Good practices guidance handbook for national TB surveys

How to apply good clinical and good data management practices for national TB surveys

World Health Organization

TDR For research on diseases of poverty
UNICEF • UNDP • World Bank • WHO

Good practices guidance handbook for national TB surveys

How to apply good clinical and good data management practices for national TB surveys

World Health Organization

TDR For research on diseases of poverty
UNICEF • UNDP • World Bank • WHO

Good practices guidance handbook for national TB surveys: how to apply good clinical and good data management practices for national TB surveys

ISBN 978-92-4-002865-4 (electronic version)
ISBN 978-92-4-002866-1 (print version)

Suggested citation. Good practices guidance handbook for national TB surveys: how to apply good clinical and good data management practices for national TB surveys. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at http://apps.who.int/iris.

Contents

List of Figures

Foreword

The purpose of this document is to describe and explain how to apply the principles of good clinical practice (GCP) and good data management practice (GDMP) in the context of national tuberculosis (TB) surveys, namely national population-based surveys of TB prevalence, anti-TB drug resistance surveys, and surveys of costs faced by TB patients and their households.

The primary target audience for this handbook includes national TB programmes (NTPs) and partners involved in the planning, design, conduct, oversight, analysis and reporting of a national TB survey. The in-country national survey coordination team is responsible for ensuring that all survey team members conform to this guidance document.

The document is organized as follows:

- **Part A**: GCP and GDMP principles in the context of national TB surveys
- **Part B**: Application of the GCP and GDMP principles and links to the tools
- **Part C**: Glossary of terms used.

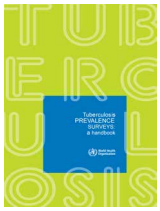
The set of tools provided in **Annex I** is intended to help end-users implement GCP and GDMP throughout the survey. Tools include checklists, report templates and tracking logs. This guidance document also refers and provides links to essential documents that are specific to each type of survey.

Most tools should be developed at the beginning of the survey. Tools are used during various phases of a survey, as illustrated in Figure 1. The use of these tools is at the discretion of the in-country survey team and they can be adapted as needed, so as to be fit-for-purpose.

HOW TO USE ICONS:

This icon is placed next to chapter for which a tool was developed as part of this handbook and that is placed in annex of it.

this icon is placed next to chapter for which guidance/ tools are provided in the WHO Global TB guidance document for TB surveys (NTPS, DRS or PCS) or in other documents.



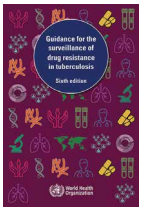


FIGURE 1. List of tools used in different phases of the survey

All tools should be developed during the survey design and planning phase. This figure shows when they will be predominantly used during the conduct and close-out of the survey.

[1] RACI: Responsible, Accountable, Consulted, Informed
[2] CAPA: Corrective And Preventive Action

Acknowledgements to all contributors

This guidance document is the result of the collaboration between the Global TB Programme (GTB) of the World Health Organization (WHO) and the Special Programme for Research and Training in Tropical Diseases (TDR). It was produced by a core writing team composed by Varalakshmi Elango (TDR consultant), Jennifer Kealy (TDR consultant) and Corinne Merle (TDR) with contributions from Anna Dean (GTB), Inés Garcia Baena (GTB), Philippe Glaziou (GTB), Christine Halleux (TDR), Annette Kuesel (TDR), Irwin Law (GTB), Nobuyuki Nishikiori (GTB), Debora Pedrazzoli (TDR), Babis Sismanidis (GTB) and Olga Tosas Auguet (GTB). Overall coordination of the production of this document was provided by Corinne Merle (TDR).

WHO would like to thank the following experts who took part in the workshop on "Good Clinical Practice in the context of national surveys of the burden of TB disease" in September 2019, which provided the initial understanding of the gaps in good clinical practice this document aims to address: Riccardo Alagna (San Raffaele Scientific Institute, Milan, Italy), Bintari Dwihardiani (WHO consultant, Indonesia), Lena Fiebig (Sokoine University of Agriculture, Tanzania), Mourad Gumusboga (Institute for Tropical Medicine, Antwerp, Belgium), Kiyohiko Izumi (WHO), Nico Kalisvaart (KNCV), George William Kasule (National Tuberculosis Reference Laboratory, Kampala, Uganda), Adam MacNeil (US Centres for Disease Control and Prevention), Farai Mavhunga (WHO), Veriko Mitskhulava (KNCV Tuberculosis Foundation, the Hague, Netherlands), Fukushi Morishita (WHO), Thuli Mthiyane (Medical Research Council, Pretoria, South Africa), Jane Nabongo Rahedi - Ong'ang'o (Kenya Medical Research Institute, Nairobi, Kenya), Ikushi Onozaki (WHO), Welile Sikhondze (Ministry of Health Eswatini), Marina Tadolini (Alma Master Studiorum University, Bologna, Italy), Elisa Tagliani (San Raffaele Scientific Institute, Milan, Italy), Fasil Tsegaye Kassa (Nitsuh, Addis Ababa, Ethiopia), Zeleke Alebachew Wagaw (National TB Programme, Accra, Ghana) and Norio Yamada (Research Institute of Tuberculosis, Japan Anti-TB Association, Japan).

Funding for this work was provided by the United States Agency for International Development (USAID).

Abbreviations

ALCOAC	attributable, legible, contemporaneous, original, accurate and complete
CAPA	corrective action preventive action
DRS	anti-TB drug resistance surveys
GCP	good clinical practice
GDMP	good data management practice
ICH	International Council for Harmonisation
IEC	independent ethics committee
KNCV	KNCV Tuberculosis Foundation
LAR	legally authorized representative
NTBS	national tuberculosis surveys
NTP	national tuberculosis programme
NTPS	national tuberculosis prevalence survey
PCS	patient cost survey
QA	quality assurance
QC	quality control
QMS	quality management system
RACI	responsible, accountable, consulted, informed matrix
RM	risk management
SRL	supranational reference laboratory
SOP	standard operating procedure
STROBE	strengthening the reporting of observational studies in epidemiology
TB	tuberculosis
WI	work instruction

Glossary

Applicable regulatory requirement(s)	Domestic laws and regulations addressing the conduct of public health program in general and NTBS in particular.
Approval	The affirmative decision from the IEC that the survey documents have been reviewed and that the survey may be conducted at the identified sites in accordance with the applicable regulatory requirements and the WHO survey guidelines.
Audit trail	Documentation of all data needed to track changes, edits or corrections to the source data. This allows for tracking details of any change/s that were made, the person who made the change and the reasons for the change, without overwriting the source data. In the event of electronic systems, traceability should be documented via computer generated audit trails, for example, the data and time when change was made and the user ID and password that was used for making the change.
Case report form	A paper or electronic document designed to record all of the protocol required information to be reported to the data manager on each survey participant.
Certified copies	Refers to a paper or electronic copy that either has been verified against the source document or was generated using a validated process to produce a copy, for instance, a photocopy of a thermal sheet generated from a lab machine, in which data would fade over time.
Compliance	Adherence to all applicable regulatory requirements
Confidentiality	Prevention of disclosure, to other than authorized individuals, of information or identity of a NTBS participant.
Conformance	Adherence to the respective WHO survey guidelines, Good Practices Guidance document for NTBS, protocol and SOP.
Corrective and preventive action (CAPA)	Refers to the actions taken to improve NTBS processes and to eliminate causes of non-compliance. The process focuses on the systematic investigation of the root causes of identified risk or an error in an attempt to prevent their recurrence or occurrence.
Data	All NTBS source data, their certified copies, metadata, transformations and reports of these data, which are generated during the NTBS and which allow full and complete reconstruction and evaluation of the NTBS activities. Data may be in paper or electronic forms, and include audit trails, photographs, audio or video files or any other media whereby information related to NTBS activities are recorded.
Data archiving	The process of secure storage of NTBS records with authorized access and measures being taken to protect records throughout the retention period from the possibility of being changed or deleted.
Data backup	A copy of NTBS electronic files to be used as an alternative, in case the original data or system are lost or become unusable (for example, in the event of a system crash or corruption of a disk/device).
Data life cycle	All processes by which NTBS data are captured from survey participants, recorded, processed, reviewed, analyzed, reported, transferred, stored, retrieved and monitored until disposal. There should be a planned approach to assessing, monitoring and managing the data and the risks to those data in a manner commensurate with potential impact on participant safety, and/or the reliability of the decisions made, throughout all stages of the data life cycle.
Data integrity	Refers to complete, consistent, accurate, trustworthy and reliable NTBS data throughout the data life cycle. It requires adherence to good documentation practices and appropriate quality and risk management systems.
Data sources	Sources that already have collected the data of interest and from which NTBS data are sometimes abstracted, for example, TB register or the microscopy results laboratory register.

