REPUBLIC OF KENYA

MINISTRY OF HEALTH

NATIONAL TUBERCULOSIS, LEPROSY AND LUNG DISEASE PROGRAM

GUIDELINES FOR IMPLEMENTATION OF ACTIVE TUBERCULOSIS DRUGS SAFETY MONITORING AND MANAGEMENT IN KENYA

2026

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List of Abbreviations

ADRs	Adverse Drug Events
aDSM T	Active Drugs Surveillance, Monitoring and Management Tool
AEs	Adverse Events
AMREF	African Medical Research Foundation
BAT	Bioequivalence Analysis tool
Bdq	Bedaquiline
CA T	Causality assesment Tool
CoA	Certificate of Analysis
Co PI	Co Principal Investigator
CoEs TB	Centres of Excellence for TB
DEA	Drugs Efficacy analysis
Dl	Delaminide
DNTLDP	Division of National Tuberculosis, Leprosy and Lung Diseases Program
DR-TB	Drug Resistant Tuberculosis
DUR T	Drugs Utilisation Review Tool
DTDSA T	Drugs Toxicology Detox and substance Abuse Tool
ECT	Extemporaneouse compounding Tool.
HBC	High Burden Country
IP	Intensive Phase
KNH	Kenyatta National Hospital
MDR TB	Multi Drug resistant Tuberculosis
MOH	Ministry of Health
MTM T	Medicines Therapeutic Monitoring Tool
NACOSTI	National Commission for Science, Technology and Innovation-Kenyan commission
NMRA	National Medicines Regulatory Agency
NQCL	National Quality Control Laboratory
NTPs	National TB programs
NSP 2023-2028	National Strategic Plan 2023-2028
PCP T	Pharmaceutical Care Plans Tool.

PMDT	Programmatic management of drug-resistant TB
PMS	Post Marketing Surveillance
PI	Principal Investigator
PK	Pharmacokinetics
PKIT	Pharmacokinetic individualized dosing tool.
PPB	Pharmacy and Poisons Board
PV-aDSM	Pharmacovigilance –aDSM Subcommittee in TB program
RR TB **SAEs**	Rifampicin Resistant Tuberculosis Severe Adverse Events
TB	Tuberculosis
TDM T	Therapeutic Drugs Monitoring Tool.
WHO	Word Health Organization

Glossary of terms

The following definitions describe terminologies in the context of this guideline.

Active TB drug safety monitoring and management (aDSM) – 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 drug toxicities.

Active surveillance - Active measures are taken to detect adverse events. It involves active followup after treatment where the events may be detected by asking patients directly or screening patient records. It is best done prospectively. Active pharmacovigilance is sometimes very descriptively referred to as, "hot pursuit"

Adverse Event/ Adverse Experience - Any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment.

Adverse Drug Reaction - A response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function. An adverse drug reaction, in contrast to an adverse event, is characterized by the fact that a causal relationship between a medical product and an occurrence is suspected.

Adverse event of clinical significance: Is an AE that is either: (i) serious, (ii) of special interest, (iii) leads to a discontinuation or change in the treatment, or (iv) is judged as otherwise clinically significant by the clinician.

Adverse event of special interest: Is any AE documented to have occurred during clinical trials and for which the monitoring programme is specifically sensitized to report regardless of its seriousness, severity or causal relationship to the TB treatment.

Board - The Pharmacy and Poisons Board

Case Control Study - Study that identifies a group of persons with the unintended drug effect of interest and a suitable comparison group of people without the unintended effect. The relationship of a drug to the drug event is examined by comparing the groups exhibiting and not exhibiting the drug event with regard to how frequently the drug is present.

Cohort Event Monitoring (CEM) - A prospective, observational, cohort study of adverse events associated with one or more medicines

Cohort Study - A study that identifies defined populations and follows them forward in time, examining their rates of disease. A cohort study generally identifies and compares exposed patients to unexposed patients or to patients who receive a different exposure.

Causality assessment: Is the evaluation of the likelihood that a TB medicine was the causative agent of an observed adverse reaction or adverse event.

Causal relationship: The relationship between an exposure (A) and an event (B) in which A precedes and causes B. This may refer to the causal association between an exposure to a TB medicine and the occurrence of an adverse reaction

Cohort event monitoring sentinel sites: are centres that, in addition to the core package of aDSM, undertake intermediate or advanced levels of drug-safety monitoring.

Centres of Excellence for TB: They are level 5 and level 6 facilities pre-qualified by an assessment tool to offer specialized, referral and advanced care and treatment for TB.

De-challenge: withdrawal of a drug: Resolution of suspected ADR when the drug is withdrawn is a strong, although not conclusive indication of drug-induced disease. In cases where a withdrawal reaction is experienced, a de-challenge is when the drug is again given to the patient.

Drug - In this context also known as medicine or medical product

Drug-safety profile: Is a description of the benefits, risks and toxicity of a given TB drug or regimen, specifying any known or likely safety concerns, contraindications, cautions, preventive measures and other features that the user should be aware of to protect the health of a TB patient.

ECGs: Electrocardiogram records of electrical signals from the heart, indicating different signals from the heart. These records will be used to monitor the toxicities to heart by quinolones: Levofloxacin, moxifloxacin molecules and Delaminide used by Drug resistant TB patients.

KNH: the Kenyatta National Referral hospital, a regional referral Hospital to offer specialized care and teaching and referral.

Lancet laboratories: (LR) the Referral laboratories collaborating with the public sector to undertake pathological chemistry analysis and TDM analysis.

"Positive" de-challenge: improvement of reaction when de-challenge occurs

Q-T interval: Is the measurement made on an electrocardiogram used to assess some of the electrical properties of the heart.

Re-challenge : reintroducing the drug after a de-challenge: This is only justifiable when the benefit of re-introducing the drug to the patient outweighs the risk of recurrence of the reaction. This is rare. In some cases, the reaction may be more severe on repeat exposure.

TB Nurse: The Nurse deployed in the chest clinic to undertake care and treatment of the patients` drugs therapy.

Therapeutic Drugs monitoring: This is both the observational and analytical monitoring and management of the patient from monitoring of the signals and subjecting the blood sample to TDM analyzer to give a range of results from the pharmacokinetics to pharmacodynamics parameters of the drug and the patient. This will inform other calculations, by a clinical pharmacist that will adjust the dosing to its safety dosing profile or withdrawal of the medication.

Serious adverse event (SAE): an AE which either leads to death or a life-threatening experience; to hospitalization or prolongation of hospitalization; to persistent or significant disability; or to a congenital anomaly. Any SAE that does not immediately result in one of these outcomes but that require an intervention such as termination of the drug suspected of having caused the event.

Signal: reported information on a possible causal relationship between an adverse event and a TB medicine, the relationship being unknown or incompletely documented previously or representing a new aspect of a known association

TIBU: Patient management software by the Division of National Tuberculosis, Leprosy and Lung Health Program, Ministry of health Annex.

CAP 242: Public health act in Kenyan Republic, under Ministry of Health.

Foreword

Tuberculosis (TB) care continues to present significant challenges, driven by the increasing use of repurposed medicines, frequent regimen changes, and the high burden of medication-related problems. These realities informed the adoption of the World Health Organization's (WHO) 2018 strategic plan, which underscored the importance of active drug safety monitoring and management (aDSM) in TB care.

In Kenya, aDSM is firmly anchored within the National Strategic Plan (2023/24–2028/29) of the Division of Tuberculosis, Leprosy and Lung Disease Program as a core strategy under patient-centered care to improve quality of treatment and outcomes. This commitment is reflected in the government's rapid adoption of WHO advisories, including the shift to injection-free, repurposed medicines in the management of drug-resistant TB.

The implementation of aDSM in Kenya began in 2022 through broad-based stakeholder participation and engagement. As part of operationalizing the National Strategic Plan, the development of these national guidelines was necessary to provide a clear framework for implementation. The Government of Kenya acknowledges the unique expertise of pharmacy specialists and recognizes their pivotal role in advancing this agenda. Their skills in pharmacovigilance, pharmacotherapeutics, clinical pharmacy, extemporaneous compounding, toxicology, and pharmaceutical analysis are essential in guiding multidisciplinary healthcare teams and ensuring the success of this initiative.

Successful implementation of this guideline will require strong intersectoral collaboration among the Pharmacy and Poisons Board (PPB), the Directorate of Health Products and Technologies (DHPT), the Division of Health Informatics (DHI), intergovernmental health coordination mechanisms, county governments, development partners, and other stakeholders. Equally critical is the alignment of reporting and data systems with the Data Protection Act, 2023 to safeguard patient confidentiality and program integrity.

The Government of Kenya calls upon all stakeholders to demonstrate commitment and partnership in ensuring the effective roll-out of these guidelines. Together, we can realize the vision of the Kenya Health Policy—to guarantee universal access to safe, effective, and high-quality medicines for all.

Dr. Patrick Amoth, CBS
Director General for Health

Acknowledgement

The Division of National Tuberculosis, Leprosy and Lung Disease Program extends its heartfelt appreciation to all institutions, partners, and individuals whose invaluable contributions, participation, and collaboration made the development of this guideline possible.

Access to the highest standards of healthcare is a constitutional right of every Kenyan. This guideline serves as a critical roadmap for ensuring the optimal, safe, and effective use of medicines in the management of tuberculosis and related conditions, including prophylaxis. It underscores the Government of Kenya's commitment, as enshrined in the Constitution of Kenya (2010), to guarantee quality healthcare for all citizens.

We are especially grateful to our implementing and technical partners—the Clinton Health Access Initiative (CHAI) and the Global Fund (GF)—for generously funding and supporting this process from inception to completion. We also recognize the African Medical and Research Foundation (Amref Health Africa) and the World Health Organization (WHO) for their strategic partnership throughout this journey.

Our appreciation further goes to the Pharmacy and Poisons Board (PPB), the Directorate of Health Products and Technologies (DHPT-MOH), the Division of Health Informatics (DHI-MOH), the University of Nairobi College of Health Sciences (UoN-CHS), the Kenya Medical Research Institute (KEMRI), the Kenyatta National Hospital Department of Pharmacy, and many other stakeholders for their unwavering support in strengthening resilient lung health systems. Special thanks are extended to the Global Fund for financial support and to Health IT for developing vital digital tools.

Finally, we acknowledge with gratitude the leadership of the Ministry of Health for championing the integration of lung health into broader primary healthcare reforms, and for providing strategic direction, policy guidance, and alignment with national health standards and jurisprudence.

It is our sincere hope that this guideline will close existing gaps in product safety and quality assurance, and enhance pharmacotherapeutics interventions at the patient-provider interface, thereby strengthening the continuum of care within our programs.

Dr. Immaculate Kathure, OGW

Ag. Head, Division of Tuberculosis and other Lung Diseases

Executive Summary

The National Guidelines for Enhancing Active Drug Safety Surveillance, Monitoring, and Management (aDSM) in Tuberculosis Care provide a framework for strengthening pharmacotherapeutic practices within the TB program's continuum of care at the patient– provider interface across the country. These guidelines outline the roles and responsibilities of pharmacists and pharmacy specialists in line with the Pharmacy and Poisons Act, Cap 244.

