained in pharmacovigilance in the previous calendar year through in-service training program	How many healthcare workers has the centre/program trained on PV in the previous calendar year (through **in-service** training)?			Quantitative Data from PV Coordinator
		a. Health professionals	>280	Multiple trainings were organized for different types of staff by different organizations and projects, including PROFORMA, ASCEND, and WHO. Most trainings were for TMDA staff. For HCW, per job description, there is the following information: - 17 Clinicians - 170 Nurses - 57 Pharmacy Technicians - 9 Dentists and Laboratory Technicians	
		b. Community health workers	NA	Community leaders and community health workers are included in public health education outreach activities, but their numbers are not recorded.	
		How many training events/sessions were conducted in the previous calendar year?	15		
		a. Health professionals	2	1 training on active surveillance for DTG, and 1 on VigiFlow data entry for PV focal persons from 28 PV centres and all national specialized hospitals.	
		b. Community health workers	1	See above	
2.12	Adoption and use of harmonized web-based	Are web-based PV training tools available?			PV coordinator
		a. For health professionals	Yes	e-learning materials from the blended learning training programme.	

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
	pharmacovigilance training tools	b. For the general public	No		
2.13	Existence of a functioning platform, mechanism or strategy for the coordination of pharmacovigilance activities - **National Level**	Does a platform, mechanism or strategy for the coordination of pharmacovigilance activities (such as PV technical working group, forum or regularly scheduled meetings) exist among **national stakeholders**?	Yes	There is a national PV TWG and an annual stakeholders meeting. Also, the PAVIA triangle meetings (including representatives from TMDA, KCRI, NTLP, and several health facilities) meets regularly. It is planned to add the NACP to this triangle.	PV coordinator
		Have the key **national stakeholders** convened at least once in the previous calendar year?	Yes	Last PAVIA triangle meeting held in July 2022	PV coordinator
2.16	Submission of AE reports by health-care facilities in the previous year	From how many health facilities were AE reports received in the previous calendar year?	NA	Health facilities send their reports to the zonal TMDA offices or the regional PV coordinators, who then report on their behalf. Not always, the original reporter is mentioned in VigiFlow.	(1): https://www.statista.com/statistics/1249210/number-of-health-facilities-in-tanzania-by-type/ (2): https://en.wikipedia.org/wiki/List_of_hospitals_in_Tanzania#:~:text=According%20to%20the%20Health%20Facilities,hospitals%20listed%20in%20the%20register, quoting the Health Facility Registry of the MoH.
		How many health facilities are there in the country?	Approx. 8,500	Data for 2020: 8,458:7,163 dispensaries, 926 health centers, 369 hospitals (1), 8,497 medical care facilities, of which 337 are hospitals, of all facilities 62% are public (2).	
		How many health facilities submitted >10 reports to the PV centre in the previous calendar year?	NA	See comment above. At least Muhimbili, Dodoma General Hospital, Kilimanjaro Christian Medical Center submitted >10 reports.	
2.17	Evidence of consideration of safety data when developing and updating standard treatment guidelines	When developing standard treatment guidelines is evidence on safety data being described and taken into consideration?	Yes	The process has been described by Mori et al., PLoS One 2014; 9:384824: *"Efficacy, safety, availability and affordability were the most frequently utilised criteria in decision-making, although these were largely based on experience rather than evidence. In addition, recommendations from international guidelines and medicine promotions also influenced decision-making. Cost-effectiveness (…) was not utilised. (…)largely used experience and discretionary judgement, leaving evidence with only a limited role in decision-making process."*	https://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0084824&type=printable
2.18	National PV centre is a full or associate member of the WHO Program for International Drug Monitoring	Is the national pharmacovigilance centre a full or associate member of the WHO Program for International Drug Monitoring?	Full Member	Since 1993	Interview
Component 3. Signal Generation and Data Management					
3.1	Existence of a national database for	Does a central database exist for managing PV data?	Yes	VigiFlow	