Documentation	All records that describe the methods, conduct, and/or results of any test(s) conducted during the NTBS, the factors affecting a NTBS, and the actions taken.
Electronic system	It includes computer hardware, NTBS software and database, peripheral devices, networks and allied documentations.
Essential document	Document which individually and collectively permits evaluation of the conduct of a NTBS and the quality of the data produced (see 11. Essential Documents).
Funding agencies	Sources of fund for NTBS, including domestic budgets, donor financing from bilateral and multilateral donors, and donor financing from foundations.
Good Clinical Practice	Good clinical practice (GCP) is an international ethical and scientific quality standard for designing, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and wellbeing of trial subjects are protected and that clinical-trial data are credible.
Good data management practice (GDMP)	Measures to ensure that data is attributable, legible, contemporaneous, original, accurate, and complete. If not implemented diligently, the quality of the data will be impacted, so also, the decisions made, based on these data.
Good documentation practice	Measures to ensure that paper and electronic documentation is secure, attributable, legible, traceable, permanent, contemporaneously recorded, original and accurate.
Impartial witness	A person independent of the NTBS, who cannot be unfairly influenced by people involved with the NTBS, who attends the informed consent process if the NTBS participant or his/her legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the participant. This person is present throughout the informed consent process and endorses that the information in the consent form was completely and correctly read out to the NTBS participant.
Informed consent	Informed consent is a process that ensures providing the potential NTBS participant with all the requisite information, to enable making an informed decision and voluntarily confirm his or her willingness to participate in a particular NTBS. Informed consent is signed and dated by the participant.
Independent Ethics Committee (IEC)	A multi-disciplinary committee responsible for reviewing the ethical aspects of the survey, detailed in the protocol and other essential documents and approving the conduct of the survey, ensuring the protection of the rights, safety and well-being of participants in a NTBS. The legal status, composition, function, operations and regulatory requirements pertaining to IEC may differ among countries.
Legally authorized representative (LAR)	An individual or legal or other body authorized under applicable law to consent, on behalf of a prospective NTBS participant, to his/her participation in the NTBS.
Metadata	Metadata are data about data that provide the contextual information required to understand those data. Such data describe the structure, data elements, interrelationships and other characteristics of data. They also permit data to be attributable to an individual. Metadata necessary to evaluate the meaning of data should be securely linked to the data and subject to adequate review. This may include the time/date stamp of an activity, the operator identification (ID) of the person who performed an activity.
Monitoring	The act of overseeing the progress of NTBS, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, SOPs, good practices guidance documents for NTBS, and applicable regulatory requirement(s).
Monitoring plan	A plan and framework describing the period and frequency, responsibilities, criteria, methods and entities for monitoring the NTBS.
Monitoring report	A written report provided by the monitor to the survey coordination team, after each site (or facility or laboratory) visit and/or other related communication, according to the monitoring SOPs.
NTBS national team	All national personnel responsible for overseeing the conduct of activities related to NTBS, at all levels of the survey.

NTBS participant	An individual who participates in a NTBS.
NTBS participant identification code	A unique identifier, assigned by the NTBS field team, to identify the participant and protect his/her identity from being disclosed when reporting NTBS related data.
NTBS site	The location(s) where NTBS related activities are actually conducted; this includes field sites, health facilities, laboratories and central data management sites.
NTBS survey coordination team (survey management team)	A team of personnel responsible and accountable for the implementation of all activities related to NTBS, at all levels of the survey.
Protocol	A document that describes the background and rationale, objective(s), design, methodology, statistical considerations, ethical aspects and organization of an NTBS.
Protocol amendment	A written description of a change(s) to or formal clarification of a NTBS protocol.
Quality	In simple terms, quality means 'conformance to a set of standards. ISO defines quality as "Degree to which a set of inherent characteristics of a product or service, fulfil requirements". American Society for Quality Control defines this as "The totality of features and characteristics of a product or service that bear on its ability to satisfy stated or implied needs" *(15)*. In the context of NTBS, quality refers to the fact that all NTBS activities satisfy the various requirements laid down in this and other guidelines and applicable national regulations.
Quality assurance (QA)	All planned and systematic actions assuring that the NTBS is performed and the data are generated, documented, and reported in conformance with good practices guidance documents for NTBS, respective WHO survey guidelines and compliance with applicable regulatory requirement(s).
Quality control (QC)	The activities undertaken within the QMS to verify that the requirements for quality of the NTBS related activities have been fulfilled.
Quality improvement (QI)	A systematic approach to continuously improving the performance of an organisation, through the analysis of performance data, identifying non-conformances and CAPA.
SIte	A site is a place where data are generated/managed, or a survey related process is carried out, which may impact participant rights, saftey and/or data quality.
Source data	All information in original records and certified copies of original records, findings, observations or other activities in a survey necessary for the reconstruction and evaluation of the survey, in paper or electronic forms. This includes data collected exclusively for the purpose of the survey, for example, X-ray in NTPS, drug resistance data from the laboratory in DRS and interview in PCS. Source data are contained in source documents.
Source documents	The documents in which the source data is first captured. At times, the source document may be a certified copy.
Standard operating procedures (SOPs)	Detailed, written instructions to be adopted/followed to achieve uniformity of the performance of a specific function.
Stakeholders	All parties than can influence or be influenced by NTBS (for example NTBS participants, community, ministry of health, national TB program, funding agencies, WHO).
Supervision	Supervision is a process of self-check of survey processes and data, either performed by someone within the survey team or a member from the quality unit – for instance to verify the completeness of informed consent forms; review of critical data collection and entry, through verification by a second person.
Survey report	A written description of a survey, in which the clinical and statistical description, and presentation of analyses are fully integrated into a single report
Validation	An action of proving and documenting that any process, procedure or method actually and consistently leads to the expected results.

Vulnerable participant	Any individual who either lacks the competency (refers to the legal status of being a major/ adult / emancipated minor) or the capacity (medical, psychological) to voluntarily decide to participate in a NTBS; or may be unduly influenced by the expectation of benefits associated with participation, e.g. the sick, physically challenged, poor or marginalized; or under risk/threat of a retaliatory response from senior members of a hierarchy in case of refusal to participate.
Well-being of the NTBS participants	The physical and mental integrity of the participants in a NTBS.

PART A
General guidance

1. Background

National population-based surveys of the prevalence of bacteriologically confirmed pulmonary TB (NTPS) *(1)* are essential tools used to directly measure the burden of TB disease in countries that do not yet have routine surveillance data that meet quality and coverage standards. They not only measure the burden of TB disease, but also help to improve the understanding of barriers to TB diagnosis and care, in turn enabling policy and programmatic action. Anti-TB drug resistance surveys (DRS) *(2)* are a health facility-based survey aimed at collecting data in a systematic manner in order to inform programmes about the prevalence and patterns of anti-TB drug resistance among patients with TB. The End TB Strategy *(3)* includes the target that no TB patients and their households face catastrophic costs due to TB disease. To monitor the progress in each country on this target, health facility-based 'patient cost surveys' (PCS) *(4)* are designed to assess the direct and indirect costs incurred by TB patients and their households. These three types of surveys will be referred to as national TB surveys (NTBS) in this document.

Robust methodologies for NTPS were developed by the WHO Global Task Force on TB Impact Measurement. Effective implementation requires commitment from the national TB programme (NTP) entity/authority to invest significant resources into staff availability, staff training, availability of adequate equipment and community mobilization. With this level of investment, all possible measures should be taken to ensure that the emerging data are comprehensive and reliable. A meeting of this Global Task Force held in April 2016 discussed progress made on the national surveys and the future direction of NTPS *(5)*. In several surveys, major challenges included the quality of processes, in particular the laboratory (culture testing) and data management for tens of thousands of participants interviewed and screened in the community. To address and mitigate such challenges in future surveys, not just for the NTPS, but also for DRS and PCS, one major recommendation was to develop guidance on how to apply the principles of good clinical practice (GCP) and good data management practice (GDMP) in the context of NTBS to ensure (1) the protection of the rights, safety and well-being of all survey participants and (2) the integrity of the data.

2. Objectives and scope of the guidance document

The purpose of this document is to describe how to apply the principles of the International Council for Harmonisation (ICH) GCP E6 guidelines *(6)* and good data and record management practices *(7)* in the context of NTBS. The guidance document is an ethical and scientific quality standard for designing, implementing, recording and reporting NTBS, namely NTPS, DRS and PCS. It includes several practical tools (checklists, plans, logs and report templates) that can be

used in the design, planning, implementation, analysis and reporting of the surveys. Along with the respective survey technical guidance documents, this document and tools are intended for use by survey team members at all levels, from ministries of health to field staff. Compliance with the guidance and tools provides stakeholders with the assurance that rights, safety and well-being of survey participants are protected and that evidence-informed national policies can be developed based on reliable, accurate and complete data.

3. Principles of ICH GCP and GDMP applicable to NTBS

This section outlines the principles relevant to GCP and GDMP; their application is elaborated in **part B**.

3.1. All NTBS should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki *(8)*, ethics guidance for the implementation of the End TB Strategy and applicable national regulatory requirement(s) *(9)*. The rights, safety and well-being of the survey participants are important considerations and should prevail over interests of science and society, except when required to balance against the risk of TB to the population in question. The ethical principles of respect for persons agreed for research with human participants are applicable to NTBS: these include "do no harm" and "ensure beneficence and justice to individuals and communities". Ethical considerations in the design and conduct of NTBS are further elaborated in **Annex II**.

3.2. NTBS should be scientifically sound, and methods should be described in a clear, detailed protocol, as prescribed in the applicable respective survey technical guidance documents.

3.2.1. Evidence in the form of in-country data (national and subnational) and a thorough literature review should be adequate to justify support for the proposed NTBS in countries.

3.2.2. Before a survey is initiated, foreseeable risks and inconveniences should be weighed against anticipated benefits for the survey participants and the population they represent. A survey can be initiated and continued only if the expected benefits justify the risks.

3.2.3. NTBS should be conducted in compliance with the protocol that has received prior approval from an independent ethics committee (IEC).

3.3. The medical care given to, and medical decisions made for, survey participants should always be the responsibility of qualified physician(s), or trained health care provider(s), and in accordance with the NTP and existing WHO guidelines.

3.4. Each individual involved in the design, planning, implementation, analysis and reporting of the survey should be qualified by education, training and experience to perform his or her respective task(s). There must be clear definition of roles and responsibilities of the survey team members at all levels.

3.5. Community education and engagement should be performed in an appropriate and culturally sensitive manner throughout the survey period.

3.6. Voluntarily given informed consent[1] should be obtained from every survey participant prior to participation in the survey.

