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MINISTRY OF HEALTH

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Timely Accurate Diagonostics for a TB-Free Africa

Training on Proficiency Testing Scheme GeneXpert DTS

Module 1: Overview of proficiency testing

Venue:

Presenter:

Date:

Introduction

Proficiency testing is a essential part of the quality management system that supports laboratories in checking and maintaining quality.

Objectives

By the end of this module participants should be able to

- Define EQA
- Understand the different proficiency testing schemes implemented in TB network
- Understand the different factors to consider before establishing a PT scheme

Module outline

- Introduction
- Uganda SRL scenarios
- Getting started: Issues to Consider for a PT scheme

The Need for Better Diagnostics

- **TB remains one of the world's top infectious killers of our time**

- **Many people die from TB due to delayed diagnosis and treatment initiation**
  - Demonstrates the need for more rapid diagnostics

l tuberculosis report 2018. Geneva: World Health Organization; 2018. WHO/CDS/TB/2018.20.
https://www.who.int/tb/publications/global_report/en/

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Working to End TB

The World Health Organization (WHO) End TB Strategy calls for an end to the global tuberculosis (TB) epidemic, aiming to:

- Reduce deaths by 95%
- Cut new TB cases by 90%,
- Ensure that no family is burdened with catastrophic expenses due to TB

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End TB Strategy – global strategy and targets for tuberculosis prevention, care and control after 2015. http://www.who.int/tb/strategy/End_TB_Strategy.pdf

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The End TB Strategy

WHO-recommended rapid TB diagnostics (WRDs) should be available to all persons with signs or symptoms of TB

- **All bacteriologically confirmed TB patients should receive drug-susceptibility testing (DST) at least for rifampicin (RIF)**
- **All patients with RIF-resistant TB should receive DST at least for fluoroquinolones and second-line injectable drugs**

l tuberculosis report 2018. Geneva: World Health Organization; 2018. WHO/CDS/TB/2018.20.
https://www.who.int/tb/publications/global_report/en/

Cepheid Xpert MTB/RIF

The Xpert MTB/RIF® test is a cartridge-based, automated WRD run on the GeneXpert® platform (Cepheid Inc.; Sunnyvale, CA, USA).

- **The test can simultaneously detect Mycobacterium tuberculosis complex bacteria (MTBC) and resistance to RIF in less than two hours.**

Potential Gains

The Xpert MTB/RIF test has the potential to:

- Significantly decrease diagnostic dela
- Increase the detection of drug resista
- Impact TB transmission

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Significant Challenges

There are a variety of challenges to providing quality Xpert MTB/RIF results:

- Inadequate training and mentoring
- Lack of, or poor adherence to, standard operating procedures (SOPs)
- Stock-outs and use of expired reagents
- Inadequate maintenance of equipment
- Poor quality of samples being tested
- Lack of regular on-site supportive supervision
- Lack of monitoring and evaluation of the TB diagnostic network

Introduction to Quality Assurance and Continuous Quality Improvement

Quality assurance (QA) is a system that monitors the various aspects of a diagnostic process ensuring that the results it produces are *accurate*, *reliable* and *timely*.

Implementation of quality assurance (QA) activities across the TB diagnostic network is part of the continuous quality improvement (CQI) process. CQI is a cyclical, continuous process-based, data-driven approach to improving the quality of diagnostic testing.