The development of these guidelines has been informed by global and national best practices. We acknowledge the leadership of the World Health Organization (WHO) in advocating for structured drug safety surveillance, particularly in the context of drugresistant TB treatment and the introduction of new regimens. We further recognize Amref Health Africa for approving prerequisite protocols that laid the foundation for this work.

Our overarching goal is to safeguard the safety, quality, and effectiveness of medicines for all patients undergoing TB treatment. This will be achieved by fostering close collaboration among healthcare professionals, enhancing communication across the continuum of care, and integrating systems for regulatory oversight. In particular, these guidelines establish critical linkages with the Pharmacy and Poisons Board (PPB) through its online platform and with the Ministry of Health's Kenya Health Information System (KHIS2). These linkages will facilitate surveillance, regulation, and policy alignment through automated reporting and data sharing.

The guidelines will be regularly reviewed and updated to reflect evolving evidence, emerging therapies, and global advancements in pharmacotherapy. Their successful implementation relies on strong collaboration with stakeholders, including the PPB, the Directorate of Health Products and Technologies (DHPT), the County Pharmacists' Forum, County TB and Leprosy Coordinators, the Kenya Medical Research Institute (KEMRI), Kenyatta National Hospital Department of Pharmacy, and the University of Nairobi College of Health Sciences. These partners will support training, mentorship, and capacity building for pharmacists and clinicians to strengthen pharmacovigilance, prevent adverse events, and optimize therapeutic outcomes.

Central to these guidelines is the accurate and timely recording, reporting, and monitoring of all relevant data on drug safety and treatment outcomes. Enrolling patients promptly into aDSM services, and ensuring data flows seamlessly from facility to county and national levels, is essential for informed decision-making and continuous improvement of patient safety within the National TB and Lung Diseases Program.

The prudent use of anti-tuberculosis medicines requires careful surveillance, individualized treatment planning, and close monitoring of drug-related toxicities. These guidelines equip pharmacists, pharmacy specialists, clinicians, and other medical professionals to work together as a multidisciplinary team at the patient–provider interface. By integrating their expertise, we aim to enhance patient safety, uphold quality of care, and improve overall treatment outcomes.

In addition, the guideline package includes practical tools, recording and reporting templates, job aids, and standard operating procedures designed for routine use at treatment facilities. These resources will enable healthcare workers to apply best practices consistently, optimize pharmacotherapy, and ensure that patients undergoing TB treatment receive the safest and most effective care possible.

Chapter 1

Background concept of aDSM and the roles and responsibilities of a Pharmacist in aDSM Implementation

Globally, TB continues to be a major public health concern. In 2019, there were an estimated 10 million new cases and 1.4 million deaths. The number of people receiving TB preventive treatment rose significantly from 1.0 million in 2015 to 4.1 million in 2019, in a Global tuberculosis report (1-3)

Kenya is among the 22 high-burden countries for TB globally and is one of the top five highest-burden countries in sub-Saharan Africa in Annual tuberculosis report (2). The 2016 Kenya TB prevalence survey reported a prevalence rate of 426 per 100,000 population. In 2017, an estimated 158,000 new cases occurred, with 47% going undetected or unreported. While the incidence rate is estimated to be declining by 6% per annum (298 per 100,000 population, or 150,000 patients, in 2019), Drug-Resistant TB (DR-TB) notifications are increasing in a TIBU data Report (3).

In the same TIBU data report (3), DR-TB case notifications rose from 444 in 2016 to 688 in 2019, further increasing to 962 patients in 2020 (TIBU). In 2020, Rifampicin-Resistant/Multi-Drug Resistant (RR/MDR-TB) contributed approximately 62% of cases, INH Mono at 35%, PDR at 1.9%, Pre-XDR at 1%, and XDR at 0.1%. Patients are currently managed with an All-Oral treatment regimen as WHO rapid advisory requirement to transit to all oral DRTB treatment 2018 (4).

In a National strategic plan document Division of National Tuberculosis, leprosy and Lung Diseases 2019 (5).for NTLDP estimated 35% of DRTB patients who interrupted treatment in the course of therapy with non-adherence and side effects issues. The Ministry of Health through the Pharmacy and Poisons Board and the Division of National Tuberculosis, Leprosy and Lung Disease program were mentioned in the NSP (2018-2123) to partner to establish pharmacotherapy practices to enhance active drugs surveillance and monitoring to improve the quality of care and treatment outcomes in TB programming continuum of care(5-7).

33%

One-third of the world's population is infected with Mycobacterium tuberculosis

While the Pharmacy and Poisons Board (PPB) and the NTLDP currently conduct safety surveillance through spontaneous reporting of suspected Adverse Drug Reactions (ADRs) and product quality defects, there is a critical need to enhance the active real time identification and intervention

of ADRs to ensure patient safety and optimize treatment outcomes, in Annual Program Forecasting And quantification review Report (8,&9).

The current adoption of WHO guidelines for DR-TB management in a Global tuberculosis report (2) includes regimens comprising Bedaquiline, Delamanid, Preteonamide and other repurposed drugs. Despite these risks, there is a scarcity of data regarding the occurrence of ADRs and the safety profile of these newer and repurposed molecules. Establishing an aDSM system is essential to generate the necessary evidence on ADRs associated with DR-TB and DS-TB drugs, which will guide the formulation of appropriate interventions and policies, in the Interim policy guidance(10-12).

The findings in a joint operational research activity, sponsored by Global Fund, in 2021. shed light on the need to address the key critical issues therein: Firstly, Data Disconnect: While some Adverse Drug Reactions (ADRs) were reported via the PPB online platform, essential data recording and reporting tools were absent at the facility level. More importantly, the spontaneous ADR data collected by the PPB is used exclusively for regulatory action and is not integrated into programmatic monitoring, preventing an effective programmatic response. Secondly, Gaps in Active Drug Safety Monitoring (aDSM): Similar Joint Research Protocol reports (13-15) highlighted minimal awareness and practice of aDSM among TB coordinators.

Furthermore, there is a noted absence of pharmacists—who are professionally equipped in drug surveillance and whose expertise in pharmacotherapeutics interventional services is foundational to aDSM—within the patient care continuum. Wherefore, amplifying the need to develop a strategy and guideline to integrate pharmacovigilance data into programmatic monitoring and ensure pharmacists are involved in patient care to strengthen aDSM.

As outlined in the WHO publications Policy implementation package for new TB drug introduction (2014) and Active tuberculosis drug-safety monitoring and management: framework for implementation (2015), aDSM is mandatory for patients on new or repurposed drugs or novel regimens, particularly those with drug-resistant TB. The aDSM system focuses on recording and reporting Serious Adverse Events (SAEs) and ensures the appropriate and timely management of Adverse Drug Reactions (ADRs) as an integral part of patient care (16-18).

