TMDA
Tanzania Medicines & Medical Devices Authority

DRUG SAFETY Bulletin

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Contents

Editorial Note

Dear readers,

It is my pleasure to present the Second Volume of the 5th Edition of the Drug Safety Bulletin for 2026. This issue provides critical updates on the safety of medicines within Public Health Programmes and beyond, reflecting TMDA's steadfast mandate to safeguard public health.

The Tanzania Medicines and Medical Devices Authority (TMDA) is an Executive Agency under the Ministry of Health, established in 2003 as the Tanzania Food and Drugs Authority (TFDA). Following the Finance Act, 2019, the regulation of food and cosmetics was transferred to the Tanzania Bureau of Standards (TBS). Since then, TMDA has focused its expertise on regulating the quality, safety, and effectiveness of medicines, medical devices, and diagnostics.

As a Maturity Level 3 Authority, TMDA remains dedicated to strengthening its regulatory systems to ensure they are robust, efficient, and transparent. A vital component of this mission is the timely dissemination of safety information to the public and our stakeholders through platforms such as this Bulletin.

Continuous engagement with our stakeholders is essential for deepening the public's understanding of quality and safety. To that end, the Drug Safety Bulletin serves as a primary tool for sharing regulatory updates and addressing emerging safety concerns.

I encourage you to read the articles featured in this Edition and welcome your constructive feedback, particularly regarding content and design, to help us refine future publications.

I trust that you will find this Bulletin informative and valuable.

Enjoy reading.

Dr. Adam Fimbo
Editor-in-Chief

VISION

To be the leading regulatory authority in ensuring safe, quality, and effective medicines, medical devices, diagnostics, and other health-related products for all.

MISSION

To protect and promote public health by ensuring the quality, safety, and effectiveness of medicines, medical devices, diagnostics, and other health-related products.

PHILOSOPHY

TMDA strives to offer quality regulatory services in the pursuit of protecting public health and the environment by using competent and dedicated staff.

Public Health Programme Contribution in Pharmacovigilance

Spontaneous reporting of adverse drug events is a cornerstone of pharmacovigilance in Tanzania. It involves unsolicited reporting of adverse events associated with the use of medicines and vaccines by healthcare workers and the community. These reports are systematically assessed to establish a clear benefit–to–risk balance, which ultimately guides critical regulatory decisions.

Spontaneous reporting relies on collaboration across multiple stakeholders, including Public Health Programmes (PHPs). From July to December 2025, these PHPs contributed a total of 889 reports (10%) out of the 8,915 individual case safety reports (ICSRs) documented.

Data was primarily sourced from four key programmes, namely the National AIDS, STIs and Hepatitis Control Programme (NASHCoP), National Malaria Control Programme (NMCP), National Tuberculosis and Leprosy Programme (NTLP), and Neglected Tropical Disease Programme (NTDP).

NASHCoP submitted the highest volume, accounting for 581 reports (6.5% of the national total) in that period whereas the NTDP recorded the fewest **(Figure 1).**

