Medicine Use Evaluations: A strategy for therapeutics committees to monitor the use of antiretroviral medicines and medicines for opportunistic infections

January 2015

USAID
FROM THE AMERICAN PEOPLE

SIAPS
Systems for Improved Access to Pharmaceuticals and Services

Medicine Use Evaluations: A strategy for therapeutics committees to monitor the use of antiretroviral medicines and medicines for opportunistic infections

Bayobuya Phulu MSH/SIAPS
Harriet Kagoya MSH/SIAPS
Malaika Ludman MSH/CPM/SIAPS

May 2015

This report is made possible by the generous support of the American people through the US Agency for International Development (USAID), under the terms of cooperative agreement number AID-OAA-A-11-00021. The contents are the responsibility of Management Sciences for Health and do not necessarily reflect the views of USAID or the United States Government.

About SIAPS

The goal of the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program is to assure the availability of quality pharmaceutical products and effective pharmaceutical services to achieve desired health outcomes. Toward this end, the SIAPS result areas include improving governance, building capacity for pharmaceutical management and services, addressing information needed for decision-making in the pharmaceutical sector, strengthening financing strategies and mechanisms to improve access to medicines, and increasing quality pharmaceutical services.

Recommended Citation

This report may be reproduced if credit is given to SIAPS. Please use the following citation.

B.Phulu. 2015. *Medicine Use Evaluations:A strategy for therapeutic committees to monitor the use of antiretroviral medicines and medicines for opportunistic infections***.** Submitted to the US Agency for International Development by the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program. Arlington, VA: Management Sciences for Health.

Key Words

medicine use evaluation, antiretroviral, standard treatment guidelines, medicine and therapeutics committees, rational use of medicines, antimicrobial resistance.

Systems for Improved Access to Pharmaceuticals and Services
Center for Pharmaceutical Management
Management Sciences for Health
4301 North Fairfax Drive, Suite 400
Arlington, VA 22203 USA
Telephone: 703.524.6575
Fax: 703.524.7898
E-mail: siaps@msh.org
Website: www.siapsprogram.org

TABLE OF CONTENTS

Abbreviations and Acronyms iv

Overview 1

Background 3
About Namibia 3
Rational use of medicine 3
Promoting RUM; justification for medicine use evaluations (MUEs) in Namibia 3

Therapeutics Committee—Overview 5
Importance of TCs 5

How to Implement a Medicine Use Evaluation 7

Phase 1. Plan the MUE Strategy 8
Step 1. Establish Responsibility for the MUE Process 8
Step 2. Develop Procedures 9
Step 3. Orient Staff to the Process 16
Step 4. Prepare Data Collection Forms 16
Step 5. Orient Data Collectors 21

Phase 2: Conduct the MUE 23
Step 6. Collect Data 23
Step 7. Tabulate Data 23
Step 8. Interpret Data 26
Step 9. Make Recommendations for Improvement 27
Step 10. Disseminate Results and Discuss the Improvement Plan 28
Step 11. Implement the Improvement Plan 28

Phase 4: Assess the Effectiveness of the Intervention 29
Step 12. Conduct a Follow-up MUE 29
Step 13. Review and Discuss Follow-up Data 29
Step 14. Evaluate the Strategy 29
Step 15. Plan and Implement the Next Cycle 30

Conclusion 31

Annex A. An Example of Published Criteria for First Line Anti-Tuberculosis Treatment 32

Annex B. Sample Data Collection Forms 44

Annex C: MoHSS Terms of Reference (TOR) for TCs June 2011 52

ABBREVIATIONS AND ACRONYMS

AIDS	acqcuired immono defficiency syndromme
ADR	adverse drug reaction
AMR	antimicrobial resistance
ART	antiretroviral therapy
ARV	antiretroviral medicine
Div: PhSs	Division of pharmaceutical Services
DR-TB	drug-resistant tuberculosis
EWI	early warning indicators
HIV	human immunodeficiency virus
HIV-DR	HIV drug-resistance
MDR-TB	multidrug-resistant tuberculosis
MoHSS	Ministry of Health and Social Services
MSH	Management Sciences for Health
MUE	medicine use evaluation
Nemlist	Namibia Essential Medicines List
OI	opportunistic infection
PMIS	pharmaceutical management information system
RUM	Rational use of medicine
SIAPS	Systems for Improved Access to Pharmaceuticals [program]
SSVs	support supervision visists
STG	standard treatment guidelines
TB	tuberculosis
TC	therapeutics commmittee
TOR	Terms of reference
XDR-TB	extensively drug-resistant tuberculosis
WHO	World Health Organization

OVERVIEW

This manual is intended to assist therapeutic committees (TCs) in monitoring medicine use in their health facilities through regular medicine use evaluations (MUEs). The manual lists and describes the various steps involved in conducting an MUE. It also:

- describes the conditions of rational use of medicines (RUM)
- describes the extent and nature of the inappropriate use of medicines
- seeks to raise awareness of practices that lead to the development of antimicrobial resistance (AMR)
- describes and discusses irrationalities pertaining to the use of antimicrobials, including those used in the treatment of HIV and AIDS and TB
- helps TCs to understand the adverse impacts of inappropriate medicine use
- highlights roles of TCs in promoting RUM
- supports TCs in designing action plans to improve medicine use in their health facilities
- supports TCs in drafting interventions to improve poor performance as it relates to the pharmaceutical management information system (PMIS), supportive supervision visits (SSVs), and antiretroviral therapy (ART) early warning indicators (EWIs) of HIV drug resistance (HIV-DR).

Medicine use evaluation—sometimes referred to as medicine use review—is an **ongoing**, systematic process designed to maintain the appropriate and effective use of medicines.

Planning overambitious and extensive MUEs can lead to challenges, delays, and frustration. During the initial phases of the MUE process, it is best to focus only on those few selected aspects of medicine use that contribute to poor quality treatment.

Factors Contributing to Poor Medicine Use

Inappropriate standard treatment guidelines
Non-compliance to standard treatment guidelines
Absence of standard treatment guidelines
Inadequate training for health care providers
Financial disincentives
Lack of patient education
No/ limited monitoring of treatment
Poor management of adverse medicine reactions
Insufficient treatment support

The institutionalization of an on-going MUE strategy among TCs will strengthen the health system and support the various building blocks of the health system by:

- ensuring access to effective treatment for common diseases and conditions
- using systematic qualitative and quantitative data collection procedures to accumulate evidence-backed informed decision making
- improving the delivery of effective, safe, and cost-effective services as a result of review and improvement in practices
- enhancing stewardship and governance as a result of audit and feedback, and improving transparency in detecting patterns of medicine use
- using findings to advocate for financial and human resources

A portion of these guidelines are based on a publication by Management Sciences for Health (MSH) entitled *Guidelines for Implementing Medicine Utilization Review Programs in Hospitals*[1], and from training materials developed by MSH through Rational Pharmaceutical Management Plus for training District-level Therapeutic Committees[2].They have been adapted to this manual to focus on principles and content that can be used by TCs to conduct MUEs in their institutions.

Most of the recommendations provided in this manual are generic and simple, and are meant to assist TCs to conduct and implement a MUE strategy. The manual provides a step-by-step explanation of:

1. Developing context specific MUE criteria according to best available evidence
2. Collecting and analyzing existing available data
3. Providing feedback and taking action based on MUE findings when indicated
4. Reviewing the MUE strategy to identify opportunities for program improvement to provide high quality treatment

[1] Moore T, Bykov A, Savelli T, et al. 1997. Guidelines for Implementing Medicine Utilization Review Programs in Hospitals.
[2] Management Sciences for Health and World Health Organization. 2007. Medicine and Therapeutics Committee Training Course

BACKGROUND

About Namibia

Namibia is located in Southern Africa and has a population of over 2.2 million people[3]. The country has 14 administrative regions which are divided into 35 districts, each with a public district hospital. Each district has a Thereapeutics Committee, the structute established with documentetd terms of reference (ToR) and responsible for promoting and ensuring rational use of medicines and providing management oversight to health facilities, among other roles. Namibia's Ministry of Health and Social Services (MoHSS) manages approximately 350 public health facilities in Namibia including 35 hospitals, 43 health centers and about 255 clinics. Namibia is among the countries with the highest prevalence of HIV; in 2013, an estimated 13.1% of the adult population was living with HIV[4] .

Rational use of medicine

Rational use of medicines (RUM) requires that patients receive appropriate medications for their clinical needs, in doses meeting individual requirements, for an adequate period, and at the lowest cost to them and their community. Irrational medicine use occurs when one of these conditions are not met. Irrational use of medicines may contribute to resistance to ARVs, anti-TB, and other medicines commonly used for treatment of opportunistic infections affecting people living with HIV and AIDS. Hence, the need for medicines use evaluations (MUEs) to provide information for informing strategies to improve RUM.

Promoting RUM; justification for medicine use evaluations (MUEs) in Namibia

Namibia has attained high (over 80%)[3] coverage of ART services for its HIV positive population through rapid scale up programs; the next challenge the country faces is sustaining the quality of HIV treatment services and improved outcomes, including adherence to ART treatment to improve retention in care and slow the emergence of HIV drug resistance (HIV-DR). The Division of Pharmaceutical Services (Div: PhSs) of the Ministry of Health and Social Services (MoHSS), through its National Medicines Policy Coordination subdivision, regularly monitors TC activities during supportive supervision visits and pharmaceutical management information system (PMIS) reporting on number of TC meetings held. Findings from annual supportive supervision visits (SSVs) conducted between 2012 to 2015[(4-7)] show that TCs have done very little with regards to evaluating medicine use, and implementing and documenting interventions to improve medicine use and treatment outcomes. In addition, raising awareness on AMR and rational use of medicines (RUM) has mainly been implemented at a national level[8], whereas this needs to be implemented at an operational level through active support to TCs.

[3] Namibia 2011 population and housing census report
[4] Namibia National Guidelines for Antiretroviral Therapy • Fourth Edition.

An analysis of PMIS data in the 2013/2014 financial year demonstrated an increase in antibiotic prescribing in public sector health facilities. Similarly, the standard treatment guidelines (STG) post-implementation assessment report, published in December 2013_, revealed low compliance to guidelines in the treatment of major diseases, including HIV and AIDS[5]. In response, the USAID-funded Systems for Improved Access to Pharmaceuticals and Services (SIAPS) program supported the training of stakeholders in Namibia on strategies to combat AMR and improve RUM. Coalitions such as Namibians Against Antibiotic Resistance were formed as a result and have been tasked with providing stewardship in AMR related activities. TCs are among the entities responsible for leading AMR/RUM activities in health facilities, promoting rational medicine use, providing oversight, and promoting accountability in the pharmaceutical sector. In this regard, SIAPS is collaborating with Div: PhSs to provide technical support to regional health management teams (RHMTs) to train representatives from district TCs on the role of the TC in promoting RUM and combating AMR and HIV-DR.

