WHO/HTM/TB/2015.28

Active tuberculosis drug-safety monitoring and management (aDSM)

Framework for implementation

November 2015

GLOBAL TB PROGRAMME

World Health Organization

Active tuberculosis drug-safety monitoring and management (aDSM)

Background

Health programmes that systematically monitor patient safety are in a better position to prevent and manage adverse drug reactions (ADRs), improve health-related quality of life, and improve treatment outcomes. Likewise, national tuberculosis (TB) programmes that actively pursue drug-safety monitoring and management are better prepared to introduce new TB drugs and novel regimens.

The prospects of new anti-TB drugs and use of novel regimens led WHO to release its first implementation manual for pharmacovigilance of anti-TB drugs in 2012 (1). Later in 2012, WHO provided interim advice that the use of shorter regimens for multidrug-resistant TB (MDR-TB) be accompanied by the collection of drug-safety data within a framework of observational research (2). In 2013 and 2014, the WHO interim policies on bedaquiline and delamanid recommended active pharmacovigilance as one of the five conditions to be met when these drugs are used to treat MDR-TB patients (3),(4).

National TB programmes (NTPs) and other stakeholders are now starting to introduce new anti-TB drugs and novel MDR-TB regimens according to WHO recommendations. A number of programmes managing MDR-TB patients have also introduced active pharmacovigilance to monitor drug-safety and to take early action to avert treatment interruption and other unfavourable patient outcomes (5),(6),(7).

The application of pharmacovigilance methods such as cohort event monitoring described in the 2012 WHO Handbook – which were largely based on experience with the use of drugs for malaria, HIV and non-communicable diseases – led to practical questions related to the implementation of drug-safety monitoring alongside other components of programmatic management of drug-resistant TB (PMDT).

The lack of familiarity of many TB practitioners with the principles of drug-safety monitoring, and the limited capacity of national drug-safety authorities in some countries to provide the necessary support, have resulted in requests for more explicit guidance. A recent survey conducted by Médecins Sans Frontières (MSF) and the Stop TB Partnership's Global Drug Facility (GDF) in the 27 high MDR-TB burden countries showed concerns about ADRs as one of the main barriers identified for the introduction of bedaquiline and delamanid (MSF/GDF, unpublished information).

Several stakeholders have also expressed concern that the introduction of new anti-TB drugs may be slowed down or even prevented due to a lack of capacity by countries to mount conventional active pharmacovigilance. The WHO Global

TB Programme (WHO/GTB) therefore convened key technical and funding agencies to a meeting in Geneva, Switzerland on 28-29 July 2015 to discuss essential requirements for the implementation of active pharmacovigilance and proper management of ADRs when introducing new anti-TB medicines or novel MDR-TB regimens. This document reflects the consensus achieved during this meeting and in subsequent discussions also involving NTP managers of selected countries and the WHO Essential Medicines and Health Products Department (see list of contributors in Annex 1).

Other WHO documents – particularly the Companion Handbook to the WHO guidelines for the programmatic management of drug-resistant TB (the PMDT Handbook) (8), the Policy Implementation Package for new TB drug introduction (9), and the current WHO/GTB website on TB drug safety and the associated frequently asked questions (10) - will also be updated accordingly.

Introducing active TB drug-safety monitoring and applicable terminology

The concept of 'cohort event monitoring' and other conventional terminology of pharmacovigilance are foreign to many TB practitioners and recent recommendations for their introduction in PMDT programmes have created some confusion. Moreover, not all countries are at equal levels of maturity in implementing general pharmacovigilance activities (11), (12).

This document therefore outlines the agreed essential requirements for active drug-safety monitoring and management in patients on treatment for drug-resistant TB.[1] It proposes key terms that were adapted to the specific context of active TB drug-safety monitoring (see Annex 2 for a glossary of the main terms). This adaptation should help the TB community to speak the same language while implementing the required drug-safety activities.