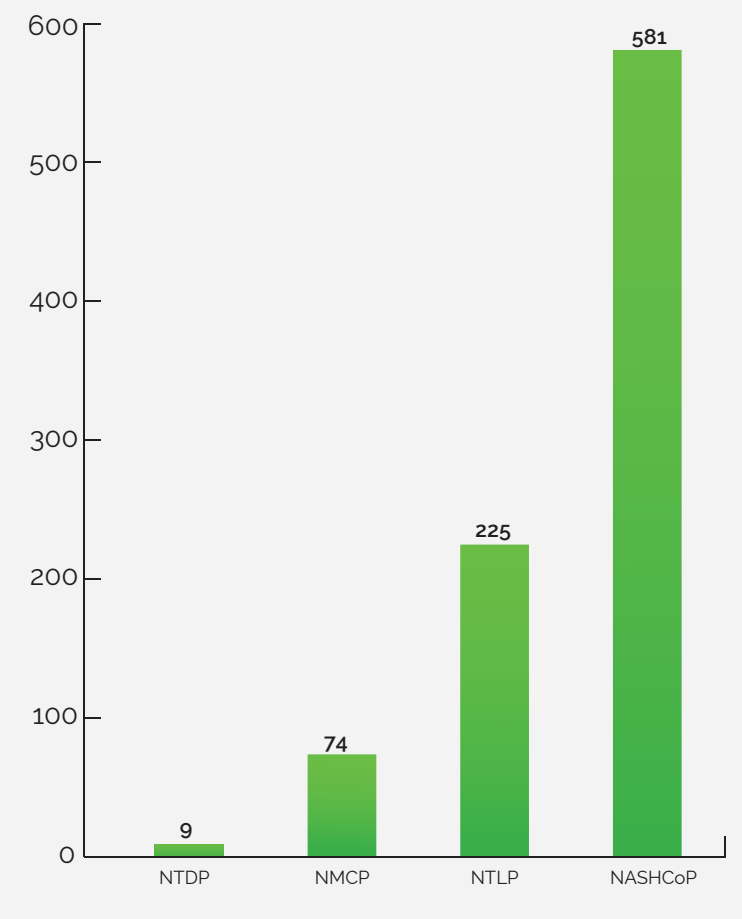


Figure 1: Number of ADR reports per Programme

An analysis by active ingredient reveals that the highest volume of reports was attributed to Tenofovir Disoproxil Fumarate/Lamivudine/Dolutegravir (TDF/3TC/DTG): 530 reports; Rifampicin/Isoniazid (RH): 133 reports; and Sulphadoxine/Pyrimethamine (SP): 50 reports. These findings are summarized in **Figure 2.**