TCs are well placed to improve medicine use at health facilities and support efforts directed toward combating the development of AMR through ongoing MUEs. The purpose of this manual is to support TCs in designing and conducting MUEs to assess medicine use in their health facilities, and enable them to use the results to draft interventions to improve poor performance in PMIS, SSVs, and ART early warning indicators (EWIs) of HIV-DR. MUEs can also create awareness among health care workers on their role in monitoring HIV-DR EWIs and promoting rational use of antiretrovirals (ARVs).

[5] Assessment of compliance to the Namibian Standard Treatment Guidelines of outpatient prescriptions in ministry of health and social services health facilities: a medicine use evaluation, December 2013

THERAPEUTICS COMMITTEE—OVERVIEW

Importance of TCs

Therapeutics committees are MoHSS established structures at district level responsible for providing management oversight to public health facilities in Namibia. There are 35 TCs operating under the terms of reference (ToR) included in annex C. Among their roles, the TCs are responsible for promoting RUM. Medicines can save lives and improve quality of life, but they are also expensive–accounting for significant proportions of hospital budgets. When medicines are used inappropriately, adverse drug reactions [ADRs] become more common, morbidity and mortality increase, and the likelihood of developing drug resistance rises. Figure 1 below shows the percentages of patients receiving antbiotics from selected PHC facilities.

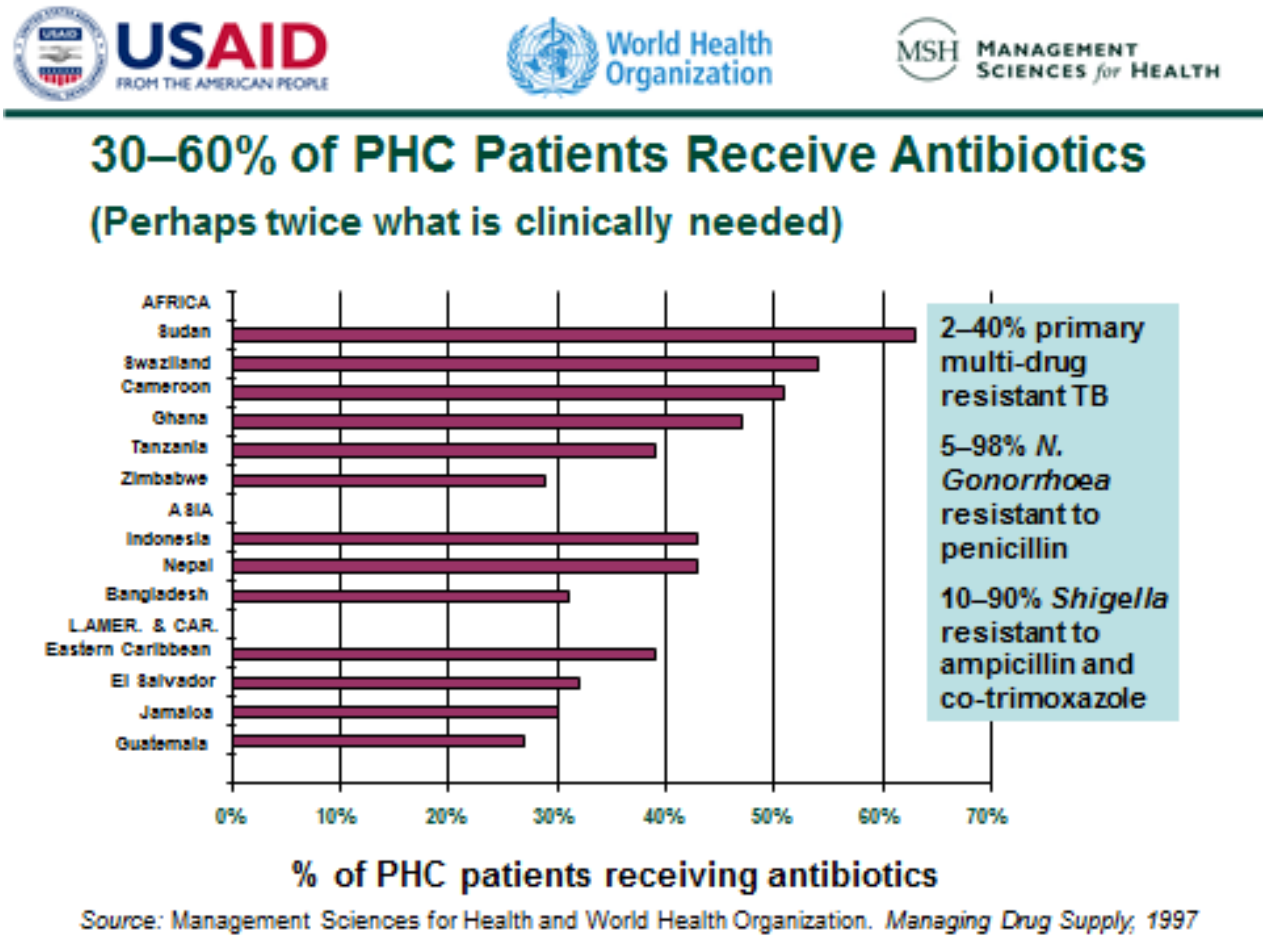

Figure 1. Percentage of primary health care patients receiving antibiotics in select countries

TCs have an important role in ensuring that medicines are managed and used optimally, safely, and effectively. The following TC activities promote rational medicine use:

- Selection of effective, safe, high quality, cost-effective medicines for the formulary
- Monitoring and identification of medicine use problems
- Improved quality of patient care and health outcomes
- Management of antimicrobial resistance (AMR)
- Increased staff and patient knowledge
- Management of ADRs and medication errors
- Improved medicine procurement and inventory management
- Management of pharmaceutical expenditures

Adverse drug reactions are a significant cause of morbidity and mortality in the United States. Estimated costs in the U.S from medicine-related morbidity and mortality range from 30 million to 130 billion US dollars. In the U.S. and Australia, ADRs account for four (40 to six (6) percent of hospitalizations. The most common and expensive adverse events include bleeding, cardiac arrhythmia, confusion, diarrhea, fever, hypotension, itching, vomiting, rash, and renal failure. [6]

In Namibia, an analysis of potential medication safety signals from 842 spontaneous reports of medication adverse events in the TIPC database, submitted from 2011 to 2013, showed that highest frequencies of ADRs were associated with skin disorders and in particular Stevenson Johnson Syndrome (SJS -94 reports out of 218). With regard to ADRs associated with blood disorders anemia 96/97 (99%) were associated with Zidovudine (AZT)[7].

[6] *White, T.J., A. Arakelian , and J. P. Rho. 1999. Counting the cost of medicine related adverse events. Pharmacoeconomics 15(5): 445-58

[7] Chinedum, A, Mazibuko, G, Mengistu A, Sagwa, E. (2014). Therapeutics Information Pharmacovigilance Centre (TIPC) report on the analysis of ART spontaneous adverse event report

HOW TO IMPLEMENT A MEDICINE USE EVALUATION

A MUE strategy is divided into four phases: plan the MUE strategy, implement the MUE, implement the improvement plan, and assess the effectiveness of the intervention. Listed below are the steps involved in each phase. Each of these steps is described in detail in the subsequent sections of the manual.

Phase 1. Plan the MUE Strategy

Step 1. Establish responsibility for the MUE process
Step 2. Develop procedures and data collection tools
Step 3. Orient staff to the process
Step 4. Prepare data collection forms
Step 5. Orient data collectors

Phase 2. Conduct the MUE

Step 6. Collect data
Step 7. Tabulate data
Step 8. Interpret data

Phase 3. Implement an Improvement Plan

Step 9. Make recommendations for improvement
Step 10. Disseminate results and discuss the improvement plan
Step 11. Implement the improvement plan

Phase 4. Assess the Effectiveness of the Strategy

Step 12. Conduct a follow-up MUE
Step 13. Review and discuss follow-up data
Step 14. Evaluate the strategy
Step 15. Plan and implement the next cycle

PHASE 1. PLAN THE MUE STRATEGY

During the planning phase, decisions are made about what needs to be done, why it should be done and who does what, when, and where. The following six steps will help in planning a successful strategy.

Step 1. Establish Responsibility for the MUE Process

MUEs are primarily a medical staff function, with pharmacists and nurses providing expertise. In health facilities, TCs are responsible for implementing STGs to ensure rational medicine use for ARVs and other medicines, monitoring medicine safety (pharmacovigilance), and ensuring patient safety. As such, TCs are in the best position to lead MUE activities.

In intermediate hospitals with a large number of TC members, a MUE subcommittee may be formed depending on feasibility, motivation, workload, and available expertise. Regardless of whether a MUE sub-committee is formed by the TC, the health facility TC will assume a supervisory role.

Regardless of its structure, the TC is the body responsible for MUEs and should be composed of professionals with an interest in improving medicine therapy at treatment facilities, and should have ready access to experts and other resources to facilitate the MUE initiative. The committee may require input from a variety of medical specialists in this first step. Pharmacists should be included as full integral members of the committee.

The TC is responsible for the initial establishment of MUE procedures, and the planning and implementation of all MUE activities. Data collection may or may not be the direct responsibility of the committee members, however, the committee must ensure that data collectors are qualified and adequately oriented.

The most important tasks of the TC in its functions as the MUE Committee are to:

- Set the objectives or purpose of the MUE
- Select the medicines
- Develop or select criteria and thresholds for evaluation
- Oversee the implementation of interventions (if needed)
- Measure medicine use improvement
- Ensure the MUE activity remains an ongoing, systematic process designed to maintain the appropriate and effective use of ART and other key medicines for treating OIs

Step 2. Develop Procedures

Prior to conducting the MUE, the TC or MUE sub-committee should draft and approve procedures that will govern its work. A clear statement of goals and major committee activitiesare important because these procedures may be disseminated to medical personnel for educational purposes.

Designation as a "Process"

The MUE procedures should specify that MUE is a **continuous** process**.** It is not a one-off project. Formal approval of the process by the health facility is recommended so that health care providers whose practices are under review understand that the institute is committed to ensuring safe and effective medicine use, and the review is not intended as a punitive activity that takes place on an ad hoc basis after problems are identified.