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
	pharmacovigilance information	Does the central database contain data from various PV sources and methods (including PHPs?)	Yes	• HCP reports received on yellow forms • Patient reports received on green forms • NTLP enters aDSM reports into the SQRT developed by TMDA. TMDA hand-copies these reports into VigiFlow. • SMS-reports via the USSD system via the number *152*00# are automatically uploaded into SQRT. TMDA hand-copies these reports into VigiFlow. • Electronic reporting through a website link (https://imis.tmda.go.tz/arrt, NOTE: link not active at time of checking, Sept 2022)	Interviews, TMDA website (https://www.tmda.go.tz/pages/electronic-submission-of-adverse-drug-reactions) .
		Is there a dedicated computer for pharmacovigilance activities?	Yes	Staff members of TMDA have VigiFlow available on their personal laptops. There are also some desktop computers available in the data entry unit. Interns conduct data entry.	Interview, observations
		Does the computer have internet access?	Yes		
		Is data stored on a cloud/server?	Yes	VigiFlow is a cloud-based platform.	Internet (https://who-umc.org/pv-products/vigiflow/)
		Is there a back-up system?	Yes	VigiFlow does back-ups automatically.	Internet (https://who-umc.org/pv-products/vigiflow/)
3.2	Evidence of a process or mechanism for sharing information with other regulatory functions, other regulatory agencies and global databases	Has information in the database been shared (either electronically or via report) with other regulatory functions, other regulatory agencies and/or global databases?	Yes	Data is shared internationally via VigiBase.	Interview
3.3	Existence of a standard adverse event (AE) reporting form and subset indicators	Is there a standard AE reporting form?	Yes	Yellow form for healthcare providers (includes ADR and AEFI reporting form), green form for general public, aDSM form for DR-TB patients	Observations
		How is the reporting form offered? (e.*g.,* paper form, web, app)	See notes	• Paper forms (yellow, green, aDSM) • SMS-reports via the USSD system via the number *152*00# • Electronic reporting through a website link (https://imis.tmda.go.tz/arrt, NOTE: link not active at time of checking, Sept 2022)	Interview
		Are there relevant fields in the standard AE form (or a separate form) to report:			
		- adverse drug reactions?	Yes	In the new form (2021), it is not very clear where that field is (no clear header, little space for reporting)	Interviews, observations https://www.tmda.go.tz/uploads/1627451154-en1627306193-Yellow%20Form-%20Revised%202021.pdf
		- Suspected medication errors?	Yes		
		- therapeutic ineffectiveness?	Yes		
		- misuse, abuse and/or dependence on medicines?	No	There is a field where additional information can be added, but it is not explained that this may include information on misuse.	
		- suspected/ observed poor quality issues?	Yes	To be reported on a separate form	
		- adverse events following immunization?	Yes	To be reported on reverse side of the form	

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
		- medical devices and diagnostics?	Yes	To be reported on a separate form (the blue form). These reports are not uploaded in VigiFlow.	
3.4	Existence of a form or mechanism for the public to report AEs (Patient reporting system)	Is there a standard reporting form for the general public to report AEs?	Yes	Green form	Interview
3.5	Existence of electronic AE reporting system that complies with international reporting format standards	Is there an electronic AE reporting system?	Yes	ARRT and SQRT. ARRT is phasing out and seems no longer accessible through internet (see above), but the app is still available and can be used for reporting. The SQRT replaces ARRT and is used for transferring aDSM and SMS reports and can also be used by regional PV coordinators to enter their paper forms. Other regional PV coordinators and the zonal PV coordinators use VigiFlow to enter their paper forms.	Observations
		If yes, please provide technical details.		SQRT is a custom-made application meant to serve as a reporting platform, linking all reporting modalities.	Interviews
		Is the system compliant with the international reporting standards (E2B)?	Yes	No. Hand-copying of reports from SQRT into VigiFlow is still needed.	Interviews
3.6	A process is in place for collection, recording and analysis of ADR reports	Is there a process in place for collection, recording and analysis of ADR reports?	Yes	These are described in the following SOPs: • Procedure for receiving and processing ADR reports • Procedure for reviewing and annotating ADR reports	SOPs
Component 4. Risk Assessment and Evaluation					
4.1	Number of registered products with a PV plan and/or a risk management strategy	How many registered products with a pharmacovigilance plan and/or a risk management strategy from market authorization holders exist in the country?	6,812	All products registered in the country have a Risk Management Plan, but not all locally manufactured medicines are registered. TMDA contributed to the registration of new drugs through international collaborations with EAC (10 out of 29 new requests approved), SDAC (9/12 approved), and the WHO collaborative registration mechanism (5/5 approved).	PV coordinator
4.2	Total number of AE reports received in the previous calendar year (also expressed as number of AEs per 100 000 persons in the population). And number of reports of sub-indicators	What is the total number of AE reports received in the previous calendar year? Of the total, what is the number of reports of:	9,468	This includes all spontaneous and active AE reports received between 1st Jul 2021 and 30th Jun 2022. (spontaneous reports: 6,157)	VigiFlow
		- ADR?	3,704	Preliminary and quick analysis shows that 164 of these were related to TB medicines	
		- suspected medication errors?	NA		
		- therapeutic ineffectiveness?	NA		
		- suspected misuse, abuse, dependence?	NA		
		- AEFI?	5,764	80 due to routine vaccines, others related to COVID-19 vaccinations	
		- medical devices and diagnostics?	NA		
		- suspected counterfeit / substandard drugs?	NA		