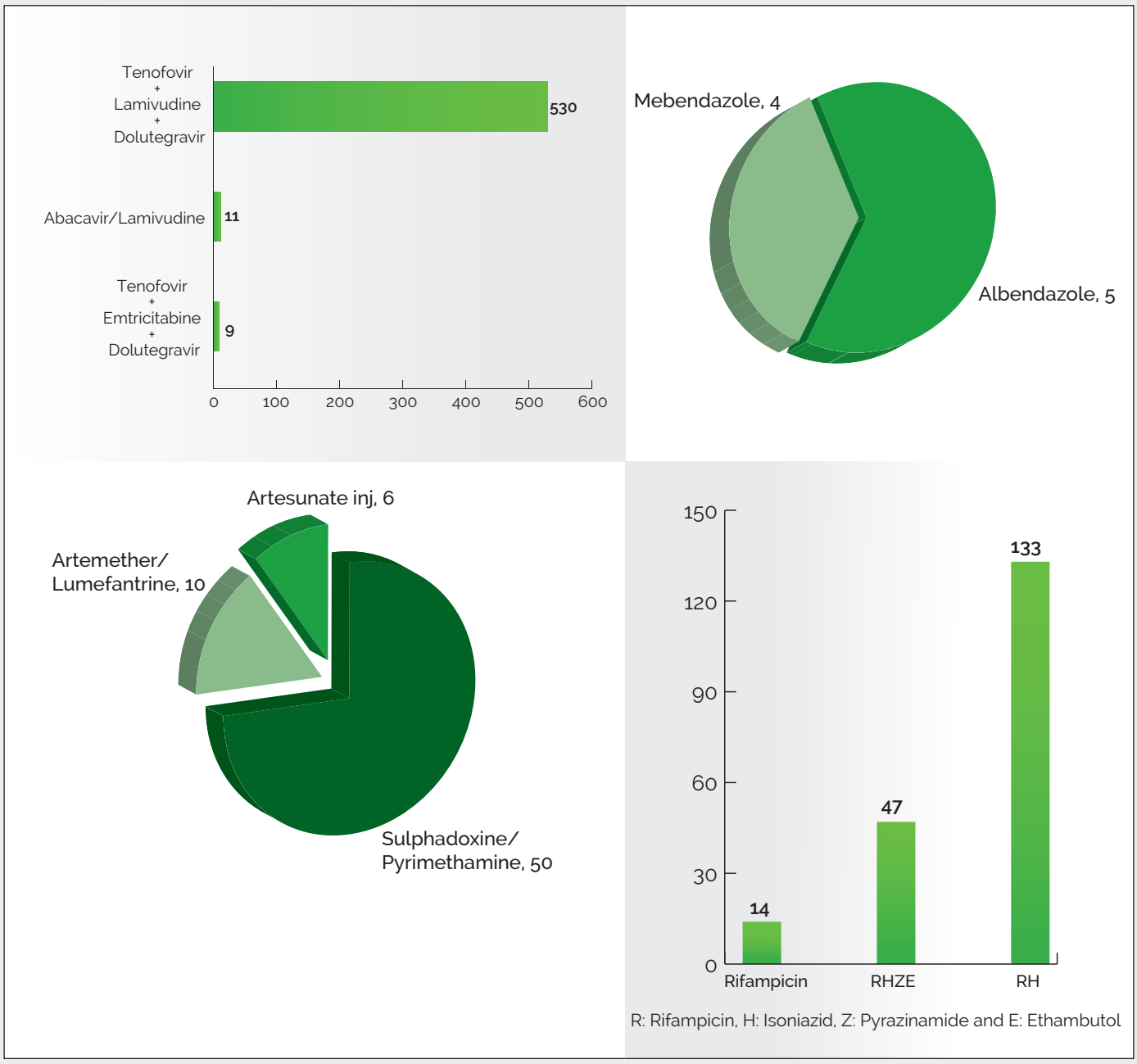


Figure 2: Three medicines with most adverse reactions reports from each of the public health program.

Tenofovir/Lamivudine/Dolutegravir safety profile: Analysis of passive surveillance data

As Tenofovir Disoproxil Fumarate/Lamivudine/Dolutegravir (**TLD**) serves as the primary first-line antiretroviral therapy in Tanzania, it accounted for **530 (5.8%)** of all adverse events reported to the Authority between July and December 2025. The most frequent clinical manifestations associated with TLD use were **Kidney injury:** 83 reports; **Headache:** 27 reports; **Nausea:** 23 reports, as detailed in **Figure 3**