3.7. Good Data management practice: All survey-related information should be recorded, handled and stored in a way that allows accurate reporting, interpretation, verification and reconstruction; this is applicable to all records on paper and electronic media.

3.7.1. A data life cycle should be clearly defined before starting the survey, comprising all stages from collection through analysis, storage or final disposal, based on the setting and the type of survey.

3.7.2. A system for data management should be instituted; details should be documented in a data management plan prior to the implementation of the survey.

3.7.3. A qualified data manager should be designated. The data manager should be aware of the unique environment (such as available resources and data management practices in the field and laboratories) in which survey data are being generated and handled.

3.7.4. Data at all levels (field, laboratories and central) should be attributable, legible, contemporaneous, original, accurate, and complete (ALCOAC principles).

3.7.5. Systems and procedures for validating data form an essential aspect of the survey.

3.7.6. A data integrity risk assessment *(10)* should be performed to identify, assess and mitigate possible risks throughout the data life cycle.

3.7.7. Confidentiality should be ensured throughout the data life cycle. Records that could identify survey participants through any personal identifiers should be duly protected, in accordance with applicable national regulatory requirement(s).

3.7.8. A data backup policy should establish the backup schedule, frequency, storage media, and access, as well as set out for how long data must be kept.

3.7.9. A system for archiving, sharing, use/re-use and disposal of data should be in place.

3.7.10. A policy for data ownership should be clearly defined.

3.8. Systems to assure quality of every aspect of the survey should be implemented throughout the design, implementation, recording, reporting and archiving of the survey. The focus should be on those activities related to ensuring participant protection and the integrity of survey data. Towards this end, a risk-based approach to monitoring the survey processes and data should be implemented; this will ensure timely identification of any noncompliance and the implementation of corrective and preventive actions (CAPA) to continuously improve process and data quality through quality improvement (QI).

[1] "Consent" here includes the consent and assent process.

3.9. The prevailing best practice methods should be applied in the performance of the data analysis.

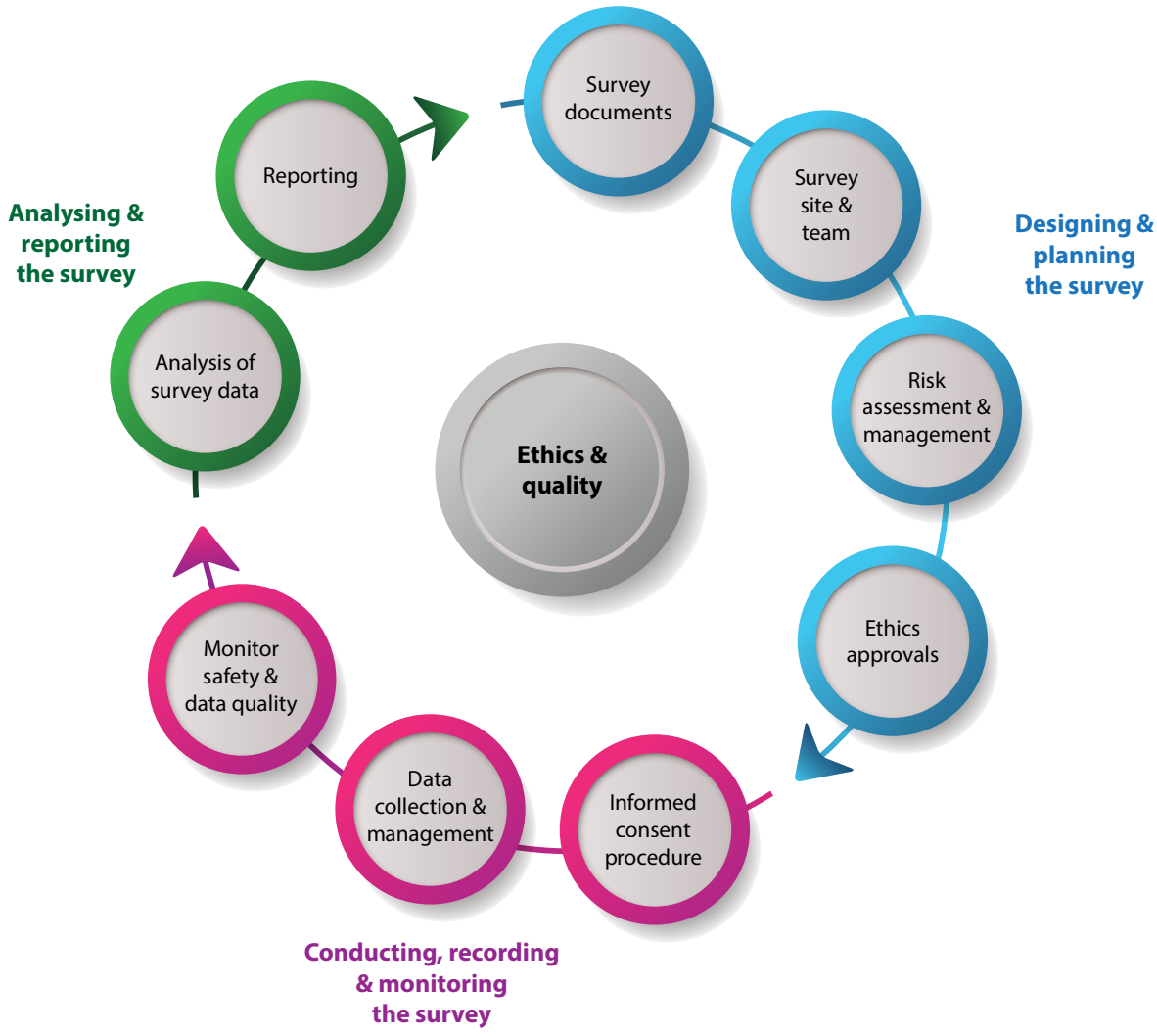
3.10. Results of the survey must be reported and should be published. They should be also be widely disseminated to all stakeholders, including the community.

PART B

Step by step implementation of the guidance to practice

This section details the application of the principles laid out in **section 3** of part A into practice and links to a set of tools detailed in **Annex I**. While some tools are specific to a given step or phase in the survey, others related to communication, risk assessment and monitoring are cross-cutting and applicable across stages. The schema below depicts the key steps in the three phases of the survey: (1) designing and planning; (2) conducting, recording and monitoring; and (3) analyzing and reporting.

FIGURE 2. Steps in the various phases of a survey



Designing and planning 1

Topics

1.1. Quality plan

TOOL 1.1

A quality management system (QMS) is a formal approach to strengthening and continuously improving performance by ensuring all activities in the context of NTBS are carried out consistently and according to pre-defined standards. A QMS consists of resources (people, time and money), Standard Operating Procedures, training of personnel, competency assessments, facilities, equipment and supplies, documents and records as well as Quality Control and Quality Assurance activities. While implementation of a QMS does not guarantee an error-free environment, it allows for early detection of process and data errors and continuous quality improvement throughout the survey life cycle.

To define quality assurance (QA) and quality control (QC) systems in the conduct of NTBS and ensure all the survey processes and data fulfil quality standards, the survey teams are encouraged to develop a quality plan. An example of a quality plan supported with illustrations is outlined in **tool 1.1**.

1.2. Essential survey documents

TOOL 1.2

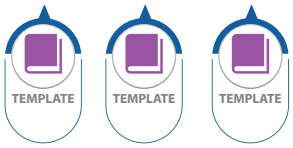
Essential survey documents individually and collectively guide the conduct of the survey and permit evaluation of the quality of data generated. A checklist of essential survey documents needed before, during and at the close-out of the survey is provided in **tool 1.2** and a brief description of each type of essential survey document is provided below.

1.3. Document management

A process for the development, review and approval of essential survey documents must be instituted. Documents need to be version-controlled with a version number and date, number of pages and approval signatures; this ensures that everyone uses the most recent version of the approved document. Once approved and version-controlled, the document is either distributed or posted online so that respective users can access it according to their roles and responsibilities. All documents are "living" and subject to amendments as part of a routine review or as needed, during the course of the survey. Amendments if any, will go through a review and approval process. Details are outlined in **tool 1.3** (management of controlled documents).

A survey master file, which is either a physical file or an electronic folder, should be established at the beginning of the survey; this will contain all versions of all essential survey documents. The survey coordination team including the data manager should have control of all essential survey documents and records generated before, during and at the end of the survey; one or more members of the survey team should be assigned the responsibility of maintaining and updating the file. The file, whether paper or electronic, should be stored in a secure place and allow for document identification, search and retrieval.

1.4. Protocol



A survey protocol is developed during the planning phase, preferably by a team of experts from diverse scientific backgrounds. The protocol serves as the key reference document for the conduct of the survey and helps to achieve consistency. The contents of the protocol are in accordance with the checklist provided in the respective survey technical guidance documents *(1, 2 and 4)*. The protocol must be submitted and approved by an IEC in-country prior to starting the survey.

1.5. Tools to ensure uniformity of survey procedures

Standard operating procedures (SOPs) and accompanying work instructions (WIs), including job-aids such as flow charts, ensure accuracy, repeatability and reproducibility of the data. Survey teams are encouraged to map SOPs required for any given survey; an example of an SOP Index is illustrated in **tool 1.1** (Quality Plan). A set of SOPs for NTPS has been published by the KNCV Tuberculosis Foundation and is available on the WHO website *(11)*. SOPs/WIs must be made available to staff responsible for carrying out the procedures.

1.6. Participant information sheet and informed consent/assent form

The participant information sheet and informed consent/assent forms are used to convey information about the survey to potential participants and to document their consent/assent. An informed consent checklist detailing these key components can be found in **tool 1.4**. Templates of informed consent for sample storage and re-use, as well as assent for minors, are available on the WHO website *(12)*. Participant information that is age-appropriate must be written in a simple, non-technical and clear language, easily understandable for a layperson. If translation to the local language is required, the document should be back-translated into the original language. Refer to **section 2.1** for more details about the informed consent process.