The term 'active TB drug-safety monitoring and management' (abbreviated as aDSM) defines the active and systematic clinical and laboratory assessment of patients while on treatment. aDSM applies to patients on treatment with i) new anti-TB drugs; ii) novel MDR-TB regimens; or iii) XDR-TB regimens, in order to detect, manage and report suspected or confirmed drug toxicities.

The recording and reporting activities of aDSM primarily target the serious adverse events (SAEs) as a core requirement. PMDT sites with additional resources may also monitor other AEs which are of clinical significance or of special interest to the PMDT programme, as part of an extended aDSM approach (see below and also Annexes 2 and 3).

[1] While drug-safety issues are also relevant in the management of drug susceptible TB, the safety profiles of first-line TB drugs are well-described and not considered necessary to be covered by *active* drug-safety monitoring.

The appropriate and timely management of all AEs and ADRs is an integral component of aDSM and patient care. Details on the management of AEs and ADRs are included elsewhere (see Chapter 11 of the PMDT Handbook (8)) and are not repeated in this document.

Setting up aDSM for patients on treatment for drug-resistant TB implies additional responsibilities and resource needs. In contrast to the surveillance of drug-resistance and treatment outcomes, the active systematic monitoring of the occurrence of SAEs is relatively new to TB programmes. Implementation, management and supervision necessary for aDSM should be systematically built into the PMDT component of the TB programme and be conducted in step with other activities related to patient care and monitoring.

Close coordination of aDSM activities with the main pharmacovigilance structures at country level is essential to avoid overlap and duplication. Even countries with mature conventional pharmacovigilance systems may need to establish an aDSM component within PMDT programmes to ensure that patients are adequately monitored and all SAEs (at least) are detected, managed, and reported rapidly.

Patients to whom aDSM applies

- MDR-TB and XDR-TB patients treated with new medicines, such as bedaquiline or delamanid;
- MDR-TB patients enrolled on treatment with novel regimens, such as those much shorter than currently recommended by WHO;
- All other XDR-TB patients on second-line treatment (as these regimens often include multiple repurposed drugs),

Once these groups of patients are covered, aDSM can be extended to other patients on treatment with conventional MDR-TB regimens, depending on the resources available.

Objectives of aDSM

aDSM is not expected to meet all the criteria for conventional cohort event monitoring. The overall objectives of aDSM are to reduce risks from drug-related harms in patients on second-line treatment for drug-resistant TB and to generate standardised aDSM data to inform future policy updates on the use of such medicines.

To achieve these objectives, aDSM includes **three essential activities**:

- Patients targeted for aDSM should undergo active and systematic clinical and laboratory assessment during treatment to detect drug toxicity and AEs. Proposed schedules have been developed for use in patients on shorter regimens or on new medications (5),(8);

- All AEs detected should be managed in a timely fashion in order to deliver the best possible patient care. Management of AEs is beyond the scope of this note and further details are provided in other implementation documents such as the PMDT Handbook (8);

- Standardised data should be systematically collected and reported for any SAE detected[2]: these will eventually be used to characterize the types of SAEs, assess the safety of the treatment and to inform future policy on the use of these medicines.

All SAEs detected should be reported to the national authority responsible for pharmacovigilance according to individual country requirements (including time limits for reporting) and should be regularly assessed for causality.

WHO will work with partners to establish a global database for aDSM to enhance the detection of new signals and to inform future updates of global policies on the use of anti-TB drugs and novel regimens. This is distinct from existing mechanisms for the global coordination of spontaneous reports from national pharmacovigilance systems.

Three levels of monitoring in aDSM

1. **Core package**: requiring monitoring for and reporting of all SAEs
2. **Intermediate package**: includes SAEs as well as AEs of *special interest*[3]
3. **Advanced package**: includes all AEs of *clinical significanc*[3]

