WARN/CARN-TB

West and Central African Regional Networks for Tuberculosis control

THE ACCESS AND DELIVERY PARTNERSHIP

Training guide for trainers on Active Tuberculosis Drug Safety Monitoring and Management (aDSM)

A guide to train Health Care Workers and /or National TB Programme and pharmacovigilance managerial staff involved in the management of aDSM

This 'Training package on active tuberculosis drug safety monitoring and management (aDSM)' was originally put together in 2016 by representatives of five technical partners on the WHO Task Force on aDSM:

- KNCV Tuberculosis Foundation
- Management Sciences for Health (SIAPS)
- Médecins sans Frontières
- World Health Organization / Global TB Programme
- Special Programme for Research and Training in Tropical Diseases (TDR) at WHO Headquarters

The materials were updated in 2022-23, with addition of this training guide, by Mahamadou Bassirou Souleymane (TDR consultant) with Marie-Eve Raguenaud (TDR), Branwen J Hennig (TDR), and Corinne Merle (TDR), and reviewed by Linh Nhat Nguyen (WHO/GTB), Medea Gegia (WHO/GTB), and Fuad Mirzayev (WHO/GTB).

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NTP – National TB Programme; PV – Pharmaco-Vigilance Programme ; MDR-TB – Multi-drug-resistant TB ;

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Abbreviations

aDSM	Active tuberculosis drug safety monitoring and management
AE	Adverse event
DR-TB	Drug-resistant TB
HCW	Health care worker
NTP	National Tuberculosis Programme
PV	Pharmacovigilance
TB	Tuberculosis
WARN-CARN TB	West and Central Africa networks for TB control
WG	Working group
WHO	World health Organization
WHO/GTB	WHO global tuberculosis program
WHO/TDR	WHO program on research and training in tropical diseases

1. Background

Active tuberculosis (TB) drug safety monitoring and management (aDSM) is a key component for the use of new TB drugs such as bedaquiline and delamanid approved by the Food and Drugs Agency of the United States in 2012. Additionally, aDSM also includes the use of repurposed drugs such as linezolid and clofazimine introduced in drug-resistant TB (DR-TB) management. Despite widespread use of these drugs by some National Tuberculosis Programmes (NTPs) among the West and Central African Regional Networks for TB control (WARN/CARN-TB), scaling up of aDSM remains suboptimal. In 2021, an assessment conducted across the networks showed that only 25.9% (7/27) NTPs had developed national guidelines for aDSM[1]. To overcome this challenge, standardized tools, regular training, and supervision of health care workers (HCWs) and their managers are crucial to build capacity towards optimising aDSM practices and reporting.

In 2022, a generic guideline and standard procedure[2] for effective implementation of aDSM was developed by a WARN-CARN TB working group (WG) with support from the Special Programme for Research and Training in Tropical Diseases (TDR). In addition to the aDSM generic guideline and procedure of implementation guide, this training pack was developed to aid HCWs and NTP managers towards successful implementation of the aDSM.

The training modules are based on WHO global tuberculosis program (GTB) training materials developed in 2016 and include (i) Background & overview, (ii) Basic components of aDSM and (iii) Implementing aDSM, with an update drawn from WHO rapid communication on DR-TB management available as of May 2022.

This training guide intends to serve as a resource document in organising the training targeted at specific audiences (Health Care Workers **(**HCWs), NTP managers and pharmacovigilance managerial staff). It further provides an orientation for the trainer on aspects to cover through interactives sessions to maximise the delivery of key information. Trainers will usually be country focal points with experience in aDSM or pharmacists.

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[1] C.S. Merle, October 2021, EP-19-281 Implementation of TB active drug safety monitoring: a cross-sectional survey in West and Central Africa. Poster presented in the framework of the 52nd World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease (The Union)

[2] aDSM guideline – Active tuberculosis drug-safety monitoring and management (aDSM): framework for implementation (who.int)

Participants will be introduced by the trainer to the learning objectives and guided through the training materials by module using the teaching slides. They will complete a short quiz before and after the training course as means to monitor learning.

2. Audiences targeted for aDSM training

The aDSM knowledge required differs depending on the level of involvement of a given person in its implementation. Frontline HCWs in DR-TB clinics need to have a good understanding of the clinical management of severe adverse events (SAE) and adverse events (AE) of interest, and on the reporting process. In contrast, at the central/regional level, aDSM managers need to have solid knowledge on the coordination aspects, causality assessment, signal detection and communication to the Ministry of health.