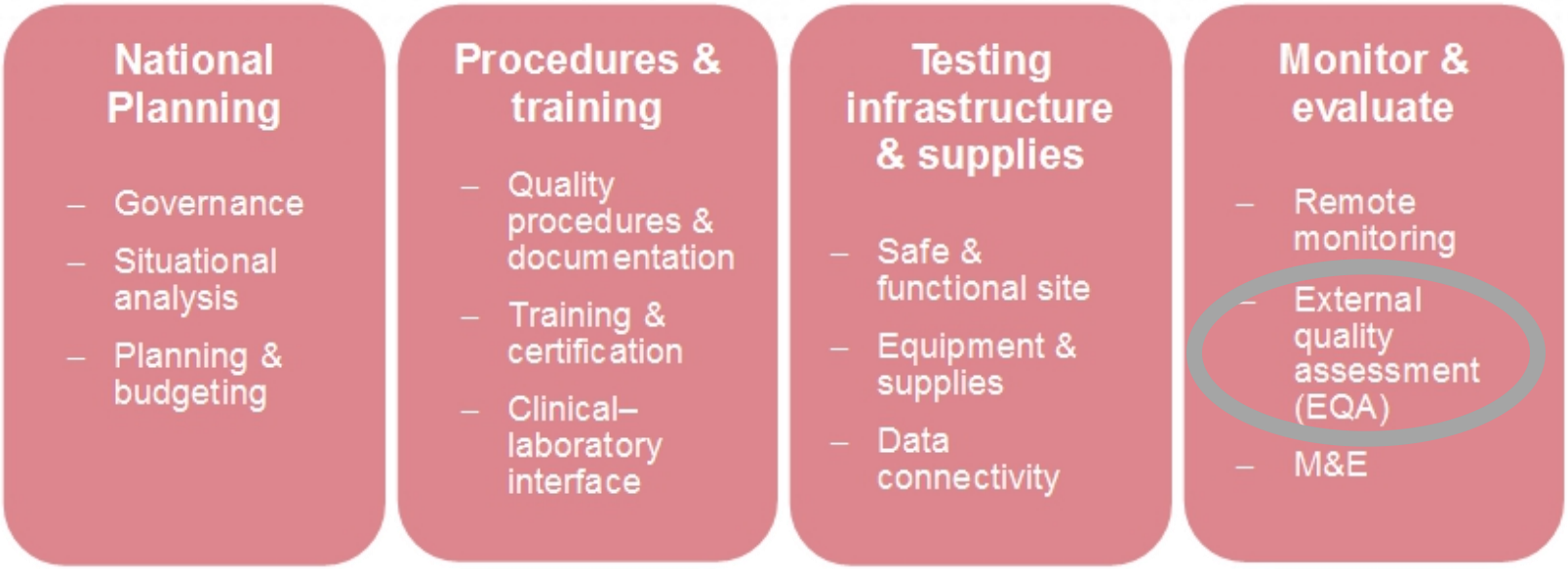
CQI operates under the belief that there is always room for improving operations, processes, and activities to increase quality.

CQI: Two Parts

- **National and Supervisory Levels**
  - Focuses on establishing or integrating Xpert MTB/RIF QA activities into the TB diagnostic network in a country or region.
- **QA at Xpert MTB/RIF Testing Sites**
  - addresses key activities to be carried out at the testing sites to ensure the production of quality Xpert MTB/RIF results

Part 1: National and Supervisory Levels

Pillars of a Quality Assurance System



Xpert MTB/RIF PT Panel Availability

- **Availability of affordable proficiency testing (PT) material was identified as an important gap in CQI programs**
  - In 2012 less than 43% (387/907) of global Xpert MTB/RIF testing sites participated in PT
  - Only 24% (77/317) of Xpert testing sites in the African region participated in PT

WHO TB Laboratory Diagnostic Services Dataset (https://www.who.int/tb/country/data/download/en/)

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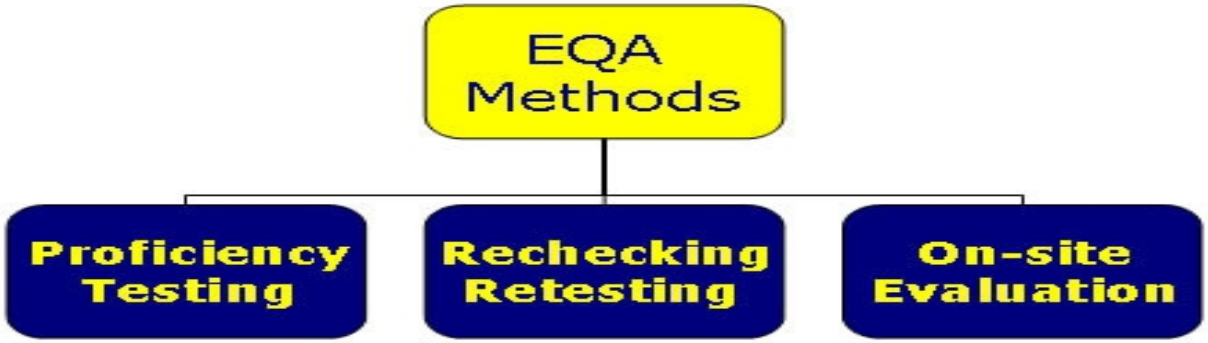
Overview of Quality Assessment

Assessment is a critical aspect of laboratory quality management, and it can be conducted in several ways with the commonest being EQA;

- **Define EQA??**

Method that allows for comparison of a laboratory's testing to a source outside the laboratory

Types of EQA



What is Proficiency Testing?