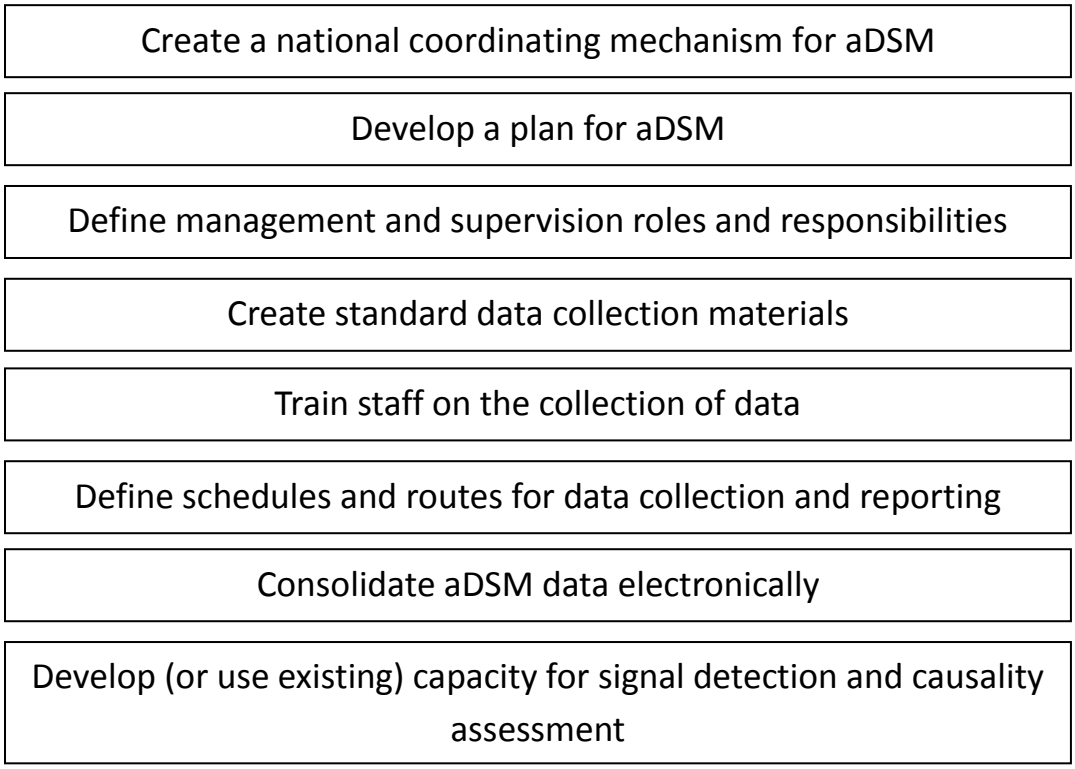
All PMDT sites treating eligible patients with new anti-TB drugs, novel MDR-TB regimens or for XDR-TB require the Core package. These treatment centres should, as a minimum, also be taking part in spontaneous reporting of ADRs as required by local regulations. Expansion of aDSM should be implemented in a phased approach as and when resources permit.

Implementing aDSM

Based upon the experience of the successful implementation of other care and monitoring components of PMDT programmes, eight key steps have been identified for programmes to follow when introducing aDSM (Figure 1).

[2] Countries and stakeholders may also monitor other AEs of special interest or clinical significance (see next section).
[3] See Annexes 2 and 3 for definitions of these terms.

Figure 1. Key steps to implementing aDSM



Ideally, all eight steps should be in place before patients are enrolled on treatment with new drugs, novel MDR-TB regimens or XDR-TB treatment. As this may not always be feasible, two steps are essential **ahead** of any patient enrolment, i.e.

i) creating standard data collection materials; and
ii) training staff on the collection of data

By having these minimum conditions in place there is less likelihood that data are lost and that opportunities to manage AEs and ADRs are missed.

The responsibility for the coordination of aDSM at national level should be assigned to an existing TB expert body, such as the MDR-TB committee (or *consilium*) or the technical working group on new drugs. These committees should primarily have scientific and clinical expertise for MDR-TB care and drug safety monitoring but may also include expertise important for coordination and communication (e.g. funding, advocacy, patient representation). Until such group is tasked with this role the NTP needs to assign someone to coordinate the necessary aDSM activities and ensure that the two key steps mentioned above are in place prior to patient enrolment.