Mission Statement and Goals

Any TC should discuss and develop its own mission statement and goals through consensus, and determine the types of activities that are needed in its respective setting.

The following is a sample mission statement of a MUE committee: *"The mission of the MUE Committee is to enhance quality of patient care by assuring appropriate medicine therapy, optimal patient treatment, and education for health care providers through the development and maintenance of a systematic, ongoing, criteria-based review."*

Listed below are examples of MUE Committee goals[8] along with ideas for discussion when defining the purpose of the review.

- Promote optimal medication therapy according to the national treatment guidelines
    - What are the key issues with following the treatment guidelines?
    - What percentage of ART paatients have viral load monitoring performed according to the guidelines?
    - Are patients receiving the correct ART regimen, at the correct dose, administered at the correct frequency?
- Evaluate the effectiveness and safety (pharmacovigilance) of medication therapy
    - What is the loss to follow-up rate for ART patients and why?
    - What is the treatment success rate for ART patients and why?
    - How can the TC find reasons for loss to follow-up?
    - How can a MUE identify unmet needs to address treatment success rate?

[8] American Society of Health-System Pharmacists. 1996. ASHP Guidelines on Medication-Use Evaluation. Am J Heal Pharm. 53:1953–5.

- Evaluate the safety (pharmacovigilance) of medication therapy
    - Are adverse medicine reactions properly recorded and reported?
    - Are anticipated adverse medicine reactions properly managed?
    - Are trends in adverse drug reactions identified and addressed?
- Prevent errors and minimize adverse effects to patients associated with medication therapy
    - Are patients receiving baseline and follow-up evaluations according to the STGs?
    - Are adverse events being managed according to the STGs?
    - Are patients receiving adequate counseling about their medications and managing adverse drug reactions?
- Establish interdisciplinary consensus on medication use processes
    - Are prescribers, pharmacists, nurses, laboratorians, audiologists, psychologists, administrators, and patients involved in the process?
- Stimulate improvements in medication-use processes
    - Once unmet needs are identified, who is responsible for deciding on the interventions needed and ensuring they are implemented?
- Identify areas in which further information and education for health care providers may be needed
    - Do all treatment facilities have a copy of the new guidelines?
    - Has key staff been trained on the guidelines?
    - Once unmet needs are identified, who is responsible for providing information and education?
- Meet or exceed internal and external quality standards
    - Are there monitoring and evaluation mechanisms in place?
    - Are there opportunities to exceed quality standards?

TCs that manage health facility data using electronic systems with data quality assurance processes in place may be able to obtain data for MUEs from regularly collected electronic data[9]. The following are advantages of using an electronic-based system over a paper-based system:

[9] World Health Organization. 2012. Electronic recording and reporting for tuberculosis care and control. Geneva: World Health Organization. Available at: http://whqlibdoc.who.int/publications/2012/9789241564465_eng.pdf.

- Data quality is assured due to data entry edit checks that prevent the input of invalid or incomplete data
- Cost-efficiencies are regularly collected electronically by generating MUE data
- Less time is spent retrieving the data

Table provides examples of the additional resources required when planning a budget for implementing a MUE strategy.

Table 1. Illustrative Examples of Budget Items for a Medicine Use Evaluation Strategy[10]

MUE Costs*	Implementation or Strategy Costs	Institutional Costs
• Personnel including all staff, data collectors, data managers, statisticians, etc., as well as consultants who could provide short-term technical support • Supplies and materials including printing of data collection instruments, notepads, pens, etc. • Equipment such as computers, printers, cell phones and airtime. • Travel and transportation • Per diem or travel allowances • Dissemination costs including renting halls for seminars or attending conferences	• Job aids for health care providers • Training programs for implementers • Commodities needed for intervention which are not being provided by the existing program (e.g., electrocardiogram and audiology equipment, laboratory commodities)	Overhead costs or basic operating costs ranging from electricity to support staff. Most institutions have a standard overhead charge as operating costs are difficult to itemize directly.

*These costs will be minimal if MUE is done mainly by the staffs within the facility

Process Cycle

A MUE cycle should include the following major activities:

- Planning (including selection of medicines to be targeted through the MUE, their criteria and thresholds)
- Implementation (data collection and interpretation)
- Interventions
- Evaluation

A yearly MUE cycle is strongly recommended. Conducting MUEs annually allows the TC to identify trends and assess the impact of medicine use interventions over time.

[10] SIAPS. 2014. Medicine Use Reviews—A Practical Strategy to Ensure the Appropriate Use of Anti-Tuberculosis Medicines. Submitted to the US Agency for International Development by the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program. Arlington, VA: Management Sciences for Health.

Elements of Medicine Use Evaluations

The three components to measuring medicine use are: criteria, indicators, and performance thresholds. Each of theseis described in detail below.

Criteria

Criteria are predetermined measureable aspects of medicine prescribing and use. The TC or MUE committee determines whether guidelines are being followed in actual practice. Three aspects of criteria for appropriate medicine use are justification for use, process (or method of use), and outcome.

Justification for use. This is the medicine's indication, or the standard condition under which the medicine being evaluated should be prescribed. Persons responsible for establishing the criteria may choose to revise the indication definition based on national standard treatment guidelines.

Process (or method of use). This is the standard that describes various elements of how a medicine that is being evaluated is used, and should be monitored during therapy. The main elements are:[11]

- Dosage and administration—recommended dosage, starting dose, dose range, and critical differences among population subsets
- Medicine interactions——a list of other medicines (or classes of medicines) or foods that interact or are predicted to interact in clinically significant ways with the medicine along with practical instructions for preventing or decreasing the likelihood of the interaction
- Contraindications—situations in which the medicine should not be used because the risk clearly outweighs any possible therapeutic benefit
- Adverse medicine reactions—a listing of the most frequently occurring adverse medicine reactions that are important for reasons other than frequency (e.g., leading to discontinuation of medicine or dosage adjustments) and how they are best managed
- Monitoring—recommendations for laboratory tests and treatment monitoring to ensure safe use of medicines
- Patient counseling information—important information regarding patient medicine regimens, weight-based dosing, adverse medicine reactions, treatment monitoring, and duration of treatment to be shared with the patients to engage and empower them in the decision-making process

[11] Food and Medicine Administration. 2006. Requirements on Content and Format of Labeling for Human Prescription Medicines. USA: Food and Medicine Administration. Available at: http://www.fda.gov/ohrms/dockets/98fr/06-545.pdf.

- Storage and handling—When applicable and important, special storage or handling information (e.g., need for refrigeration, reconstitution prior to medicine administration)

Traditionally, the cost of medicines is also monitored (e.g., choosing an expensive oral hypoglycemic to treat type-2 diabetes when a less expensive oral hypoglycemic would have been just as effective with the same number or fewer adverse medicine reactions).

Outcome. The standard anticipated results of medicine (e.g., cured, treatment completed, treatment failed, died, lost to follow-up, not evaluated, or treatment success— the sum of cured and treatment completed).

Annex A provides sample criteria for some anti-TB medicine use reviews. They are comprehensive and some criteria may not be relevant to the context of TCs.The intent of Annex A is to provide examples of a complete, valid, and reliable list of criteria from which the users of these guidelines deduce how a meaningful subset of criteria can be selected and adapted to focus on identifying medication errors, preventable adverse medicine reactions, toxicity, or signs of treatment failure for a particular medicine. An example of select criteria for cycloserine appears in **Error! Reference source not found.**.

Process criteria to consider when prescribing cycloserine
1. Patient history has been reviewed for:
a. Cycloserine or terizidone allergy
b. Epilepsy
c. Depression, severe anxiety, or psychosis
d. Severe renal insufficiency
e. Excessive concurrent use of alcohol
2. HIV status is documented in case records
3. Cycloserine was available for the duration of treatment
4. Dose and Frequency
a. Appropriate cycloserine dosing for adult • 15 to 20 mg/kg daily Not to exceed 1000 mg daily
b. Appropriate cycloserine dosing for pediatric patients • 10 to 20 mg/kg once or twice daily Not to exceed 1000 mg daily

Figure 2. Select Criteria for a Cycloserine MUE

Selecting Criteria

The most important task of the TC orMUE sub-committee is to develop or select criteria and thresholds that serve as the basis for program monitoring and evaluation, then implement interventions (if needed).

Too many criteria create information overload and become burdensome to maintain while too few criteria may only provide a partial picture of medicine use at the facility. Selecting between one and five criteria that are meaningful for the facility can strike a balance between undue burden on human resources and provide results.

Procedures for medicine use criteria should be developed and updated as new information becomes available. Suggested resources include peer-reviewed medical literature (that is, scientific, medical, and pharmaceutical publications in which original manuscripts are published only after having been critically reviewed by unbiased independent experts), compendia (e.g., American Hospital Formulary Service Medicine Information, United States Pharmacopeia-Medicine Information, British National Formulary, WHO International Formulary, Vidal, and Martindale: The Extra Pharmacopeia), package inserts, WHO guidelines, TB specialists, and clinical staff. The list of references used in developing criteria should also be included with the procedures.

Indicators

Indicators are the means to measure achievement and track performance by determining if performance thresholds are being met.

For example, potentional ART program indicators could be:

- Percentage of ART patients receiving a treatment regimen in accordance with national approved STGs
- Percentage of ART patients withdocumented viral load results 12 months from starting ART

Performance Thresholds

A performance threshold (also known as tolerance level or targets) defines a minimum acceptable standard that identifies the point at which non-compliance with medicine use review criteria is of such magnitude to warrant an intervention.

An example of a performance threshold of 95% means that a problem exists if less than 95% of the data collected for a given criterion shows compliance. If serious consequences could result from noncompliance with a given criterion, the threshold should be 100%.

For example, the threshold for correct dosing and administration of all ART treatment must be 100%, since prescribing incorrectly can lead to further medicine resistance, poor treatment outcomes, avoidable adverse effects, and waste of health care resources.
Although a threshold of 100% is ideal, it is not realistic for every criterion. A threshold for documenting results of medicine susceptibility testing may be 90%, as the TC may determine that some deviations may be due to occasional problems at the laboratory, or that deviations are random occurrences that do not signify an ongoing problem.

A smaller threshold percentage may be more appropriate for a new laboratory test that is not yet customarily performed (e.g., second-line medicine resistance testing), then gradually increased as the laboratory test become routine for all cases. Table shows thresholds for sample indicators.