1.7. Data collection tools

Source data refers to the original data, where it is first collected. The document in which the source data is captured is referred to as the source document. Data could be collected on paper or via electronic data capture tools. The list of source data and the relevant source documents should be clearly defined, according to the survey type and settings. This may include for example:

- informed consent
- census form
- screening questionnaire
- X-ray data sheet or X-ray films
- sputum examination request form, specimen register, specimen transportation log, or specimen transportation form
- laboratory results form
- interview data collection tools.

If a source document will fade over time or must be returned to the patient, staff should make a certified paper or electronic copy, which has either been verified against the source document or generated using a validated process to produce a copy. For example, a photocopy of a thermal sheet generated from a machine that is signed and dated is a certified copy.

In the NTBS, data are sometimes abstracted from administrative or health facility registers (for instance population censuses, TB registers or microscopy results from the laboratory register) that have already been collected as part of the routine surveillance system. These are referred to as 'data sources' and it is good practice to clearly define the different data along with their relevant data sources, according to the survey type and settings. A case report form is a paper or electronic document designed to record and capture all of the protocol-required information to be reported to the data manager on each survey participant.

All survey forms/registers/logs/electronic systems should be user-friendly, and capture all relevant data including date and time, initials of the person completing it, equipment ID, batch numbers of reagent, as necessary. Avoid capturing the same data multiple times, unless there is a clear reason to do so. Prior to the survey start, data collection forms should be pilot-tested to ensure no data fields are missing and/or confusing.

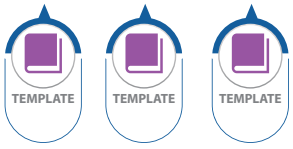
A well-designed system for linking participant data from various sources, using codes (e.g. numeric, character-based or both), should be instituted in order to ensure smooth flow of data between different stages of the survey in the field (such as interviews, X-rays, laboratory in NTPS, interviews, laboratory in DRS); between different levels (field, health facilities, peripheral and central laboratories and central coordination team); and in correct matching of the various records to a given participant. Rigorous testing of the system should be undertaken before survey implementation.

Electronic data collection: When using an electronic data capture system, consider the following points:

- availability of documented design of software and database;
- easy mechanisms for software upgrade in the field;
- how to ensure that range and other quality checks are built in the entry fields, to be able to perform automatic validation;
- generation of quality indicators for monitoring the data quality;

- synchronization of data from different sources, including importing data from other software (for instance, laboratory Information System data in DRS database);
- ownership of the database, especially when stored on the servers of a third party; and
- transfer of data across systems are fully validated and compatible, such that the final output is consistent with the source data.

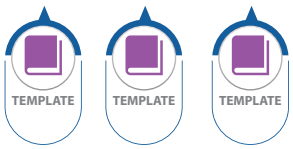
1.8. Data management plan



A data manager, or authorized designee, should be responsible for the data management process, including the development of a centrally-managed database. Prior to the initiation of the survey, a data management plan should be developed. The plan should include the following considerations:

- data collection, to encompass completion of the different data collection forms and other survey-related documents, with clearly defined procedures for correcting errors in these documents;
- coding/terminology for participant characteristics and medical history (data dictionaries/ metadata);
- database design, testing and validation;
- data entry and verification (such as random checks for errors), regular checks for systematic errors and procedures for reporting such issues to the survey coordinator and team;
- merging of data from different sources;
- data validation "which data will be validated", when and how; who is responsible and how to handle the validation outcomes;
- database closure;
- secure, efficient and accessible data storage;
- data quality assessment (such as reliability of data) for issues such as valid value and range checks, and alerts for missing values or discrepant values between forms;
- QA through standardized procedures and training of survey staff; and
- ensuring confidentiality of the data at all times during the data life cycle.

1.9. Statistical analysis plan



The statistical analysis plan provides a detailed and comprehensive description of the analysis for NTBS, including the planned tables and figures for the presentation of results. It is to be developed in line with the survey protocol, reviewed and agreed upon at the study start. Additionally, standard codes for analysis are available for the different surveys[2] that could then be adapted to accommodate country-specific analysis.

1.10. Monitoring plan and associated tools

Monitoring aims to ensure that the rights and well-being of survey participants are protected and that reported data are accurate, complete and verifiable against the source documents. Monitors who are qualified by education and training are selected by the survey team and should be familiar with the survey protocol. The monitor may be part of the survey team or independent (e.g. an external monitor from WHO or other technical agency). Monitoring activities focus on key data and include source document and source data review as well as compliance checks with the protocol and applicable regulations. A variety of risk-based monitoring approaches can be used to include a combination of central/remote and/or on-site monitoring. The survey

[2] For TBPS: https://github.com/GTB-TBPS for DRS: https://github.com/GTB-DRS for PCS: https://github.com/GTB-PCS

coordination team should develop a monitoring plan that takes into consideration costs, time, logistics and experience of the survey team and site(s).

A monitoring plan template is provided in **tool 1.5**. This is a "living" document and should be updated throughout the survey to reflect the frequency and type of monitoring changes over time. Examples of various logs and report templates a monitor can use to document their QC activities are provided within **tool 1.5**. These logs and templates should be adapted to the needs of the survey, prior to the start of the survey. Refer to **section 2.4** for a description of how these tools are used.

1.11. Survey sites

Sites (field site, health care facility and laboratory) selected for the survey should be evaluated against a pre-defined set of criteria to determine their ability to conduct the survey and identify any areas in need of attention (such as equipment, lack of personnel or training)[3]. A feasibility assessment checklist in **tool 1.6** can be used to document site readiness. Equipment, electrical power and other resources specific to the survey should be available and fully functional. The site should have sufficient space to store paper records under appropriate conditions, for instance protection from fire, water and pests. Any deficiencies identified should be addressed prior to initiating the survey.

Additional measures for laboratories

Participation in external quality assessment, either through testing a panel of proficiency samples distributed by the SRL or re-testing of samples and cultures at the SRL, is an additional measure to assure quality of the laboratory. Similarly, accreditation of a laboratory by a national or international accrediting body provides assurance with respect to the credibility of the laboratory performance, for example through ensuring that laboratories have ISO certification.

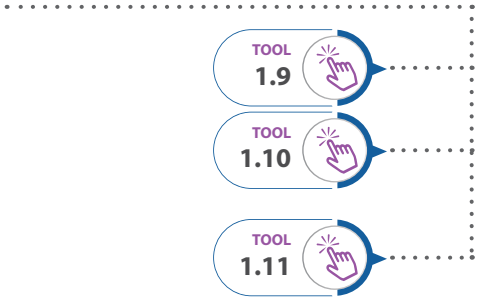
1.12. Survey team

The survey team is generally composed of national representatives and international technical experts. The global management of the survey and its implementation is organized in a three-tier structure composed of a scientific advisory committee; survey coordination team (sometimes referred to as the steering committee); and survey field team.

Adequate numbers of appropriately qualified and trained staff, with access to highly-specialized international technical assistance where required, should be made available during the entire survey period, covering all the different aspects of the survey, without affecting TB control routine activities. **Annex III** provides details of the different stakeholders and their roles and responsibilities. Taking into account all the survey activities, the survey coordination team should perform the following tasks:

- define an organizational structure and communication lines preferably detailed in an organogram (see template in **tool 1.7**);
- assign roles and responsibilities to survey staff, detailed in delegation logs (see template in **tool 1.8**), and ideally pre-define criteria for the different roles and match the curriculum vitae of the survey staff against these criteria to ensure that qualified staff are delegated for the correct roles;

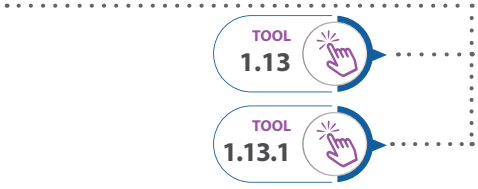
[3] For prevalence surveys, the willingness of the community to participate in the survey needs to be researched carefully based on previous experience of refusal of some communities.



- map the roles of the different stakeholders using a responsibility-accountability-consulted-informed (RACI) matrix; details are outlined in **tool 1.9**;
- capture the contact details of the survey team members in a contact list (see template in **tool 1.10**);
- provide initial training and re-training to all the survey team members on the survey processes and procedures and document details of the training conducted in training logs, templates for which are outlined in **tool 1.11**;
- assess competency of trained personnel, where necessary – for instance, it is recommended to perform competency assessment for those reading chest X-rays in NTPS, performing drug susceptibility tests in DRS and interviews in the PCS;
- where any tasks are outsourced to third party organizations, ensure that an agreement on data ownership, the tasks delegated, timelines and the terms and conditions of contracts are in place; and
- develop a communication plan to ensure timely and accurate information is communicated to all stakeholders throughout the survey.

This communication plan describes lines of communication and escalation as well as how noncompliance and suspected cases of misconduct and fraud should be handled. An example communication plan template is outlined in **tool 1.12**. Prior to writing this plan, team members are encouraged to perform a stakeholder analysis and determine their communication needs (for instance with respect to mode and frequency.

1.13. Risk assessment and management

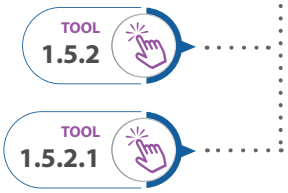


Risk management is the process of identifying, assessing, monitoring, responding to and reporting risks. Risks could impact the project, process or data integrity; they need to be identified and managed prior to and throughout the survey process. Further details and illustrations on how to perform the risk assessment and management are elaborated in **tool 1.13** (risk management plan) and **1.13.1** (risk assessment matrix tool).