The aDSM plan should define clearly the activities and the standard operating procedures, including the plan for data collection, reporting of indicators, analyses and communication. The final document should be incorporated within

the national TB or PMDT guidelines. Local and/or international experts in drug-safety as well as the national pharmacovigilance centre should be engaged.

While some of the data collection tools for aDSM are separate from those used for routine PMDT programme monitoring, the process should be integrated with the other cohort-based monitoring for bacteriological response and outcomes that has been a standard feature of the PMDT component of TB programmes for several years (see Chapter 2 and Annexes of (8)). WHO is working closely with NTPs and partners towards further integration of aDSM within routine PMDT programme monitoring.

In the Core Package of aDSM, clinical and laboratory test records at baseline (treatment initiation) and during regular review (e.g. monthly intervals) should be integrated into an expanded version of the programmatic MDR-TB (Second-line TB) Treatment Card (see Annex 4 for an example). The treatment initiation form should be completed before the start of treatment (to document any abnormality which could later be confused with a drug-related SAE) and the review form should be completed at scheduled encounters with the patient. In addition, information on SAEs occurring in-between visits should also be captured using the same forms.

A standard form (in paper or electronic format) to alert the programme when any SAE occur will need to be developed (see Annex 5 for an example). Its content could be similar to that used by the national pharmacovigilance centre for spontaneous reporting.

For the Intermediate and Advanced Packages of aDSM, additional data collection forms will have to be used to record data at baseline and during regular follow-up. Templates of such forms have been developed and can be adapted to individual programme needs (13).

Staff at the different levels of health services should be informed and trained on the use of the new anti-TB drugs or novel regimens ahead of any patient enrolment. This training would need to include instruction on the completion of the aDSM forms. It is important that this activity is completed ahead of any patient enrolment to ensure timely identification of adverse events which need to be managed as well as proper and complete collection of information.

All adverse events detected during routine clinical patient care should lead to an appropriate and timely management response in order to limit potential harms to the patient. In terms of monitoring, the minimum requirement for aDSM is that all SAEs be registered and reported, regardless of their severity or whether they are known to have been caused by any of medicines to which the patient is exposed.

Some centres with sufficient resources may be designated as "sentinel sites" and undertake additional monitoring to that required by the Core Package of aDSM,

such as the reporting of AEs of special interest or AEs of clinical significance (see above). In addition, in many countries the reporting of ADRs to the national pharmacovigilance centre is mandated by law. As for all other public and private health services, TB practitioners should comply with the national legal requirements for such reporting.

The creation of an electronic database - or preferably the adaptation of an existing TB patient database to accommodate the additional data fields required - is an important step in aDSM implementation. It will ensure the standardisation and safekeeping of the data. If data are collected on paper forms these need to be entered regularly into the electronic database. The management of data in electronic format is indispensable and will facilitate the sharing of data, generation of indicators and analysis.