Table 2 Examples of Performance Thresholds for Different Indicators

Indicator	Threshold
Percentage of ART patients receiving a treatment regimen in accordance with national approved standard treatment guidelines	100%
Percentage of ART patients with documented viral load results 12 months after starting treatment	80%
Percentage of ART patients treated with zidovudine with documented heamoglobin results within 6 months of starting treatment	50%, increase by 10% each quarter

Types of Interventions

The TC or MUE sub-committee should develop a document that specifies procedures for the major types of interventions needed to correct medicine use problems. Such interventions might include:

- In-service and continuing education programs
- Written guidelines for medicine use
- Development of special medicine prescription forms
- Changes in health facility policies and procedures
- Namibia essential medicines list (Nemlist) additions and deletions
- Prescribing restrictions or reviews
- Formal and informal counseling

The procedures should also emphasize that interventions are aimed at improving performance and are not punitive.

Strategy Evaluation

Procedures should specify an evaluation at the end of each MUE cycle to make improvements and to assess the clinical and economic impact to the treatment center.

Step 3. Orient Staff to the Process

Prior to data collection in the first process cycle, medical and pharmacy staff should be oriented to the strategy and objectives of the MUE, and build support for the process and get review and input. Medical staff orientation may best be accomplished by disseminating all or part of the MUE procedures -- this includes the monitoring and evaluation schedule, and criteria for each medicine for the staff members' review and input. Dissemination may be done through various print and electronic methods (e.g., memo, newsletter, text, e-mail, website).

Before subsequent MUE cycles, distribution of the monitoring schedule and criteria may be sufficient, but the medical staff should always be informed of changes to MUE procedures.

Step 4. Prepare Data Collection Forms

Before the actual monitoring and evaluation of a medicine begins, the TC or MUE sub-committee must establish methodology for data collection including data elements, data sources, data collection forms, persons responsible, and the number of samples to review.

Data elements: Describe each data element that must be collected during the evaluation (e.g., medicine name, dose, amount prescribed, and duration of therapy). Data elements will vary with criteria. See Annex A for examples.

Data sources: Indicate on a data source table where the selected data elements can be found (e.g.,in-patient histories, laboratory records, pharmacy records, and standard WHO recording and reporting forms).

Data collection forms: Once the data elements are selected, modify the forms to be consistent with those data elements.

Persons responsible: Indicate the persons who will be responsible for collecting, verifying, organizing, and reporting the data.

Number of cases to review: Decide how many patient charts or prescriptions to review, after considering the following aspects:

- Objectives of the evaluation
- Dates to be evaluated
- Time, personnel, and financial resources available

A facility with less than 30 patients should review all prescriptions. Facilities with more than 30 patients should review at least 30 prescriptions, or 5% of prescriptions to a maximum of 100 cases, whichever is greater.[12]

[12] Management Sciences for Health. 2012. MDS-3: Managing Access to Medicines and Health Technologies.

Patient confidentiality: The data collection team, the TC, and medical facilities must ensure that confidentiality of medical records is maintained throughout the MUE process. Each patient's identifiable private information or information related to the patient's past, present, or future medical condition, treatment or payment for care must be protected according to national laws.

Prospective MUE: A prospective MUE compares medicine prescriptions with criteria and implements the intervention before the patient receives the medicine. Its main advantage is its preventive potential, and it should be used when significant non-compliance with criteria has been identified. The impact of this approach is noticeable immediately, and physicians may become accustomed to formal monitoring as a "double check." Various medicine use problems can be detected and prevented from occurring with prospective monitoring, such as:

- Incorrect dosage
- Inappropriate dosage form
- Incorrect route of administration
- Incorrect duration of therapy
- Medicine-medicine interactions
- Medicine-disease contraindications
- Medicine-allergy and other adverse medicine reactions
- Incorrect laboratory orders
- Incorrect therapy monitoring orders

A prospective MUE is most useful for short-term therapy, and does not usually apply to ART and tuberculosis therapy.

The clinical team should routinely perform prospective MUEs in their daily practice (but not collect medicine use criteria data) when evaluating a patient's planned treatment regimen before the patient starts medicine therapy.

This kind of review can be done as a part of the pharmacy's review of new patient medicine orders. Its success depends on a number of factors, including access to full pharmacy records, sufficient workforce, and appropriate knowledge base of potential medicine-medicine and disease-medicine interactions.

Concurrent MUE: A concurrent review involves comparing medicine use with the same criteria as prospective reviews during therapy. The main difference between the two types is that with concurrent monitoring, interventions are corrective.

For example, criteria may be established stating that kanamycin dosage and frequency of administration should be adjusted based on renal function and audiometry tests. The criteria are checked regularly by the clinical team and the prescriber is notified when dosage adjustments may be needed.

Concurrent MUE data collection is similar to prospective MUE data collection in that it may be done in the pharmacy or at the facility. It differs from prospective MUE data collection in that the data collection does not have to occur prior to administration of a first dose.

A concurrent MUE is beneficial at the facility level, as this type of review allows a patient's treatment to be altered if necessary without delay. The clinical team routinely performs concurrent MUEs in their daily practice (but medicine use criteria data are not collected) when they assess the ongoing therapy of their patients and, when necessary, intervene to modify the patient's regimen.

Retrospective MUE: A retrospective review involves reviewing prescribed medicines **after** they are dispensed to the patient. Its main drawback is that interventions cannot be implemented to correct medicine use irregularities for patients who have completed treatment, but can be effective for patients who are still on treatment. It can be used to monitor the same aspects of medicine use listed for a prospective MUE, as well as:

- Comparing medicine prescribing among different physicians
- Comparing medicine prescribing to standard treatment guidelines

Example, a treatment center performs a MUE on kanamycin, and one of the criteria under review is that its use is contraindicated in renal failure. Records for newly diagnosed cases over from the previous three months are reviewed. The review may show that a prescribing problem exists. The medical staff decides to do a more intensive review of all aminoglycosides, with similar results. An education program is conducted for the entire medical staff on aminoglycoside use in renal failure.

Since almost all required data elements are contained in case histories, data collectors typically work in cooperation with the medical records department. Retrieval of data elements that are not contained in the case history, such as treatment preparation, may require visits to the pharmacy or laboratory.

The method of data collection will vary greatly with the approaches (prospective, concurrent or retrospective) chosen. In all cases, forms will be necessary for documenting results.

Retrospective MUEs will be used in most cases by TCs, as they will usually be incorporated into routine supervision and supportive supervision visits, and most patient records reviewed during the visit will be of patients on treatment or of patients who have completed treatment. Also, a retrospective MUE presents the fewest problems with data collection and, therefore, is often the method of choice.

Figure 3,
Figure 4, and Figure 5, show data collection forms evaluating the use of kanamycin.

Page 1 of 3

Kanamycin medicine Retrospective Use Review

[Name of TB Treatment Center]

Case Reviewed	**1**	**2**	**3**	**4**	**5**
Patient Unique Identifier	SC	RK	HW	LH	PD
Health Service Setting (enter one) I—In-patient O— Out-patient C – Community	O	O	O	O	I
Gender	M	M	M	M	F
Age at start of treatment (years and months)	28	52	36	44	37
Weight at start of treatment (kg)	65	59.7	59	61.2	42
Date treatment initiated	20 Oct 11	27 Oct 11	01 Nov 11	11 Nov 11	11 Nov 11
Planned Treatment Duration Intensive Phase (months)	6	7	6	6	6
Planned Treatment Duration Continuation Phase (months)	18	17	18	18	18

Have these patient records been previously inspected During this MUE cycle? If yes enter last month of treatment reviewed	Y 6	Y 3	Y 3	N	N
Enter the last month of treatment inspected today	18	17	18	18	18
Data collector's initials	VK	VK	VK	VK	VK
Date of data collection	25 Feb 13	25 Feb 13	25 Feb 13	25 Feb 13	25 Feb 13

Figure 3. Kanamycin Medicine Use Review

Page 2 of 3 Kanamycin Medicine Use Review [Name of TB Treatment Center]						
Case Reviewed		**1**	**2**	**3**	**4**	**5**
Threshold %		Yes (Y), No (N), or Not Applicable (NA)				
1. HIV status is documented prior to starting treatment	100	N	N	N	Y	Y
2. Pregnancy status is documented for female patients of childbearing potential prior to starting treatment	100	N	N	N	Y	Y
3. Audiometric testing conducted prior to starting treatment	95	Y	Y	N	Y	Y
4. Renal function testing conducted prior to starting treatment	100	N	N	Y	Y	N
5. Serum potassium testing conducted prior to starting treatment	100	N	N	Y	Y	N
6. Serum potassium testing conducted at least monthly During treatment	100	N	N	Y	Y	N
7. Patient has not been coadministered or sequentially administered potentially nephrotoxic, neurotoxic, or ototoxic medicines (**Error! Reference source not found.**)	100	Y	Y	N	Y	Y

Figure 4. Kanamycin Medicine Use Review—Selected Criteria Page

Page 3 of 3 Kanamycin Medicine Use Review [Name of TB Treatment Center] Comments Page	
Data collector Comments Sign and date each entry Patient 3 was taking furosemide (self-medicated). Patient complained of ringing in the ears. Furosemide was stopped. No antihypertensive was required. *VK 25 Feb 13*	MUE/TC Committee Comments

Figure 5 Kanamycin Medicine Use Review—Comments Pages

Step 5. Orient Data Collectors

Data collection for MUEs is usually carried out by physicians, pharmacists, or nurses. Pharmacy interns are often used to conduct data collection. Data collectors should be chosen carefully, and should be familiar with how information is arranged in the patient's history or the prescription, since data are often collected from the case history and prescriptions. Knowledge of the national STGs is important. Depending on their availability, physicians, pharmacists, and nurses that are not directly affiliated with the treatment facility help to avoid the potential for bias.

Ideally, data collection will be conducted during routine supervision visits. If data collection for MUEs is incorporated into routine supervision and supportive supervision visits, supervisors will need orientation be oriented to the MUE process and data collection forms even though they are experienced staff and are quite familiar with the data sources (e.g., patient charts, dispensing records, medication administration records, laboratory reports, electronic records, and standard WHO DR-TB recording and reporting forms).

The objectives of the orientation for data collectors are to:

- Understand the rationale for MUEs
- Discuss the overall MUE process
- Become familiar with the data collection instrument
- Become familiar with acceptable sources of data
- Practice skills required to use the instrument effectively
- Develop a plan for field implementation
- Clarify the logistical issues related to field implementation
- Appreciate that , when appropriately collected, the information derived can facilitate decision-making and improve medicine use

The duration of orientation will depend on the data collectors' experience, the number of medical records to review, the number of medicines to be reviewed, and the number of working hours per day. The schedule should be flexible enough to allow for a few extra days in case the facilities are not ready for data collection.