Therefore, two separate training packs were developed for i) HCWs and ii) NTP and pharmacovigilance (PV) managerial staff, respectively, figure 1:

i) aDSM training pack for HCWs containing technical components of **aDSM in everyday practice.** This training is targeting HCWs responsible for DR-TB patients (operational level keys staff: clinician, nurses, etc.) with a focus on clinical management and reporting of aDSM.

ii) aDSM training pack for NTP managers containing components for **implementation and coordination of aDSM.** This training is targeting NTP staff both at the central and implementation level in addition to pharmacovigilance (PV) management staff with a focus on aDSM implementation, coordination aspects as well as causality assessment, signal detection and communication/reporting.

A more detailed overview of the training packs is provided as Training plan in Annex 1.

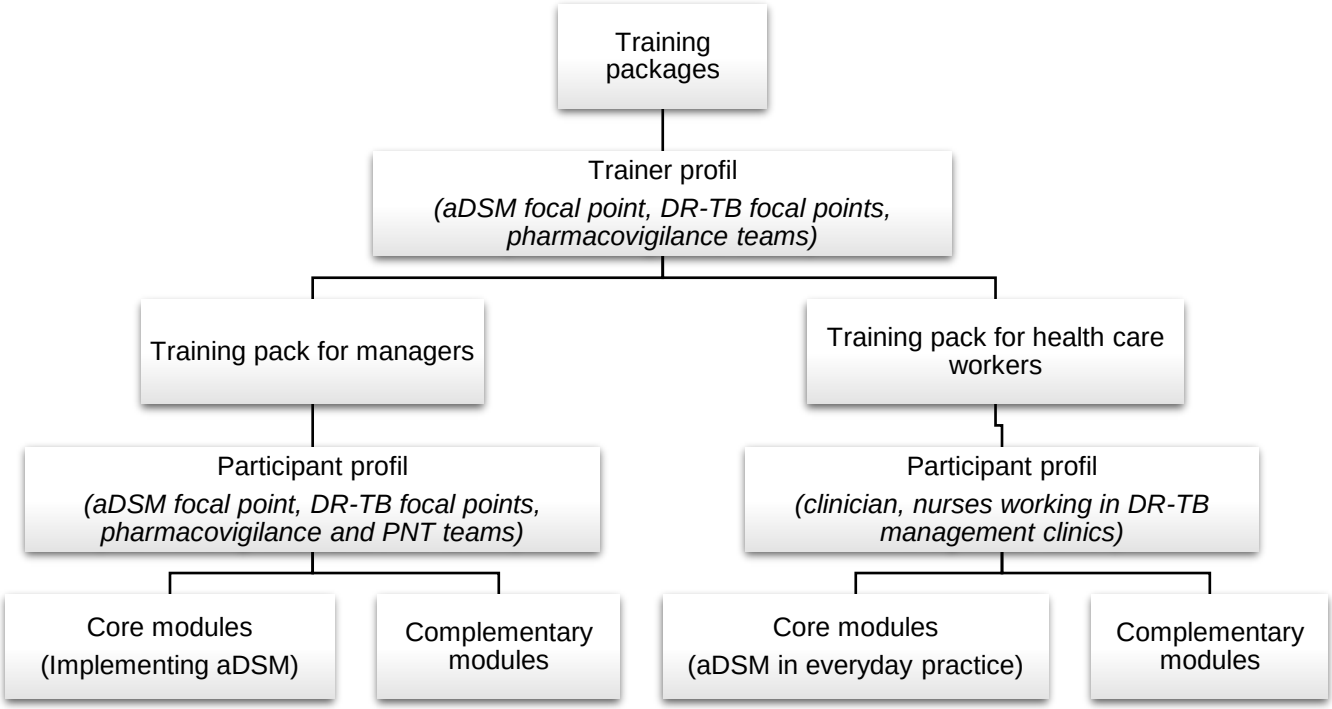

Figure 1: Schematic overview of aDSM training materials for key audiences

3. Aim and objectives

The overall aim of this training package on active TB drug safety monitoring and management (aDSM) is to provide training to two categories of staff involved in aDSM, health care workers and managers. The specific objectives per category are as follows

3.1. aDSM training objectives for health care workers

By the end of this training course the participants (according to the level of work) should be able to:

i) Identify and understand the key concepts and definitions of aDSM
ii) Correctly identify AE and culprit drug(s) during the clinical monitoring of DR-TB treatment
iii) Effectively manage adverse drug reactions during treatment
iv) Properly record AE per system affected and by severity (mild, moderate, severe)
v) Properly and regularly notify AE to the NTP or the pharmacovigilance (PV) department of the MoH

3.2. aDSM training objectives for managers

By the end of this training course, the participants (according to the level of work) should be able to:

i) Identify and understand the key concepts and definitions of aDSM
ii) Describe how to implement and manage aDSM within a TB programme and/or pharmacovigilance system
iii) Properly summarize AEs and regularly forward results to the pharmacovigilance department of the MoH
iv) Understand key concepts of causality assessment, signal detection and safety risk management

4. Training packs for trainers

The packs for trainers consist of this guide and teaching materials organised as a series of slides decks available in English and French. This covers:

i) Background, Overview, Objectives (Note: This module is the same for HCW and manager training)
ii) Core and complementary modules (for each of the target audiences)
iii) A short quiz (before and after the training).