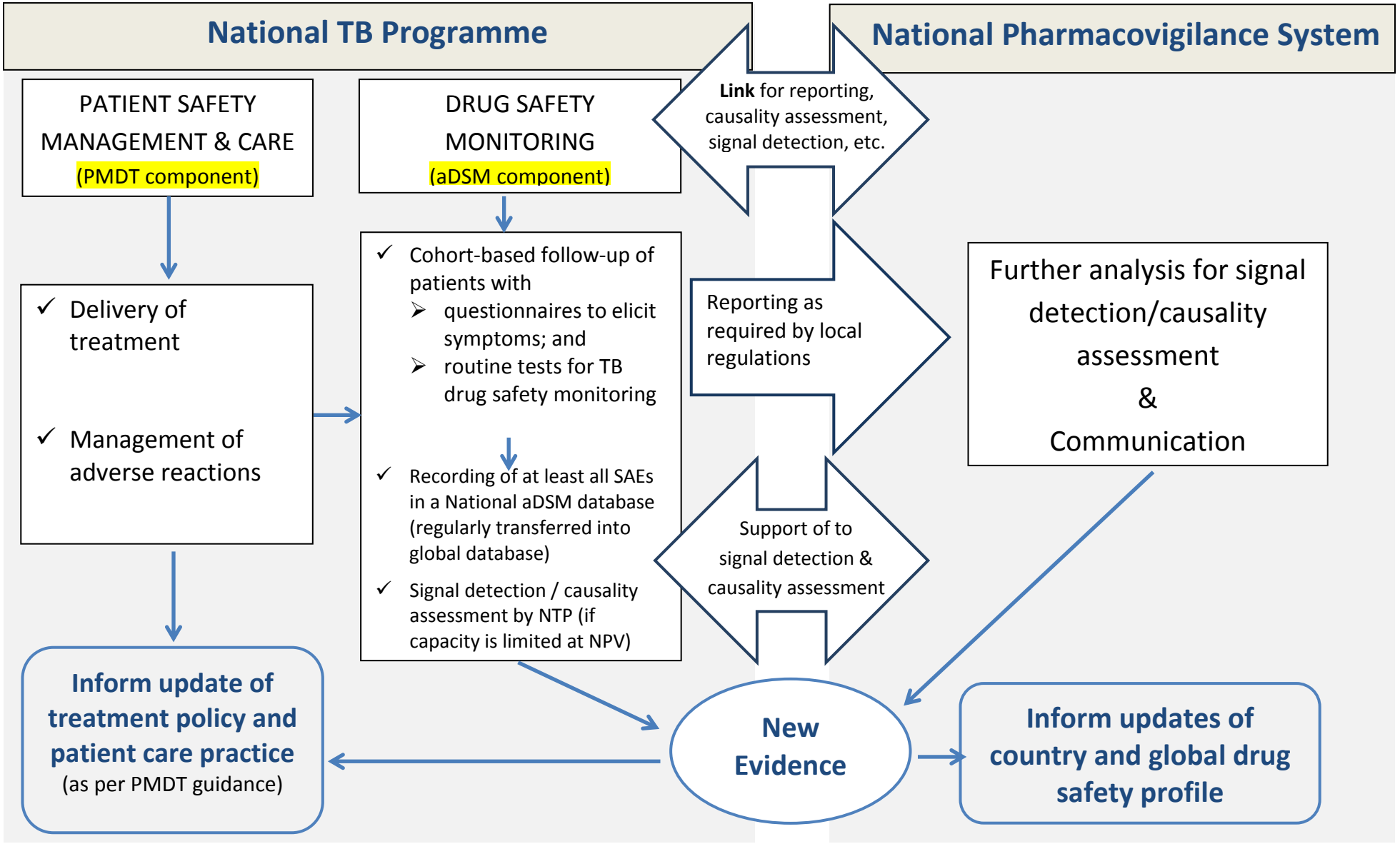
Measures should be taken to avoid duplication of work by revising existing databases, ensuring interoperability of data management systems, consulting with local pharmacovigilance authorities and granting access rights to users for different data as needed (see Figure 2). The roles and responsibilities for data management and analysis should be specified in the aDSM plan to avoid the creation of parallel systems of ADR reporting and make use of the best possible expertise and capacity in the country on drug safety.

The ultimate purpose of systematic data collection within aDSM is to enable causality assessment for serious adverse events, determine their frequency (rates) and to detect signals. Physicians skilled in MDR-TB management already attempt to assess relationships between drugs and ADRs and take appropriate clinical action. Nevertheless, formal causality assessment is a separate process that requires involvement of other experts. In a number of countries, the capacity of the national pharmacovigilance centres to conduct formal causality assessment is very limited but where such capacity exists it should be availed of.

National TB programme staff should acquire the skills necessary to undertake the essential activities related to aDSM. This is a long-term goal but needs to be started as part of the plan to introduce new anti-TB drugs and novel MDR-TB regimens. Local and/or international expertise in causality assessment needs to be sought by the programme to carry out such capacity building. WHO is also working with partners to accelerate such capacity building efforts.