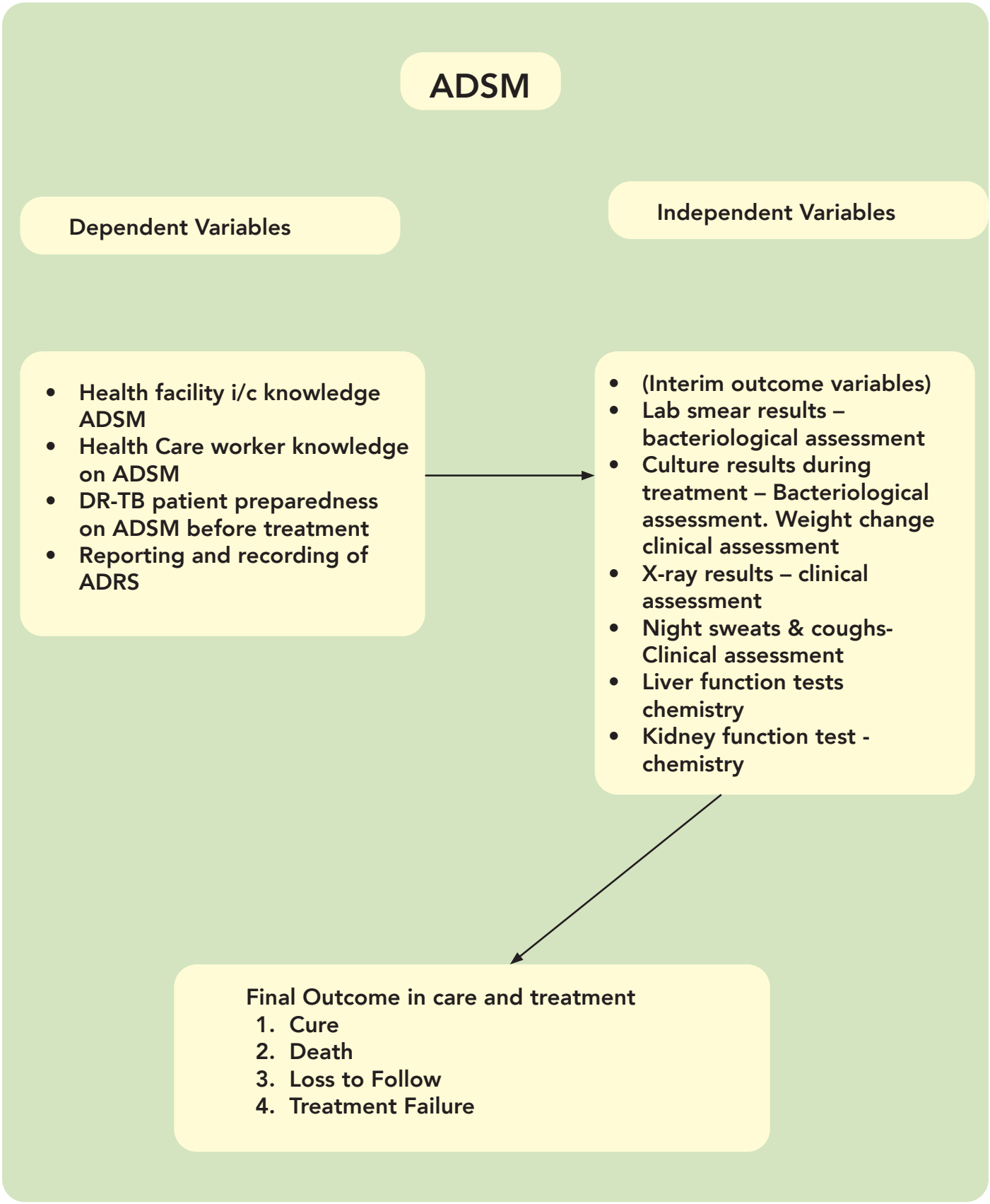


Fig 1.0 : Infographic showing integration of services & ADSM variables

ADSM Management Recording and Reporting

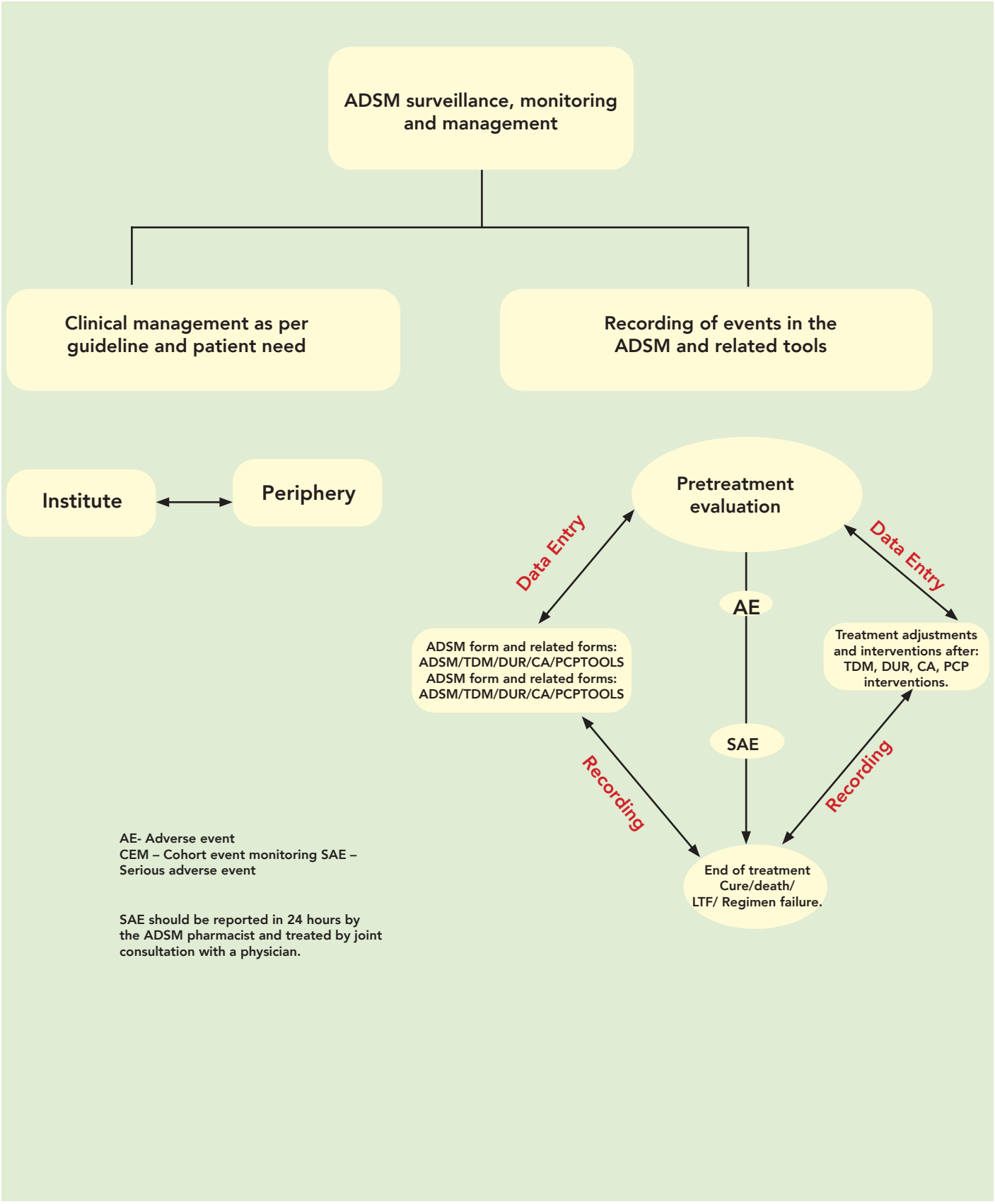


Fig 2.0: showing the interaction points of patient care cascade and ADSM

This guideline outlines Active Tuberculosis (TB) Drug Safety Monitoring and Management (aDSM), a new and crucial component of the TB program. aDSM focuses on providing proactive and systematic pharmacotherapeutics interventions. This includes pharmacological correlationship of drugs with biochemistry and pathological chemistry assessments for patients undergoing treatment for extensively drug-resistant TB (XDR-TB), those on new TB drugs, or those following innovative multidrug-resistant TB (MDR-TB) regimens.

The core activities of aDSM involve delivering pharmacotherapeutics interventions through drug therapeutics monitoring, adverse drug reaction (ADR) surveillance, prediction, and detection. It also encompasses the appropriate and timely management and reporting of any suspected or confirmed ADRs. Notably, the recording and reporting efforts of aDSM primarily target serious adverse events (SAEs) as a fundamental requirement.

The World Health Organization (WHO) introduced aDSM as a prerequisite for implementing new drugresistant TB treatment regimens that include repurposed medicines like bedaquiline and delamanid. This was in response to increasing concerns regarding drug toxicity and the failure of first-line TB medications.

The 2021 conference in London identified four key pillars of aDSM:

1. Enhanced patient monitoring and management
2. Data capture
3. Research and development of evidence-based practice standards
4. Greater integration and collaboration among healthcare professionals

For TB programming, our central goal is to ensure quality of care throughout the TB treatment continuum of care.

To support aDSM, various pharmacotherapeutics interventional services will be utilized, including:

- Therapeutics Drug Monitoring (TDM),
- Medicines Therapeutic Monitoring (MTM),
- Extemporaneous compounding (EC),
- Pharmaceutical Care Plans (PCP),
- Bioequivalence Testing (BET),
- Pharmaceutical Toxicology Detox (PTD),
- Causality Assessment on a case-by-case basis (CA).

Scope of aDSM

aDSM is applicable to the following patient groups:

1. MDR-TB and XDR-TB patients receiving treatment with new medications such as bedaquiline or delamanid.
2. MDR-TB patients enrolled in treatment with novel regimens, including those significantly shorter than current WHO recommendations.
3. All other XDR-TB patients on second-line treatment regimens, which often include multiple repurposed drugs.
4. Drug-susceptible TB (DS-TB) and TB preventive treatment (TPT) patients.

5. All programmatic TB co morbidities (Hypertension, Diabetes mellitus, HIV, Asthma, COPD, Lung cancer, Leprosy, Mycobacterium Other than TB(MOTs), Aspergillosis, Covid 19).

Once these patient groups are covered, the implementation of aDSM can be expanded to include other patients regimens, depending on available resources and implementation framework in the national drug policy.

Rationale of aDSM

The rationale behind aDSM stems from the evolution of MDR-TB treatment. This includes the approval and use of new medicines before the completion of Phase III trials, the increased use of repurposed drugs for XDR-TB treatment, and the development of innovative second-line anti-TB regimens. These approaches necessitate careful monitoring for potential drug-related harms, some of which may not yet be fully understood.

Goal of aDSM

The primary goal of aDSM is to systematically monitor and manage the safety of patients undergoing treatment primarily for drug-resistant tuberculosis. This aims to improve patient outcomes and ensure the safe utilization of new and repurposed TB drugs.

Objectives of aDSM

1. To minimize risks associated with drug-related harm in patients on second-line treatment for drug-resistant TB.
2. To generate standardized safety data that can inform future policy updates regarding the use of these medications. It's important to note that aDSM is not intended to meet all the criteria of conventional cohort event monitoring.

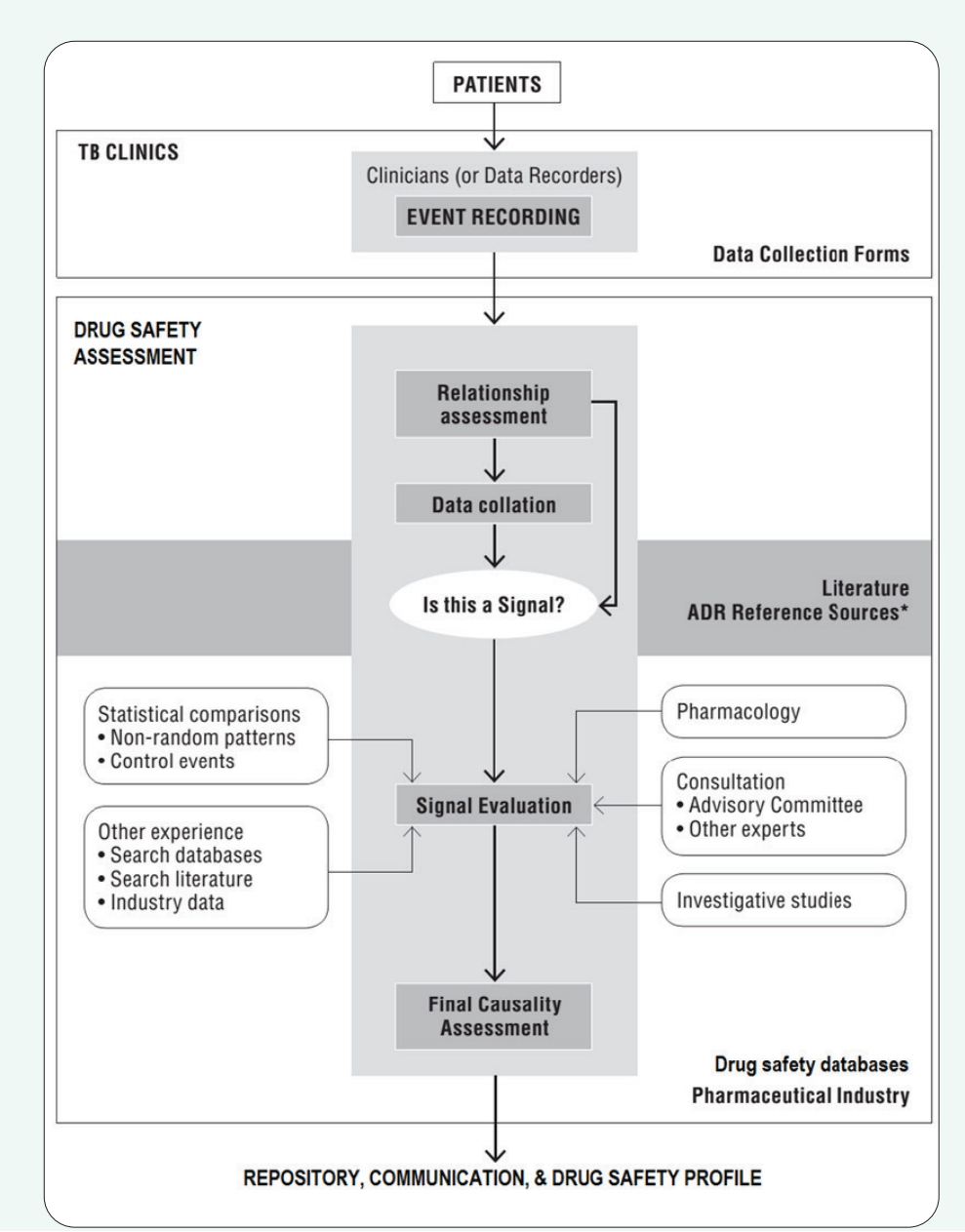
To achieve these objectives, aDSM incorporates three essential activities:

- Patients targeted for aDSM should undergo proactive and systematic clinical and laboratory assessments during their treatment to identify drug toxicity and adverse events (AEs). The patients hould be enrolled for aDSM alongside regular enrolment of patients on tuberculosis. Proposed schedules for these assessments have been developed for patients on shorter regimens or new medications (refer to page xx for details).
- All detected AEs should be managed promptly to ensure the best possible patient care. (Chapter 11 provides guidance on the management of specific adverse drug reactions).
- Standardized data on all detected SAEs should be systematically collected and reported. This data will be used to characterize the types of SAEs, evaluate the safety of the treatment regimens, and inform future policy decisions regarding the use of these drugs. All detected SAEs must be reported to the Pharmacy and Poisons Board through the Pharmacovigilance Electronic Reporting System (PvERS) or TIBU.