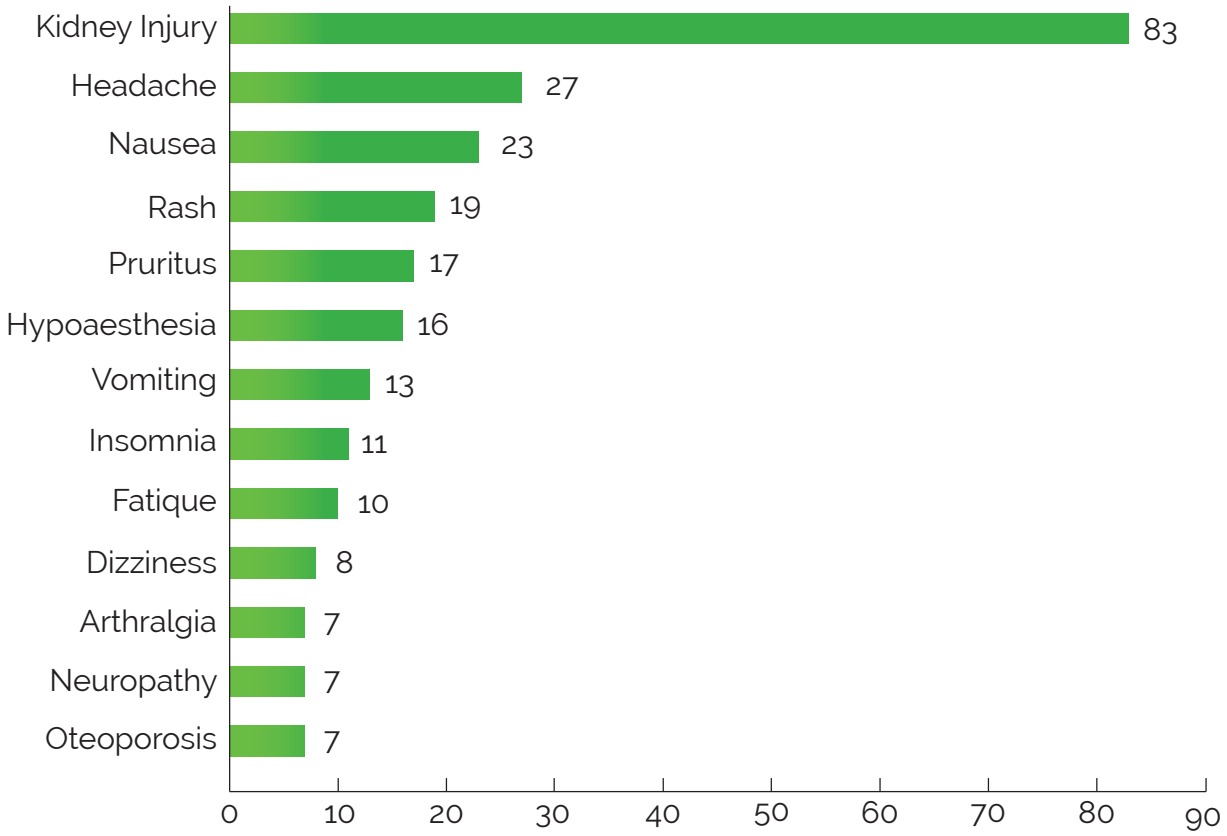


Figure 3: Most frequently reported adverse drug events associated with TLD

The high incidence of kidney injury associated with TLD aligns with both the Summary of Product Characteristics (SmPC) and established clinical evidence. Literature confirms that advanced age and long-term exposure (≥2 years) to Tenofovir Disoproxil Fumarate (TDF) significantly increase the risk of both acute and chronic renal impairment.

The hypothesized mechanism involves mitochondrial toxicity within the proximal tubular cells. This leads to Dysfunctional oxidative phosphorylation, Depletion of Adenosine Triphosphate (ATP) and Cellular apoptosis.

Routine monitoring of renal and hepatic function is essential for all patients on TLD, with a specific focus on creatinine clearance, estimated Glomerular Filtration Rate (eGFR), and clinical signs such as urinary changes fluid retention etc is emphasized. Healthcare facilities should implement standardized assessments and regular follow-ups to enable early detection of kidney problems and timely intervention.

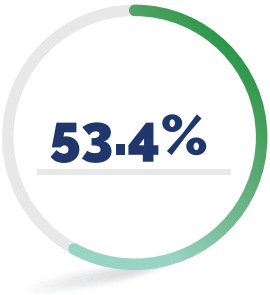
This may include a clinical switch from TDF to Tenofovir Alafenamide Fumarate (TAF). As a potent, targeted prodrug, TAF achieves higher intracellular concentrations with lower systemic blood levels, offering superior renal and bone safety profiles.

Other reported adverse events in descending order of frequency, other reported events included: -

a. **Common:** Malaise, tachycardia, confusion, peripheral neuropathy, cough, dizziness, pain in extremities, pollakiuria, and decreased appetite.

b. **Additional:** Amnesia, asthenia, hunger, throat irritation, flatulence, myalgia, and hyperhidrosis (excessive sweating).

Surveillance of Pentavalent Vaccines: Insights from spontaneous adverse event reports



TMDA received a total of 3,700 reports, of which 1,975 (53.4%) were related to the pentavalent vaccine.

The pentavalent vaccine is a 5-in-1, single-shot immunization for infants that protects against diphtheria, tetanus, pertussis (whooping cough), hepatitis B, and *Haemophilus influenzae* type b (Hib). It is typically administered in a three-dose series at 6, 10, and 14 weeks of age. Despite its critical role in preventing these five serious illnesses, it can be associated with adverse events following immunization (AEFI), as is the case with any vaccine.

TMDA collects and assesses all AEFIs to identify any changes in the safety profile that may warrant regulatory action. Between July and December 2025, TMDA received a total of 3,700 reports, of which 1,975 (53.4%) were related to the pentavalent vaccine.

The multi-component nature of this vaccine likely contributes to this volume, as recipients may react differently to the various individual antigens.

AEFIs can occur following the first, second, or third dose, and recipients may experience multiple events simultaneously. The most frequently reported AEFIs were Pyrexia (fever): 1,374 reports; Persistent crying: 473 reports; and Swelling of the vaccinated limb: 180 reports (**Figure 4**).

Other reported events included seizure, somnolence, febrile convulsion, erythema, itching scar, rash, asthenia, chills, nausea, oral mucosal scar, loss of appetite, and rectal abscess.