Figure 2. Generic model of how aDSM is positioned within drug-safety structures at the national level

aDSM adapted to the local situation to avoid the creation of parallel systems of reporting



Support to the implementation of aDSM

The implementation of aDSM at TB programme level will be greatly facilitated by familiarity with the concept of cohort-based follow-up of patients, which is the basis of monitoring and evaluation of TB and MDR-TB treatment programmes. To date a number of countries have already successfully integrated clinical and laboratory testing schedules for active drug-safety monitoring within the TB patient cohort framework which they use to monitor treatment response and outcomes (5),(6). The testing schedules used in these projects have largely followed those generally recommended when second-line TB drugs are used (8).

Experience from observational studies of shorter regimens for MDR-TB has shown that active drug-safety monitoring can be feasibly implemented within programmes if dedicated funding is provided. Most of the additional resources are needed to undertake clinical testing (e.g. electrocardiography, audiometry) and laboratory analyses, as well as undertaking the added work to collect the safety data.

It is envisaged that once the right skills have been acquired, and links established with appropriate experts in drug-safety, causality assessment and signal detection could be organised within the PMDT programme with appropriate capacity building and support from drug-safety experts (if such capacity is missing at the national pharmacovigilance system). More work is needed to quantify the costs of aDSM and these will eventually be reflected in tools to help users with budgeting.

While clinicians treating patients with second-line anti-TB drugs are usually familiar with clinical monitoring for adverse events, this knowledge may not be shared by many other health care workers within the programme. The monitoring component of aDSM is also likely to be novel to many health care workers. WHO/GTB and technical partners will be supporting national TB programmes to build such capacity and to integrate aDSM into routine PMDT monitoring. A training plan and resources for building capacity will be created by early 2016.

Likewise, the creation of a global central database to pool anti-TB drug-safety data collected through aDSM projects in different countries is envisaged from early 2016. This could increase the likelihood of detecting rare adverse events. Separate guidance will be prepared to guide national programmes on how to submit their data to the global database.

Summary – aDSM in brief

- Active TB drug safety monitoring and management (aDSM for short) refers to the active and systematic clinical and laboratory assessment of patients on treatment with i) new anti-TB drugs; ii) novel MDR-TB regimens; or iii) XDR-TB regimens, to detect, manage and report suspected or confirmed drug toxicities.

- While all detected adverse events (AEs) need to be managed clinically, the Core Package of aDSM requires the reporting of serious AEs (SAEs) only. PMDT sites with additional resources may also monitor other AEs which are of clinical significance or of special interest to the programme, as part of comprehensive aDSM. aDSM may also be expanded in a phased approach to eventually cover TB patients on treatment with any second-line drugs should programmes wish to do so.

- aDSM is intended to be an integral component of PMDT programmes. Its rationale is based on recent developments in MDR-TB treatment, particularly the approval for use of new medicines ahead of the completion of Phase 3 trials, increased use of repurposed drugs for XDR-TB treatment and the development of novel second-line anti-TB regimens. Such approaches need careful monitoring for drug-related harms, some of which may as yet not be described.

- aDSM is not aimed at replacing or duplicating efforts of national pharmacovigilance units but to complement current capacities and address barriers to undertake active pharmacovigilance within the context of TB care. In addition to drug-safety monitoring, aDSM also incorporates a component which promotes the clinical management of all ADRs and AEs regardless of seriousness. This monitoring and management needs to be adapted to the realities of TB programmes which are often under-resourced.

- In order for national programmes to undertake aDSM effectively, a series of activities need to be coordinated to ensure that the right expertise is developed through interaction with local and external drug-safety experts, and that sufficient funds are made available to ensure that the clinical monitoring activities are performed, the data collected, reported and analysed, and decisions made based on the new knowledge gained.