Further, this guide provides suggested training time tables, a list of materials and equipment required as well as a course evaluation form and report.

4.1. aDSM training modules for health care workers

This training focuses on competencies, knowledge, skills, and attitudes to be gained by health care workers to enable successful monitoring of aDSM in the field and reporting to NTP and PV managerial staff.

These slide decks contain the following components of training :

- ✓ 1. Background, Overview, Objectives (Note: This module is the same for HCW and manager training)
  - Training objectives for this course & key references
  - Key definitions
  - Active TB drug-safety monitoring: rationale and mechanisms in the context of TB & DR-TB treatment
- ✓ 2. Core modules (aDSM in everyday practice)
  - Clinical monitoring and management of adverse events

- Train staff on the collection of data
- National and international reporting of AE: mechanisms, routes, and resources
- Records Management & Quality Assurance of Data

✓ 3. Complementary modules (aDSM)

- Indicators of aDSM implementation and programme management

4.2. aDSM training modules for Managers

This training focuses on competencies, knowledge, skills, and attitudes required for successful implementation and monitoring of aDSM by NTP and PV managerial staff.

These slide decks contain the following components of training :

✓ 1. Background, Overview, Objectives (Note: This module is the same for HCW and manager training)

- Training objectives for this course & key references
- Active TB drug-safety monitoring: rationale and mechanisms in the context of TB & MDR-TB treatment
- Key definitions

✓ 2.Core modules (Implementing aDSM)

- The 8 key elements for the implementation of aDSM in a national TB programme
- National and international reporting of adverse events: mechanisms, routes, and resources
- Indicators of aDSM implementation and programme management

✓ 3. Complementary modules (aDSM)

- Record management and quality assurance of data
- Causality assessment: scales & methods
- Signal detection introduction
- Overview on risk communication and new knowledge integration
- Role of national and international technical and funding partners in the implementation of aDSM

5. Duration of the training for each of the target audience

The anticipated duration required for delivery of this aDSM training is three days, a suggested timetable is presented in Annex 2 here attached.

The training could be extended over a longer period especially for health care professionals who have not been previously trained in aDSM in DR-TB, since they may then need more emphasis on practical examples and participatory techniques in a DR-TB treatment centre.

6. Materials and equipment

The course materials provided as series of slide decks available in English and French.

See annex 3 for further equipment needed to deliver the training.

7. Methodology

Different training methods are used to enhance active participation and knowledge sharing among participants such as working in groups, role-playing, and other practical exercises e.g. to discuss the current aDSM situation in participants countries and planning future improvements. Participants are therefore encouraged to come prepared with a case study related to a specific challenge they face in their respective country for peer discussion during the training course.

It is important that the training achieves a high level of understanding, comprehensive knowledge acquisition, and retention of simple key messages, clear attitudes, and useful practices. At the end of the training, participants should have acquired the necessary skills for successful implementation of the aDSM at various level of the health care system.

Supportive supervision should be provided after the training to respective participants to ensure appropriate implementation of the knowledge gained during aDSM training in the various countries who participated and within an agreed time.

8. Evaluation

During the course, participants complete

i) an evaluation form to measure their satisfaction with the course (annex 4), and

ii) a pre/post-test to assess the improvement of their knowledge (annex 5).

The results of these evaluations, as well as suggestions on the content and methodology of the training will be collected in a training report and used for future improvement of the training packs (annex 6: report example template).

The impact of the course should be evaluated during follow-up supervision visits in countries who participated.

9. References

All information included is fully consistent with the WHO recommendations on the implementation of an active surveillance system for TB drug safety (aDSM) developed in 2015[3], the WHO/GTB training materials developed in 2016 and the latest available WHO recommendations on DR-TB treatment in May 2022[4] and WHO operational handbook on tuberculosis. Module 4, update in 2022[5].

[3] World Health Organization, Active tuberculosis drug-safety monitoring and management (aDSM) https://apps.who.int/iris/bitstream/handle/10665/204465/WHO_HTM_TB_2015.28_eng.pdf?sequence=1&isAllowed=y

[4] Rapid communication: key changes to the treatment of drug-resistant tuberculosis. Geneva: World Health Organization; 2022 (WHO/UCN/TB/2022.2). Licence: CC BY-NC-SA 3.0 IGO.