1.14. Independent ethics review and approval

A multi-disciplinary IEC, independent of the NTP and survey team members, must approve the survey prior to implementation. The submission package and process time for review by the IEC should be ascertained during the planning phase of the survey. An authorized designee in the team is responsible for communication with the IEC secretariat and submission of the package of documents to the IEC for review and approval. At a minimum, this package will include the survey protocol, participant information sheet including the consent / assent form, data collection tools, curriculum vitae of the key survey team members. A document outlining the approval of the survey must be obtained from the ethics committee; this document should state the version of the documents reviewed and approved, the period of approval, the members who sat on the committee and be duly signed by the Chair of the IEC. All communications with the IEC and the approval letter are filed in the survey master file. Subsequent amendments made to the protocol, informed consent forms or data collection tools should be approved by the IEC and well-documented. It is good practice to encourage community representation in the ethical review process.

1.15. Assessment of readiness



A monitoring visit may be conducted on-site or remotely to assess the readiness of the site to commence the survey. Action items and findings are documented in a site initiation visit report outlined in **tool 1.5.2**. Upon satisfactory review of the report, the steering committee / survey coordination team gives approval for the survey to begin.

Conducting, recording and monitoring 2

Topics

2.1 Informed consent procedure

The informed consent process ensures that potential survey participants are provided with all the requisite information to make an informed decision as to whether or not they wish to participate in the survey. The process has three steps:

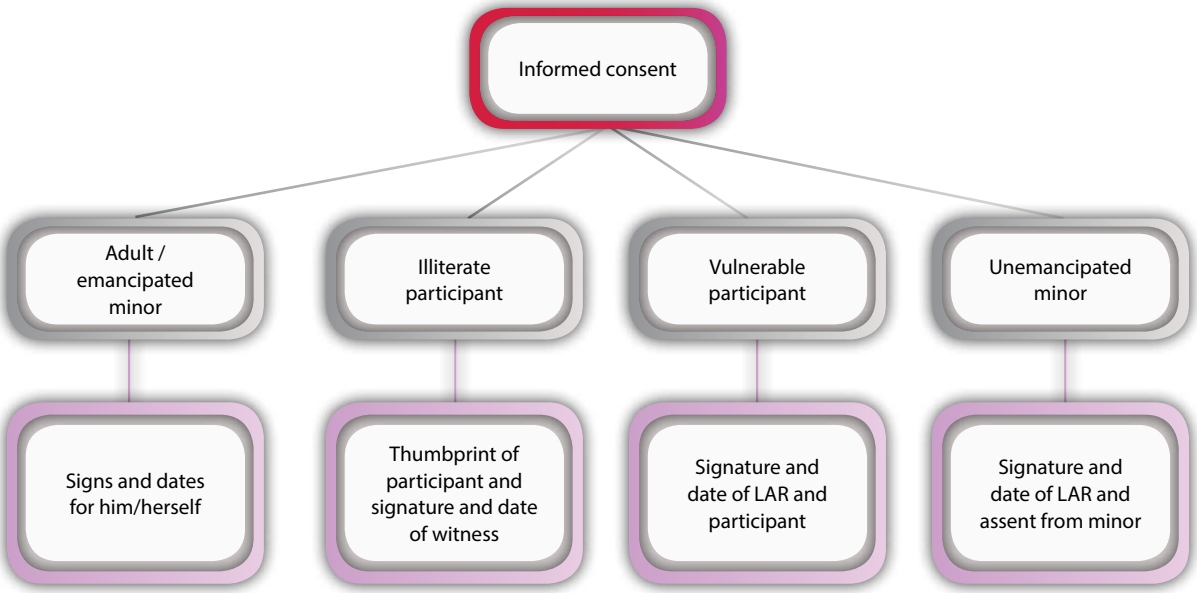
1. provision of the information and answering all the questions a potential participant may have;
2. ensuring that the participant has understood all the information provided; and
3. allowing the participant to voluntarily decide his/her willingness to participate, providing enough time for consideration.

An adult participant or an emancipated minor must sign and date the informed consent form in order to give his/her consent for participation in the survey. A legally authorized representative (LAR) must sign and date the consent in the case of a vulnerable participant who does not have the capacity and competency to make his/her own choices or in the case of an unemancipated minor, whose interests need to be protected *(13)*. Children or vulnerable participants should be provided with information that is age-appropriate and provide their assent, in so far as possible and in line with the national laws of the country. If a participant (or his/her LAR, where applicable) is unable to read or write, the process must be witnessed by an impartial literate adult. The witness should sign and personally date the consent form. An authorized designee in the survey team must sign and date the informed consent form. Signatures are obtained on two copies; one copy is returned to the participant and the other must be stored securely, with access limited to authorized staff.

In the event that several participants need to be enrolled on a given day as in NTPS the field team may opt for a two-step process in which information is first provided in groups, and subsequently consent is obtained as a one-on-one process with individual participants. Verbal

informed consent may be an option under exceptional circumstances, provided this has been approved by the IEC; obtaining the verbal consent will need to be duly documented by the survey team designee.

FIGURE 3. Who should sign and date the informed consent form?



In addition to upholding the principle of autonomy, informed consent ensures that participants understand the consequences of testing positive and will adhere to treatment protocols. It also builds trust with the survey team and the health care system, which is essential for successful implementation of the survey.

2.2 Screening, enrollment and assignment of participant ID

TOOL 1.14

Participants are screened and enrolled into the survey based on eligibility according to the inclusion and exclusion criteria of the protocol. Every participant is assigned a unique identification code, preferably using barcodes, that will be used throughout the survey. Details are maintained in a participant ID, screening and enrolment Log, a sample of which is outlined in **tool 1.14**. As this log bears personal identifiers, it must be stored securely, with access limited to authorized staff.

2.3 Data collection and management

2.3.1 Good documentation practices

Good practices related to the documentation of data collected are described in this section. ALCOAC refers to the following documentation principles and are applicable to data written on paper and/or generated electronically:

Attributable: data collected should be attributable to a person, date and time, method and machine as applicable.

Legible: if data are handwritten, the data should be readable with ease and written with an indelible ink, so it cannot be erased or over written. Also, electronic data should be collected on media, where data can be securely stored for a considerable duration.

Contemporaneous: data should be documented immediately after it is generated and not left to memory and be recalled later.

Original - refers to the source document, on which the data are captured and it may either be paper or electronic – for instance, it may be the recording of microscopy results in a logbook or an electronic output from an automated machine performing the drug susceptibility testing; or interview responses directly entered into the electronic device. All original data should be reviewed; if on paper, with approval signatures and if electronic either an electronic signature or an approval process with a specific user ID and password. Review process helps to assure the accuracy and integrity of the data and that the data have been generated in compliance with standardised procedures.

Accurate - refers to valid and reliable data, collected following standardized procedures and controls. In the event of data transfer from a machine to the computer, it is to be ensured that data transfer process is validated.

Complete - all data required are collected and there are no missing data.

2.3.2 How to make changes to the data?

An audit trail should be set up to track changes, edits or corrections to survey source data. This should allow for tracking details of the content, any change(s) that were made and identification of who made the change, the reasons for the change and the date/time of the change. With electronic systems, traceability should be documented via computer-generated audit trails, for instance the date and time when change was made and the user ID and password that was used. Use of computerized systems that lack audit trails should be discouraged.

2.3.3 Ensuring privacy and confidentiality

Privacy: As TB is associated with social stigma in many parts of the world, special care must be taken to protect the privacy of the individuals who are being followed up after being diagnosed with TB in NTPS and drug-resistant TB in DRS or in interviews conducted in field sites and home visits, as in the NTPS and PCS. Survey team members must ensure that the modality of the follow-up, whether by telephone or home visit, is discussed and agreed upon with the participants beforehand. In the event of a home visit, the survey team member must reveal the identity of the organization he/she represents to the interviewee, but not to the others in the community.

Confidentiality: The use of codes instead of names and personal identifiers that might lead to the identification of individual participants should be encouraged in all data collection tools to protect confidentiality. Use of personal identifiers is restricted to the screening and enrolment log and the informed consent form; records with identifiers should be stored securely, and with access limited to authorized survey team members. Names and other personal identifiers may be used only for clinical purposes to follow up in cases where the participant tests positive for TB or has an ancillary disorder diagnosed. In many countries, TB is a notifiable disease and a diagnosis of TB must be reported to public health authorities. Where this is the case, ethics committees and participants should be told about the potential consequences of participating in a TB survey, namely investigation and action by the public health authorities. Any electronic data collection and transmission system should be designed to ensure data confidentiality, using documented and tested processes that require an authorized login to enter, correct and

review data by specific users. Policy and procedures may be established to grant data access to additional team members under special circumstances.

2.4. Monitoring participant safety and data quality

Routine monitoring visits are conducted throughout the survey process as described in the monitoring plan; visits may be remote, central and/or on-site. Tools that should be customized for the particular survey include:

- informed consent verification log (**Tool 1.5.1**), to verify consent was obtained correctly;
- monitoring visit reports (**Tools 1.5.3** and **1.5.4**) to document monitoring activities and any action items.

The monitor should verify that essential survey documents are maintained and on file. This includes various logs used by the site (for instance, screening and enrolment log or delegation log).

In addition to monitoring, other measures to ensure participant safety and data integrity include:

- QC of the key survey processes by the survey team. For example:
  - In a NTPS, a certain percentage of X-rays that have been read in the field (first) are re-read by a central reviewer (second); discordant results are either read by a third reviewer or resolved (through consultation or interaction) between the first and the second reader.
  - In a DRS, drug-susceptible or drug-resistant TB strains are used as controls during every test run to validate the process of drug susceptibility testing.
  - In a PCS, a certain percentage of interviews can be redone, focusing only on key critical data, to ensure the quality of the interview process.