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
		What is the total population of the country?	63.3 million (2022)		Internet (https://www.unfpa.org/data/world-population/TZ)
4.3	Number and percentage of total AE reports received by the national pharmacovigilance centre in the previous calendar year from:	What is the number of AE reports received by the national pharmacovigilance centre in the previous calendar year from:		This differentiation cannot be made and needs in-depth analysis.	
	- Marketing Authorization Holders	- Marketing Authorization Holders	0	Expectation is that no, or very little, individual case safety reports are sent in by MAHs. Reports received through PSURs are not included in VigiFlow. Also, SAEs received from clinical trials are not included.	
	- PHPs	- PHPs	NA	16 reports were received from the NTLP in 2021 (source: PV focal person of NTLP)	
	- Health care providers	- Health care providers	NA	These are the main reporters.	
	- Patients	- Patients	NA	Some patient reports are received, but it is not clear how many. A quick unconfirmed analysis found 40 patient reports for 2021.	
	-Distributors	-Distributors	0		
	-Suppliers	-Suppliers	0		
4.4	Number and percentage of total AE reports received that are entered in the national database in the previous calendar year	What is the total number of AE reports received that have been entered in the national database in the previous calendar year?	9,468	Note that regional PV coordinators sometimes decide not to enter incomplete reports, even though this is allowed in VigiFlow as all must-enter information was available (observation made in one of the regional PV centres visited by the assessors)	VigiFlow
4.6	Number and percentage of total AE reports acknowledged and/or issued feedback in the previous calendar year	What is the total number of AE reports acknowledged/issued feedback in the previous calendar year?	NA	Only paper forms sent to TMDA headquarters receive acknowledgement of receipt (and this is a minor part of the reports). SMS report also receive an automatic acknowledgement of receipt.	
4.7	Number and percentage of AE reports subjected to causality assessment in the previous calendar year	What is the total number of AE reports subjected to causality assessment in the previous calendar year?	9,468	SAEs are undergoing causality assessment by the PV Technical Committee that meets quarterly. Other AEs are causality assessed by staff of the Clinical Trial Control and PV unit of TMDA.	
4.8	Number and percentage of AE reports submitted to Vigibase in the previous calendar year	How many of the AE reports received at the national PV centre were submitted to Vigibase in the previous calendar year?	4,383	This includes 744 spontaneous AE reports. Reports that miss >1 of 1) information about drugs received; 2) information about the AE; 3) information about the facility where the drugs was received; 4) key information from the patient and/or 5) information on date of starting medication and/or of onset of the ADR are not submitted to VigiBase	
4.9	Average completeness score of quarterly reports submitted to Vigibase in the previous four quarters (= one year)	What was the average completeness score of quarterly reports submitted to Vigibase in the previous calendar year? *Consult quarterly reports from VigiGrade for*	0.55		Uppsala Monitoring Centre

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
		completeness scores of submitted reports			
4.10	Number of active surveillance activities initiated, ongoing or completed during the previous three years	How many active surveillance studies have been conducted in the last three years (36 months)?	2		PV coordinator
		Indicate what type (e.g. cohort event monitoring, targeted spontaneous reporting, etc.) and stage of completion (e.g. initiated, on-going or completed) for each study.		• CEM on dolutegravir for persons living with HIV (PLHIV). Study included 4,442 PLHIV receiving dolutegravir-containing anti-retroviral treatment. Data collection completed, data cleaning and analysis in progress. Supported by WHO. • CEM on AEFI following J&J COVID vaccination. Financially supported in part by WHO.	
4.11	Number and percentage of total AE reports received at the national pharmacovigilance centre in the previous calendar year from healthcare providers by type of provider	What is the number of AE reports received in the previous calendar year submitted by:			PV coordinator
		- doctors?	NA	This information is often not filled in the forms, as reporters do not include their job description. See also above for further clarifications.	
		- nurses or midwifes?	NA		
		- pharmacists?	NA		
		- manufacturers and pharmaceutical companies?	0		
		- dentists?	NA		
		- the general public?	NA		
		What is the total number of AE reports received in the previous calendar year?	9,468	1 Jul 2021 - 30 Jun 2022	
4.12	Evidence of supervision visits to marketing authorization holders by NMRA that address PV	Does the NMRA conduct supervision visits of MAHs that address PV?	Yes	The MAHs have been trained on their duties re. PV last year. In the upcoming year, TMDA plans to conduct more supervision visits.	PV coordinator
		How many supervision visits have been conducted in the previous calendar year?	1		
Component 5. Risk Management and Communication					
5.1	Number of regulatory actions taken in the previous calendar year as a consequence of national pharmacovigilance activities. *Request documentation to verify*	How many regulatory actions were taken in the previous calendar year as a consequence of pharmacovigilance activities that resulted in:	3		PV coordinator
		- product label changes (variation)?	0		
		- safety warnings on medicines to health professionals?	0		
		- safety warnings on medicines to the general public?	0		
		- withdrawals of medicines?	1	One batch of medformin failed quality control checks and was removed from the market.	