- Is an evaluation of participant performance against pre-established criteria by means of inter-laboratory comparison.

- A PT program is a quality assessment tool that provides a retrospective measure of technical quality and verifies the reliability of lab results

- However such programs are expensive to establish hence meagre in developing countries.

Types of PT schemes

- **Quantitative scheme** – Quantifies one or more measurands of the proficiency test item;
- **Qualitative scheme** – Identifies or describes one or more characteristics of the proficiency test item. The results of qualitative tests are descriptive and reported on a categorical or ordinal scale, e.g. identification of micro-organisms, or by identifying the presence of a specific measurand (such as a drug or a grading of a characteristic).
- **Simultaneous scheme** – where proficiency test items are distributed for concurrent testing or measurement within a defined time period
- **Continuous scheme** – where proficiency test items are provided at regular intervals

PT schemes for laboratories

- PT is an EQA program involving sending a panel of sample to a group of participating labs.
- Means of verifying the reliability of lab results
- The main objective is to assess proficiency of the labs in the diagnostic TB sites

However, such programs are not readily

Objectives of EQA schemes for laboratories

- Evaluation of Lab testing competence
- Assessment of individual testing performance of the lab staff
- Evaluation of reliability of a test procedure
- Production of relevant information to participating labs when necessary

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Objectives of EQA schemes for laboratories

- Providing the basis for the comparability of results during epidemiological surveillance and disease control
- Collecting information on laboratory measurements (intra- and inter-laboratory)
- Collecting information for the purpose of licensing or accreditation of laboratories

Group Exercise

- In a group of 3 or individually list the EQA programmes available in your country and explain the limitation of each. (5 minutes)

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Uganda SRL PT scheme overview

- The Uganda National Tuberculosis Reference Laboratory (NTRL) Proficiency testing scheme covers
  - Microscopy,
  - Culture,
  - Line probe Assays,
  - GeneXpert MTB/RIF,
  - and Drug susceptibility testing techniques.
  - SARS-C0V-2

Design of the NTRL PT scheme;

- randomly selected sub-samples from a bulk homogeneous supply of material
- distributed simultaneously to participating

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Uganda SRL PT schedule

EQA panels provided	Microscopy	LPA	Genexpert	Culture	DST	Sars-COV 2
Frequency/ year	Biannual	Annual	Biannual	Biannual	Annual	Biannual
Sending out month	February and August	August	February and August	February and August	August	February and August
Quantity	10 slides/round	10 Dried Tube Specimens /round	05 Dried Tube Specimens /round	10 isolates/round	20 isolates/round	05 Dried Tube Specimens / round
Expected TAT (from date of Dispatch)	44 days	44days	44 days	91 days	116 days	44 days

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Uganda SRL: GeneXpert PT Scheme

- Materials; Standard control strains of *Mycobacterium tuberculosis (MTB)* eg H37R*v* , Non-MTB strains (NTM) PBS, Cryovials, Cryo labels, Ziplock bags etc,
- Composition; 5 PT panels
- Must be **non-viable**
- Frequency;
  - Availability of funds and purpose
  - Twice a year

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Uganda SRL: LPA PT Scheme

- Materials; Standard control strains of *Mycobacterium tuberculosis (MTB)* eg H37R*v* , Non-MTB strains (NTM) PBS, Cryovials, Cryo labels, Ziplock bags etc,

- Composition; 5 PT panels

- Must be **non-viable**

- Frequency;
  - Availability of funds and purpose
  - Twice a year

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Uganda SRL: Microscopy PT Scheme