PHASE 2: CONDUCT THE MUE

This is the execution phase of the MUE. The following three steps describe activities to operationalize the MUE.

Step 6. Collect Data

The quality of the information that the MUE generates depends on the accuracy of data collection. The TC has the overall responsibility for data quality, though all data collectors have a role to play in ensuring data accuracy.

Carry out the following to help ensure greater data accuracy:

- Thorough preparation and orientation
- Test the forms out on three to five patients before collecting data on all patients is helpful in ensuring that the forms and instructions for completion are accurate and understood
- Make sure that each data collector has enough copies of and is familiar with all the data collection instruments they will need for the site(s) for which he or she is responsible
- Give a copy of explicit, written instructions for using the data collection forms to each data collector
- Give each data collector supplies such as pens, notebooks, bags for carrying forms, cell phone airtime, etc.
- Make sure that all the site visits have been approved and scheduled by facility management
- Give data collectors copies of letters of introduction that confirm their identity and authorization to evaluate that site/department.
- Establish procedures to check for data completeness, consistency, plausibility, and legibility in the field when it is still possible to correct errors or to fill in missing information
- At the end of the day, the supervisor should randomly check the quality and completeness of data collection, if feasible. The supervisor should return to randomly selected facilities/departments to collect the same data so as to check the accuracy of the data collected earlier, or if a team of supervisors is conducting a visit, one of the supervisors can check the accuracy of the data collected.
- Develop a system for collecting, grouping, and storing completed data collection forms

Step 7. Tabulate Data

Now you would like to see the results of your work. As information is collected from a small number of patient records (usually not more than 30) it can be tabulated by hand or using an Excel® spreadsheet.

For larger volumes of data, a variety of free software packages are available to download and install on computers for stand-alone (offline, non-web-based) forms development, data entry, and analysis. Examples include Epi-Info[13] and EpiData[14]

A sample data summary table is presented in
Figure 6 below.

[13] Management Sciences for Health. 2012. MDS-3: Managing Access to Medicines and Health Technologies. Arlington, Virginia: Kumarian Press

[14] Dean AG, Arner TG, Sunki GG FR, Lantinga M, Sangam S, Zubieta JC, Sullivan KM, Brendel KA GZ, Fontaine N, Shu M, Fuller G, Smith DC, Nitschke DA and FR. 2011. Epi InfoTM, a database and statistics program for public health professionals. Atlanta, Georgia: CDC. Available at: ftp://ftp.cdc.gov/pub/software/epi_info/7/Epi_Info_7_User_Guide-V1.0_cleared.pdf.

Number of patient records reviewed: 120					
Date(s) data collected: 08 August 14					
Criteria	**Total Number Met**		**Threshold Met**		**Comments**
	YES	**NO**	**Target %**	**Observed %**	
1. CD4 count is done at initiation and patient is eligible for ART.	**120**	**0**	**100**	100	
2. Clinical monitoring done a. There is documented laboratory testing before therapy start	**100**	**0**	**100**	100	
b. There is documented clinical staging prior to commencing treatment	**20**	**0**			
3. Documentation that patient has been evaluated for: a. Kidney function b. Adherence	**92**	**28**	**95**	77	
4. Adult patients were administered 300 mg	**108**	**12**	**100**	90	
5. Tenofavir was administered daily	**99**	**21**	**100**	83	
6. Kidney function is monitored every six months	12	3	**95**	80	
7. Documentation that at least every 3 months patients are advised to abstain from alcohol	***100***	***20***	***95***	83	Patient information sheets are not available at the clinic. Check if there is a problem with providing information or documenting providing information
8. Patient experienced diarrhea	***44***	***76***	***Not Applicable***		
9. Diarrhea was managed by: • Assessing dehydration • Rehydration initiated (if indicated) • Anti-diarrheal therapy was initiated (e.g., loperamide)	***39***	***5***	**100**	89	

Figure 6. Tenofavir Medicine Use Review Summary

Step 8. Interpret Data

Data interpretation is one of the most critical steps in the MUE process. Conclusions drawn from data interpretation could result in changes in treatment, policies, formulary additions or deletions, prescribing restrictions, and counseling of treatment center staff. Information must be carefully aggregated when determining if thresholds were met or exceeded. Whenever feasible, a TC member should review the data collection forms for completeness, and verify questionable data with the prescriptions, or other treatment center records.

If a threshold set at 100% is met (indicating complete compliance with the criteria), it is usually sufficient to simply report the results to the MUE committee.

If a threshold is set at less than 100% (e.g., 80%) and that threshold is not met or exceeded (e.g., 63%), the TC should decide if it is necessary to review those cases that were not in compliance with the criteria. The main purpose of any such review is to determine if there was a justifiable reason for non-compliance. It is not uncommon for a MUE committee to justify cases of non-compliance. In this case, they may decide to change the criteria prior to re-evaluation of the medicine. If non-compliance is determined, a recalculation of the threshold percentage may be considered.

A threshold that is not met may indicate a medicine use problem. As above, cases of non-compliance should be reviewed to determine if medicine use was actually appropriate. If the committee determines that a medicine use problem does exist, the data should be evaluated to determine if the problem is widespread or limited to a few individuals, if the problem is localized to a particular ward or department, or if the problem occurs on one particular treatment center shift. A common finding is that the notes are incomplete or illegible.

PHASE 3: IMPLEMENT AN IMPROVEMENT PLAN

Phase 3 is the key phase to achieving improvement. It consists of using findings from Phase 2 to identify areas that need improvement, and schedule interventions to address any medicine use deficiencies.

The following steps describe activities for effecting change in medicine use practices.

Step 9. Make Recommendations for Improvement

The MUE findings should be discussed at the TC meeting and reported to all stakeholders. When the MUE is conducted by the TC, the findings can also be discussed at supportive supervision visits. When the MUE committee determines that a medicine use problem exists, it recommends one or more interventions that will result in improved medicine use. Interventions can be educational or operational and can target groups, or only those individuals whose performance was not in compliance with medicine use criteria. Some possible interventions are listed below.

Educational interventions can include the following:

- Educational meetings (e.g., conferences, lectures, workshops, or trainings
- Informal and formal counseling
- Letters to health care providers
- Newsletters, medicine use guidelines , and other informational materials
- Clinical literature
- E-mail and text alerts
- Clinical mentoring
- Patient counseling
- Audit and feedback
- Reminders (specific information, provided verbally, on paper, or on a computer, which is designed or intended to prompt a health care provider to recall information)

Operational interventions can include the following:

- Development of medicine prescriptions forms with systematic review
- Changes in treatment center policies and procedures
- Nemlist additions and deletions
- Prescribing restrictions based on level of prescriber's credentials
- Counter signing patient medicine orders
- Implementing or revising STGs
- Improved record keeping
- Purchasing new equipment
- Skill mix changes (changes in number, type, or qualification of staff members)
- Supervisory changes

Step 10. Disseminate Results and Discuss the Improvement Plan

The results of the review and the strategy for improvement are disseminated to appropriate treatment center staff or national policymakers. This step is important because it will help prevent the perception among the medical staff that problem identification was based on anecdotal information, or that interventions are unnecessary or chosen arbitrarily.

The most common dissemination formats are oral presentations at staff meetings, fact sheets, slide or computer presentations, and written reports. Visual aids such as tables, charts, graphs, and photographs can be used effectively to summarize information and add a visual aspect to a written report or oral presentation.

Step 11. Implement the Improvement Plan

Identify the Target Audience

The target audience for an intervention depends primarily on the extent of the problem. If non-compliance with criteria is widespread, the intervention may be aimed at the entire medical staff, or at groups of specialists (e.g., laboratory, nursing, pharmacy, or prescribers). If a small number of prescribers or staff members are non-compliant, interventions may be directly aimed at only those who did not meet the criteria. Those who were fully compliant should be recognized and involved in follow on activities.

Assign Responsibility for Designing and Carrying Out Intervention

Interventions may be designed and carried out by a combination of committee members, treatment center staff, or outside experts. The committee chair is usually responsible for sending letters and counseling activities. Other interventions, such as writing an informational newsletter, or drafting new policies, may be assigned to specialists on the committee or on the treatment center staff. Outside experts may be used to conduct seminars for treatment center staff.

PHASE 4: ASSESS THE EFFECTIVENESS OF THE INTERVENTION

Phase 4 is a crucial step for reviewing the entire cycle of the MUE process and for developing long-term plans to ensure that improvement is sustained and progresses.

Step 12. Conduct a Follow-up MUE

Typically, a re-review is done 6 to 12 monthsfollowing the implementation of an intervention, and involves collecting the same data as in the original MUE from later records. If a comprehensive evaluation with a large number of criteria reviewed revealed a small number of deficiencies, the committee may decide to narrow the focus of the re-review to target only the criteria where results showed that the threshold was not met.

Step 13. Review and Discuss Follow-up Data

At the TC meeting (or post-supportive supervisory meetings), assess the effectiveness of the intervention and document any improvements or remaining deficiencies. When the results show improvement, it is important to communicate that success to the appropriate treatment center staff or national policymakers. When results indicating deficiencies remain, criteria and thresholds may need to be adjusted for the next cycle, or a new corrective action plan may need to be implemented.

Step 14. Evaluate the Strategy

At the end of each cycle, the TC should review the process to identify opportunities for its improvement, and if necessary, make procedural changes to reflect actual practices, or to facilitate desired changes.

Considerations for evaluation include:

- Were criteria developed according to procedures?
- Were thresholds appropriate?
- Were problems identified and appropriately addressed?
- Were interventions appropriate?
- Were medicine use problems solved?
- Are there any remaining deficiencies that need corrective action?
- Did the MUE have an impact on the incidence of inadequate clinical follow-up, adverse medicine reactions, medicine-medicine, medicine-food, medicne-disease, or medicine-laboratory interactions, or medication administration errors?
- Were results disseminated according to procedures?
- Are additional resources (human or financial) required to improve medicine use?

Step 15. Plan and Implement the Next Cycle

Once procedural changes have been made and the guidelines have been updated, plan activities for the next cycle in order to continue improving the use of medicines and measure the impact of MUE activities on medicine use.

CONCLUSION

Providing patients with the correct treatment regimen for the entire treatment period is fundamental to preventing the development of drug resistane, especially for HIV and TB. With new ARV and anti-TB medicines becoming available, rational and responsible medicine use is critical to preserving the effectiveness of current medicines and new medicines.