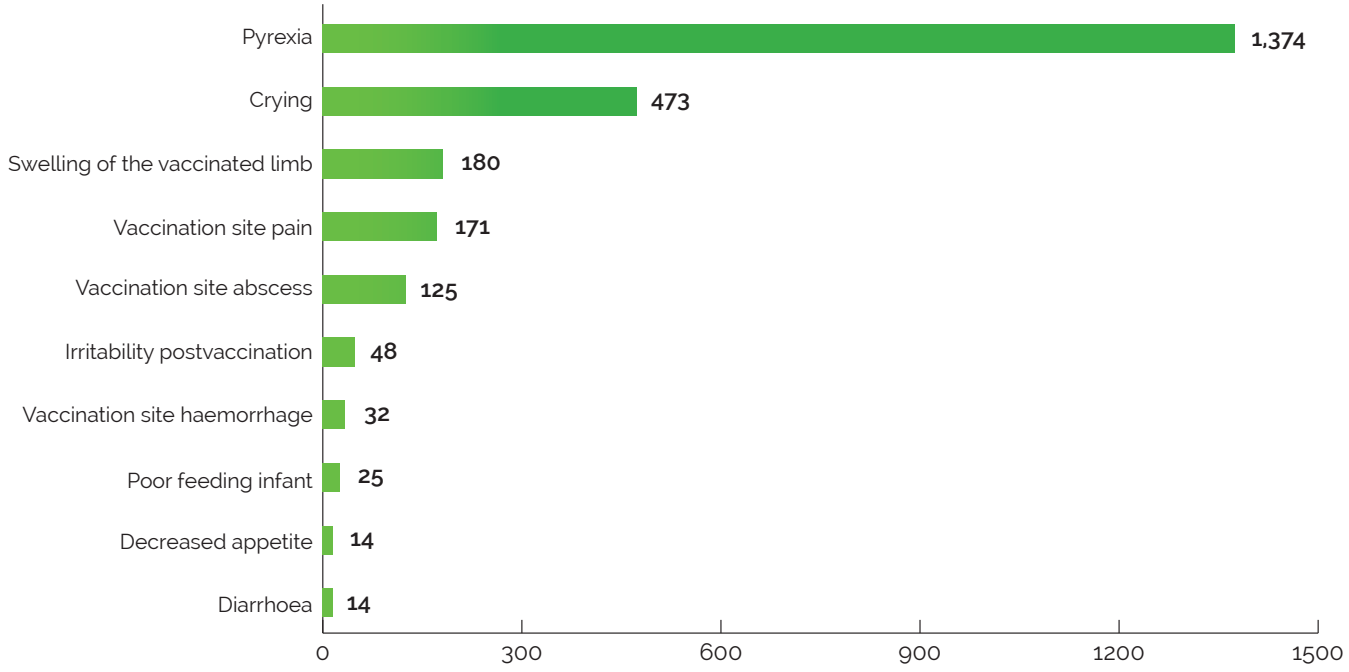


Figure 4: Most reported AEFI following Pentavalent Immunization

All reported adverse events were classified as *non-serious* and were consistent with the Summary of Product Characteristics (SmPC). This data confirms that the pentavalent vaccine maintains a favourable safety profile and remains safe for public administration.

Enforcement of Pharmacovigilance to Marketing Authorization Holders

TMDA continuously employs a risk-based approach when conducting Good Pharmacovigilance Practice (GVP) inspections of Marketing Authorization Holders (MAHs). These inspections ensure strict compliance with the TMDA Pharmacovigilance (Regulations) 2018.

In December 2025, TMDA Inspected 53 MAHs nationwide to verify that these entities have established effective and efficient pharmacovigilance systems. The primary goal was to ensure that these systems are capable of collating adverse event reports and continuously monitoring medicinal safety throughout the product life cycle.

The inspections identified several instances of non-compliance (Table 2). Consequently, the affected MAHs were directed to rectify the observed non-conformances and submit Corrective and Preventive Action (CAPA) reports to the Authority.

Table No. 2: Summary Findings of Pharmacovigilance Practice (GvP) Inspection

S/N	Description	Compliance (n)	Compliance (%)
1	Presence of Qualified Personnel for Pharmacovigilance	25	47.2
2	Presence of Designated Pharmacovigilance Office/Space	24	45.3
3	ADRs report submission	6	11.3
4	Presence of Pharmacovigilance System Master File (PSMF)	14	26.4
5	Periodic Safety Updates Reports (PSUR) Submission	13	24.5
6	Risk Management Plans (RMPs) Submission	12	22.6
7	Presence of SOPs for PV activities	19	35.8
8	Presence of Qualified Personnel for Pharmacovigilance (QPPV)	31	58.5
9	Pharmacovigilance Self Audit	13	24.5

These findings indicate that significant challenges persist among MAHs in meeting their pharmacovigilance obligations. This underscores the critical need for continued regulatory oversight and enhanced capacity building for the Qualified Persons Responsible for Pharmacovigilance (QPPVs).