- Materials; Standard control strains of *Mycobacterium tuberculosis (MTB)* eg H37R*v* , Non-MTB strains (NTM) PBS, Cryovials, Cryo labels, Ziplock bags etc,

- Composition; 10 PT panels At least 10 slides provides a valid and fair test Batch of stained and unstained smears

- Must be **non-viable**

- Frequency;
  - Availability of funds and purpose
  - Twice a year

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Uganda SRL: Culture PT Scheme

- Materials; Standard control strains of *Mycobacterium tuberculosis (MTB)* eg H37R*v* , Non-MTB strains (NTM) PBS, Cryovials, Cryo labels, Ziplock bags etc,
- Composition; 10 PT panels
- Must be **viable**
- Frequency;
  - Availability of funds and purpose
  - Twice a year

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Uganda SRL: SARS Cov -2 PT Scheme

- Materials; Standard control strains of *SARS-Cov 2* PBS, Cryovials, Cryo labels, Ziplock bags etc,
- Composition; 5 PT panels
- Must be **non-viable**
- Frequency;
  Availability of funds and purpose
  - Twice a year

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Uganda SRL: DST PT Scheme

- Materials; Standard control pure strains of *MTB,* PBS, Cryovials, Cryo labels, Ziplock bags etc,

- Composition; 20 PT panels

- Must be **viable**

- Frequency;
  Availability of funds and purpose
  - Once a year

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Getting Started: Issues to Consider (1)

- Capacity of NRL
  - HR
  - Training and expertise
- Type and Composition of PT panels
- Internal QC procedures to ensure
  - Homogeneity
  - Stability
- System for sending PT panels
- Frequency of testing
- Forms to record and report results
- Time allowed for technicians to complete PT
- Performance criteria
- Feedback and corrective action if needed
- Mechanism to resolve discrepant results

Getting Started: Issues to Consider (2)

Dispatch of PT panels

- Delivery system based on services, regulations, resources available:
  - mail/post
  - courier
  - supervisory visit
- Turnaround time; consideration of
  - total no. of days from dispatch of panels to closing dates,
  - preparation of individual and summary reports,
  - presentations to PT team,
  - dispatch of the individual and summary reports

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Getting Started: Issues to Consider (3)

- Safe package to prevent breakage/damage of PT materials:
  - strong plastic slide holders
- A standardized PT reporting form / an accompanying letter to provide instructions
- No incentives or punitive actions as a result of the PT exercise
- Time allowed to complete the PT exercise

Getting Started: Issues to Consider (4)

Analysis of PT Results

- A scoring system is to be developed prior to test
- Distinguish major and minor errors
- Determine successful score
- Determine plan of action for poor performances
- Database for analysis

Getting Started: Issues to Consider (5)

Feedback to Laboratories on PT results

- Timely and confidential
- Individual and aggregate test results
- Criteria for acceptable performance
- Reports to TB program coordinator should provide appropriate background information and recommendations and not simply scores
- Poor performance often requires a visit to laboratory

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Getting Started: Issues to Consider (6)

Feedback to Laboratories on PT results

- Timely and confidential
- Individual and aggregate test results
- Criteria for acceptable performance
- Reports to TB program coordinator should provide appropriate background information and recommendations and not simply scores
- Poor performance often requires a visit to laboratory

Roles of Participating labs

- . To be successful, PT instructions must be followed carefully, all paper work completed accurately, and results submission deadlines met.
- All PT results, as well as corrective actions, should be recorded and the records maintained for an appropriate period of time.
- There must be no difference in the treatment of PT samples and the patient's sample
- Avoid discussion of results with other laboratories.

Limitations Of PT Schemes

- PT results are affected by variables not related to patient samples Such as preparation of the sample, clerical functions, selection of statistical methods of evaluation.
- PT will not detect all problems in the laboratory, particularly those that address the pre- and post-examination procedures.
- A single unacceptable result does not necessarily indicate that a problem exists in the laboratory.

Assessment

- Define the term EQA and discuss its importance
- What factors might drive the choice of an EQA program to implement
- List the 3 EQA programmes that a TB network can implement

Summary

- EQA plays a crucial role in evaluating the performance of a laboratory network
- Proper planning and considerations are vital to drive the choice of an EQA program to implement

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