[5] WHO operational handbook on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment, 2022 update

Annex 1: Training plans

1. aDSM training plan for health care workers

Name of training: aDSM FOR HCWs	
Training type	Presentations and Exercises*
Target audience	Health Care Workers (HCWs) responsible for DR-TB patients/facilities (keys staff: clinician, nurses)
Training goals	1. Identify and understand key concepts and definitions of aDSM 2. Correctly identify adverse events and culprit drug(s) during the clinical monitoring of DR-TB treatment 3. Effectively manage adverse drug reactions during treatment 4. Appropriately record adverse events by body system affected and severity (mild, moderate, severe). 5. Appropriately and regularly notify adverse events to NTP or the PV department of the MoH
Training pre-requisite	Knowledge of clinical management of DR-TB patients
Duration	3 days
Time	Daily 9am to 5pm (with two short breaks 2x30' and one lunch break of 60')
Key modules	✓ Background, Overview, Objectives o Training objectives for this course & key references o Active TB drug-safety monitoring: rationale and mechanisms in the context of TB & MDR-TB treatment o Key definitions ✓ Core modules (aDSM in everyday practice) o Clinical monitoring and management of adverse events o Train staff on the collection of data o Records Management & Quality Assurance of Data o National and international reporting of adverse events: mechanisms, routes and resources ✓ Exercises
Complementary modules	✓ Indicators of aDSM implementation and programme management ✓ Exercises
Evaluation	- Pre and post-test (multiple choice quiz before and after the training) - Course evaluation by participants
*** Exercises**	Country-specific case studies, guides, reporting forms etc. brought by participants for discussion and updating if required.

2. aDSM Training plan for managers

Name of training: aDSM FOR MANAGERS	
Training type	Presentations and exercises*
Target audience	NTP (managers and coordinators at both central and regional level) and pharmacovigilance (PV) managerial staff
Training goals	1. Identify and understand key concepts and definitions of aDSM 2. Describe how to implement and manage aDSM within a TB programme 3. Appropriately summarize AEs and regularly forward results to the pharmacovigilance department of MoH 4. Understand key concepts of causality assessment, signal detection and safety risk management
Training pre-requisite	Knowledge of the pharmacovigilance system and DR-TB management in the country Systematic reporting of aDSM to national and international systems.
Duration	3 days
Time	Daily 9am to 5pm (with two short breaks 2x30' and one lunch break of 60')
Key modules	✓ Background, Overview, Objectives o Training objectives for this course & key references o Active TB drug-safety monitoring: rationale and mechanisms in the context of TB & MDR-TB treatment o Key definitions ✓ Core modules (Implementing aDSM) o The 8 key elements for the implementation of aDSM in a national TB programme o National and international reporting of adverse events: mechanisms, routes and resources o Indicators of aDSM implementation and programme management ✓ Exercises
Complementary modules	✓ Record management and quality assurance of data ✓ Causality assessment: scales & methods ✓ Signal detection introduction ✓ Overview on risk communication and new knowledge integration ✓ Role of national and international technical and funding partners in the implementation of aDSM ✓ Exercises simulation
Evaluation	- Pre and post-test (multiple choice quiz before and after the training) - Course evaluation by participants
*** Exercises**	Country-specific case studies, guides, reporting forms etc. brought by participants for discussion and updating if required

Annex 2: Training timetables – examples

1. Three-day aDSM training schedule for HCW

Day	Time	Topic	Facilitator
D1	(45')	Welcome and introduction	Organizers, trainers, participants
	(15')	Objectives	Organizers
	(30')	Pre-course Quiz	Participants
	(30')	*Break*	
	(30')	Background & overview	Organizers
	(30')	Key definitions	
	(30')	Rationale & mechanisms	
	(1h)	*Lunch*	
	(2x30')	Clinical monitoring of adverse events (AE) and management of adverse drug reactions	Organizers
	(30')	Management of adverse drug reactions: Case presentations	
	(30')	*Break*	
	(30')	Management of adverse drug reactions: Case presentation	Organizers
	(15')	Discussion	
D2	(45')	Recap day 1 and Introduction of day 2	Organizers
	(15')	Results of the pre-test	
	(30')	Train staff on the collection of data	
	(30')	*Break*	
	(2x30')	National and international reporting of adverse events: mechanisms, routes, and resources	
	(30')	Records Management & Quality Assurance of Data	
	(1h)	*Lunch*	
	(30')	Indicators of aDSM implementation and programme management	
	(2x30')	Reporting of AEs per system and grades: short cases exercises	
	(30')	*Break*	All
	(30-45')	Discussion	
D3	(45')	Recap day 2 and Introduction of day 3	ALL
	(30')	Post-course Quiz	
	(30')	*Break*	
	(1h)	Evaluation of the training	
	(1h)	*Lunch*	
	(1h)	Discussion, Clarifications, closing remarks	