There are three levels of monitoring within aDSM:

- Core package: Requires the monitoring and reporting of all SAEs.
- Intermediate package: Includes SAEs as well as AEs of special interest.
- Advanced package: Encompasses all AEs of clinical significance.

All Programmatic Management of Drug-Resistant Tuberculosis (PMDT) sites that treat eligible patients with new anti-TB drugs, novel MDR-TB regimens, or for XDR-TB are required to implement the core package. As a minimum, these treatment centers should also participate in the spontaneous reporting of ADRs, as mandated by the Pharmacy and Poisons Board regulations on Pharmacovigilance. The expansion of aDSM should be carried out in a phased manner as the necessary resources are mobilized.



Adapted from WHO 2012 (www.who.int/entity/medicines/publications/pharmacovigilance_tb/)

Fig 3.0: The data flow for aDSM involves collection, recording, assessment, storage, transmission, communication and utilization of the knowledge gained in improving the drug safety profile.

To successfully implement aDSM and achieve the best possible outcomes for TB treatment, close collaboration between the Pharmacist and the TB clinic staff is essential.

To foster this harmony, establishing clear structures that support regular clinical review meetings and facilitate daily consultations is crucial. These initiatives should actively involve the patient and all key healthcare professionals who contribute to their care journey.

Chapter 2

Structural requirements for operationalising the active Tuberculosis Drugs Safety Monitoring and Management (aDSM)

A. Clear organizational Structure:

This guideline outlines a proposed framework to strengthen our Adverse Drug Reaction Surveillance and Management (aDSM) program and integrate pharmacotherapeutics interventional services more effectively within our healthcare system.

1. Defined Leadership and Roles:

To ensure the success of the aDSM program, we recommend establishing a dedicated leadership team at the county level (26). This team should include the aDSM County Coordinating Pharmacist, County TB and Leprosy Coordinators, and County Medical Lab Technologists.

2. Standardized Workflow:

Below are standardized processes for the initiation, documentation, and follow-up of aDSM cases and related pharmacotherapeutics interventions. These activities should be coordinated within a Medicines Pharmacotherapeutics Monitoring (MTM) clinic, interacting with the Chest (TB) clinic, with a valid PBB premise license, established in public hospitals, adhering to the design principles outlined in the Good Pharmacy Practice guidelines 2024. It is crucial that these MTM activities and processes are integrated seamlessly into existing healthcare workflows within hospitals, clinics, and Main pharmacy (20, &22).

3. Accountability Mechanisms:

A robust system for tracking and monitoring the completion of aDSM and pharmacotherapeutics intervention services is essential. This system should also assess the impact of these services on patient outcomes. We recommend designating qualified pharmacists, as per cap 244 and Director General advisory 2025 August on the Authorized/qualified pharmacist, who will be accountable for ensuring the effective implementation of these processes (7, &22).

4. Human Resource Roles & Expertise:

We envision that each facility should have at least one pharmacist, serving as the facility aDSM coordinator within the TB clinic on every clinic day. To facilitate their work, each pharmacist should have a dedicated workspace suitable for screening and consultation services. Collaboration between

pharmacists, clinicians, nurses, medical lab technologists, and other healthcare professionals will be vital for the successful implementation of aDSM. Furthermore, establishing an MTM clinic within each facility will enable pharmacists to collaborate with colleagues providing complementary services to support aDSM (7, &22).

Ideally, the MTM center would serve as the primary location for the aDSM coordinator to provide aDSM and pharmacotherapeutics services after a patient's clinical review in the chest clinic. The MTM center would be the final point of contact for TB patients to receive aDSM review services.

5. Capacity Building

We are rolling out aDSM across 30 counties, mapped as ADSM sentinel counties. targeting clinical. pharmacy departments linked to laboratory services for comprehensive therapy assessments. Due to resource constraints, we will emphasize synergy between these teams and prioritize Monitoring & Evaluation (M&E) sensitization to ensure reliable recording and reporting on ADSM. The pharmacy team will be central in coordinating reporting and recording of active surveillance of drug safety and efficacy (13).

Implementation of the training curriculum begins at nine Level 6 hospitals, followed by Level 5 county referral facilities designated as centres of excellence. Subject to resources. Cascading this to level 4 and level 3 is the projection we want to strengthen ADSM recording and reporting. These sites were prequalified based on program criteria and the AMREF-approved aDSM protocol. The two-day sensitization curriculum, developed with stakeholders including KEMRI, UoN, KNH, PPB, and MOH, will be updated annually based on data reviews and quarterly technical assistance. We plan to expand the number of sentinel sites (counties) to cover the entire country. as more counties meet the eligibility threshold for TB drug aDSM.

6. Technology Infrastructure:

To support these efforts, we will leverage the following technological infrastructure (8,13 & 26):

- **Data Management:** The TIBU Meds platform, which is currently linked to KHIS, TIBU, and PPBPVERs, will serve as our primary data management system.
- **Drug Therapeutics Monitoring:** We will utilize both paper-based and electronic tools to conduct drug therapeutics monitoring and pharmacotherapeutics services.
- **Telehealth/Tele pharmacy Support:** Communication platforms, including Tele pharmacy and social media, will be utilized to enhance patient support and follow-up.

7. Patient Enrollment:

Enrollment of patients for aDSM and related pharmacotherapeutics services will be conducted in the MTM clinic following guidance and referral by the TB clinician from the chest/TB clinic. The clinical evaluation and review of the patient to be moderated at the Chest clinic.

8. Quality Assurance and Continuous Improvement:

Safety data entered into TIBU Meds will be the primary source for data collection. This data will interface with TIBU for interoperability. KHIS 2 and PvERS will serve as relay platforms for aggregate data and analysis, informing policy and regulatory decisions, respectively. The aggregated data will be analyzed,

and feedback will be provided to healthcare workers to enable them to assess their practices. This feedback will also inform policy development for new practice frameworks, drug manufacturing, and medicines marketing for regulatory purposes.

9. National Coordinating Mechanism for aDSM:

A clear framework for coordination is proposed between the National TB Program (TIBU Meds and TIBU mainstream), the Product Safety Directorate in PPB (PPB PVERs), the Directorate of Health Products and Technologies (DHPT), and the Health Informatics Directorate (KHIS2).

This comprehensive framework will significantly enhance our ability to monitor, manage, and learn from adverse drug reactions, ultimately improving patient safety and outcomes.

B. Responsibilities:

The responsibilities regarding the documentation of various tools into the TIBU Meds system below (6,7,22,& 26):

1. ADSM tools documentation: This is to be completed by the County aDSM coordinator, sub county aDSM coordinator, and facility pharmacist aDSM coordinator. With Registration Number from PPB.

2. Causality assessment (case by case) tool documentation: The responsible parties are the County aDSM coordinator, sub county aDSM coordinator, and facility PV specialist pharmacist aDSM coordinator with Pharmacy and Poisons Board Registration Number from PPB and pharmacy Specialist recognition from PPB.

3. Medicines therapeutics monitoring tool documentation: This task falls to the County aDSM coordinator, sub county aDSM coordinator, and facility pharmacist coordinator. With Registration Number from PPB.

4. Extemporaneous compounding Tool documentation: The County aDSM coordinator, sub county aDSM coordinator, and facility pharmacist coordinator are responsible for this. With Registration Number from PPB.

5. Pharmaceutical care plan tool documentation: This needs to be completed by the County aDSM coordinator, sub county aDSM coordinator, and facility clinical pharmacist coordinator.

6. Therapeutic Drug monitoring tool documentation: The designated individuals are the County aDSM coordinator, sub county aDSM coordinator, and facility pharmacist coordinator. Specialist pharmacist aDSM coordinator with Pharmacy and Poisons Board Registration Number from PPB and pharmacy specialist recognition from PPB.

7. Bioequivalence Testing Tool documentation: This is assigned to the County aDSM coordinator, sub county aDSM coordinator, and facility analysis/industrial pharmacist coordinator. Specialist pharmacist aDSM coordinator with Pharmacy and Poisons Board Registration Number from PPB and pharmacy specialist recognition from PPB.

8. Pharmacokinetic tool documentation: The responsible parties are the County aDSM coordinator, sub county aDSM coordinator, and facility pharmacist coordinator. Clinical Specialist pharmacist aDSM coordinator with Registration Number from PPB and pharmacy specialist recognition from PPB.

9. Pharmaceutical toxicology detox Tool documentation: This task falls to the County aDSM coordinator, sub county aDSM coordinator, and facility pharmacist coordinator. Clinical Specialist pharmacist

aDSM coordinator with Pharmacy and Poisons Board Registration Number from PPB and pharmacy specialist recognition from PPB.

Chapter 3

Overview of Guidelines and medicines used in TBmanagement in Kenya

This outlines the policy statement regarding the requirements for pharmacists to adhere to the established guidelines for managing and treating tuberculosis (TB) in Kenya. The National Tuberculosis (TB) and other Lung Diseases Program has developed these guidelines to ensure a consistent and effective approach to TB diagnosis, treatment, and prevention across the country (26).

These guidelines offer a structured framework covering various aspects of TB management, including the specific medicines to be used, key treatment protocols, and recommendations for providing appropriate care to TB patients.

The National Tuberculosis Policy in Kenya is specifically designed to achieve the following critical objectives:

Provide Universal Access to TB Diagnosis and Treatment

The policy aims to guarantee that all individuals affected by TB, whether pulmonary or extra pulmonary, have consistent access to high-quality diagnostic services and effective treatment regimens.

Support Integrated and Patient-Centered Care

It promotes a holistic approach to care that extends beyond medication. This includes the integration of psychosocial support, counseling services, and active engagement with the community to support patients throughout their treatment journey.

Promote Drug Sensitivity Testing

The guidelines emphasize the importance of conducting drug sensitivity testing for TB patients. This is crucial for accurately identifying and effectively managing cases of drug-resistant TB.

Prevent and Control the Spread of TB

A strong focus is placed on proactive measures to prevent TB transmission. This includes the implementation of TB preventive therapy (TPT), the administration of the BCG vaccine, the enforcement of stringent infection control protocols within healthcare facilities, and the promotion of public awareness campaigns.

Ensure Equity in Access to TB Services

The policy is committed to providing TB services that are readily available and accessible to all segments of the population, with particular attention to reaching marginalized and underserved groups such as people living with HIV, individuals in correctional facilities, and refugees.

By outlining these requirements and objectives, the National Tuberculosis Policy seeks to engage pharmacists as key stakeholders in the effective management and control of TB in Kenya.

Medical management and quality of care assurance.