To address these gaps, the Authority remains committed to fostering compliance through rigorous monitoring and technical support, ensuring that all MAHs maintain the standards necessary to safeguard public health.

Picture 1: Good Pharmacovigilance (GVP) Inspection at JD Pharmacy Limited in Dar es Salaam on 3rd December, 2025

Inauguration of New Vigilance Technical Committee (VTC)

The Vigilance Technical Committee (VTC) is a statutory advisory body established under Section 13(1) and 13(2) of the Tanzania Medicines and Medical Devices Act, Cap. 219. Its primary mandate is to provide independent technical expertise to the Director General of the TMDA on pharmacovigilance matters.

The VTC is a multidisciplinary body comprising experts from academic institutions, national Public Health Programmes, and Healthcare Facilities (Clinical Settings). This diverse composition ensures a balanced, evidence-based review of safety emerging safety information related to medicines and vaccines. Members serve a three-year term, with appointments or reappointments occurring at the end of each tenure.

The 5th VTC was appointed by the Director General on 4th November 2024 and officially inaugurated on 4th March 2025. The committee will serve until December 2027. The current VTC consists of nine (9) members, as detailed in **Table 3**.

Table 3: Composition of the Vigilance Technical Committee - (2025–2027)

S/N	Name	Title	Speciality	Affiliation
1	Prof. Kennedy.D. Mwambete	Chairperson	Pharmaceutical Microbiology	Muhimbili University of Health and Allied Sciences (MUHAS)
2	Dr. Yonah H. Mwalwisi	Secretary	Regulatory Sciences	Tanzania Medicines and Medical Devices Authority (TMDA)
3	Prof. Omary Minzi	Member	Clinical Pharmacy	Muhimbili University of Health and Allied Sciences (MUHAS)
4	Pharm. Anna Kajiru	Member	Pharmacist	Immunization and Vaccine Development (IVD)
5	Pharm. Chrispin Mamkinga	Member	Pharmacist	National Tuberculosis and Leprosy Programme (NTLP)
6	Dr. Florence Salvatory Kalabamu	Member	Paediatrics and Child Health	Hubert Kairuki Memorial University (HKMU)
7	Pharma. Anna David Mwasomolo	Member	Pharmacist	National Malaria Control Programme (NMCP)
8	Dr. Amina Mgunya	Member	Internal Medicine	Muhimbili University of Health and Allied Sciences (MUHAS)
9	Pharm. Saulo Sarungi	Member	Pharmacist	National AIDS, STIs and Hepatitis Control Programme (NASHCoP)

The inauguration ceremony for the 5th VTC was held on 4th March 2025 (**Picture 2**). During the proceedings, members were formally oriented on the committee's Terms of Reference (ToR) and received comprehensive briefings on all regulatory frameworks governing pharmacovigilance.

Picture 2: Acting Director General, Dr. Danstan Hipolite (4th from the left – front line) with newly appointed Chairman Prof. Kennedy Mwambete (3rd from the left – front line) and other appointed VTC members during the inauguration ceremony held on 4th March, 2025 at Edema Hotel in Morogoro Municipality

The responsibilities of the **VTC** include, but are not limited to, the following:-

a	**Technical Advisory**	Providing expert guidance to the Director General on pharmacovigilance and post-marketing safety matters.
b	**Safety Signal Review**	Reviewing and making formal recommendations on safety signals, serious adverse events (SAEs), and the ongoing benefit–risk assessments of medicines and vaccines.
c	**Risk Management**	Advising on risk minimization measures, necessary regulatory actions, and official safety communications.
d	**System Strengthening**	Supporting TMDA in enhancing the national pharmacovigilance framework and promoting the rational use of medicines and vaccines.

Publications

A peer-reviewed article titled: "The ASCEND Project (2020-2023): Strengthening clinical trial ethics review and pharmacovigilance in Tanzania Mainland and Zanzibar" was published in Open Research Europe. This article can be accessed via the following DOI: 10.12688/openreseurope.17124.1

Open Research Europe
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CASE STUDY

The ASCEND Project (2020-2023): Strengthening clinical trial ethics review and pharmacovigilance capacity in Tanzania mainland and Zanzibar

[version 1; peer review: awaiting peer review]

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Summary of the Publication

Clinical trials and related health research in Sub-Saharan Africa continue to expand in volume and complexity, increasing the need for strong and responsive research ethics oversight, regulatory reviews, and pharmacovigilance systems. The ASCEND Project was implemented in Tanzania Mainland and Zanzibar from November 2020 to December 2023 to support these functions through capacity development and system- strengthening activities.