Strategies to ensure the rational and responsible use of medicines should be an intrinsic part of ART and TB programs and implementing and using MUEs is an excellent strategy. ART managers, clinicians, health care providers, patients, educators, donors, and pharmaceutical companies all contribute to preventing the development of HIV-DR, drug resistant TB (DR-TB), multidrug-resistant TB (MDR-TB), or extensively drug resistant TB (XDR-TB), and optimizing patient outcomes. The experience gained by these individuals and groups in implementing and using this manual will provide valuable recommendations for local adaptation and improvement of future editions.

ANNEX A. AN EXAMPLE OF PUBLISHED CRITERIA FOR FIRST LINE ANTI-TUBERCULOSIS TREATMENT

Please be aware of the following when using information in this annex. Although the medicine information in this document is extensive, it is not intended to replace national standard treatment guidelines, package inserts, or other printed material that may be available or accompany a particular medicine.

Only medicines on the WHO Model Essential Medicines Lists[15][16] are referenced in this document. Ancillary medicines or concomitant medicines on National Essential Medicine Lists that do not appear on the WHO Model Lists should be checked for

- Interactions with anti-TB medicines
- Contraindications for coadministration with anti-TB medicines
- Correct dose and administration for treatment of adverse medicine reactions

These should be added to the information in Annex A.

Children older than 12 years of age can be managed as adults.[17]

Consult with a TB specialist or clinical pharmacist about the clinical use of **any** medicine administered to a patient.

[15] World Health Organization. 2013. WHO Model List of Essential Medicines. Available at: http://apps.who.int/iris/bitstream/10665/93142/1/EML_18_eng.pdf?ua=1.
[16] World Health Organization. 2013. WHO Model List of Essential Medicines for Children. Available at: http://apps.who.int/iris/bitstream/10665/93143/1/EMLc_4_eng.pdf?ua=1.
[17] The Sentinel Project for Pediatric Medicine-Resistant Tuberculos. 2012. Management of Tuberculosis in Children : A Field Guide. Boston, USA.

Criteria for Rifampicin[1]

I. ***Justification criteria*** for prescribing rifampicin

1. TB is microbiologically confirmed (e.g., smear, culture, WHO-approved rapid diagnostics)
2. Clinically diagnosed by a TB medical provider (e.g., X-ray abnormalities or suggestive histology)
3. Laboratory medicine susceptibility testing (DST) documents that the organism is susceptible to rifampicin
4. According to national TB treatment guidelines

II. ***Process criteria*** to consider when prescribing rifampicin

1. Administer in conjunction with other effective chemotherapy and not as the sole therapeutic agent
2. Patient history has been reviewed for:
   a. Previous discontinuation of rifampicin
   b. Hypersensitivity to rifampicin or other rifamycins
   c. Impaired liver function
   d. Impaired kidney function
   e. History of diabetes
   f. Excessive concurrent use of alcohol
   g. Porphyria
3. HIV status is documented in case records
4. Rifampicin was available for the Duration of treatment
5. **Dose and frequency**
   a. Appropriate dosing for adult patients
      - 10 mg/kg (8 to 12 mg/kg) daily
        Not to exceed 600 mg daily
   b. Appropriate dosing for renal dysfunction (creatinine clearance less than 30 mL/min or patients receiving hemodialysis)
      - No adjustment necessary
        Administer rifampicin following dialysis on dialysis days

[1] SIAPS. 2014. Medicine Use Reviews—A Practical Strategy to Ensure the Appropriate Use of Anti-Tuberculosis Medicines. Submitted to the US Agency for International Development by the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program. Arlington, VA: Management Sciences for Health.

Criteria for Rifampicin[1]

c. Appropriate dose for pediatric patients
   - 10 to 20 mg/kg daily
     Not to exceed 600 mg daily

6. **Administration**
   - For oral use
   - Give by mouth on an empty stomach, one hour before or two hours after meals
   - May be given with a small amount of food if it irritates the stomach

   a. For parenteral use—May be administered intravenously if patient cannot tolerate oral medication
      - Must not be administered intramuscularly or subcutaneously
      - The reconstituted solution is stable at room temperature 15 to 25°C, for 24 hours
      - Rifampicin can be added to the following diluents for infusion:
        - glucose 5% for injection (stable at room temperature for up to 4 hours)
        - normal saline (stable at room temperature for 24 hours)
      - Administer 500 mL infusion over 3 hours, or 100 mL infusion over 30 minutes
      - Store vials of powder at 25°C excursions permitted to 15 to 30°C
      - Avoid temperatures above 40°C
      - Protect from light

   b. In pregnancy, phytomenadione (vitamin K) should be administered at birth to the infant of a mother taking rifampicin because of the risk of postnatal hemorrhage

7. **Duration**

a. Medicine susceptible TB	Intensive phase	2 months
	Continuation phase	4 months

8. **Patient monitoring**

   Adults—Prior to treatment and then at least monthly During treatment

   a. Weight

   b. Pregnancy testing—according to standard clinical protocol

   c. Liver function
      - AST (SGOT)
      - ALT (SGPT)
      - Total bilirubin

   Note: for patients with impaired liver function— Prior to treatment and then every 2 to 4 weeks During treatment:

Criteria for Rifampicin[1]

d. Renal function
   One or more of the following laboratory measurements:
   - Blood
     - Creatinine clearance rate (either carefully measured or estimated from published nomograms or equations based on patient's age, sex, body weight, and serial creatinine concentrations— preferred over BUN)
     - Serum creatinine concentration (preferred over BUN)
     - Blood urea nitrogen (BUN)
     - Non-protein nitrogen (NPN)
   - Urine
     - Proteinuria
     - Presence of cells and casts
     - Specific gravity

e. Complete blood count with differential

f. Platelet count

Pediatrics—none required unless a complicating condition is known or clinically suspected

Patients with diabetes—Prior to therapy and then at least daily until stabilized During therapy:

- Blood glucose

g. HIV testing —according to standard clinical protocol

9. **Therapeutic medicine monitoring—**rifampicin blood levels
   a. Recommended only for patients suspected of having malabsorption or treatment failure
   b. Peak concentrations should be obtained 2 hours after a dose, and if delayed absorption is considered, a concentration at 6 hours should also be collected
   c. Peak concentrations of 8 to 24 mcg/ml are expected
   d. Dose increase should be strongly considered for low concentrations (but not for delayed absorption), as rifampicin exhibits a dose response in treatment of TB.
      See **Error! Reference source not found.** for guidance on how to adjust dose based on serum concentration.
10. **Medicine interactions**

Criteria for Rifampicin[1]

a. The dose of rifampicin may need to be decreased when coadministered with the following medicines or classes of medicines
   - Antimycotics—azole derivatives (e.g., fluconazole—reduce rifampicin by half)
   - Calcium channel blockers (e.g., verapamil, enalapril)
   - Chloramphenicol
   - Clarithromycin (reduce rifampicin dose by half)
     - Other macrolide antibiotics (e.g., azithromycin, erythromycin)
   - Fluoroquinolones (e.g., levofloxacin)
   - Haloperidol
   - Indinavir (reduce rifampicin dose by half)
     - Other protease inhibitors (**do not coadminister ritonavir or saquinavir**)
   - Levothyroxine
   - Progestins (e.g., norethindrone enantate)
   - Pyrazinamide
   - Sulfamethoxazole
   - Sulfasalazine
   - Tricyclic antidepressants (e.g., amitriptyline)
   - Trimethoprim
   - Zidovudine
b. The dose of rifampicin may need to be increased when coadministered with the following medicines or classes of medicines:
   - Carbamazepine
   - Mifepristone
   - Omeprazole
   - Quinine

Criteria for Rifampicin[1]

c. The dose of the following medicines or classes of medicines may need to be increased when coadministered with rifampicin
   - Anticonvulsants (e.g., carbamazepine, ethosuximide, phenytoin, valproic acid)
   - Antimycotics—azole derivatives (e.g., fluconazole)
   - Barbiturates (e.g., phenobarbital)
   - Benzodiazepines (e.g., diazepam, midazolam)
   - Beta blockers (e.g., propranolol)
   - Calcium channel blockers (e.g., verapamil)
   - Cardiac glycosides (e.g., digoxin)
   - Ciclosporin
   - Clarithromycin
   - Other macrolide antibiotics (e.g., azithromycin, erythromycin)
   - Corticosteroids (e.g., prednisolone, methylprednisolone)
   - Coumarin anticoagulants (e.g., warfarin)
   - Dapsone
   - Indinavir
     - Other protease inhibitors (**do not coadminister ritonavir or saquinavir**)
   - Lidocaine
   - Mifepristone
   - Non-nucleoside reverse transcriptase inhibitors (e.g., nevirapine; do not coadminister delavirdine)
   - Nucleoside and nucleotide reverse transcriptase inhibitors (e.g., zidovudine)
   - Estrogens
   - Opiate analgesics (e.g., morphine)
   - Oral hypoglycemics (e.g., metformin)
   - Praziquantel
   - Pyrazinamide
   - Sulfamethoxazole
   - Trimethoprim
   - Vincrisinte

d. If co-infected with HIV, patient is not coadministered ritonavir-boosted protease inhibitors ritonavir or saquinavir

e. Patient is not coadministered halothane

f. Rifampicin impairs the effectiveness of oral contraceptives
   - Recommend the use of another form of contraception

g. Antiretrovirals may have additive or synergistic toxicities, or cause sub-therapeutic levels when coadministered
   - If necessary to coadminister, monitor adverse medicine reactions carefully. Refer to **Error! Reference source not found.**.
   - Adjust doses as described in **Error! Reference source not found.**

Criteria for Rifampicin[1]

h. Hepatotoxic and nephrotoxic medicines
   - May potentiate toxicities
   - If necessary to coadminister, monitor adverse medicine reactions carefully
     Refer to **Error! Reference source not found.**

i. May cause false-positive urine opiate screening test results
   - Confirm with gas chromatography/mass spectrometry
   - May inhibit microbiological assays for serum folate (vitamin B9) and hydroxocobalamin (vitamin B12)
   - Consider alternate assay methods

j. May case abnormalities in liver function tests (LFTs) and reduce excretion of gall bladder contrast media
   - Conduct LFTs and gall bladder imaging prior to morning dose of rifampicin