- A trained member of the field team may supervise the survey processes and data – for example by verifying the completeness of informed consent forms, by reviewing critical data collection and entry at periodic intervals, and by documenting the findings in a QC check log (**Tool 1.5.6**).

QC checks can help to identify errors or noncompliance related to a procedure or data. A systematic error (one which has occurred across participants in a particular site or laboratory) should be thoroughly investigated. Root cause analysis can be used identify the underlying cause(s) of a problem. Based on the findings of root cause analysis, appropriate CAPA should be implemented to correct the error (if possible) and to prevent the recurrence of such events. This should be documented in a CAPA Log (refer to example in **Tool 1.15**) and reviewed by a monitor to ensure that systematic errors are not re-occurring and that the CAPA plan is effective.

Misconduct (details outlined in **Annex II**) is most often detected by a monitor during on-site visits or through an analysis of data listings done by central monitoring/routine QC checks. A process can be outlined in the communication plan which addresses how suspected cases of misconduct are reported, investigated and escalated.

2.5. Survey closure

On completion of data collection, query resolution and data cleaning, the survey coordination or management team should formally close the survey. This can be done on-site or remotely. The monitor or the survey coordination team should:

- confirm that query resolution is complete and the database can be locked for analysis;
- ensure all survey documents are filed in the appropriate sections of the survey master file - whether paper or electronic, the survey master file should be stored in a secure place for several years, and allow for document identification, search and retrieval (the length of archiving might vary depending on the country requirements but should be around 5 to 7 years); and
- document the findings in the close-out visit report, (see the example provided in **Tool 1.5.5**).

Analysis, reporting and dissemination 3

Topics

3.1. Analysis of survey data

Survey data should be analysed in a timely manner in accordance with the statistical analysis plan developed during the planning phase. The results should be presented in accordance with the guidance provided in the respective survey guidelines and according to best practice and up-to-date methods. A survey report detailing the results and methodology should be prepared following "strengthening the reporting of observational studies in epidemiology" (STROBE) *(14)* or any other recognized standard depending on the type of the survey. When expertise is not available within the country, international experts should be hired; such an opportunity should be used also for building national (in-country) capacity for analysis and preparation of reports.

3.2. Reporting and dissemination

There is an ethical obligation to report and publish survey results to a wider scientific audience and share the findings with the communities. Publication of an official report of the survey by the NTP (ministry of health) is encouraged. Clear lines of communicating and disseminating the reports and findings should be instituted at the point when the survey is initiated. At a minimum, the results of the survey should be communicated to two groups. Results should be shared with the scientific community through publications in peer-reviewed scientific journals and presentations in scientific events including conferences, where possible. In addition to the results, the details of the process of implementation of the survey and the lessons learned should also be published; this will be very helpful for other countries that are planning similar surveys in the future. They must be shared with the participants and their communities in an appropriate language and using culturally sensitive media and strategies.

3.3. Data archiving, ownership and sharing

For data archiving, clear timeline for storage and disposal of data and records at all levels (field, laboratories and central) and a process for disposal should be defined in accordance with institutional polices and applicable national laws. In NTPS, these are stored for at least seven years, either by the implementing agency or the NTP in-country; for DRS and PCS, storage time will depend on the country and the recommendations of the IEC. Final datasets should be stored in secure media with adequate back-up, and allow for easy retrieval. Access should be restricted to authorized personnel, for example in a data repository administered by WHO.

With respect to data ownership, the final dataset in the database is owned by the NTP; copies of dataset may additionally be archived under the custody of WHO for purpose of security.

With respect to data sharing, if publications arise from particular surveys, journals may require that the dataset are posted on open-access sites. External requests for access to data should be made directly to the NTP. Communication can be facilitated by WHO, where appropriate.

PART C

References*

1. Tuberculosis prevalence surveys: a handbook. Geneva: World Health Organization; 2011. (https://apps.who.int/iris/handle/10665/44481, accessed 17 December 2020).

2. Guidance for the surveillance of drug resistance in tuberculosis, sixth edition. Geneva: World Health Organization; 2020.

3. The End TB strategy [website]. Geneva: World Health Organization; 2014. (https://www.who.int/teams/global-tuberculosis-programme/the-end-tb-strategy, accessed 17 December 2020).

4. TB patient cost surveys - A Handbook. Geneva: World Health Organization; 2017, (https://www.who.int/publications/i/item/9789241513524, accessed 17 December 2020).

5. WHO Global Task Force on TB Impact Measurement: Sixth Task Force meeting, 19-21 April 2016, Glion-sur-Montreux, Switzerland [website]. Geneva: World Health Organization; 2016 (https://cdn.who.int/media/docs/default-source/hq-tuberculosis/global-task-force-on-tb-impact-measurement/tf_meeting_report_2016.pdf, accessed 17 December 2020).

6. Step 4 in Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6 (R2). Geneva: International Council for Harmonisation (ICH); 2016.

7. World Health Organization TRS No: 996, 2016 - Annex 5 Guidance on good data and record management practices. WHO expert committee on specifications for pharmaceutical products. Geneva: World Health Organization; 2016. (https://www.who.int/publications/m/item/trs-966---annex-5-who-good-data-and-record-management-practices, accessed 17 December 2020).

8. World Medical Association. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. JAMA. 2013;310(20):2191–2194. doi:10.1001/jama.2013.28105.

9. Ethics guidance for the implementation of the End TB strategy. Geneva: World Health Organization; 2017. (https://www.who.int/publications/i/item/9789241512114, accessed 17 December 2020),

10. Guideline on data integrity (Draft Working Document for Comments) (Working document QAS/19.819/Rev.1). Geneva: World Health Organization; 2020. (https://www.who.int/docs/default-source/medicines/norms-and-standards/current-projects/qas19-819-rev1-guideline-on-data-integrity.pdf?sfvrsn=653c05c0_2, accessed 17 December 2020).

* Where possible, this guidance document has been harmonized with other published documents and should be read with other WHO guidelines and publications.

11. National Tuberculosis Prevalence Survey Guidance: document for development of standard operating procedures (SOPs). The Hague: KNCV Tuberculosis Foundation; 2010 (https://documents.pub/document/national-tuberculosis-prevalence-survey-guidance-document-this-document.html?page=1)

12. Research Ethics Review Committee (ERC): Templates for informed consent forms [Website]. Geneva: World Health Organization. (https://www.who.int/ethics/review-committee/informed_consent/en/, accessed 17 December 2020).

13. UN General Assembly, Convention on the Rights of the Child, 20 November 1989, United Nations, Treaty Series, vol. 1577, p. 3, available at: (https://www.refworld.org/docid/3ae6b38f0.html, accessed 18 December 2020)

14. STROBE statement: strengthening the reporting of observational studies in epidemiology [website]. Bern: University of Bern; 2009. (strobe-statement.org, accessed 17 December 2020).

15. What is quality [Website]. Wollerau: International Six Sigma Institute; 2020. (https://www.sixsigma-institute.org/What_Is_Quality.php, accessed 17 December 2020).

16. International Ethical Guidelines for Epidemiological Studies. Geneva: World Health Organization and Council for International Organizations of Medical Sciences; 2009 (https://cioms.ch/wp-content/uploads/2017/01/International_Ethical_Guidelines_LR.pdf, accessed 17 December 2020).

Annex I

Tools for the adapted GCP principles for NTBS

Tool C=checklist; F=Form; T=Template L=Log	Tool number and title	Description & link to the tool	Comments and where to source if not part of the package
T	**1.1.** Quality plan	The template for creating a quality plan for the survey should include management of controlled documents; master SOP index for the survey, QA/QC; and roles/responsibilities specifically for actions such as quality, training, handling deviations and corrective action, misconduct investigations.	Training is mentioned briefly in this plan, as this is part of a QMS, but teams may also have a stand-alone training manual they will use.
C	**1.2.** Essential survey documents checklist	A list of essential survey documents should be kept on file before, during and at the close-out of the survey	
T	**1.3.** SOP - management of controlled documents	This is an example of a SOP on SOPs.	An example has been provided. Teams need to determine how they will manage controlled documents (SOPs/WIs) through the course of their lifecycle---from writing/review/approval/ distribution/obsolete.
C	Protocol checklist	This is a checklist for required elements of a survey protocol/ review.	NTPS and DRS have a checklist of components in the protocol; DRS is further working on the checklist as part of updating the DRS guidelines. PCS does not have a checklist.
C	SOP index	As part of the quality plan, the SOP index provides a common list of SOPs for sites and laboratories participating in surveys to assist with planning needs for the specific survey.	KNCV has a set of SOPs for the NTPS available at: http://158.232.12.119/tb/advisory_bodies/impact_measurement_taskforce/resources_documents/3_1_generic_guidance_for_development_of_sops.pdf
T	SOP and WIs template	These are templates for SOPs and WIs (standardized format).	Teams could use existing templates.
C	**1.4.** Informed consent contents check	This checklist should verify that the informed consent to be used in the survey meets all applicable requirements.	ICF reference templates are available on the WHO ERC website: https://www.who.int/ethics/review-committee/informed_consent/en/.
T	Data management plan		This will be developed by the technical team; NTPS has a data management plan.
T	Statistical analysis plan		This will be be developed by the technical team; NTPS has a statistical analysis plan.
T	**1.5.** Monitoring plan	This template for creating a plan describes key data and how QC checks and oversight of the survey will be carried out (e.g. on-site visits, remote/central reviews) in order to ensure data integrity and participant protection	This plan will reference the various other report formats/ ICF log/ checklists the monitor has available for use.