Objective

To describe the implementation approach and documented outputs of the ASCEND Project as a case study focusing on operational processes that may inform similar initiatives.

Approach

Project documentation produced during implementation, mainly training materials, activity reports, system development records, and consortium deliverables, was compiled and synthesized. We summarized the implementation components and verified the output counts across the available records.

Outputs

The following outputs were delivered under the ASCEND Project: -

a. Training packages for clinical trial protocol reviews and Good Clinical Practice inspection;

b. 30 clinical trial protocol assessors and 25 GCP inspectors trained, including on-the-job inspection exposure for Zanzibar Food and Drug Authority staff;

c. 19 early- and mid-career researchers and 50 trainers from institutional ethics committees trained on research ethics and clinical trial-related issues;

d. Digital tools developed and/or upgraded to support ethics review workflows;

e. A Community Pharmacovigilance Engagement Model developed and deployed to sensitization activities in both rural and urban settings; and

f. Networking forums were convened to support interactions among researchers, institutional review boards, and regulators.

Conclusion

This case study documents the implementation of a multicomponent capacity development initiative that combines training, digital tools, community engagement, and stakeholder networking. The experience highlights practical considerations for similar programmes, including institutional ownership, integration of electronic tools into routine workflows, and early planning for sustainability within existing structures.

Co-Administration of Bupivacaine-Propofol and Diazepam, a case report of Local Anaesthesia Systemic Toxicity (IST) post-Caesarean Section

Background:

Cesarean sections are common in Tanzania (29% regionally in 2022, exceeding the WHO's 15% recommendation), with spinal anaesthesia using bupivacaine preferred for safety. However, pregnant women face a risk of increased local anesthetic systemic toxicity (LAST) due to elevated cardiac output and reduced protein binding.

Case Report:

A full-term woman in her 30s (72 kg) underwent elective cesarean section (CS) at a primary health facility under spinal anaesthesia with bupivacaine (suspected) and propofol 1%, delivering a healthy 3.4 kg baby. Fifteen (15) minutes post-administration, she developed low back pain, sweating, irritability, intermittent convulsions, loss of consciousness (at 2 hours), and oxygen desaturation, progressing to death despite no allergies, illnesses, or procedural errors. Upon investigation, it was confirmed that the case was related to bupivacaine-induced Local Anaesthetic Systemic Toxicity (LAST) exacerbated by propofol/diazepam synergy on GABA_A receptors.

Management of the patient was done by administration of Magnesium sulfate (loading dose), diazepam, and adrenaline. Despite this effort, the patient encountered Central Nervous System (CNS) and Cardiovascular collapse and died instantly.

Discussion:

This rare fatal case of LAST post-cesarean in Tanzania highlights co-administration risks of bupivacaine-propofol-diazepam in resource-limited settings where lipid emulsion availability is critical.

Discussion

The patient's symptoms—low back pain, sweating, irritability, loss of consciousness, and dehydration—align with the Summary of Product Characteristics describing bupivacaine's induced LAST. Similar adverse reactions were reported by Shafiel and his colleagues, including back pain, sweating, irritability, chills/shivering, and severe outcomes like loss of consciousness or coma (1). A study done by Dudley reported (seizure, bradycardia, cardiac arrest post-nerve block) (2).

Panagiotis and his colleague reported (rapid CNS/cardiovascular toxicity)(3), and Mayo Clinic (confusion, nervousness, sweating, chills, irritability)(4). This supports the hypothesis of local anaesthetic systemic toxicity (LAST), though Micromedex notes an unknown incidence for irritability, shivering, and sweating.(5).

Bupivacaine use risks severe CNS toxicity (convulsions, coma), cardiovascular collapse (bradycardia, arrest), and dehydration/excitement symptoms, especially in pregnancy/post-caesarean with added magnesium sulfate and adrenaline.(6). Monitoring needs include immediate vital signs (heart rate, blood pressure, respiration), neurologic status, fluid status, and readiness for lipid emulsion therapy or airway support for LAST; pregnancy heightens vulnerability to rapid symptom onset. (7).