11. **Patient counseling**

a. Advise patient
   - Rifampicin may produce a reddish coloration of the urine, tears, saliva, sweat, semen, and sputum; contact lenses and clothing may be permanently stained
   - Rifampicin may affect the reliability of oral or other systemic hormonal contraceptives and should consider using non-hormonal contraceptive measures During treatment and four to eight weeks after stopping treatment
   - Take rifampicin one hour before or two hours after food or antacids with a full glass of water

b. Advise patient to contact a health care provider immediately if they experience
   - Unusual fatigue or loss of appetite
   - Severe abdominal upset
   - Fever or chills
   - Nausea or vomiting
   - Darkened urine
   - Yellowish discoloration of the skin and eyes
   - Pain or swelling of the joints

c. Advise patients who are pregnant or planning to become pregnant of the potential risks and potential benefits of starting TB treatment
   - US Food and Medicine Administration Pregnancy Category C
   - Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans
   - Potential benefit should outweigh the potential risk

d. Advise patients who are breastfeeding
   - Most medicines used to treat TB cross into breast milk at low levels
   - The amount of anti-TB medicines that babies receive through breast milk will not treat or prevent TB in the infant

Criteria for Rifampicin[1]

III. ***Complications*** that could occur During therapy with rifampicin and how to respond if the complication presents as follows:[2]

Severe or common toxicities are indicated by **bold** font

1. **Hepatitis and other hepatotoxicity** (less than five times the upper limit of normal) with or without jaundice (greatly increased or decreased frequency of urination or amount of urine, increased thirst, loss of appetite, nausea, vomiting)
   - Monitor liver function tests and bilirubin weekly
   - Once resolved, monitor liver function monthly
2. **Hepatitis and other hepatotoxicity** (more than five times the upper limit of normal) with or without jaundice (greatly increased or decreased frequency of urination or amount of urine, increased thirst, loss of appetite, nausea, vomiting)
   - Stop all hepatotoxic medicines
   - Continue with three non hepatotoxic medications (e.g., the injectable agent, fluoroquinolone, and cycloserine)
   - If hepatitis does not resolve, stop all medications
   - Rule out other potential causes of hepatitis (e.g., viral hepatitis, alcohol induced hepatitis); and if identified, treat according to standard clinical protocol
   - Reintroduce medicines, individually with the least hepatotoxic agent first while monitoring liver function every three days, and if the most likely agent is not essential consider not reintroducing it
   - Once resolved, monitor liver function monthly
3. Nephrotoxicity or renal failure
   - Consider dosing two or three times a week if medicine is essential to the regimen
   - Monitor creatinine closely
   - Adjust all anti-TB medications according to the creatinine clearance
   - Discontinue rifampicin if serum creatinine is greater than 100 mcg/mL
   - Modify regimen according to national TB treatment guidelines
4. **Hypersensitivity, mild** (skin itching, redness, rash, swelling)
   - Initiate antihistamine therapy (e.g., loratadine); corticosteroids (e.g., prednisolone, methylprednisolone), and hydrocortisone cream or calamine lotion

     Note: Concurrent antihistamine administration with regimens containing aminoglycocides may mask the symptoms of ototoxicity such as tinnitus, dizziness, or vertigo
5. **Hypersensitivity, severe** (e.g., eosinophilia, medicine fever, blood dyscrasias, angioedema, exfoliative dermatitis, stomatitis, shortness of breath, edema of face and extremities, hypotension, anaphylactic shock, Stevens-Johnson syndrome)

[2] For mild reactions, encourage patients to continue to take the medication and assure them that for most patients many adverse reactions lessen over the first several weeks and may become tolerable or resolve entirely

Criteria for Rifampicin[1]

- Initiate antihistamine therapy (e.g., loratadine); corticosteroids (e.g., prednisolone, methylprednisolone)

  Note: Concurrent antihistamine administration with regimens containing aminoglycocides may mask the symptoms of ototoxicity such as tinnitus, dizziness, or vertigo

- Stop all therapy under cover of antihistamines
- Stop all therapy until reaction resolves
- Modify regimen according to national TB treatment guidelines
- Serious acute hypersensitivity reactions may require treatment with epinephrine and other resuscitative measures, including oxygen, intravenous fluids, antihistamines, corticosteroids, pressor amines, and airway management, according to standard clinical protocol
- Rechallenge cutaneous hypersensitivity reactions with or without desensitization

  DO NOT attempt medicine desensitization with severe skin, mouth, or mucous membrane reactions (e.g., exfoliative dermatitis and Stevens-Johnson syndrome)

6. **Reddish coloration of body fluids** (e.g., urine, stools, tears, saliva, sweat, semen, and sputum)
   - Counsel patients to expect discoloration
   - Advise patients that contact lenses may be stained
   - Reassure patient that symptoms are harmless and will subside as treatment progresses
7. Hematological abnormalities (e.g., **thrombocytopenia**, disseminated intravascular coagulation, leukopenia, **acute hemolytic anemia**, decreased hemoglobin, agranulocytosis)
   - Stop all therapy pending resolution of toxicity
   - Eliminate other potential causes of toxicity
   - Consider suspending most likely agent permanently
   - Reintroduce remaining medicines, one at a time with the least myelotoxic agents first, while frequently monitoring hematology
8. Purpura
   - Suspect thrombocytopenia
   - Discontinue rifampicin as soon as purpura occurs
   - Modify regimen according to national TB treatment guidelines
   - Cerebral hemorrhage and fatalities have been reported when rifampicin administration has been continued or resumed after the appearance of purpura
9. Nausea, vomiting, anorexia
   - Administer with small meals and advise patient to swallow tablets slowly with small sips of water
   - Give medication at a time of day to minimize the effects (consult the patient as to timing of medicines)
   - Assess for dehydration, electrolyte disturbances, hepatitis

Criteria for Rifampicin[1]

- Initiate rehydration if indicated
- Initiate antiemetic therapy (e.g., metoclopramide, ondansetron)
- Decrease frequency of rifampicin administration
- Discontinue rifampicin if this can be done without compromising regimen—rarely necessary

10. **Gastritis and abdominal pain**
    - Rule out other causes (e.g., pancreatitis, lactic acidosis, hepatitis)
    - Treat with H2-blockers (e.g., ranitidine), or proton-pump inhibitors (e.g., omperazole)
    - Stop rifampicin for short periods of time (e.g., one to seven days)
    - Discontinue rifampicin if this can be done without compromising the regimen
    - Modify regimen according to national TB treatment guidelines
11. **Flu-like syndrome** (e.g., fever, chills and malaise)
    - Change from intermittent to daily rifampicin
    - Provide symptomatic treatment as listed for individual
12. Fever
    - Rule out other causes
    - Paracetamol or ibuprofen can be given to lower the temperature

      Note: NSAIDs, such as ibuprofen, may contribute to renal toxicity
      Exercise caution with use and monitor renal function

    - Fluids may be given by mouth or IV to prevent dehydration, if necessary
13. Headache
    - Rule out other causes (e.g., meningitis or other central nervous system infections)
    - Give medication at a time of day to minimize the effects (consult the patient as to timing of medicines)
    - Encourage adequate fluid intake
    - Treat with ibuprofen, paracetamol, or aspirin
    - Treat migraine headaches with analgesics, low-dose beta-blockers, supportive measures

      Note: NSAIDs, such as ibuprofen, may contribute to renal toxicity
      Exercise caution with use and monitor renal function

    - Address stressors potentially contributing to tension-related headaches
    - Consider administering amitriptyline 50 to 150 mg at night
    - Consider administering mild opiate-containing analgesics (e.g., paracetamol with codeine)
    - Consider neurology consultation
    - Consider reducing the frequency of rifampicin administration to five times or even three times per week

Criteria for Rifampicin[1]

14. Central nervous system-related adverse medicine reactions (confusion)
    - Generally occurs During first few weeks of therapy
    - Reassure patient that symptoms will subside as treatment progresses
    - Suspect medicine-induced acute liver failure if there is jaundice
    - Give medication at a time of day to minimize the effects (consult the patient as to timing of medicines)
    - Consider reducing the frequency of rifampicin administration to five times or even three times per week
    - Discontinue rifampicin if this can be done without compromising regimen— rarely necessary
15. Visual disturbances
    - Generally occurs During first few weeks of therapy
    - Reassure patient that symptoms will subside as treatment progresses
    - Refer to ophthalmologist if condition persists
16. Menstrual disturbances
    - Reported when used with hormonal contraceptives
    - Consider non-hormonal contraceptive measures
17. Diarrhea, flatulence
    - Encourage patients to tolerate some degree of loose stools and flatulence
    - Encourage fluid intake
    - Assess for dehydration; initiate rehydration if indicated
    - Assess for electrolyte disturbances; initiate replacement therapy if indicated
    - Initiate anti-diarrheal therapy (e.g., loperamide)
    - Administer lactobacillus or encourage foods such as yogurt
    - Evaluate for *C. difficile* and other infections
    - Decrease frequency of rifampicin administration
    - Discontinue rifampicin if this can be done without compromising regimen— rarely necessary
18. *Clostridium difficile*-associated diarrhea
    - Bowel rest
    - Appropriate fluid and electrolyte management
    - Protein supplementation
    - Antibiotic treatment of *C. difficile*
    - Surgical evaluation should be instituted as a last resort, if clinically indicated
    - Discontinue rifampicin
    - Modify regimen according to national TB treatment guidelines
19. Blood glucose disturbances
    - Monitor blood glucose
    - Initiate or adjust oral hypoglycemic agent or insulin—according to standard clinical protocol

Criteria for Rifampicin[1]

20. Metabolic acidosis
    - Monitor serum electrolytes and arterial blood gasses
    - Initiate sodium hydrogen carbonate therapy—according to standard clinical protocol
21. Ergocalciferol (Vitamin D) deficiency
    - Check Vitamin D
    - If Vitamin D is low also check for hypocalcemia, hypophosphatemia, and elevated parathyroid hormone
    - Initiate Vitamin D therapy—according to standard clinical protocol
22. Porphyria
    - Discontinue rifampicin
    - Consider dosing 2 to 3 times a week if medicine is essential to the regimen and patient can tolerate
    - Provide symptomatic therapy, high carbohydrate intake, and intravenous administration of hematin
    - Modify regimen according to national TB treatment guidelines
23. Overdosage
    - Intensive support measures should be instituted and individual symptoms treated as they arise
    - The airway should be secured and adequate respiratory exchange established
    - Since nausea and vomiting are likely to be present, gastric lavage within the first 2 to 3 hours after ingestion is probably preferable to induction of emesis
    - Following evacuation of the gastric contents, instilling activated charcoal slurry into the stomach may help absorb any remaining medicine from the gastrointestinal tract
    - Antiemetic medication may be required to control severe nausea and vomiting
    - Active diuresis (measuring intake and output) will help promote rifampicin excretion
    - For severe cases, extracorporeal hemodialysis may be required. If this is not available, peritoneal dialysis can be used along with forced diuresis

ANNEX B. SAMPLE DATA COLLECTION FORMS[1]

Kanamycin Retrospective Medicine Use Review **Adult Patients** **[Name of Treatment Center]**			**Page 1 of ___**
Case Reviewed	**1**	**2**	**3**
DR-TB Case Number			
Health Service Setting (enter one) I—Inpatient O—Outpatient C—Community			
Diagnosis	DR-TB	DR-TB	DR-TB
Gender			
Age at start of treatment (years and months)			
Weight at start of treatment (kg)			
Date Treatment Initiated			
Planned Treatment Duration Intensive Phase (months)			
Planned Treatment Duration Continuation Phase (months)			

[1] SIAPS. 2014. Medicine Use Reviews—A Practical Strategy to Ensure the Appropriate Use of Anti-Tuberculosis Medicines. Submitted to the US Agency for International Development by the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program. Arlington, VA: Management Sciences for Health.