Tool C=checklist; F=Form; T=Template L=Log	Tool number and title	Description & link to the tool	Comments and where to source if not part of the package
L	1.5.1. Informed consent verification log	Referenced in the monitoring plan, this log will be used by the monitor to verify that informed consent was obtained correctly.	This log is in Excel format. It is important for teams to know that review of ICFs is not 100%; it should be risk-based and described in the monitoring plan.
T/C	1.5.2. Survey initiation report template	Referenced in the monitoring plan; this template documents the training and readiness of the site to start survey.	
T/C	1.5.3. On-site monitoring visit report template	Referenced in the monitoring plan; this template includes checklists of on-site monitoring activities and report templates.	
F	1.5.4. Central/ remote monitoring report template	Referenced in the monitoring plan, this will document ongoing central monitoring activities.	
F	1.5.5. Survey close-out report template	Referenced in the Monitoring Plan; this will document close-out activities, resolution of all data queries and identify where survey results/ original records will be archived.	
L	1.5.6. Supervisor QC check log	As part of the monitoring plan, this log serves as an internal QC check.	This log is in Excel format. The log can be used by the supervisor to perform random quality checks.
C/F	**1.6.** Feasibility assessment	This is a checklist to assess whether a particular site fulfills the requirement to participate in a survey.	
T	**1.7.** Organogram	This shows governance structure and reporting lines for survey.	
L	**1.8.** Delegation log	This log documents key staff and their delegated responsibilities.	
T	**1.9.** RACI matrix	This serves as a template for defining roles and responsibilities for all stakeholders and key parties.	This log is in Excel format. This would be a stand-alone document and not part of the communication plan, so that it can be easily updated.
T	**1.10.** Survey contact list	This provides a list of survey team members and their contact details.	This would be a stand-alone contact list that can be easily updated without having to amend the communication plan.
L	**1.11.** Training log	This log will document any training that is done throughout the survey	
T	**1.12.** Communication plan	The template for creating a communication plan describes organogram, list of key contacts, methods of communication (for instance, meetings, TCs, etc.) and issue escalation within the teams.	
T	**1.13.** Risk management plan	The template for creating an overall risk management plan addresses risks to data integrity and protection of survey patient rights, safety and well-being.	
L	1.13.1. Risk assessment matrix	Referenced in the risk management plan this Excel spreadsheet contains various examples of approaches to risk assessment (such as qualitative or quantitative).	Teams can select their approach to risk management from this matrix and then describe this in their risk management plan.

Tool C=checklist; F=Form; T=Template L=Log	Tool number and title	Description & link to the tool	Comments and where to source if not part of the package
L	**1.14.** Participant ID, screening and enrolment log	This tool tracks who was screened and enrolled in the survey.	Teams should determine format; currently this is a Word document but could be an Excel Log. This form must be kept confidential with limited access.
L	**1.15.** Incident and CAPA log	Referenced in the quality plan and monitoring plan, this log documents instances where a problem was identified (e.g. protocol deviation) and the plan to correct it and prevent it from happening in future.	The log is an Excel spreadsheet to capture incidents and CAPAs, and follow up, throughout the survey.
T	Survey final report	This is a template to be used to report the final results of the survey.	This may be either a report structure as for PCS or the tables as in all three surveys
F	Lessons learned	This form is used to document lessons learned during the conduct of the survey for quality improvement purposes.	Teams should verify whether a database of lessons learned is already maintained by the different surveys

Annex II

Ethical considerations in the design and conduct of NTBS

The overarching goal of the NTBS as a public health activity is to promote a country's health, both short-term and in the future. NTBS results are aimed at benefitting people and communities beyond the survey participants and are therefore generalizable. In addition, surveys are data-intensive, collecting personal information and samples for current and future use. It is imperative to subject the survey protocol to an ethical review in order to ensure adherence to ethical standards laid down in the Declaration of Helsinki and the ethics guidance for the implementation of the End TB strategy, and to provide public assurance of respecting the rights, safety and well-being of the survey participants.

General ethical principles

The following ethical principles agreed for 'research with human participants' are also applicable to TB surveys:

1. Respect for persons: Every survey participant is an autonomous individual and has the right to decide what should or should not happen to him or her. This is embedded in the concept of informed consent. TB patients may be illiterate, sick, poor or marginalized, and may not have the capacity and competency to make their own choices, making them vulnerable. In order to protect the interests of the vulnerable, there should be adequate safeguards, in accordance with the national laws / regulations. Country-specific laws govern the age for consent or assent and procedures with respect to LARs who could consent on behalf of a minor or other vulnerable participant. Verbal consent or waiver of consent might be allowed under exceptional circumstances, but only after obtaining due approval from the IEC.

Respect for participant's privacy and confidentiality also fall within the scope of this principle. Further details on contents of the document, informed consent process and confidentiality are furnished in **part B** of the guidance document.

2. Do no harm and ensure beneficence: A thorough risk benefit analysis will need to be carried out prior to and during the course of the survey, in order to ensure that benefits outweigh the risk to the individual at all relevant points in time. This means maximizing benefits and minimizing harm.

Some examples of risks related to the implementation of TB surveys are as follows:

- The limited diagnostic testing accuracy for the identification of drug-resistant TB may risk false diagnosis of TB (NTPS) or drug resistance (DRS), resulting in unnecessary treatment.
- Use of digital technologies may lead to inadvertent disclosure of confidential information like the Geographic Information System (GIS), resulting in stigma.
- Comorbidities might be detected as part of the NTBS. Another possibility is psychological distress associated with the interview process of PCS, as this requires the recall of patients on their socio-economic hardship. Interviewers should be equipped with basic counselling skills and aware of referral points for further follow up and support.

The above risks could be mitigated by:

- assuring the quality of the laboratory processes and data;
- using robust security measures to enhance confidentiality, minimizing the likelihood that any individual participant would be inappropriately identified;
- establishing a referral mechanism for management of ancillary / co-morbid conditions; and
- seeking consent from participants for sputum and data storage and re-use.

With respect to consent, the informed consent form should explicitly specify "the conditions and duration of storage; who will have access to the samples; the foreseeable uses of the samples, whether limited to an already fully defined study or extending to a number of wholly or partially undefined studies; and the intended goal of such use, whether only for research, basic or applied, or also for commercial purposes" *(16)*, if samples and data are to be used further. The sample be stored and re-used only if the participant consents; otherwise the sample should be suitably disposed of or destroyed.

As the list is not exhaustive, the survey management/coordination team should conduct a detailed risk versus benefit assessment, considering risks and benefits to the individual and their communities in the country settings. Risks with the potential for harm will need to be mitigated.

3. Justice to individuals and communities: Planners must ensure that individuals and populations are treated fairly and that burdens are equitably distributed, so that no one community or sub-population bears more risks or harm for the benefit of the population as a whole. For example, participant selection process in DRS and PCS should be fair and aim to achieve equitable representation of all TB patients, based on the inclusion / exclusion criteria laid down in the protocol. The principle of reciprocity requires finding ways to give back to individuals or communities that had borne a disproportionate share of risk for the benefit of others. It is fair to leave the population that was surveyed in a better position than they were originally; this can be ensured through better access to TB diagnosis, treatment and care.

4. Community engagement: In the current research ethics framework such as that of Council for International Organizations of Medical Sciences (CIOMS) (15), ethical obligations

are not just limited to research participants but extend to consulting, engaging and protecting the broader community which may be affected by the research. Similarly, the community is a key stakeholder in the end TB strategy, and it is therefore crucial to engage with groups such as people with TB, civil society, and representatives from TB-affected communities, and local authorities as appropriate. This engagement should span the planning and designing phase until the dissemination of the results of the survey and preferably even thereafter. Community engagement can either be through 'community advisory boards', which is a group of non-scientific members, or selected community representatives, called as gatekeepers.

Selection of the representatives should be vested with the community, either through nomination or election. This can ensure that individuals truly interested in the welfare of the community represent and facilitate communication between the community and the survey team, thereby building trust and ensuring smooth conduct of the survey.

5. Misconduct and fraud: There are many definitions of research misconduct. The US Public Health Service definition focuses on fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results:

- Fabrication: making up data or results and recording or reporting them
- Falsification: manipulating materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record
- Plagiarism: using another person's ideas, processes, results, or words without giving appropriate credit

In simpler terms, misconduct as defined by the EFGCP Research Integrity Sub-Group[4] is "The generation of false data with the intent to deceive". Anyone, alone or in a group, can commit misconduct and the motivations to do so vary (examples include job stress, lack of time, greed, laziness, improper training).

Misconduct can be categorized into low, medium and high grade, depending on the type and impact to the overall survey.

- Low grade refers to unintentional errors that are random, often due to inattention or sloppiness. These can be fixed by correction and/or additional training. These are easy to detect, easy to fix and would have low impact on the survey overall.
- Medium grade refers to intentional errors, such as enrolling participants who do not meet inclusion/exclusion criteria. These errors can be difficult to detect and may be unfixable. The impact on the survey would be variable depending on the parameter and extent.
- High grade refers to wilful deception, such as falsified test results, fictitious data or abuse of participant rights. This type of misconduct can be difficult to detect, is rarely fixable and can have a very negative impact on the survey, including the possibility of data having to be discarded.

[4] See https://efgcp.eu/

Annex III

Stakeholders and their roles and responsibilities

The main stakeholders and their activities in NTBS (NTPS, DRS and PCS) are listed in this annex along with their roles and responsibilities.

1. Roles and responsibilities of funding agencies include:

- liaising with NTP with respect to the need, feasibility of conducting and the terms of reference for the survey;
- setting up a documentation agreement on all financial matters;
- financing the survey as planned and ensuring timely release of funds to avoid delays; and
- establishing mechanisms for alignment of several funding sources (such as forming a steering committee to align several donors).