2. Three-day aDSM training schedule for managers

Day	Time	Topic	Facilitator
D1	(45')	Welcome and introduction	Organizers, trainers, participants
	(15')	Objectives	
	(30')	Pre-course Quiz	Participants
	(30')	*Break*	
	(30')	Background & overview	Organizers
	(30')	Key definitions	
	(30')	Rationale & mechanisms	
	(1h)	*Lunch*	
	(30')	Create a national coordinating mechanism for aDSM	Organizers
	(30')	Discussion and exercises simulation	
	(30')	Develop a plan for aDSM	
	(30')	Discussion and exercises/simulation	
	(30')	*Break*	
	(15')	Define management and supervision roles and responsibilities	Organizers
	(30')	Discussion	
D2	(15')	Recap/Introduction of the day	Organizers
	(15')	Pre-test results	
	(15')	Create standard data collection materials	
	(30')	Review of existing data collection materials and exercises	
	(30')	*Break*	
	(30')	Train staff on data collection	
	(30')	Exercises/simulation	
	(30')	Define schedules and routes for data collection and reporting	
	(1h)	*Lunch*	
	(30')	Consolidate aDSM data electronically	Organizers
	(30')	Exercises/simulation	
	(15')	Develop capacity for signal detection and causality assessment	
	(30')	National and international reporting of adverse events: mechanisms, routes and resources	
	(30')	*Break*	
	(30')	Indicators of aDSM implementation and programme management	Organizers
	(30')	Discussion/questions	

D3	(30’)	Recap day 2 and Introduction to day 3	ALL
	(30’)	Records Management & Quality Assurance of Data	
	(15’)	Exercises/simulation	
	(30’)	*Break*	
	(30’)	Causality assessment: scales & methods	
	(30’)	Signal detection introduction	
	(30’)	Overview on risk communication and new knowledge integration	
	(1h)	*Lunch*	
	(30’)	Role of national and international technical and funding partners in the implementation of aDSM	
	(30’)	Discussion, clarifications	
	(30’)	Post course Quiz	
	(30’)	*Break*	
	(1h)	Evaluation of the training	
		closing	

Annex 3: Training materials and equipment required

General	Per participant	Trainers
aDSM for HCWs		
Invitation letter Training room Laptop and projector White board/flip charts Marker pens (different colours) Printed pre-and post-test forms and/or online test forms (depending on availability) Internet connection	Training kit (pen, notebook…) PV form used in the country (if available) DR-TB patients treatment card Course evaluation form Copy of the National aDSM guideline (paper/electronic)	Training slide decks for HCW (as pptx and pdfs) aDSM guide aDSM SOP National DR -TB guideline National PV guideline (if available)
aDSM for managers		
Invitation letter Training room Laptop and projector White board/flip charts Marker pens (different colours) Printed the pre- and post-test forms and/or online test forms (depending on availability) Internet connection	Training kit (pen, notebook…) PV form used in the country DR-TB patients treatment card Course evaluation form Copy of the National aDSM guideline and SOP (paper/electronic)	Training slide decks for managers (as pptx and pdfs) aDSM guide aDSM SOP National DR -TB guideline National PV guideline (if available)

Annex 4: Course evaluation form

Course evaluation

How do you rate the training course program?

4= Excellent, 3= Very good 2= Satisfactory 1= Poor

A: EVALUATION OF THE TRAINING METHODOLOGY

How do you rate the quality of this training course on the following

Topic/Score	4	3	2	1
Quality of training materials				
Competence of teachers				
Personal satisfaction				
Duration of the course				
Logistics and organization of the course (venue, Information before the start of the training course)				

B: LEARNING RESULTS

The overall aim of this training package on active TB drug safety monitoring and management (aDSM) is to provide training to health care workers and management staff involved in aDSM. By the end of this training course the participants should be equipped to conduct clinical management and appropriate reporting of adverse events within aDSM.

1. ***Did the training course meet your expectations?***
2. ***To what extent did you meet the goal of the training course?***

3. What are the three most important things you have learned?
4. Do you have any suggestions to improve this training course program?

Annex 5_A: Quiz for health care workers (HCW)

Tick or circle the letter that corresponds to your answer. More than one answer can be true per question. To get the point(s) for the question, all relevant answers must be ticked/circled.