Annex 1. List of Contributors

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Annex 2. Glossary of terms for active tuberculosis drug-safety monitoring and management (aDSM)

In addition to the new terms (marked with an asterisk), the definition of other terms may have been modified slightly from those in general usage to apply better to the context of national tuberculosis programmes.

active TB drug-safety monitoring and management (aDSM)* is the active and systematic clinical and laboratory assessment of patients on treatment with i) new anti-TB drugs; ii) novel MDR-TB regimens; or iii) XDR-TB regimens; to detect, manage and report suspected or confirmed drug toxicities. While all detected adverse events (AEs) need to be managed, the core package of aDSM requires the reporting of serious AEs only. M/XDR-TB treatment sites with additional resources may also monitor other AEs which are of clinical significance or of special interest to the programme, as part of comprehensive aDSM.

adverse drug reaction (ADR) is a response to a TB medicine which is noxious and unintended, and which occurs at doses normally used in humans.

adverse event (AE) is any untoward medical occurrence that may present in a TB patient during treatment with a pharmaceutical product, but which does not necessarily have a causal relationship with this treatment.

serious adverse event (SAE) is an adverse event which either leads to death or a life-threatening experience; to hospitalization or prolongation of hospitalization; to persistent or significant disability; or to a congenital anomaly. Serious events which do not result immediately in one of these outcomes but which might require an intervention to prevent it from happening are included (14). SAEs may require a drastic intervention such as termination of the drug suspected of having caused the event.

adverse event of clinical significance* is an adverse event which is either (i) serious, (ii) of special interest, (iii) leads to a discontinuation or change in the treatment, or (iv) is judged as otherwise clinically significant by the clinician (see Annex 3). The centres which offer the advanced package of aDSM will include all adverse events of clinical significance in their reporting.

adverse event of special interest* is an adverse event documented to have occurred during clinical trials and for which the monitoring programme is specifically sensitized to report regardless of its seriousness, severity or causal relationship to the TB treatment (see Annex 3). The centres which offer the intermediate and advanced packages of aDSM will include all adverse events of special interest in their reporting.

adverse event leading to treatment discontinuation or change in drug dosage*, is an adverse event which leads a clinician to stop, interrupt temporarily or change the dosage of one or more drugs, regardless of its seriousness, severity, or causal relationship to the TB treatment.

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

causality assessment is the evaluation of the likelihood that a TB medicine was the causative agent of an observed adverse reaction.

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

sentinel sites* are centres which, in addition to the core package of aDSM, also undertake intermediate or advanced levels of drug-safety monitoring.

signal is reported information on a possible causal relationship between an adverse event and a TB medicine, the relationship being unknown or incompletely documented previously or representing a new aspect of a known association. The information may arise from one or multiple sources that are judged to be of sufficient likelihood to justify verification(15).

Annex 3. Adverse events of clinical significance or special interest for aDSM

See Annex 2 for the definition of types of adverse events mentioned on this page

1) All serious adverse events (SAEs)

2) All adverse events of special interest (suggested list)[4]:

- Peripheral neuropathy (paraesthesia),
- Psychiatric disorders and central nervous system toxicity (e.g. depression, psychosis, suicidal intention, seizures)
- Optic nerve disorder (optic neuritis) or retinopathy,
- Ototoxicity (hearing impairment, hearing loss).
- Myelosuppression (manifested as anaemia, thrombocytopenia, neutropenia or leukopenia),
- Prolonged QT interval (Fridericia correction; see (8))
- Lactic acidosis
- Hepatitis (defined as increases in alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥5x the upper limit of normal (ULN), or increases in ALT or AST ≥3x ULN with clinical manifestations, or increases in ALT or AST ≥3x ULN with concomitant increase in bilirubin ≥1.5 x ULN)
- Hypothyroidism,
- Hypokalaemia,
- Pancreatitis
- Phospholipidosis
- Acute kidney injury (acute renal failure)

3) Adverse events leading to treatment discontinuation or change in drug dosage

4) Adverse events not listed above but judged as otherwise clinically significant by the clinician

Adapted from (16)

[4] The list shown here is provisional and may be modified according to the regimen composition or the patient cohort.