Overlapping of Propofol and Diazepam Effects

Propofol and diazepam overlap with bupivacaine via enhanced CNS depression on GABA_A receptors—bupivacaine potentiates propofol's hypnosis, diazepam

adds sedation (drowsiness, confusion), amplifying risks of respiratory depression, hypotension, and prolonged recovery cited by Pency. (8). Diazepam's effects (drowsiness, confusion) overlap with patient irritability/loss of consciousness, synergizing with propofol's depressant action for profound sedation in this multi-drug caesarean context. (9).

Conclusion

The timing of these symptoms and a review of existing literature suggest a possible causal link between the use of bupivacaine and LAST as per the WHO–UMC causality grading system

Recommendations

a. Reduced bupivacaine doses by 10-20% in pregnancy; slow injection administration (<1 mL/s) practice with aspiration; use of intralipid emulsion (20-30% solution) as rescue for severe LAST; and close monitoring of vitals during bupivacaine administration is recommended. This should be coupled with the evaluation of the risk of CNS depression due to drug-drug interactions between Propofol, diazepam and bupivacaine.

b. Training of all staff involved in the administration of Bupivacaine anaesthesia should be mandated to all respective facilities that use this anaesthetic agent;

c. Equipment to facilitate operation procedures, such as pulse oximetry (monitoring oxygen concentration), capnography (monitoring end-tidal carbon dioxide among patients), sphygmomanometers (monitoring of blood pressure every 5 minutes), etc., should be available in theatres.

d. Levobupivacaine as an alternative to Bupivacaine should be sought when necessary to avoid heart and CNS toxicity.

References on Bupivacaine Case Report

1. Shafiei FT, McAllister RK, Lopez J. Bupivacaine. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2026 Jan 19]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK532883/

2. Dudley MH, Fleming SW, Garg U, Edwards JM. Fatality Involving Complications of Bupivacaine Toxicity and Hypersensitivity Reaction*: FATALITY INVOLVING BUPIVACAINE. Journal of Forensic Sciences. 2011 Sept;56(5):1376–9.

3. Cotileas P, Myrianthefs P, Haralambakis A, Cotsopoulos P, Stamatopoulou C, Ladakis C, et al. Bupivacaine-induced myocardial depression and pulmonary oedema: A case report. Journal of Electrocardiology. 2000 July;33(3):291–6.

4. The Mayo Clinic Diet. Propofol (intravenous route) [Internet]. 2026 Jan [cited 2026 Jan 19]. Available from: https://www.mayoclinic.org/drugs-supplements/propofol-intravenous-route/description/drg-20488192

5. Merative, Micromedex. Bupivacaine (injection route) [Internet]. Arizona - Scottsdale/Phoenix; 2025 Nov [cited 2026 Jan 19]. (Drugs & Supplements). Available from: https://www.mayoclinic.org/about-mayo-clinic/contact

6. Karam RS, Mohammad FK. The use of anaesthetics for cesarean section delivery in women in Duhok, Kurdistan region, Iraq. jidhealth [Internet]. 2022 Nov 30 [cited 2026 Jan 19];5(4). Available from: http://www.jidhealth.com/index.php/jidhealth/article/view/257

7. Sánchez-Romero J, Falcón-Araña L, Blanco-Carnero JE, García-Ferreira J, Herrera-Giménez J, Fuentes-García D, et al. Randomized clinical trial of the use of Propofol as a sedative agent versus spinal analgesia with bupivacaine in External Cephalic Version (PropoSpinECV): study protocol for a randomized clinical trial. Trials. 2025 Oct 9;26(1):398.

8. Pence A, Hoyt H, McGrath M, Forman SA, Raines DE. Competitive Interactions Between Propofol and Diazepam: Studies in GABAA Receptors and Zebrafish. J Pharmacol Exp Ther. 2022 Dec;383(3):238–45.

9. Molly Becze, PharmD, BCPS —. Diazepam, oral tablet [Internet]. Healthline Media UK Ltd, London, UK; 2024 Aug [cited 2026 Jan 19]. Available from: https://www.medicalnewstoday.com/articles/diazepam-oral-tablet#_noHeaderPrefixedContent

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