There are new drugs like Bedaquiline and Delamanid currently approved for conditional use by drug regularity authorities and for which WHO had provided interim guidance for their use under programmatic settings few years back. Moreso, some of the earlier drugs like Clofazimine and Linezolid are being repurposed and recommended for use in the management of DRTB. Recently WHO has recommended an all-oral longer regimen with new drugs for the treatment of MDR / RR TB patients (10, &11). Therapeutic management is the main stay mode of care and treating TB. Quality and safety of the medicines is an integral factor in disease care and treatment. Ensuring quality of care needs a concerted effort of all stakeholders in the supply chain of the medicines and patient care cascade. The regulatory authority in our country has a fundamental role in ensuring that quality, safety and efficacious medicines are in circulation. It`s the direct mandate of the county, sub county and pharmacists working in health facilities to ensure that this mandate is accomplished their core practice obligation, regulated by Pharmacy and poisons Board (PPB) (7).

There is a need to Move to patient centric approach focusing patient's needs and preferences for better adherence. There are newer drugs like Bedaquiline (Bdq) and Delamanid (Dlm) currently approved to be used under the Programme only. However, drugs are reclassified based on the evidences to manage the patient and recommended for use in the management of DR-TB. The few shorter MDR-TB regimens are being studied worldwide using combination therapy with newer drugs (12).

For national TB programs (NTPs) to undertake aDSM effectively, a series of activities need to be coordinated in a bid to have the right expertise developed through interaction with local and external drug-safety experts, sufficient funds are made available so that clinical monitoring activities are performed, data gets collected, reported and analyzed; and decisions are made on the basis of new knowledge gained (12). The aDSM program is not aimed at replacing or duplicating efforts of national pharmacovigilance units but to complement current capacities and address barriers by undertaking active pharmacovigilance within the context of TB care. In addition to drug-safety monitoring, aDSM also incorporates a component that promotes the clinical management of all ADRs and AEs regardless of their seriousness (13).

The aDSM includes four essential activities to achieve safety and quality of care and treatment in the patient care cascade:

1. Patients targeted for aDSM should undergo active and systematic clinical and laboratory assessment during treatment to detect drug toxicity and AEs. Proposed schedules have been developed for use in patients on shorter regimens or on new medications 11, 12. This is what is commonly known as pharmacokinetics (PK) Therapeutics drugs monitoring (TDM).

2. All AEs detected should be managed in a timely manner in order to deliver the best possible patient care. Management of AEs is beyond the scope of this note and further details are provided in other implementation documents, such as the PMDT Handbook 13. This is managed in the aDSM tool alongside the pharmaceutical care plan as the accessory tool.

1. Standardized data should be systematically collected and reported for any detected SAE.2 these will eventually be used to characterize the types of SAEs, assess the safety of the treatment, and inform future policy on the use of these medicines. This is well managed under causality assessment tools and Drugs utilization review tools.

2. Drugs analytical laboratory to undergo systematic chemistry, biological and genetic evaluations in bioequivalence analysis. This to be done in cases where different brands of the same generic molecules are passing the chemical analysis but failing the clinical outcomes in care and treatment cascade.

aDSM And Treatment of Tuberculosis

This chapter outlines the key steps for implementing active TB drug safety monitoring and management (aDSM). Ideally, all ten steps listed below should be in place before enrolling patients on new drugs or novel/extreme drug-resistant TB regimens. However, steps (iv) creating standard data collection materials and (v) training staff for data collection are essential prerequisites before any patient enrollment to minimize data loss and missed opportunities for managing adverse events (AEs) and adverse drug reactions (ADRs).

Here are the key steps to implementing aDSM:

1. Create a national coordinating mechanism for aDSM.

2. Develop a protocol for aDSM.

3. Define management and supervision roles and responsibilities.

4. Create standard data collection materials.

5. Train staff for data collection.

6. Define schedules and routes for data collection and reporting.

7. Consolidate aDSM data electronically.

8. Develop (or use existing) capacity for signal detection and causality assessment.

9. Set up cohort event monitoring sites in the centers of excellence for tuberculosis.

10. Create Therapeutic Monitoring clinics in CoEs to conduct therapeutic drug monitoring and network with laboratory networks for drug efficacy and bioequivalence testing.

All DR-TB treatment should adhere to WHO-recommended standards, including patient-centered care, informed consent, good clinical practice principles, active TB drug safety monitoring and management (aDSM), and regular patient monitoring for regimen effectiveness. aDSM is recommended for all patients on any MDR-TB regimen, and an appropriate schedule of laboratory tests and clinical examinations should be included in the patient's chart to identify adverse events. In situations where aDSM may not be fully implemented or national guidelines fully updated, patients should not be delayed in receiving potentially life-saving interventions.

Regular culture testing, preferably monthly, is recommended throughout treatment for early detection of treatment failure. Furthermore, findings from clinical examinations (ECG, urinalysis, blood tests, and radiographs) and pharmacokinetic examinations (dose-response curve, therapeutic drug monitoring (TDMs), drug interactions, drug efficacy, and effectiveness) are crucial for safety monitoring. The specific monitoring tests required depend on the medicines included in the regimen. For instance, Linezolid requires

clinical and biochemical assessment; monitoring for peripheral neuropathy and psychiatric disturbances is needed; and electrocardiography and electrolyte monitoring are important when using multiple QT interval prolonging agents like Bedaquiline, Delamanid, Moxifloxacin, and Clofazimine. Any adverse events during treatment must be managed promptly to alleviate suffering, minimize treatment interruptions, and prevent morbidity and mortality. Schedules for clinical, biochemical, and microbiological testing are detailed in the aDSM module of the companion handbook, while drug efficacy, pharmacokinetics, and TDM require pharmaceutical analysis and calculations by a pharmacy specialist.

Table 1: Standard DR-TB treatment regimens by Resistance pattern

Pattern of Drug Resistance	Regimen	Duration
MDR/ RR TB	Intensive phase:6Bdq/Cfz/Lfx/Cs/Lzd Continuation phase: 12 Cfz/Lfx/Cs	18 months
Pediatric MDR / RR TB (<6yrs and <25kg)	Intensive phase: 6 Mfx/Cfz/Cs/Lzd Continuation phase: 12 Mfx/Cfz/Cs	18 months
Pre-XDR - Injectable resistant	Intensive phase:6Bdq/Cfz/Lfx/Cs/Lzd Continuation phase: 12 Cfz/Lfx/Cs	18 months
Pre-XDR - Fluoroquinolones Resistant	Intensive phase:6Bdq/Dlm/Lzd/Cfz/C Continuation phase: 14 Dlm/Cfz/Cs	20 months
Pre - XDR Pediatrics'* - Fluoroquinolone Resistance	Intensive Phase: 6Bdq**/**Dlm/Lzd/Cfz/Cs Continuation phase:14 Dlm/Cfz/Cs/Z	20 months
ISONIAZID mono resistance	6 RZE/Lfx (with pyridoxine)	6 months
Bedaquiline Intolerance (In cases of Severe Adverse Events or hypersensitivity)	Intensive Phase: 6Dlm/Lzd/Lfx/Cfz/Cs Continuation phase: 12 Lfx/Cfz/Cs	18 months
Poly-drug resistance (PDR TB) (HE/HEZ +-S)	9 RZE/Lfx (with pyridoxine)	9 Months
Pyrazinamide mono-resistance(Z) or Pyrazinamide and Ethambutol (EZ) without INH resistance or Ethambutol Mono-resistance(E)	2 RHZE 4 RH (with pyridoxine)	6 months
Extensively Drug-resistance (XDR)	Individualized regimen	18-24 months
Any case excluded from any of the regimens above	Individualized regimen	18-24 months

Classes of Anti-TB Drugs Recommended for Treating DR- TB Patients

Group A: Include all three medicines:

1. Levofloxacin OR Moxifloxacin (Lfx /Mfx)
2. Bedaquiline (Bdq)
3. Linezolid (Lzd)

Group B: Add one or both medicines:

1. Clofazimine (Cfz)
2. Cycloserine OR Terizidone (Cs Trd)

Group C: Add to complete the regimen and when medicines from Group A and B cannot be used:

1. Ethambutol (E)
2. Delamanid (Dlm)
3. Pyrazinamide (Z)
4. Imipenem-Cilastatin OR Meropenem (Ipm-Cln/Mpm)
5. Amikacin OR Streptomycin (Am/(S)
6. Ethionamide OR Protionamide (Eto /Pto)
7. P-amino salicylic acid (PAS)

DR-TB Regimen Used in the DNTLDP-Kenya

In MDR/RR-TB patients on longer regimens, all three Group A agents (Lfx/Mfx, Bdq & Lzd) and one Group B agent (Cfz & Cs) should be included initially to ensure at least four likely effective TB agents, with at least three agents continued after Bedaquiline is stopped. If only one or two Group A agents are used, both Group B agents should be included. If the regimen cannot be composed using only Groups A and B, Group C agents are added to complete it.

Cautious Side Effects in Group A and B Drugs in IFR Regimen

- Linezolid (Lzd) may cause anemia, thrombocytopenia, peripheral neuritis, and optic neuritis. Appropriate precautions should be taken.
- Cycloserine (Cs) should be used cautiously in patients with pre-existing seizure disorders not well-controlled by medication. Neurologist consultation is recommended before initiating Cs in such patients, and psychiatric evaluation is advised for severe depression due to the risk of Cs-induced depression and suicidal tendencies.
- Clofazimine (Cfz) causes dark brown discoloration of the skin. Patients should be counseled about this before starting treatment.

Treatment Initiation on Outpatient Basis

All-oral longer MDR-TB regimens can be initiated on an outpatient basis if the patient meets all the following risk assessment criteria:

- QTcF < 450 ms in males and < 470 ms in females at baseline.
- Normal serum potassium (K), magnesium (Mg), and calcium (Ca) at baseline.
- No history of structural cardiac abnormalities (though LVH secondary to hypertension may cause ECG changes and is not necessarily an exclusion criterion) or other ECG abnormalities.

Patients with QTcF between >450 to 500 ms in males and > 470 to 500 ms in females require daily ECG monitoring for 3 days along with evaluation and correction of any electrolyte abnormalities. A cardiologist's opinion may be necessary.

The first dose should be administered under supervision at the treatment-initiating facility for ambulatory patients. Treatment should be initiated using a monthly patient-wise box, and the entire one-month supply should be given at the time of discharge.

Principles for Replacement of Drugs

The regimen should ideally be fully oral. However, in some cases, an injectable may be necessary based on efficacy and side-effect profile. Five drugs should be used in the intensive phase (IP) and at least four drugs in the continuation phase (CP). Newer drugs (Bdq or Dlm) should be given for 24 weeks only. Delamanid (Dlm) and Amikacin (Am) will not be used in the CP. The preferred replacement sequence is Z*, Am*, Eto*, PAS, E, Imp/cln or Mpm with Amx/clv (*Z if no resistance detected, Am if SL LPA suggests, and Eto if no Inh A mutation detected).