Have these chart notes been previously inspected During this Medicine Use Review cycle? If yes, enter last month of treatment inspected.	No	No	No
Enter the last month of treatment inspected today.			
Data Collector's initials			
Date Data collected			

Kanamycin Retrospective Medicine Use Review **For Adult Patients** **[Name of Treatment Center]** **Page ___ of ___**				
Case Reviewed		**1**	**2**	**3**
DR-TB Case Number				
Threshold, %		Y (Yes), N (No), ND (Not Documented), NA (Not applicable)		
Justification Criteria				
1. TB is microbiologically confirmed (e.g., smear, culture, WHO-approved rapid diagnostics)	100			
2. Laboratory medicine susceptibility testing (DST) documents the organism resistance is resistant to rifampicin and isoniazid	100			
3. Laboratory medicine susceptibility testing (DST) documents the organism resistance is susceptible to kanamycin	100			
Process Criteria				
1. Past medical history documents screening for a. Kanamycin allergy	100			
b. Aminoglycoside allergy	100			
c. Possibility of pregnancy (if applicable)	100			
d. Hearing disorders	100			
e. Vestibular disorders	100			
f. Neuromuscular disorders (e.g., myasthenia gravis or Parkinson's Disease)	100			

Kanamycin Retrospective Medicine Use Review **For Adult Patients** **[Name of Treatment Center]**				**Page ___ of ___**
Case Reviewed		**1**	**2**	**3**
DR-TB Case Number				
Threshold, %		Y (Yes), N (No), ND (Not Documented), NA (Not applicable)		
2. HIV status is documented in case records	100			
3. Audiometric or caloric stimulation testing conducted prior to starting treatment	100			
4. Renal function testing conducted prior to starting treatment	100			
5. Liver function testing conducted prior to starting treatment	100			
6. Serum potassium testing conducted prior to starting treatment	100			
7. Patient has not been coadministered or sequentially administered potentially nephrotoxic, neurotoxic, or ototoxic medicines (**Error! Reference source not found.**)	100			
8. Patient has been advised to contact a health care professional if they experience problems with hearing, dizziness, or balance	100			
9. Patients who are pregnant or planning to become pregnant have been advised of the potential risks and potential benefits of starting TB treatment	100			
10. Patient's weight is documented prior to starting treatment and at least monthly	100			
11. Patent's weight has changed since initiation of treatment	NA			

Kanamycin Retrospective Medicine Use Review **For Adult Patients** **[Name of Treatment Center]**				**Page ___ of ___**
Case Reviewed		**1**	**2**	**3**
DR-TB Case Number				
Threshold, %		Y (Yes), N (No), ND (Not Documented), NA (Not applicable)		
12. Appropriate kanamycin dosing for **adult** patients • 15 to 20 mg/kg **OR** Appropriate kanamycin dosing for renal dysfunction (creatinine clearance less than 30 mL/min or patients receiving hemodialysis) • 12 to 15 mg/kg per dose • Two or three times per week • After dialysis if administered on dialysis days	95			
13. Kanamycin dose is less than or equal to 1,000 mg	100			
14. Kanamycin was administered for at least 8 months				
15. Kanamycin is administered at least six times per week	95			
16. Audiometric or caloric stimulation testing conducted monthly	75			
17. Liver function testing conducted at least monthly	100			
18. Renal function testing at least monthly	100			
19. Serum potassium testing conducted at least monthly	100			

Kanamycin Retrospective Medicine Use Review **For Adult Patients** **[Name of Treatment Center]**				**Page ___ of ___**
Case Reviewed		**1**	**2**	**3**
DR-TB Case Number				
Threshold, %		Y (Yes), N (No), ND (Not Documented), NA (Not applicable)		
20. HIV-positive patients are monitored for potentially overlapping antiretroviral toxicities (See **Error! Reference source not found.**)	100			
a. Ototoxicity (e.g., clumsiness, dizziness, nausea, vomiting, unsteadiness, any loss of hearing, ringing or buzzing, a feeling of fullness in the ears)	100			
• Management – Document events and compare with prior to starting treatment – Decrease frequency (e.g., three times a week)	100			
b. Nephrotoxicity	100			
• Management – Consider dosing 2 to 3 times a week if medicine is essential to the regimen – Monitor creatinine daily	100			
c. Peripheral Neuropathy (burning of face or mouth, numbness, tingling)	100			
• Management – Administer pyridoxine 200 to 300 mg per day	100			

Kanamycin Retrospective Medicine Use Review **For Adult Patients** **[Name of Treatment Center]** **Page ___ of ___**				
Case Reviewed		**1**	**2**	**3**
DR-TB Case Number				
Threshold, %		Y (Yes), N (No), ND (Not Documented), NA (Not applicable)		
d. Injection site reactions	100			
• Management – Rotate injection sites	100			
e. Hypersensitivity, mild (skin itching, redness, rash, or swelling)	100			
• Management – Initiate antihistamine therapy (e.g., loratadine); corticosteroids (e.g., prednisolone, methylprednisolone), and hydrocortisone cream or calamine lotion	100			
f. Hypersensitivity, severe (eosinophilia, fever, blood dyscrasias, angioedema, exfoliative dermatitis, stomatitis, and anaphylactic shock)	100			
• Management – Eliminate kanamycin from regimen	100			

Kanamycin Retrospective Medicine Use Review

Adult Patients

[Name of Treatment Center] **Page ___ of ___**

Data Collector Comments **Sign and Date each comment**	**MUR Committee Comments**

ANNEX C: MOHSS TERMS OF REFERENCE (TOR) FOR TCS JUNE 2011

REPUBLIC OF NAMIBIA

Ministry of Health and Social Services

TERMS OF REFERENCE

DISTRICT THERAPEUTICS COMMITTEE

Purpose

A committee of clinical and pharmacy staff set up to share information, discuss issues, solve problems and make decisions about matters relating to prescribing and management of pharmaceuticals and related supplies. The committee shall also monitor the appropriate use of blood and blood products. The committee should act as an advisory body, recommending necessary action to the District Coordinating Committee (DCC).

Functions

1. Review and monitor usage patterns of pharmaceutical, clinical and radiographic supplies in the institution with a view to ensuring appropriate and cost-effective use of these important and essential resources.
2. Assist in revising and operationalising the Namibian Essential Medicines List (Nemlist).
3. Draw up and maintain an institution-specific list of essential supplies (i.e. medicines and clinical supplies), within the national essential lists, based on local health conditions and expertise.
4. Monitor and control institutional expenditure on medicines and related supplies and to ensure adherence to budget allocation.
5. Coordinate and approve all requests for items that are not authorised for the institution.
6. Monitor and coordinate reports of medicine related adverse events which may influence the quality of patient care and to coordinate reporting of such adverse events to the Regional level and to the national Therapeutic and Pharmacovigilance Centre (TIPC).
7. To help to develop guidelines on the use of medicines and to implement and enforce their use.
8. To discuss matters arising from National Level and the Regional Therapeutics Committee meetings, with a view to devising strategies to ensure implementation.
9. To discuss any problems that concern prescribing or medicine supply. Examples are as follows;
   - Improper use of specialist medicines.
   - Nurses prescribing AB medicines.
   - Prescribing of medicines not on the Nemlist.

Terms of Reference for District Therapeutics Committee

- Incomplete prescriptions.
- Illegal prescriptions.
- Use of generic names of medicines.
- Uneconomical use of clinical supplies.
- Problems with medicine supplies and distribution.
- Medicines out of stock.
- Short dated medicines that could be prescribed preferentially to avoid wastage due to expiry.
- Inappropriate prescribing habits.
- Following of guidelines.
- Recommendations for changes to the Nemlist.
- Control and prescribing of Schedule 4 medicines.

10. To discuss any problems that concern the appropriate use of blood and blood products. Examples are as follows;
    - To develop a maximum surgical blood ordering schedule and other procedures as defined in Guidelines for the Appropriate Clinical Use of Blood and Blood Products (GACUB).
    - To monitor the availability, safety, adequacy and reliability of the supply of blood, blood products and other alternatives to blood transfusion (Crystalloids, colloidal and haematinics)
    - To promote the effective implementation of GACUB including the monitoring of the usage of blood and blood products
    - To review incidents of severe adverse effects or errors associated with transfusion and to identify any corrective action required.
    - To ensure appropriate bio-safety and waste management of blood and blood products.

Composition

The committee should consist of all Medical Officers, Nursing Managers, PHC Supervisor, Nurse in charge of OPD, Nurses in charge of wards and theatre, all Pharmacist's Assistants and all Pharmacists (*where available*). Any private doctors who admit patients to state hospitals should attend or be represented. A representative of Namibia Institute of Pathology (NIP) should be present at all meetings during discussions around use of blood and blood products. Representatives from Radiography, Environmental Officers, Dentists, Dental Therapists and the Control Officer can also be included.

The Chairperson of the District Therapeutic Committee shall be the Principal Medical Officer (PMO). The Chairperson shall organise the meetings and ensure that a clear agenda is distributed in advance. The Pharmacist or Pharmacist's Assistant should be the secretary and where there is no Pharmacist or Pharmacist's Assistant a secretary should be appointed to co-ordinate the committee and write minutes.

Terms of Reference for District Therapeutics Committee

Procedures

1. Meetings shall be held at least once a month.
2. The secretary shall send an agenda specifying matters to be discussed, to all members, one week prior to the meeting. Members should contribute agenda points before that time.
3. More than half of the members shall constitute a quorum at any meeting.
4. If the chairperson is unavailable to attend any meeting he/she can delegate that function to another member.
5. The proceedings of the meeting shall be recorded in the form of minutes and shall be signed and dated by the chairperson and secretary. Corrections of the minutes will be recorded on the next minutes.
6. Within 2 weeks of the meeting the secretary shall send copies of the minutes to all Therapeutics Committee members and to the regional level.