2. Roles and responsibilities of WHO and scientific experts include:

- providing technical advice in conducting the TB survey throughout the survey life cycle;
- supporting the process of developing survey documents in general and protocol in particular, analysing survey data and preparing survey report; and
- assisting with the performance of monitoring, identifying and addressing potential issues and risks, thereby improving data quality.

3. Countries:

a. Roles and responsibilities of NTP and ministries of health include:

- developing detailed funding proposal and financial plan;
- ensuring that a mechanism for alignment of several funding sources has been put in place at a very early stage of planning the survey;

- coordinating funding with the donor(s) and avoiding/minimizing delays;
- identifying the national survey coordination team composition, qualification and agreements;
- ensuring availability of adequately qualified human resources to conduct survey tasks in a timely manner without disrupting routine TB control activities, and ensuring they are aware of their duties and have the information and tools needed to conduct these tasks;
- ensuring timely procurement and availability of functioning equipment, maintenance plan and backup solutions;
- ensuring availability of adequate supplies and logistics support;
- ensuring smooth conduct of the survey in compliance with applicable national regulations;
- tracking the progress through regular communication; providing necessary support to the national survey team in periodic risk assessment and management, as appropriate;
- developing plans for report writing and wide dissemination that identify local sources for effective advocacy; ensuring adequate funds to facilitate more rapid generation of transparent methodological reports and greater dissemination of results to a broader audience;
- identifying reporting standards such as STROBE, plan external support for writing the publication and build capacity of country experts; and
- putting in place systems to ensure scientific publications of the survey results, processes and lessons learned are made within a year after completion of the survey.

b. Roles and responsibilities of national survey coordination teams include:

i. Survey design, development of protocol and essential survey documents:

- forming committees of qualified specialists for the development of survey design, protocol and essential survey documents, and ensure engaging the field staff in these processes, as they would be adept with the country settings.
- defining the requirements for protecting the safety and rights of vulnerable participants for the given country;
- developing a system for tracking amendments through version control of all essential documents; and
- developing training materials adapted to the country settings and covering the different roles.

ii. Coordination responsibilities incude:

- acquiring the IEC approvals through a nominated focal point, which includes studying the IEC SOP and timelines for submission of survey protocol and other essential survey documents;
- preparing the documentation package for submission and conducting peer review prior to submission of protocol and documents to IEC;
- cooperating with local authorities in the health care system and communities during the entire survey period starting from the planning phase;
- engaging community and disseminating information about the survey using appropriate media and culturally sensitive strategies; and
- coordinating with the field survey team about all aspects of the survey activities and providing timely/prompt response to their queries.

iii. Survey management includes:

- selecting the field survey team and allocating responsibilities; ensuring availability of qualified and competent people to conduct survey tasks as needed;
- developing a well-defined organogram, assignment of clear roles and responsibilities and a communication strategy;
- planning and conducting training of all teams on 'good practices guidance document for NTBS' and the procedures of the survey (training may be delegated to qualified trainers following training of trainers);
- ensuring compliance with survey protocol and procedures;
- supervising any individual or party to whom the survey tasks have been delegated;
- conducting regular/periodic meetings to assess the survey progress, identifying challenges;
- communicating the outcomes of the meeting promptly with the survey team; address their queries and feedback in a timely manner; and
- preparing progress reports, interim and final as agreed upon, including with the funding agency.

iv. Quality management includes:

- ensuring a system is in place for QA; tools and SOPs for all processes of the survey are in order after having been pilot tested;
- instituting a system for verification of processes and data through QC and reporting any opportunities for quality improvement;
- identifying key quality indicators to monitor the processes and data; facilitating monitoring-related tasks;

- preparing flexible risk-based monitoring schedule, combining on-site monitoring visits with remote (such as phone-based) monitoring, based on risk assessment;
- conducting supervision and monitoring activities to assess progress, safety and data quality;
- reporting of progress (such as regular meeting schedules), monitoring outcomes and escalation of issues, following a communication plan;
- conducting system and facility audits as appropriate; and
- ensuring that all team members conform to the principles laid out in this guidance document.

v. Risk assessment, control and communication includes:

- conducting risk assessment at a regular periodicity; identifying, assessing and performing risk mitigation measures as appropriate;
- checking the available new technologies that allow minimizing risks to humans; mainly chest X-ray and laboratory tests;
- establishing adequate follow up mechanisms to ensure timely reporting of laboratory results and access to treatment for participants with positive laboratory results in NTPS and DRS; and
- reporting and communicating the risks and mitigation actions to all concerned.

vi. Data management includes:

- assigning a qualified data manager.
- ensuring a system is in place for data cleaning and validation, including second reading of chest X-ray in NTPS.
- ensuring sufficient storing, archiving and backup systems for all forms, registers, chest X-ray films and electronic databases.
- implementing data privacy and confidentiality system.
- ensuring that any electronic systems used are fulfilling data quality requirements; and
- developing policy for data ownership, access to and re-use of survey data.

vii. Data analysis and reporting includes:

- ensuring data is analysed in accordance with the statistical analysis plan and within the agreed timelines.
- reporting and publishing survey results and lessons learned from the implementation.

c. Roles and responsibilities of the field survey team (common to all the surveys) must be detailed in a delegation log and include:

- providing participants with all the necessary information about the survey for an informed decision making, in simple non-technical terms, a language understandable to the participant and in a culturally sensitive manner;
- ensuring that participants fully understand their rights and obligations prior to consenting;
- collecting and recording data in accordance with the survey protocol and SOPs; varies according to the survey;
- reporting any noncompliance to the field supervisor for necessary actions;
- keeping all the original documents in secure storage and transferring data to the data manager;
- ensuring adequate medical care is available for participants and provided by qualified health care provider, in line with the national regulations (thereby ensuring proper clinical management for participants tested positive in the NTPS and DRS; psychological counselling for participants in the PCS; and reference to health care system for management of identified co-morbid conditions); and
- ensuring that supervising all individuals to whom the survey specific tasks have been delegated (field team lead).

d. Roles and responsibilities of field survey teams (specific to the different surveys):

NTPS roles and responsibilities include:

- conducting household census, and interviews in the households to identify eligible participants;
- conducting individual interviews using the requisite questionnaires;
- performing chest X-ray images with necessary safety precautions by allocating secure venue, ensuring privacy and following personal safety measures;
- reading the chest X-rays and transmitting the films to a central reader, for re-reading as part of internal QC;
- enrolling participants according to the defined inclusion and exclusion criteria;
- collecting, documenting, storing and transporting sputum specimen in accordance with the survey SOPs;
- ensuring privacy and following personal safety measures for collecting sputum specimens;
- providing participants with clear and realistic information on when results can be anticipated; and

- defining a system for follow-up, for example, contacting the mobile phone of the participant or by providing to the participant telephone number of a member of the field team for communication.

DRS roles and responsibilities include:

- identifying eligible participants from the data sources in the health facilities;
- conducting individual interviews using the requisite questionnaires;
- enrolling participants according to the defined inclusion and exclusion criteria;
- collecting, documenting, storing and transporting sputum specimen in accordance with the survey SOPs;
- ensuring privacy and following safety measures for handling sputum specimens;
- providing participants with clear and realistic information on when results can be anticipated; and
- defining a system for follow-up, for example, contacting the mobile phone of the participant or by providing to the participant telephone number of the health care facility for communication.

PCS:

- identifying eligible participants from the data sources in the health facilities; and
- conducting individual interviews using the requisite questionnaires either at home or the health care facility, respecting the privacy of the patient and safety of the interviewer.

Laboratory roles and responsibilities include:

- instituting and conforming to written procedures for receiving, storing, testing and reporting of sputum samples;
- maintaining QC of key processes and data, including documenting any deviations to SOPs and errors;
- participating in External Quality Assurance (EQA) program or proficiency panel testing;
- reporting of the results of testing to the survey participants, in a timely way and in accordance with agreed turnaround times;
- archiving and shipment of specimens and isolates; and
- collaborating with supranational reference laboratories for all re-test activities in DRS.

e. National / institutional ethics committees roles and responsibilities include:

- providing an advisory role by rendering necessary support to the national focal points in addressing the ethical issues and dilemma for the conduct of TB surveys, in line with the social and cultural norms that prevail in the country;
- maintaining timely well documented review (in accordance with the IEC SOPs) of the protocol, informed consent and their amendments, cvs of the national focal points and key members of the survey team, other essential documents as deemed appropriate to ensure protecting the rights, safety and well-being of the survey participants;
- carrying out timely approval of the survey documents after ensuring the committee's suggestions and recommendations, if any, have been fully addressed;
- identifying elements for the progress report to be submitted to the committee;
- reviewing periodically the survey progress report, at least once a year;
- guiding the survey team on ethical dilemmas that may arise during the survey conduct; and
- retaining all relevant records related to the documents submitted for the survey, standard operating procedures for its conduct, communications with the national TB program or the survey team as appropriate, members who sat in the committees that deliberated the survey documents and minutes of meetings, for a period, in accordance with the applicable national regulations.

f. Survey participants and the community roles and responsibilities include:

- helping to educate participants and community about their rights and responsibilities;
- helping create a supportive environment for conducting the survey;
- encouraging active participation in the survey;
- collaborating with survey teams to facilitate smooth conduct of the survey; and
- representing their welfare and interests in the IEC.

g. Monitor roles and responsibilities:

Monitors may be part of the survey team or an expert, independent of the survey team, either from the same country or from outside. Their role involves:

- ensuring that the rights and well-being of survey participants are protected and the reported data are accurate, complete and verifiable against the source documents;
- identifying noncompliance, investigating the cause and following through to resolution; and
- documenting their findings and the follow-up actions to be performed by the survey team in a report.

9789240028654