Annex 4

Active tuberculosis drug-safety monitoring and management (aDSM)

CLINICAL AND LABORATORY TESTING SCHEDULE FOR aDSM

to be adapted to the local treatment regimen and national policy (*ref.1*)

	M0	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18	M19	M20	M21	M22	M23	M24
Date																									
Clinical screen																									
Visual acuity																									
Simple hearing test																									
Audiogram																									
Neuro & psychiatric investigations																									
Serum creatinine																									
ALT (SGPT)																									
AST (SGOT)																									
Bilirubin																									
Alkaline phosphatase																									
γGT																									
ECG																									
Lipase																									
Amylase																									
Potassium																									
Magnesium																									
Calcium																									
Albumin																									
Complete Blood Count																									
Blood glucose																									
Thyroid test / TSH																									

1. Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. (WHO/HTM/TB/2014.11). Geneva, World Health Organization. 2014

Shade cells for the months when the test will not be done

Notation for marking the cells: 0= screen/test not done 1=screen/test done; result pending 2=screen/test done; no SAE 3=screen/test done; SAE detected

example

Annex 5

Alert for serious adverse events to the TB programme

CONFIDENTIAL - To be sent even upon suspicion of a serious adverse event

IS THIS REPORT A NEW EVENT? YES ☐ NO ☐ GIVE DATE WHEN PREVIOUS SAE FORM SENT : (dd/mmm/yyyy)

1. PATIENT DETAILS

SURNAME FIRST NAME

SEX Male ☐ Female ☐ DATE OF BIRTH ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY *age in yrs if DOB unknown*

PREGNANCY NO ☐ YES ☐

ID NUMBER PHONE NO.

ADDRESS

2. SUSPECTED and CONCOMITANT MEDICINE(S)

NAME (Brand name or Generic)	Total daily dose	Date started	Date stopped	Continues
				❑
				❑
				❑
				❑
				❑

3. DETAILS OF SERIOUS ADVERSE EVENT

DATE EVENT STARTED		**DATE EVENT STOPPED**	
DESCRIPTION OF EVENT			

WHY IS THE EVENT CONSIDERED SERIOUS?

- ❑ Death
- ❑ Life-threatening event (specify.....)
- ❑ Hospitalization or prolongation of hospitalization
- ❑ Persistent or significant disability (specify.....)
- ❑ Congenital anomaly
- ❑ Other (specify.....)

4. ACTION TAKEN

- ❑ Medicine withdrawn
- ❑ Dose increased
- ❑ Dose reduced
- ❑ Dose not changed
- ❑ Unknown

5. OUTCOME OF SERIOUS ADVERSE EVENT

- ❑ Recovered / resolved
- ❑ Recovering / resolving
- ❑ Recovered with sequelae
- ❑ Not recovered / not resolved
- ❑ Died
- ❑ Unknown

6. REPORTER

NAME POSITION

FACILITY/CLINIC

ADDRESS

E-MAIL PHONE NO.

SIGNATURE DATE SENT ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

example

Explanatory Note

TO BE ADAPTED ACCORDING TO THE LOCAL SITUATION

- This form is intended for the Core Package of active tuberculosis drug-safety monitoring and management (aDSM). For more details please refer to other documents on aDSM. The spontaneous reporting form in use by the national pharmacovigilance authorities may be adapted to provide for the purposes of alerting the TB programme of SAEs and avoiding parallel reporting structures.
- The completed form can be sent electronically, via email or fax to <address> and the responsible authority alerted by phone
- The report should be sent within <number> hours after it is detected, even upon suspicion of seriousness
- The report should be sent even if not all details are available and regardless of certainty of association with any particular medicine. The essential details are the identifiers of the patient and the reporter; the name of the suspected medicine(s); and basic details on the serious adverse event
- If the report relates to a previously notified event indicate this under section 3; if more than one serious adverse event occur in the same individual, send separate forms for each event
- All health care professionals are encouraged to report. Patients and relatives may also report
- Upon receipt of the information the responsible authority will review the information and contact the reporter and/or facility for more details. All information, including identity of the patient and reporter, will be handled in strict confidence. Apart from action to protect public health, anonymised statistics from these reports will be used to improve drug-safety
- When reporting please use DD MMM YYYY format to report dates. In the DESCRIPTION OF EVENT provide a single diagnosis and include anatomical location if applicable. If diagnosis is unknown, describe clinical picture.

example

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