1. **The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problems is referred to as:**

☐ A. Clinical research
☐ B. Clinical data management
☐ C. Pharmacovigilance
☐ D. Active Drug Safety Monitoring (aDSM)

2. **Pharmacovigilance (PV):**

☐ A. Increases the economic burden on healthcare system
☐ B. Improves public health
☐ C. Neglects patient safety
☐ D. Discourages effective drug use

3. **Of the two main approaches of pharmacovigilance, which one is aDSM a part of?**

☐ A. Spontaneous reporting
☐ B. Voluntary reporting
☐ C. Passive reporting
☐ D. Active reporting

4. **Adverse event are:**

☐ A. Life threatening
☐ B. Due to drug/treatment
☐ C. Have a causal relationship with treatment

5. **What changes in the management of drug-resistant TB reinforce the importance of active TB drug safety monitoring for a National TB Programme (NTP)?**

☐ A. New TB regimes and drugs incorporated into routine use
☐ B. New TB regimes and drugs used under operational research condition
☐ C. All oral bedaquiline-containing regimes

6. **In the first instance, aDSM applies to which category(ies) of patients?**

☐ A. All treated TB patients
☐ B. All DR-TB patients treated with new drugs or regimens
☐ C. All ultra-resistant TB (XDR-TB) patients

7. **Active Drug Safety Monitoring (aDSM) results in:**

☐ A. Reduced treatment interruption
☐ B. Added costs to the service (e.g. hospitalization)
☐ C. Reduced treatment failure

8. The occurrence of an adverse drug event may lead to:

☐ A. Interruption of TB treatment
☐ B. Avoidable morbidity
☐ C. Treatment failure
☐ D. Additional costs to the health care service

9. Which of the following activities is/are related to active TB drug safety monitoring and management (aDSM)

☐ A. Clinical monitoring
☐ B. Adverse event management
☐ C. Systematic recording
☐ D. Standardised reporting of adverse events

10. Basic aDSM includes:

☐ A. Monitoring and reporting of all serious adverse events
☐ B. Monitoring and reporting of all serious adverse events of special interest
☐ C. Monitoring and reporting of all clinically significant adverse events

11. A serious adverse event (SAE) is an event that may result in:

☐ A. Death
☐ B. Hospitalization
☐ C. Significant disability
☐ D. Congenital anomaly
☐ E. Change medication

12. A severe adverse event (severe AE) is an event :

☐ A. Of maximum intensity as judged by the patient/clinician
☐ B. May be determined by degree
☐ C. Often based on the outcome
☐ D. Often based on clinical or laboratory tests

13. How can adverse events be detected in a DR-TB patient on treatment?

☐ A. Listening and observation
☐ B. Systematic clinical assessments
☐ C. Hospitalisation
☐ D. Regular laboratory tests

14. Which second-line anti-TB drugs prolong the QTc interval on electrocardiogram (ECG)?

☐ A. Isonizid
☐ B. Linezolid.
☐ C. Bedaquiline.
☐ D. Cycloserine.

15. Which second-line anti-TB drugs primarily cause peripheral neuropathy?

☐ A. Linezolid
☐ B. Pyrazinamide
☐ C. Clofazimine
☐ D. Isoniazid
☐ E. Moxifloxacin

16. A TB patient during treatment for DR-TB with all-oral short course therapy develops severe hepatitis with transaminase elevation to 5 times the normal value. Should he/she:

☐ A. Continue treatment
☐ B. Promptly switch to the continuation phase even if the intensive phase has not been completed
☐ C. Stop all treatment until transaminases normalise and reintroduce all treatment at half dose.
☐ D. Stop all treatment until transaminases normalise and reintroduce the less hepatotoxic drugs Ethionamide (E), Moxifloxacin (Mfx), Clofazimine (Cfz), Bedaquiline (Bdq). Then introduce the most hepatotoxic drugs one by one Prothionamide (Pto), Pyrazinamid (Z) and observe the evolution of transaminases every 3 days in order to identify the responsible drug.
☐ E. Stop all treatment until transaminases normalise and reintroduce the drugs one by one in this order: Pyrazinamid (Z), Prothionamide (Pto), Clofazimine (Cfz), Moxifloxacin (Mfx), Ethionamide (E).

Annex 5_B: Quiz for managers

Tick or circle the letter that corresponds to your answer. More than one answer can be true per question. To get the point for the question, all relevant answers must be ticked/circled.