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
		- treatment guideline/policy changes?	0		
		- other restrictions on use of medicines?	2	Two veterinary medicines were not yet approved. TMDA requested them to apply for approval but no application was received. Therefore, the importation of these medicines was stopped.	
5.2	Number of signals detected in the past 5 years by the pharmacovigilance centre	How many signals were detected in the past 5 years by the pharmacovigilance centre?	0	11 regions had a serious AEFI that was investigated. Currently, the TMDA is investigating a potential signal re. bupivacaine	
		If any signals were detected, which ones and how were they identified?	NA		
5.3	Average time lag between identification of safety signal of a serious ADR or significant medicine safety issue generated nationally and communication to health care workers and the public	How long does it take from when a safety signal or significant safety issue is identified to when it is communicated to health workers and the public?	NA		
5.4	Number of suspected product quality issues detected through the pharmacovigilance system	What is the number of suspected product quality issues detected through the pharmacovigilance system in the previous calendar year?	0		PV coordinator
5.5	Percentage of planned issues of the medicine safety bulletin (or any other health-related newsletter that routinely features ADR or medicine safety issues) published in the previous calendar year	How many issues of the medicine safety bulletin are supposed to be published per year?	2		PV coordinator; https://www.tmda.go.tz/uploads/publications/en1661782920-DRUG%20SAFETY%20A5%20.pdf
		How many issues of the medicine safety bulletin were published in the previous calendar year?	0	The last issue (no. 4) was published in Oct 2020 (see link). No publications after 2020 due to lack of capacity (low staff number, COVID pandemic).	
5.6	Number of products voluntarily withdrawn by marketing authorization holders because of safety concerns in the previous calendar year	How many products were voluntarily withdrawn by marketing authorization holders because of safety concerns in the previous calendar year?	0		PV coordinator
5.7	Number and percentage of medicine safety information requests addressed in the previous calendar year	How many requests for information about medicine safety were received in the previous calendar year?	NA	This type of information is not recorded in TMDA.	PV coordinator
		Of the total received, how many requests for medicine safety information were addressed in the previous calendar year?	NA		
5.8	Number of summaries of product characteristics updated by MAH because of safety concerns in the previous	In the previous calendar year, how many summaries of product characteristics were updated by MAH because of safety concerns?	0		

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
	year				
5.9	Number of medicine safety issues of local relevance identified from outside sources (e.g., from another country, from region or international sources) and acted on locally in the previous calendar year	How many medicine safety issues identified from outside sources were acted on locally in the previous calendar year?	0		
5.10	Number of public or community education activities relating to medicine safety carried out in the previous calendar year	How many public or community education activities relating to medicine safety were carried out in the previous calendar year?	>100, see notes	TMDA activities include drug safety monitoring outreach campaigns reaching 125,589 persons, 8 exhibitions, 102 visits to secondary schools and colleges, 10 scripts for messages on 27 radio stations, 14 television programmes, and 2 meetings with reporters and editors from different media groups about TMDA's functions. 31 different IEC materials were prepared, e.g. an information leaflet on COVID vaccines, brochure about the SMS toll free reporting tool.	