Extension of Treatment in H Mono/Poly DR-TB Regimens

The total duration of H mono/poly DR-TB regimens is 6 months but may be extended to 9 months in patients with extensive disease, uncontrolled comorbidity, extrapulmonary TB, or if the smear is positive at the end of the 4th month (based on smear microscopy and clinical monitoring). In CNS, skeletal, and miliary TB, treatment may last up to a year. Patients remaining sputum smear- positive at the end of the 5th month or later are considered treatment failures.

Extension of Treatment in All-Oral Longer MDR-TB Regimen

The total duration of the all-oral longer MDR-TB regimen is 18-20 months. At the end of the 6th month, the dose of linezolid (Lzd) will be halved if the 4th or 5th-month culture result is negative. If the 4th or 5th-month culture remains positive, the regimen with the same Lzd dosage should be extended for one more month. However, new drugs (Bdq or Dlm) are given for 24 weeks only. The decision to continue the extended IP with Lzd (600/300 mg) beyond the 7th month is based on the 6th/5th-month culture results and the clinical/radiographic response. Extension of the IP beyond the 8th month is not permitted, and the patient should be switched to the CP (i.e., total treatment duration should not exceed 20 months). If the patient remains culture-positive or reverts to culture-positive after 8 months of treatment, they are declared a treatment failure, re- evaluated according to the integrated DR-TB algorithm, and started on an appropriate modified regimen based on extended drug susceptibility testing (DST). For XDR-TB patients, the all-oral longer MDR-TB regimen will be given for 20 months.

Management of DR-TB Patients with Treatment Interruptions and Loss to Follow-Up

- All missed doses during the IP must be completed before switching the patient to the CP. Similarly, all missed doses during the CP must be administered before ending treatment.
- Patients who interrupt treatment for less than one month during IP:
- Resume IP treatment, and the treatment duration will be extended to complete the IP. Follow-up cultures will be done as,

Chapter 4

Detection of Drug Ineffectiveness

Here's an overview of how tuberculosis (TB) drug ineffectiveness is typically detected:

Identifying when TB drugs aren't working well involves carefully tracking a patient's response to their treatment and looking for factors that might be reducing the drugs' effectiveness. This can happen for several reasons, such as the bacteria becoming resistant to the drugs, the drug levels in the body being too low, the patient not taking their medication as prescribed, or if the initial diagnosis was incorrect.

Here are the key ways drug ineffectiveness is monitored

1. Clinical Monitoring

This includes regularly checking for TB symptoms like a persistent cough, fever, weight loss, night sweats, and fatigue. If these symptoms don't improve or get worse during treatment, it could indicate the drugs aren't working. Doctors will also conduct physical exams to look for signs of ongoing infection. It's also vital to assess how well patients are adhering to their treatment plan, often through regular follow-ups and sometimes using Directly Observed Therapy (DOT) to ensure medication is taken correctly.

2. Laboratory Tests

Microbiological Monitoring

If sputum smears are still positive after a few months of treatment, this might suggest drug ineffectiveness, poor adherence, or drug resistance. Similarly, a positive culture after two months of therapy can indicate treatment failure or resistance. Cultures can be taken from sputum, blood, or other affected tissues. Rapid molecular tests like Gene xpert MTB/RIF can quickly detect both the presence of TB and resistance to Rifampicin, an important first-line drug.

Drug Susceptibility Testing (DST):

This testing determines if the TB bacteria are sensitive to specific drugs. Phenotypic DST involves growing the bacteria and exposing them to different medications to see if they are effective at stopping growth. Molecular DST looks for genetic mutations known to be associated

with resistance to drugs like Isoniazid and Rifampin. Next-Generation Sequencing (NGS) is an advanced technique that can provide a comprehensive profile of drug resistance by analyzing the TB bacteria's DNA.

Drug Concentration Monitoring

Measuring the levels of TB drugs in the blood (Therapeutic Drug Monitoring or TDM) can help identify if a patient isn't getting enough of the medication due to issues like poor absorption or altered metabolism. This is particularly useful for patients with conditions like HIV, malnutrition, or those taking multiple other medications.

3. Radiological Assessment

Chest X-rays are crucial for both the initial assessment and for monitoring how the TB is responding to treatment. If abnormalities in the lungs (like cavities or consolidations) persist or worsen despite therapy, it could be a sign of drug ineffectiveness or resistance. In more complex cases, a CT scan might be used to get a more detailed view.

4. Immunological Testing

Measuring a patient's immune response can provide insights into whether their body is fighting the infection effectively. A weak immune response despite proper drug treatment could suggest a compromised immune system or the drugs not working. Interferon-Gamma Release Assays (IGRAs) can assess if a patient has a persistent infection, though they are more commonly used for latent TB or to check for ongoing infection rather than during active treatment.

5. Monitoring Drug Resistance

If a patient with TB doesn't show improvement after several weeks on first-line drugs, drug resistance should be suspected. Multidrug-Resistant TB (MDR-TB) is defined as resistance to at least isoniazid and rifampicin. It's crucial to test for this in such cases. Extensively Drug-Resistant TB (XDR-TB) is diagnosed when there's also resistance to important second-line drugs. This makes treatment much more challenging.

6. Follow-up and Regular Re-Evaluation

Regular monthly checks of sputum samples through microscopy and culture are important in the early months of treatment to see if the bacterial load is decreasing. Ongoing clinical and radiographic assessments help track the resolution of symptoms and improvements in lung imaging. If drug ineffectiveness is suspected, the treatment plan needs to be re-evaluated, considering the possibility of drug-resistant strains and adjusting the medications accordingly.

7. Addressing Co-infections

The effectiveness of TB drugs can be affected in patients who also have HIV due to interactions with antiretroviral medications or a weakened immune system. These patients need close monitoring. Other conditions like diabetes, malnutrition, or kidney disease can also impact how the body processes and responds to TB drugs, requiring careful attention to drug levels and the patient's overall response.

In summary, detecting TB drug ineffectiveness requires a comprehensive approach that combines clinical observation, laboratory tests (including drug susceptibility testing), radiological assessments, and careful monitoring for drug resistance. Early identification of treatment failure or drug resistance is vital for successful treatment and to prevent the development of more complex forms of drug-resistant TB. Consistent follow-up, support for adherence to the treatment plan, and timely adjustments to the medication regimen are all essential components of managing TB effectively.

Chapter 5

Monitoring and Evaluation of Tools

1. aDSM

Tools (refer to appendix 2)

Active Drug Safety Monitoring (aDSM): is recommended for all patients on second line treatment and in particular those on new molecules Delamanid, Bedaquiline and repurposed medicines Linezolid, Clofazimine.
This has not been practiced in the past and there is need to strengthen pharmacovigilance. Capacity building of healthcare workers to monitor adverse events during treatment is also a gap that needs to be filled

Why drug safety monitoring?

- Early recognition and management of adverse reactions can improve adherence and treatment outcomes
- Adverse reactions pose a risk not only to the individual patient but also to the whole treatment programme.
- They may harm public confidence in a national treatment programme or in a new medicine or regimen which could bear promise
- In 2018, 35% of patients taking MDRTB experienced serious ADRS that resulted to 33% treatment success rate
- Adverse drug reactions can lead to: reduced quality of life, treatment interruption, treatment failure, avoidable morbidity, Deaths, added costs to the service (e.g., hospitalization), TB drugs: known for adverse reactions and sequelae, permanent disability, life-threatening/ lead to death
- Drug safety monitoring not a standard feature of monitoring frameworks in TB programmers (unlike bacteriological status & treatment outcomes). Not yet a priority in countries

The Goal of aDSM

- To ensure the safety of patients on second-line treatment for drug- resistant TB.
- Active and systematic clinical and laboratory assessment of patients include:
- Proper and regular laboratory tests

- Clinical evaluation
- Detection and management of ADR
- Recording and reporting ADRs
- To guide policy development

Main processes of ADSM.

- Monitoring: Active surveillance of public health program medicines, all new medicines, spontaneous reporting of ADRs/AEFI, product quality.
- Assessing benefits: Therapeutic ineffectiveness, comparative effectiveness.
- Prevention: Risk management Action Plans (RMaPs), mitigating AMR, Interactions, contraindications, polypharmacy, prescription quality, medication errors

Objectives

- To ensure active and systematic clinical and Laboratory monitoring for ADRS is conducted at recommended intervals.
- To ensure timely recognition and management of ADRS
- To ensure ADRS are documented appropriately and reported in accordance with established guidelines and National regulator.
- Reduce the incidence of serious ADRS which include: prolonged hospitalization, death or permanent disability

Supporting processes

- Assessment of medical products-related mortality
- Efficacy monitoring and AMR –Therapeutic Drug Monitoring
- Off-label use of medical products.
- Pharmacokinetic calculations
- Resistance trends in use of the antimicrobial medicines.
- Case reports of acute and chronic poisoning/ toxicity
- Drug detoxification and hyper elimination procedures.
- Adverse interactions of medical products with chemicals, other medicines, and food reports.
- Assesses traditional medicines and associated adverse events and interactions.
- Evaluate the Genetic makeup and nutrition status to drug efficacy.

Benefits of ADSM

- Provides new evidence on safety of medicine.
- Establishes benefits/risk and comparative effectiveness.
- Guides treatment guidelines review decisions.
- Maximization of benefits.
- Reduction of risk.
- Patient with risk factors not exposed to the product.
- Greater understanding of medicine induced disorders.
- Early signals/warnings to potentially serious ADRs.

Greater awareness of agents that commonly cause medicine induced disorders.

- Better patient care.
- Huge savings in healthcare costs
- Better patient confidence and trust

aDSM indicators

- To measure the prevalence and incidence of Known adverse events to standard regimens
- To measure the prevalence and incidence of unknown adverse events to standard regimens for management of TB.
- To assess the efficacy of treatment monthly.
- Pre requisite of Authorized officer to record and report on Adsm

All the providers of ADSM should have the following qualifications;

1. A Registered pharmacist with Pharmacy and Poisons Board
2. Current retention License number
3. Working in the public sector
4. Indemnity cover
5. Evidence of Continuous Professional Development courses
6. Belong to a recognized pharmacists association.

2. MEDICATION THERAPY MANAGEMENT SERVICES (MTM)

Introduction

Medication Therapy Management (MTM) is a service that aims to optimize medication use and improve patient outcomes. It involves a review of all medications a patient is taking, including prescription, over-the-counter, and herbal products, to identify and address potential issues. MTM is often provided by pharmacists and focuses on patient education, consultation, and collaboration to achieve optimal medication goals (5,6,7, &27).

The MTM services results in a review of all medications prescribed by all prescribers providing care to the patient, and any over-the-counter and herbal products the patient may be taking to identify and address medication problems. Problems may include medications not being used correctly, duplication of medications, unnecessary medications, and the need for medication(s) for an untreated or inappropriately managed condition. In-depth, medication-related education, consultation, and advice provided to patients, family and/or caregivers to help assure proper use of medications, also Collaboration with the patient, physician, and other health care providers to develop and achieve optimal goals of medication therapy (28).