1. **The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problems is referred to as:**

☐ A. Clinical research
☐ B. Clinical data management
☐ C. Pharmacovigilance
☐ D. Active Drug Safety Monitoring (aDSM)

2. **Pharmacovigilance (PV):**

☐ A. Increases the economic burden on healthcare system
☐ B. Improves public health
☐ C. Neglects patient safety
☐ D. Discourages effective drug use

3. **Of the two main approaches of pharmacovigilance, which one is aDSM a part of?**

☐ A. Spontaneous reporting
☐ B. Voluntary reporting
☐ C. Passive reporting
☐ D. Active reporting

4. **Adverse event are:**

☐ A. Life threatening
☐ B. Due to drug/treatment
☐ C. May or may not have a casual relationship with treatment

5. **What changes in the management of drug-resistant TB reinforce the importance of active TB drug safety monitoring for a National TB Programme (NTP)?**

☐ A. New TB regimes and drugs incorporated into routine use
☐ B. New TB regimes and drugs used under operational research condition
☐ C. All oral bedaquiline-containing regimes

6. **In the first instance, aDSM applies to which category(ies) of patients?**

☐ A. All treated TB patients
☐ B. All DR-TB patients treated with new drugs or regimens
☐ C. All ultra-resistant TB (XDR-TB) patients

7. **Active Drug Safety Monitoring (aDSM) results in:**

☐ A. Reduced treatment interruption
☐ B. Added costs to the service (e.g. hospitalization)
☐ C. Reduced treatment failure

8. The occurrence of an adverse drug event may lead to:

☐ A. Interruption of TB treatment
☐ B. Avoidable morbidity
☐ C. Treatment failure
☐ D. Additional costs to the health care service

9. Which of the following activities is/are related to active TB drug safety monitoring and management (aDSM)

☐ A. Clinical monitoring
☐ B. Adverse event management
☐ C. Systematic recording
☐ D. Standardised reporting of adverse events

10. Basic aDSM includes:

☐ A. Monitoring and reporting of all serious adverse events
☐ B. Monitoring and reporting of all serious adverse events of special interest
☐ C. Monitoring and reporting of all clinically significant adverse events

11. A serious adverse event (SAE) is an event that may result in:

☐ A. Death
☐ B. Hospitalization
☐ C. Significant disability
☐ D. Congenital anomaly
☐ E. Change medication

12. A severe adverse event (severe AE) is an event :

☐ A. Of maximum intensity as judged by the patient/clinician
☐ B. May be determined by degree
☐ C. Often based on the outcome
☐ D. Often based on clinical or laboratory tests

13. Regarding record keeping and data quality assurance for DR-TB: It is important that the documentation of records and/or registers is:

☐ A. Attributable
☐ B. Readable
☐ C. Contemporary
☐ D. all of the above

14. What are the indicators of good aDSM?

☐ A. Good coverage at the level of diagnosed patients
☐ B. Good data completeness
☐ C. Good reporting of serious AEs
☐ D. Good description of AEs associated with the new regimen/drug

15. Of the eight key steps for implementing the aDSM, two are essential before patients are put on new MDR-TB treatment:

☐ A. Create standard data collection tools and train staff on the collection of data
☐ B. Develop a plan for aDSM and train staff on the collection of data
☐ C. Create standard data collection tools and consolidate aDSM data electronically
☐ D. Develop a plan for aDSM and create standard data collection tools

16. The process of pharmacovigilance notification involves steps in the following order:

☐ A. Case processing -> signal management -> risk management -> international submission
☐ B. Case processing-risk management -signal management- international submission
☐ C. international submission - case processing-signal management-risk management
☐ D. Risk management- international submission - case processing-signal management

Annex 5_C: Solutions to Quiz for health care workers and managers

Correct answers are shown in *italics*, more than one answer can be true per question.

1. **The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problems is referred to as:**

☐ A. Clinical research
☐ B. Clinical data management
☐ *C. Pharmacovigilance*
☐ D. Active Drug Safety Monitoring (aDSM)

2. **Pharmacovigilance (PV):**

☐ A. Increases the economic burden on healthcare system
☐ *B. Improves public health*
☐ C. Neglects patient safety
☐ D. Discourages effective drug use

3. **Of the two main approaches of pharmacovigilance, which one is aDSM a part of?**

☐ A. Spontaneous reporting
☐ B. Voluntary reporting
☐ C. Passive reporting
☐ *D. Active reporting*

4. **Adverse event are:**

☐ A. Life threatening
☐ *B. Due to drug/treatment*
☐ C. May or may not have a causal relationship with treatment

5. **What changes in the management of drug-resistant TB reinforce the importance of active TB drug safety monitoring for a National TB Programme (NTP)?**

☐ *A. New TB regimes and drugs incorporated into routine use*
☐ *B. New TB regimes and drugs used under operational research condition*
☐ *C. All oral bedaquiline-containing regimes*

6. **In the first instance, aDSM applies to which category(ies) of patients?**

☐ A. All treated TB patients
☐ *B. All DR-TB patients treated with new drugs or regimens*
☐ *C. All ultra-resistant TB (XDR-TB) patients*