Annex 4. PHP assessment tool

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
Component 2. Systems, Structures, and Stakeholder Coordination					
P2.1	PV activities included within the strategic and/or annual operational plans of PHPs	Are PV activities included within the strategic and/or annual operational plans of public health programs?	Yes	Included in annual operational plan. Also in Global Fund plan 2017-2022 (cannot be shared because salaries are also in there, has been translated in annual plan) and in the national strategic plan 2020-2025.	https://ntlp.go.tz/site/assets/files/1090/national_tuberculosis_and_leprosy_strategic_plan_vi_final_version.pdf
P2.2	Existence of a dedicated financial provision or statutory budget for the PHPs	Is there an annual budgetary allocation for PV activities for the PHP?	Yes	This is from GFATM donor funding. It is meant for orienting regional focal aDSM persons and HCWs dealing with MDR-TB patients (pharmacist, DOT nurse, laboratory staff) on aDSM reporting. 14 regional coordinators were trained so far out of 33 (32 regions + Kibong'oto, the national TB referral hospital)	PV focal person NTLP
		In the last fiscal year, how many funds were allocated by the MoH and donors for PV activities?	52M	Tanzania shillings, from the MoH.	
P2.3	Existence of a mechanism to disseminate PV information (including one or more of the following: newsletters, information bulletin, website or phone line for dissemination of pharmacovigilance information)	Is there a mechanism in place to disseminate PV information?	Yes	aDSM committee (national NTP team + regional PV focal persons) meets every quarter. Feedback to health care workers by PV focal persons, needs to be refined	PV focal person at NTLP
		Is there a newsletter or information bulletin for dissemination of PV information?	No	A PV component will be included in the annual TB report from next year onwards	
		Is there a website for dissemination of PV information?	No	There is not a website that specifically disseminates PV information, but, if there is relevant PV data, it will be published on TB program website: www.ntlp.go.tz	
		Is there a publicly advertised phone line to receive and provide medicine safety and PV information?	No		
		Is there another mechanism for dissemination of PV information?	No	There is an aDSM whatsapp group for organizing meetings and sharing minutes between the national team and focal points. This group is also for supply chain management, not only for PV. Apart from this, there are the trainings, DR-TB coordination meetings, and regular supportive supervision visits to TB facilities.	
P2.4	Number of healthcare workers trained in pharmacovigilance in the previous calendar year through in-service training	How many healthcare workers has the centre/program trained on PV in the previous calendar year (through **in-service** training)?	20	14 regional aDSM coordinators plus some healthcare workers	Quantitative Indicators from NTLP Focal Person
		- Clinicians / nurses	NA	Multidisciplinary training involving clinicians, pharmacists, some nurses etc	
		- Community health workers	0		
		How many training events/sessions were conducted in the previous calendar year?	4	The training was provided by NTLP, they have had some OV training themselves but feel they have a knowledge gap as the trainers had not been trained on all aspects of aDSM (e.g., causality assessment and signal detection; electronic data entry) Trainings were provided as in-class trainings by NTLP staff, TB clinicians and TB focal persons.	PV focal person at NTLP

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
P2.5	National treatment guidelines or protocols in use within the public health programs that consider pharmacovigilance	Do the treatment guidelines or protocols in use in the PHP provide instruction for PV activities?	Yes	There is a chapter on aDSM in the manual for management of tuberculosis and leprosy in Tanzania (2020)	http://www.ntlp.go.tz/site/assets/files/1081/ntlp_manual_2020_2021_1.pdf
P2.6	Evidence of consideration of safety data when developing and updating standard treatment guidelines or treatment policies	When developing standard treatment guidelines is evidence on safety data being described and taken into consideration?	Yes	See previous indicator.	
Component 3. Signal Generation and Data Management					
P3.1	PHPs use the national, standard ADR/AE reporting form	Does the PHP use the national, standard ADR/AE reporting form?	Yes	aDSM form is used, HCPs in MDR-TB fill in yellow form as well	PV focal person at NTLP
Component 4. Risk Assessment and Evaluation					
P4.1	Number and percentage of ADR/AE reports received by PHPs that were submitted to the national PV centre in the previous calendar year	What is the number of AE reports received by the PHP in the previous calendar year?	16	All TB regions have an aDSM focal person, but the training and supervision focus on the regions with most DR-TB patients. Many aDSM reports end up in the patient file and are not submitted to NTLP. More joint supervision visits with TMDA are needed. There used to be airtime support for submission of electronic forms through ARRT under the Challenge TB programme but that support has stopped.	Quantitative Indicators from NTLP Focal Person
		What is the number of AE reports submitted by the PHP to the national PV centre in the previous calendar year?	16		
P4.2	Total number of ADR reports per 1000 individuals exposed to medicines in the PHP in the previous calendar year.	How many individuals received medicines under the PHP in question during the previous year?	405	All MDR TB patients given medicines in 2021	Quantitative Indicators from PV Coordinator
		How many ADR reports were received, referring to the exposed population?	16		Quantitative Indicators from NTLP Focal Person
		Total number of ADR reports per 1000 individuals exposed to medicines in the PHP in the previous calendar year	39.5	Calculation	
P4.3	Percentage of patients in public health programs for whom drug-related, serious unexpected/unknown adverse events were reported in the previous calendar year	What is the total number of patients receiving medicines under the PHP?	87,820	87,415 DS TB patients and 405 DR TB patients	Quantitative Indicators from NTLP Focal Person
		What is the total number of patients receiving medicines in the PHP who experienced drug-related, serious, unexpected adverse events?	NA	16 aDSM reports; (Quick analysis by TMDA on medicines used for TB treatment provided 164 ADR reports.)	
		How many of those were reported to the national PV centre?	16		
P4.4	Number of suspected product quality issues detected through public health programs	What is the number of suspected product quality issues detected through the PHP in the previous calendar year?	0		Quantitative Indicators from NTLP Focal Person