Recognizing the Clinical Role of Pharmacists in DRTB through MTM service delivery is critical for drug safety, eff efficacy and effectiveness. A medication that fails to produce the desired or expected therapeutic outcomes is clearly cost-ineffective, regardless of its price. The impact of inappropriate medication use and medication-related problems on patient morbidity and mortality has led leading policy makers in both the private and public sectors to provide recommendations on effective strategies to address this significant public health problem especially in DRTB. By recognizing Medication Therapy Management (MTM), many entities have acknowledged that pharmacists have the expertise necessary to effectively manage medication therapies and medication-related problems for therapy safety (28, &29).

Global MTM Landscape

Many countries have adopted MTM service delivery, these include but not limited to North America, USA, Canada, Australia, Indonesia, United Kingdom, Saudi Arabia, Ghana, Ethiopia, Italy, Switzerland

MTM and DRTB Patients

MTM provides advantages to DRTB patients;

- MTM empowers them to know the goals of their medication therapy and be in better control of your medication use.
- MTM helps them have a better understanding of their medications in the course of treatment.
- MTM helps them get the most benefit from their medications and can detect and prevent both present and future medication problems.

Benefits of MTM:

Improved patient adherence: MTM helps patients understand their medications and how to take them properly, leading to better adherence.

Reduced adverse drug events: By identifying and addressing potential problems with medication use, MTM can help prevent adverse events.

Enhanced medication-related outcomes: Optimizing medication use leads to better overall health outcomes for patients.

Reduced polypharmacy: MTM can help simplify medication regimens by identifying and eliminating unnecessary medications.

Cost savings: Improved adherence, reduced adverse events, and simplified medication regimens can lead to cost savings for patients and the healthcare system.

During an MTM Session

An MTM session typically includes sitting down with your pharmacist to discuss your medications in depth. These sessions often last 30-60 minutes.

Each session entails five aspects of a full MTM session that are completed by the pharmacist working with the patient and the patient's doctor(s):

- Conducting a Medication Therapy Review (MTR);
- Creating a personal medication record;
- Creating a medication-related action plan;
- Providing an intervention and/or referring the patient to another practitioner; and
- Documenting the session and following up with the patient and/or their doctor(s).

During this time Pharmacists will discuss and address medication problems the patient may be having. Pharmacists will also determine if there are:

- Medications being used incorrectly,
- Duplication of medication types,
- Unnecessary medications, and
- Additional medications that are needed for untreated or inappropriately treated health conditions.

Pharmacists will also provide in-depth medication education in addition to providing advice to the DRTB patients.

Guidelines for Delivering MTM services

For the purpose of developing, implementing, delivering and sustainability of MTM services, a systematic approach is crucial at all stages. A review of essential skills and knowledge in performing MTM successfully and an organized process of identifying Medication – Relate.

Problems (MRPs), drugs safety and patient drugs related needs should form the foundation of delivering MTM service (22).

All the providers of MTM should have the following qualifications;

- A Registered pharmacist with Pharmacy and Poisons Board
- Current retention License number
- Working in the public sector
- Indemnity cover

- Evidence of Continuous Professional Development courses
- Belong to a recognized pharmacists association.

3. Extemporaneous preparation

An extemporaneous preparation, also known as a compounded medication, refers to a drug or a combination of drugs that a pharmacy prepares based on a prescription. Compounding involves activities like formulating, mixing, or repackaging medications.

It's important to note that these extemporaneous preparations are not licensed by Drug Regulatory Authorities. Consequently, they do not undergo the same rigorous evaluations for quality, efficacy, and stability as commercially manufactured drugs. Additionally, the reporting of adverse events associated with these compounded products is not mandatory.

Introduction

Extemporaneous compounding involves preparing a customized therapeutic product for a specific patient when their needs cannot be met by commercially available options. This practice offers a valuable solution in situations such as when patients have difficulty swallowing solid medications, when a suitable dose or dosage form is unavailable, when an individualized dose is necessary, or when medications need to be administered through nasogastric or gastrostomy tubes.

Compounded medications can take various forms, including creams, eye drops, nasal sprays, oral formulations, and intravenous infusions. These products are often categorized as either simple or complex.

It's understood that any pharmacist can perform simple compounding, as it is a fundamental skill in pharmacy training. However, complex compounding requires further specialized training and demonstrated expertise, as outlined in the Pharmacy Board's guidelines on compounding.

Rationale

Compounded products play a valuable role in specific situations, such as during drug shortages or for the treatment of rare diseases. These altered drug forms can include topical ointments, eye drops, solid or liquid oral medications, and intravenous infusions.

Extemporaneously compounded medicines can be particularly helpful when a necessary dose or formulation isn't commercially available, or when individualized dosing is required. There are many established compounding formulas, and new ones can be created using formulation

guidelines and professional guidance. It's important to note that unlike registered medicines, compounded preparations typically have not undergone assessments for safety and efficacy. Their use is considered off-label and relies on extrapolating data from their individual components.

Compounded products are typically assigned short-term expiry dates unless their stability has been specifically evaluated (5,6,7,29,&30)

Principle involved in extemporaneous compounding.

Extemporaneous compounding, the small-scale preparation of medications from raw materials or commercially available forms, is a common practice within the TB programming patient care continuum.

This is particularly relevant for pediatric patients and in managing adverse drug reactions related to non-adherence to treatment.

The formulations are as follows:

Preparations

- Liquid. The active part of the medicine is combined with a liquid to make it easier to take or better absorbed.
- Tablet. The active ingredient is combined with another substance and pressed into a round or oval solid shape.
- Capsules.
- Topical medicines.
- Suppositories.
- Drops.
- Inhalers.
- Injections.

Regulation:

The extemporaneous compounding activities that will be conducted in the MTM clinic, specifically within the pharmaceutics laboratory. Please note that this is in accordance with the pharmacy and poisons board licensing conditions (6&7).

Furthermore, a subcommittee focused on extemporaneous compounding within the National Formulary development, stabilization, and standardization of these preparations has been formed. This subcommittee will provide guidance on the operational roadmap for these activities.

Guidelines for Delivering Extemporaneous compounding services

A systematic approach is essential for the successful development, implementation, delivery, and sustainability of extemporaneous compounding services. This includes a thorough review of the necessary skills and knowledge required for successful compounding.

An organized compounding process is crucial to preserve the pharmaceutical and therapeutic characteristics of the formulation. This also helps to avoid errors, pharmaceutical interactions, and local reactions that could lead to a toxic compound.

For an added layer of safety and accuracy, we recommend that a second reviewer, preferably a specialist in pharmaceutics or industrial pharmacy, review both the formulation and the compounding process.

The pharmaceutics lab will need (22):

- To be registered under the MTM clinic package, requirements for a compounding area on annual basis.
- Regular External quality Assurance Audits from the regulator PPB on quarterly basis.
- Regular Internal Quality Assurance on Monthly basis. By the Superintending pharmacist.
- Review of the compounding stabilizers protocols including sterility protocols.
- Review of the Standard operating Procedures (SOPs) and compounding formulary on annual basis.

- Routine standardization and calibration of the instrumentation for the MTM clinic Pharmaceutics lab.
- A biosafety cabinet. Lamina flow unit for sterile transfer.

Considering the medical legal implications and that could arise from the extemporaneous compounding,

All the providers of Extemporaneous compounding should have the following qualifications;

- A Registered pharmacist with Pharmacy and Poisons Board
- Current retention License number
- Working in the public sector
- Indemnity cover
- Evidence of Continuous Professional Development courses
- Belong to a recognized pharmacists association.
- A clear referral mechanism for a second reviewer/validation of the preparations.

Chapter 6

Legal Ethical Considerations and ADSM system Governance mechanism

Informed consent

Informed consent will be obtained from all patient (or legally acceptable representative) before any care-related procedures are performed. Each informed consent form shall include the elements required by the international Good pharmacy Practice and Good pharmacy practice guidelines by PPB. The Pharmacist must provide his registration credentials and indemnity insurance cover number, active before proceeding with the patient. Must adhere to the ethical principles that have their origin in the Declaration of Helsinki (6,7,22,32 & 33)..

Confidentiality

Patients` data confidentiality must be adhered to in accordance to the data protection act and guidelines from the data protection commission.

Indemnity obligations on recording and reporting on ADSM
Under cap 244, the indemnity cover and legal obligation for qualified person to undertake Medicine Therapeutics Monitoring and safety is someone under the pharmacy oath. They are Pharmacist and Pharmacist specialist. This is amplified in the Good Pharmacy Practice guidelines from the PPB.

The recording of events will be divided into two components:

Active drug safety monitoring (aDSM) will follow the patient pathway from registration to the treatment outcome. The patient details will be captured as baseline (before starting treatment) using the aDSM – treatment initiation form and will get updated for all SAEs using aDSM – treatment review form after it is appropriately managed (32).

Any AE will be captured additionally using the yellow form, pharmaceutical care plans (PCP) causality Assessment form, Therapeutics Drugs Monitoring Form, Drugs utilization review forms (in the annexes). The forms to be filled will be depended on interventions that will be Required. The primary responsibility of filling up of above forms will be with the Specialist
Pharmacist and Pharmacists in the Facilities.

The management of the ADRs will be in the MTM clinics through multidisciplinary involvement coordinated by the clinical pharmacist. All information about AE and SAE need to be updated in

TIBU platform and PPB online platform Once the relevant information is uploaded in the county allocation tool, TIBU Meds platform, it will automatically be visualized and pulled in PPB PVERS platform. What is captured in PPB PVERS will seamlessly flow to Vigiflow software of PPB through the electronic bridge that is functional.

These platforms are integrated by interphases centrally linked to Kenya Health Information Systems (KHIS) national aggregator platform. The sites need to ensure reporting of SAE within 24 hours to TIBU platform. Records need to be maintained in hard copies at respective sites.

The aDSM data will be analyzed at TIBU and KHIS. The relevant information will be shared with drug safety monitoring committee in Pharmacovigilance centre under pharmacy and poisons board on regular basis. The data on action required on immediate basis will be shared with PPB by TIBU.

The primary role of PPB would be to evaluate periodically, the accumulated data for patient safety and make recommendation to PMDT concerning use of the medicines in the injection free regimen (IFR) in DR-TB management protocols. Once the relevant information is uploaded in county allocation tool, TIBU and PPB platform it will seamlessly flow to Vigiflow software of PPB PVER through the electronic bridge that is functional.

These platforms are integrated by interphases centrally linked to Kenya Health Information Systems (KHIS) national aggregator platform. The sites need to ensure reporting of SAE within 24 hours to TIBU platform. Records need to be maintained in hard copies at respective sites.

The aDSM data will be analyzed at TIBU and KHIS. The relevant information will be shared with drug safety monitoring committee in Pharmacovigilance centre under pharmacy and poisons board on regular basis. The data on action required on immediate basis will be shared with PPB by TIBU.

The primary role of PPB would be to evaluate periodically, the accumulated data for patient safety and make recommendation to PMDT concerning use of the medicines in the injection free regimen (IFR) in DR-TB management protocols.