7. **Active Drug Safety Monitoring (aDSM) results in:**

☐ *A. Reduced treatment interruption*
☐ *B. Added costs to the service (e.g. hospitalization)*
☐ *C. Reduced treatment failure*

8. **The occurrence of an adverse drug event may lead to:**

☐ *A. Interruption of TB treatment*
☐ B. *Avoidable morbidity*
☐ *C. Treatment failure*
☐ *D. Additional costs to the health care service*

9. Which of the following activities is/are related to active TB drug safety monitoring and management (aDSM)

☐ *A. Clinical monitoring*
☐ *B. Adverse event management*
☐ *C. Systematic recording*
☐ *D. Standardised reporting of adverse events*

10. Basic aDSM includes:

☐ *A. Monitoring and reporting of all serious adverse events*
☐ B. Monitoring and reporting of all serious adverse events of special interest
☐ C. Monitoring and reporting of all clinically significant adverse events

11. A serious adverse event (SAE) is an event that may result in:

☐ *A. Death*
☐ *B. Hospitalization*
☐ *C. Significant disability*
☐ *D. Congenital anomaly*
☐ E. Change medication

12. A severe adverse event (severe AE) is an event :

☐ *A. Of maximum intensity as judged by the patient/clinician*
☐ *B. May be determined by degree*
☐ C. Often based on the outcome
☐ *D. Often based on clinical or laboratory tests*

13. How can adverse events be detected in a DR-TB patient on treatment?
(HCWs)

☐ *A. Listening and observation*
☐ *B. Systematic clinical assessments*
☐ C. Hospitalisation
☐ *D. Regular laboratory tests*

Regarding record keeping and data quality assurance for DR-TB: It is important that the documentation of records and/or registers is:
(Managers)

☐ A. Attributable
☐ B. Readable
☐ C. Contemporary
☐ *D. all of the above*

14. Which second-line anti-TB drugs prolong the QTc interval on electrocardiogram (ECG)?
(HCWs)

☐ A. Isonizid
☐ B. Linezolid.
☐ *C. Bedaquiline.*
☐ D. Cycloserine.

What are the indicators of good aDSM?
(Managers)

☐ A. Good coverage at the level of diagnosed patients

☐ B. Good data completeness
☐ *C. Good reporting of serious AEs*
☐ *D. Good description of AEs associated with the new regimen/drug*

15. Which second-line anti-TB drug(s) primarily cause peripheral neuropathy?
(HCWs)
☐ *A. Linezolid*
☐ B. Pyrazinamide
☐ C. Clofazimine
☐ *D.* Isoniazid
☐ E. Moxifloxacin

Of the eight key steps for implementing the aDSM, two are essential before patients are put on new MDR-TB treatment:
(Managers)
☐ *A. Create standard data collection tools and train staff on the collection of data*
☐ B. Develop a plan for aDSM and train staff on the collection of data
☐ C. Create standard data collection tools and consolidate aDSM data electronically
☐ D. Develop a plan for aDSM and create standard data collection tools
☐ E. Train staff on the collection of data and consolidate aDSM data electronically

16. A TB patient during treatment for DR-TB with all-oral short course therapy develops severe hepatitis with transaminase elevation to 5 times the normal value. Should he/she:
(HCWs)
☐ A. Continue treatment
☐ B. Promptly switch to the continuation phase even if the intensive phase has not been completed
☐ C. Stop all treatment until transaminases normalise and reintroduce all treatment at half dose.
☐ *D. Stop all treatment until transaminases normalise and reintroduce the less hepatotoxic drugs Ethionamide (E), Moxifloxacin (Mfx), Clofazimine (Cfz), Bedaquiline (Bdq). Then introduce the most hepatotoxic drugs one by one Prothionamide (Pto), Pyrazinamid (Z) and observe the evolution of transaminases every 3 days in order to identify the responsible drug.*
☐ E. Stop all treatment until transaminases normalise and reintroduce the drugs one by one in this order: Pyrazinamid (Z), Prothionamide (Pto), Clofazimine (Cfz), Moxifloxacin (Mfx), Ethionamide (E).

The process of pharmacovigilance notification involves steps in the following order:
(Managers)
☐ A. Case processing -> signal management -> risk management -> international submission
☐ *B. Case processing-risk management -signal management- international submission*
☐ C. international submission - case processing-signal management-risk management
☐ D. Risk management- international submission - case processing-signal management

Annex 6: Report template

aDSM training Report

Submitted by: ……

(Name, affiliation, date)

The training report should cover the following aspects

Note: The Training Report should cover the following aspects, but can be modified if needed.