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
P4.5	Number of reports on therapeutic ineffectiveness in the previous year	What is the number of reports on therapeutic ineffectiveness received by the PHP in the previous calendar year?	0		Quantitative Indicators from NTLP Focal Person
P4.6	Number of medicine-related hospital admissions per 1000 individuals exposed to medicines in the PHP in the previous year	What is the number of medicine-related hospital admissions of individuals exposed to medicines in the PHP in the previous year?	NA	Question on form not always clear to HCW, is now discussed in training. So data obtained may not reflect true situation. Not clear from data which AE required hospital admission	PV focal person at NTLP
P4.7	Number of active surveillance activities initiated, ongoing or completed during the past three years	How many active surveillance studies have been conducted in the last three years (36 months)?	1		Quantitative Indicators from NTCP Focal Person
		Indicate what type (e.g. cohort event monitoring, targeted spontaneous reporting, etc.) and stage of completion (e.g. initiated, on-going or completed) for each study	aDSM	Intermediate Package: Includes SAEs as well as AEs of special interest for all MDR-TB Patients	
P4.8	Functional collaboration/involvement in risk management plans with the PV centre	Do the PHP and PV centre communicate on risk management plans?	No	There isn't a platform created to discuss medicines risk management. However, the use of the aDSM electronic reporting tool was demonstrated during a training in September, 2021. TMDA and PHPs have agreed to further conduct joint activities between regulators and other PHPs	PV focal person at NTLP
		How often have the PHP and PV centre met to discuss risk management in the previous calendar year?	2		
Component 5. Risk Management and Communication					
P5.1	Average time lag between identification of safety signal of a serious ADR or significant medicine safety issue generated nationally and communication to health care workers and the public	How long does it take from when a safety signal or significant safety issue is identified to when it is communicated to health workers and the public?	NA	No signal/safety issue identified	Quantitative Indicators from NTCP Focal Person
P5.2	Existence of a program-related newsletter that routinely features ADR or medicine safety information	Is there a program-related newsletter, bulletin or other publication that routinely features ADR or medicine safety information?	No		PV focal person at NTLP
P5.3	Number and percentage of medicine safety information requests addressed in the previous calendar year	How many requests for information about medicine safety were received in the previous calendar year?	NA	Not officially documented but often called by clinicians	PV focal person at NTLP
		How many requests for medicine safety information were addressed in the previous calendar year?	NA		
P5.4	Number of medicine safety issues of local relevance identified from outside sources (e.g., from another country or international sources) and acted on locally in the previous calendar year	How many medicine safety issues identified from outside sources were acted on locally in the previous calendar year?	NA		

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
P5.5	Number of public or community education activities relating to medicine safety carried out in the previous calendar year	How many public or community education activities relating to medicine safety were carried out by the PHP in the previous calendar year?	0		Quantitative Indicators from NTLP Focal Person

Annex 5. List of documents reviewed for the endline assessment

Document	Year of publication
Relevant documents related to Pharmacovigilance:	2018
Tanzania Food, Drugs and Cosmetics Act	2003
Tanzania Food, Drugs and Costmetics Act Regulations	2018
Tanzania National Health Policy	2017
National guidelines for monitoring medicines safety, 2nd ed.	2017
Standard treatment guidelines and national essential medicines list for Tanzania mainland, 6th ed.	2021
Medicines and Therapeutics Committee Guidelines	2020
TMDA annual report 2020-2021	2021
Pharmacovigilance training manual for healthcare workers, 4th ed.	2020
Pharmacovigilance training guide for healthcare workers, 2nd ed.	2020
National pharmacovigilance roadmap 2019-2023	2021
Relevant SOPs and reports	
TMDA website (www.tmda.go.tz)	
Relevant Documents related to the NTBLCP:	
National Tuberculosis and Leprosy Strategic Plan VI 2020-2025	2020
NTLP website (www.ntlp.go.tz)	
Other relevant documents:	
EAC harmonized compendium on safety and vigilance of medical products and health technologies	2019

Annex 6. Example of documents used in an investigation

This form was used for investigating AEFIs possibly associated with vaccines administered against COVID-19. See paragraph 4.4.2 for more details on how investigations are conducted.