Data management and analysis

De-identified data will be transmitted to the NTLD-P server in real-time. At the end of each day, data transmitted to the server will be reviewed by the Pharmacovigilance - ADSM subcommittee under the commodity and PV section on daily basis. Any data quality/ issues flagged to the M&E section for immediate correction. The data requiring programmatic clinical intervention shall be flagged for PMDT to intervene. The data requiring regulatory intervention will be flagged for PPB to intervene. The data will be stored in a password protected computer with back-up on a password protected external hard-drive, only accessible to authorized program staff. The PPB PVERs and KHIS2 will be integrated for interoperability (32,33).

After completion of data collection, quantitative data will be downloaded from the server into Excel and transferred to Stata 15 (Stata Corp, USA) for statistical analysis. These will be under the custody of the ADSM coordinator and IT section team based at the NTLD-P office. A conventional approach to content analysis will be used to create coding categories and identify themes and

patterns derived directly from the data obtained. Transcribed data will then be condensed into text segments which will be coded based upon emergent themes. This will be continuously refined and compared with each other. Categories will finally be aggregated into broader themes. Data

will be stored for at least 10 years or until the interests that merit protection have been clarified legally, or NTLD-P has evaluated the data to determine whether it must be retained for historical purposes as per (Kenya, 2018).

Community engagement plans

Upon the release of the periodic report draft by the commodity & Adsm team in the Program and the IT team in a program during biannual Performance Review Workshop, the program will pave way and modality for its implementation in the hospital facilities. More so, involving community engagement strategies to the community. The program`s health preventive and promotive section will do communications in media houses, health talk shows, Stickers, Billboards and Placards on the adverse drugs and ADSM. More so, sensitize the healthcare workers attending to the patients on ADRS and ADSM. Importantly, to bring implementation partners on community engagement as AMREF to integrate ADSM in patient care cascade by coordinated interaction of Pharmaceutical Society of Kenya with Kenya Medical Association

Data Relay System

Data capture will be done using an electronic tools and paper tools depending on the facility. For the electronics tools, data will be captured on the scoped tools of ADSM and MTM Clinic Tools in TIBU Platform and TIBU Meds platform at the primary data collection stages by the hospital facility pharmacists. It will be relayed into KHIS 2 for national aggregation while PPB, PVERS for regulatory interpretation. TIBU and TIBU Meds will be for patient management and programmatic purposes. All the said four systems will be integrated for interoperability and system validation rules will be applied accordingly a per the Data commission Act. The data will then be transmitted to National TB Program servers on real time. For the paper tools, the hospital pharmacist will fill in the data at the patient data collection stages, then the sub county pharmacists will aggregate on the system on a daily basis.

Training/ capacity building.

Due to funding constraints, the capacity building will target the pharmacists with content resource: degree pharmacists and pharmacy specialists with PPB Regn Numbers and active license with indemnity insurance cover for the retention year. The modules will target the M&E aspects of aDSM. The clinicians will be enjoined to train alongside for mentorship interplaying with interoperability in this model of integrated healthcare model.

References

1. World Health Organization. Global Tuberculosis Report 2017. http://www.who.int/tb/publications/global_report/en/
2. National Tuberculosis, Leprosy and Lung Disease. (2018). Annual Tuberculosis Report. Nairobi: National Tuberculosis, Leprosy and Lung Disease.
3. Division of National Tuberculosis, leprosy and Lung Diseases. (2020). TIBU data report. Nairobi: National Tuberculosis, Leprosy and Lung Disease
4. World Health Organization. (2018). Global Tuberculosis Report. Geneva: World Health Organization.
5. Division of National Tuberculosis, leprosy and Lung Diseases. (2019). Annual Program Forecasting And quantification review Report. Nairobi: National Tuberculosis, Leprosy and Lung Disease.
6. The use of Delaminid in the treatment of multidrug-resistant tuberculosis. Interim policy guidance (WHO/HTM/TB/2014.23). Geneva: World Health Organization; 2014 (http://apps.who.int/iris/bit stream/10665/137334/1/WHO_HTM_TB_2014.23_eng.pdf, accessed 11 January 2016).
7. The 2012 implementation manual for pharmacovigilance of anti-TB drugs in 2012 (1),
8. The importance of pharmacovigilance: safety monitoring of medicinal products. Geneva: World Health Organization; 2002 (apps.who.int/medicinedocs/en/d/Js4893e/#Js4893e, accessed
9. January 2016). 12. VigiBase™. In: The Uppsala Monitoring Centre/products and services [website] (http://www.umc-products. com/DynPage.aspx?id=73590&mn1=1107&mn2=1132, accessed 11 January 2016)
10. Research protocol – effectiveness of a simplified short regimen for multidrug resistant tuberculosis treatment in Karakalpakstan, Uzbekistan. MSF Field Research. (http://fieldresearch.msf.org/msf/ handle/10144/322296, accessed 11 January 2016).
11. Recent changes in guidelines on programmatic management of drug resistant tuberculosis in India 2019: a paradigm shift in tuberculosis control.
12. Post Marketing Surveillance for antidiabetics and antihypertensive on Kenya. (2016).PPB PMS protocol.
13. Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. (WHO/HTM/TB/2014.11). Geneva: World Health Organization; 2014 (http://apps.who. int/iris/bit stream/10665/130918/1/9789241548809_eng.pdf, accessed 11 January 2016).
14. Policy implementation package for new TB drug introduction (WHO/HTM/TB/2014.22). Geneva: World Health Organization; 2014 (www.who.int/tb/PIPnewTBdrugs.pdf, accessed 11 January 2016).

15. Companion handbook to the WHO guidelines for the programmatic management of drugresistant tuberculosis (WHO/HTM/TB/2014.11). Geneva: World Health Organization; 2014 (https://apps.who.int/ iris/bitstream/handle/10665/130918/9789241548809_eng.pdf?sequence=1, accessed 20 March 2020).

16. Active tuberculosis drug-safety monitoring and management (aDSM): framework for implementation. Geneva: World Health Organization; 2015 (https://www.who.int/tb/publications/aDSM/en/, accessed 1 June 2020).

17. Mitnick CD, White RA, Lu C, Rodriguez CA, Bayona J, Becerra MC et al. Multidrug-resistant tuberculosis treatment failure detection depends on monitoring interval and microbiological method. Eur Respir J. 2016;48 (4):1160–70.

18. Guidelines on programmatic management of drug resistant tuberculosis in India 2019. Revised National Tuberculosis Control Programme, Central TB Division, Directorate General of Health Services, Ministry of Health & Family Welfare, Nirman Bhawan, New Delhi.

19. Patient identification and education: World Health Organization (WHO), Guidelines for Treatment of Drug-Susceptible Tuberculosis and Patient Care (2017 Update).

20. Treatment regimen adherence: WHO, Companion Handbook to the WHO Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis (2014)

21. Packaging and labelling: International Standards for Tuberculosis Care, Standard.

22. Drug Administration and Patient Monitoring (2021).

23. Monitoring and documentation: National TB Program Guidelines (Country- Specific Recommendations)

24. Handling Drug-Resistant TB WHO, Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis (2020).

25. Storage and stability:WHO, TB Manual: A Practical Guide to the Management of Tuberculosis in the Era of Tuberculosis Elimination (2018).

26. Directly Observed Treatment (DOT) WHO, Implementation of the End TB Strategy (2021).

27. Paediatric and special populations: Union Against Tuberculosis and Lung Disease, Management of Tuberculosis in Special Populations (2021).

28. Patient Confidentiality:WHO, Ethics Guidance for the Implementation of the End TB Strategy (2017)

29. Emergency preparedness: WHO, Operational Handbook on Tuberculosis: Emergency Preparedness and response (2022).

Annexes

APPENDICES

APPENDIX 1
SOPS

S.O.Ps :Good Documentation Practices for aDSM & Related Pharmacotherapeutics Tools.

a. For paper-based records

1. All records should be: Dated Signed/Attributed Secured
2. Sign/initial and date entries at the time of the documented event
3. Data entries must be dated on the date of entry; contemporaneous
4. Data entries must be signed or initialled by the person entering the data - attribution.
5. No other person should sign for anybody else's name - falsification
6. Do not post or pre-date documents related to aDSM
7. Whenever records require correction
    - Do not conceal previous data
    - Date the change I
    - dentify the person making the change
    - State the reason for the change
    - Do not use whiteout
    - Do not change data without knowledge that the change is correct

b. For Electronic records

1. Should be as secure as paper records
2. Maintain data security and integrity of data records

3. Control the access of data to authorised individuals
4. Utilise reliable, validated or adapted software
5. The electronic records should be have ability to copy, backup and retrieve data
6. The electronic record should have time-stamped audit trails
7. Staff should be trained on use of the electronic record

APPENDIX 2
TOOLS

1. aDSM tool.

This will be an observational/analytical descriptive of prospective cohort enrolment of a patient and case that will use qualitative/quantitative data collection methods. Data be analyzed by Stata 10 version tool. Measures of association will be done by odds ratio and test for significance will be done by regression analysis.

2. Causality assessment tool.

This will be an observational descriptive and case control survey that will use both qualitative and quantitative data collection methods. Data to be analyzed by Stata 10 tool. Measure of association will be done by risk ratio and test for significance will be done by Chi square.

3. Extemporaneuse compounding Tool.

This will be both observational in clinical settings and analytical study in laboratory setting with a case study and case series study design. The pharmacokinetic parameters of the TDM drugs under IFR regimen from the laboratory will be correlated to the clinical parameters. The data to be analyzed by the Stata 10 version tool and test for significance to be done by chi square and Anova.

4. Drugs Utilization Reviews.

This will be an observational descriptive and cross-sectional review with case by case basis case series study designs, that will use both qualitative and quantitative data collection methods. Data to be analyzed by Stata 10 version tool. Measures of association will be done by odds ratio and test for significance will be done by chi square and regression analysis.

5. Pharmaceutical Care Plans.

This will be an observational descriptive and cross-sectional survey that will use qualitative data collection methods. Data to be analyzed by Stata 10 version tool. Measures of association will be done by odds ratio and test for significance will be done by chi square and regression analysis.

6. **MTM Tool.**

This will be an observational descriptive and cross-sectional survey that will use qualitative data collection methods. Data to be analyzed by Stata 10 version tool. Measures of association will be done by odds ratio and test for significance will be done by chi square and regression analysis.

7. **TDM Tool.**

This will be both observational in clinical settings and analytical study in laboratory setting with a case study and case series study design. The pharmacokinetic parameters of the TDM drugs under IFR regimen from the laboratory will be correlated to the clinical parameters. The data to be analyzed by the Stata 10 version tool and test for significance to be done by chi square and Anova.

8. **Drugs Toxicology Detox and substance Abuse.**

This will be an observational descriptive and analytical survey that will use quantitative data collection methods. The data to be analyzed by the Stata 10 version tool and test for significance to be done by chi square and Anova.

9. **Drugs Bioequivalence analysis tool.**

This will be an observational descriptive and analytical survey that will use quantitative data collection methods. The data to be analyzed by the Stata 10 version tool and test for significance to be done by chi square and Anova.

10. **Pharmacokinetic projection/analysis tool.**

This will be a cross sectional descriptive/ cohort progressive mathematical pharmacotherapeutics modeling analysis. Laboratory analytical study design will use quantitative data collection methods. The data will be analyzed by the Stata 10 version tool and test for significance to be done by chi square.

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