THE UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH, COMMUNITY DEVELOPMENT, GENDER, ELDERLY AND CHILDREN

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

ADVERSE EVENT FOLLOWING IMMUNIZATION (AEFI) INVESTIGATION FORM FOR COVID-19 VACCINES

(Only for Serious Adverse Events Following Immunization - Death / Disability / Hospitalization / Cluster)

SECTION A: PATIENT/CASE INFORMATION

**Patient name(Use a separate form for each case in a cluster):*
.....
Patient Registration number (Case ID):.....
**Patient's full Address:* Street..... .....
Ward..... District..... ..... Region: .....
Mobile: .....
Sex: ☐Male ☐Female
Date of birth (DD/MM/YYYY): _____/_____/_____ Age:_____
Age Group: ☐ 0 < 1 year ☐1- 5 years ☐> 5 years - 18 years ☐> 18 years – 60 years ☐> 60 years

Place of Vaccination:.....
Designation (√): ☐*Govt. health facility* ☐*Private health facility* ☐*Faith based Organization* ☐*other (Specify)*
.....
Vaccination in (√):☐Campaign ☐Routine ☐other (Specify)

Type of site *(√):*☐ Fixed ☐ Mobile ☐Outreach ☐Other

Details of the vaccine used							*Diluent*		
Name of vaccine (Generic)	**Brand Name Incl. Name of Manufacturer*	**Date of vaccination*	**Time of vaccination*	Dose (1st, 2nd, etc.)	**Batch/ Lot number*	Expiry date	**Batch/ Lot number*	Expiry date	Time of reconstitution

Brief Description of AEFI
(Signs and Symptoms):

Date & Time of First/key symptom(DD/MM/YYYY):
_____/_____/_____ _____Hr_____Min
Date of Hospitalization
_____:_____/_____/_____
Date first reported to the health authority:_____/_____/_____

Status on the date of investigation : ☐Died ☐Disabled ☐ Recovering ☐ Recovered ☐completely ☐Unknown

Death:
If died, date and time of death (DD/MM/YYYY): _____/_____/_____

Was Autopsy done? ☐Yes (date)_____/_____/_____ ☐No

Planned on (date)_____ Time_____
(Attach report (If available)

SECTION B: RELEVANT PATIENT INFORMATION PRIOR TO IMMUNIZATION

Criteria	Finding	Remarks
Past history of similar event	Yes / No /Unkn	
Adverse event after previous vaccination(s)	Yes / No /Unkn	
History of allergy to vaccine, drug or food	Yes / No /Unkn	
Pre-existing comorbidity/ congenital disorder?	Yes / No /Unkn	
Pre-existing acute illness (30 days) prior to vaccination?	Yes / No /Unkn	
Has the patient tested Covid19 positive prior to vaccination?	Yes / No /Unkn	
History of hospitalization in last 30 days, with cause	Yes / No /Unkn	
Was the patient receiving any concomitant medication? (If yes, name the drug, indication, doses & treatment dates)	Yes / No /Unkn	
Family history of any disease (relevant to AEFI) or allergy	Yes / No /Unkn	

For adult women
- Currently pregnant_____/ No / Unknown
- Currently breastfeeding? Yes No

For infants

- The birth was □full-term □pre-term □post-term Birth weight:____ (kg)
- Delivery procedure was Normal Cesarean Assisted (forceps, vacuum etc)with complication (specify)

SECTION C DETAILS OF FIRST EXAMINATION OF SERIOUS AEFI CASE**

Source of information (√ all that apply): Examination by investigator □Document □Verbal autopsy □ Other_____

*if from verbal autopsy, please mention source*_____

Name of the person who first examined /treated the patient: _____

Name of other persons treating the patient: _____

Other sources who provided information (specify): _____

Signs and symptoms in chronological order from the time of vaccination:

Name and contact information of person completing these clinical details	Designation:	Date/time

****Instructions – Attach copies of ALL available documents (including case sheet, discharge summary, case notes, laboratory reports and autopsy reports, prescriptions for concomitant medication) and then complete additional information NOT AVAILABLE in existing documents, i.e. • *If patient has received medical care* -** attach copies of all available documents (including case sheet, discharge summary, laboratory reports and autopsy reports, if available) and write only the information that is not available in the attached documents below • ***If patient has not received medical care*** – obtain history, examine the patient and write down your findings below (add additional sheets if necessary)

Provisional / Final diagnosis:.....

SECTION D: Details of vaccines provided at the site linked to AEFI on the corresponding day										
Number immunized for each antigen at session site. *Attach record if available*	Vaccine name									
	Number of doses									
a) When was the patient immunized? (√ the below and respond to ALL questions)										
Within the first vaccinations of the session within the last vaccinations of the session Unknown										
In case of multidose vials, was the vaccine given within the first few doses of the vial administered? within the last doses of the vial administered? unknown?										

b) Was there an error in prescribing or non-adherence to recommendation for use of this vaccine?	Yes* / No
c) Based on your investigation, do you feel that the vaccine (ingredients) administered could have been unsterile?	Yes* / No / Unable to assess
d) Based on your investigation, do you feel that the vaccine's physical condition (e.g. colour, turbidity, foreign substances etc) was abnormal at the time of administration?	Yes*/ No / Unable to assess
e) Based on your investigation, do you feel that there was an error in vaccine reconstitution /preparation by the vaccine vaccinator (e.g wrong product, wrong diluent, improper mixing, improper syringe filling etc)	Yes* / No / Unable to assess
f) Based on your investigation, do you feel that there was an error in vaccine handling (e.g. break in cold chain during transport, storage and / or immunization session etc)	Yes* / No / Unable to assess
g) Based on your investigation, do you feel that the vaccine was administered incorrectly (e.g. wrong dose, site or route of administration, wrong needle size, not following good injection practice e.tc.)	Yes* / No / Unable to assess
h) Number immunized from the concerned vaccine vial /ampoule	
i) Number immunized with the concerned vaccine in the same session	
j) Number immunized with the concerned vaccine having the same batch number in other locations. Specify location:_____	
k) Is this case a part of a cluster?	Yes* / No / Unkn
l) If yes, how many other cases have been deleted in the cluster?	
a. Did all the cases in the cluster receive a vaccine from the same vial?	Yes* / No / Unkn
b. If no,number of vials used in the cluster (enter details separately)	

**It is compulsory for you to provide explanations for these answers separately*

Section E Immunization practices at the place(s) where concerned vaccine as used *(Complete this section by asking and / or observing practice)*	
Syringes and needles used:	
• Are AD syringes used for immunization?	Yes* / No / Unkn
If no, specify the type of syringes used: □Glass □Disposable □Recycled disposable □ Other_____	
Specific key findings/additional observations and comments:	

Reconstitution: (Complete only if applicable, (√) NA if not applicable			
• Reconstitution procedure (√)	Statu s		
Same reconstitution syringe used for multiple vials of same vaccine?	Yes	No	NA
Same reconstitution syringe used for reconstituting diferent vaccine?	Yes	No	NA
Seperate reconstitution syringe for each vaccine vial?	Yes	No	NA
Seperate reconstitution syringe for each vaccination?	Yes	No	NA
• Are the vaccines and diluents used the same as those recommended by the manufacturer?	Yes	No	NA
Specific key findings/additional observations and comments			

SECTION F: Cold Chain and transport *Complete this section by asking and / or observing practice*	
Last vaccine storage point:	
• Is the temperature of the vaccine storage refrigerator monitored?	Yes / No
If "yes", was there any deviation outside of 2-8 ^{0}C after the vaccine was placed inside?	Yes / No
If "yes", provide details of monitoring separately	
• Was the correct procedure for storing vaccines, diluents and syringes followed?	Yes / No / Unkn
• Was any other item (other than EPI vaccines and diluents) in the refrigerator or freezer?	Yes / No / Unkn
• Were any partially used reconstituted vaccines in the refrigerator?	Yes / No / Unkn
• Were any unusable vaccines (expired, no label, VVM at stages 3 or 4 frozen) in the refridgerator?	Yes / No / Unkn
• Were any unusable diluents (expired, manufacturer not matched, cracked dirty ampoule) in the store	Yes / No / Unkn
Specific key findings/additional observations and comments:	
Vaccine transportation	
• Type of vaccine carrier used	
• Was the vaccine carrier sent tothe site on the same day as vaccination	Yes / No / Unkn
• Was the vaccine carrier returned from the site on same day as vacinnation?	Yes / No / Unkn
• was a conditioned ice-pack used?	Yes / No / Unkn
Specific key findings/additional observations and comments	

Section G	*Community investigation (please visit locality and interview parents/others*
Were any similar events reported within a time period similar to when the adverse event occured and in the same locality? Yes / No Unknown If "yes" describe:	
If "yes" how many events/episodes?	
Of those effected, how many events/episodes • *Vaccinated:* • *Not vaccinated:* • *Unknown:*	
Other comments:	
Section H:	Other findings/observations/commentss

As agreed by:

Mr Adam Fimbo
Director General TMDA
Date:
Location: