WHO call for individual patient data on the treatment of multidrug- and rifampicin-resistant tuberculosis

WHO is initiating the development of new guidelines for rifampicin-resistant and multidrug-resistant TB (MDR/RR-TB) following new evidence made available this year.

Over the years, WHO has produced guidance to help countries organize their response to the challenge of drug-resistant TB. The latest evidence-based guidance for the treatment of MDR/RR-TB was published by WHO in December 2018 in accordance with the requirements of the WHO Guideline Review Committee (GRC), using GRADE process and eventually became part of the WHO Consolidated guidelines on drug-resistant TB treatment.[1]

Since these guidelines were released, new evidence became available in 2019, which has prompted WHO to initiate a new guideline development process to ensure that national TB programme managers, policy makers and medical practitioners receive the best possible advice, and MDR/RR-TB patients receive treatment in accordance with the best evidence and medication available. Ahead of the guidelines development group meeting, planned in November 2019, WHO will commission reviews of relevant evidence on the effect of different treatment regimens on patient outcomes. To enable this process and collect available evidence that may potentially contribute to this review, WHO is issuing a public call, appealing to industry, researchers, national TB programmes and other agencies to provide suitable datasets.

The request is for data on treatment of MDR/RR TB patients with the following specifics:

1. use of bedaquiline for longer than 6 months as part of longer treatment regimens
2. use of all oral bedaquiline-containing shorter regimens of 9-12 month duration
3. concurrent use of bedaquiline and delamanid
4. use of bedaquiline-containing regimens in pregnant women

Eligible data, and in agreement with data owners, will be appended to existing individual patient datasets on MDR-TB treatment which have been used in recent years for the making of global recommendations.[2,3,4]

Data requirements

Data that have already been reported to the existing individual patient dataset coordinated by McGill University should not be reported again.

Data from studies that have not yet been reported but otherwise fulfilling the below criteria will be considered for inclusion:

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[1] WHO consolidated guidelines on drug-resistant tuberculosis treatment, 2019

[2] WHO treatment guidelines for drug-resistant tuberculosis, 2016 update. October 2016 revision.

[3] WHO treatment guidelines for drug-resistant tuberculosis, 2018 update.

Essential:

- Individual datasets of at least 50 MDR/RR-TB patients who completed treatment and in whom an end-of-treatment outcome was assigned. Outcomes need to be as per WHO definitions[5,6]
- Patients with RR-TB or MDR-TB confirmed using a WHO-recommended phenotypic or molecular test (with or without additional drug resistance patterns, including extensively drug-resistant TB, XDR-TB)
- Baseline drug susceptibility results for a fluoroquinolone and a second-line injectable agent confirmed using a WHO-recommended phenotypic or molecular test
- Data should be organized in anonymized, individual records (i.e. one row per treatment episode) for the minimum set of variables, preferably coded in a standard way (see Annex 1)
- Datasets are available in a digital format with essential variables as per attached data dictionary and can be shared within a short period of time (please see below timeline)

Desirable:

- Drug susceptibility testing results of other medicines used as a part of longer regimen
- Information on adverse events during treatment

For the individual patient data (IPD) analyses, records of patients who are still on treatment and whose outcome was not evaluated cannot be used.

Also, regimens composed solely of first line agents (rifampicin, isoniazid, pyrazinamide, ethambutol, as well as streptomycin) will not be considered.

Correspondence

Please let us know if you have data to contribute by **10 August 2019.**

Individual data sharing agreement will be provided separately.

Please send all electronic correspondence, including enquiries to the WHO Global TB Programme at **LDR.POLICIES@WHO.INT**.

[5] Definitions and reporting framework for tuberculosis – 2013 revision (WHO/HTM/TB/2013.2). Available from: http://apps.who.int/iris/bitstream/10665/79199/1/9789241505345_eng.pdf Geneva, World Health Organization; 2013.

[6] Laserson KF, Thorpe LE, Leimane V, Weyer K, Mitnick CD, Riekstina V, et al. Speaking the same language: treatment outcome definitions for multidrug-resistant tuberculosis. Int J Tuberc Lung Dis. 2005 Jun;9(6):640–5.

Annex 1:

Data dictionary for MDR/RR-TB IPD

FACILITY INFORMATION					
Field	**Variable**	**Additional Information**	**Format**	**Category Coding**	**Category Labelling**
COUNTRY	Country	Country of the primary source	Char		
TREATING_SITE	Treating Site Name	Name of the primary source	Char		
SITE_ID	Treating Site Identifier	Site ID number	Char		

PATIENT IDENTIFIER AND DEMOGRAPHICS					
Field	**Variable**	**Additional Information**	**Format**	**Category Coding**	**Category Labelling**
PATIENT_ID	Patient Identifier	Patient ID number in country database	Char		
YEAR	Year	Year of treatment start for this episode	Num ###		
AGE	Age	Age of the patient in years	Num ###		
SEX	Sex	Patient's biological sex at birth	Category	F	Female
				M	Male
				U	Unknown
WEIGHT	Weight	Patient's weight in kilograms	Num ###		
HEIGHT	Height	Patient's height in centimetres	Num ###		
BMI	Body Mass Index	Patient's body mass index in kilograms per meters-squared	Num ###		

PATIENT BASELINE CHARACTERISTICS

Field	Variable	Additional Information	Format	Category Coding	Category Labelling
SMOKINGSTATUS	Smoking Status	The patient's smoking status at start of treatment	Category	Current	Current Smoker
				Ex	Ex-Smoker
				Never	Never Smoker
				U	Unknown
SMOKINGPACKPERDAY	Packs Smoked Per Day	Total number of packs per day smoked at start of treatment (if current smoker)	Num ###		
SMOKINGTOTALPACKYEAR	Total Pack Years	Total number of pack years smoked (if current- or ex-smoker)	Num ###		
ALCOHOL	Alcohol Use	Does the patient drink (defined as ≥1 drink per week in men or women)	Category	Y	Yes
				N	No
				U	Unknown
ALCOHOLABUSE	Alcohol Abuse Disorder	If the patient drinks, do they meet the definition of alcohol abuse (≥14 drinks per week in men or ≥7 drinks per week in women)	Category	Y	Yes
				N	No
				U	Unknown
DM	Diabetes Mellitus	Is the patient diagnosed with diabetes?	Category	Y	Yes
				N	No
				U	Unknown
INSULINDEPENDENT	Insulin-Dependent Diabetes Mellitus	Is the patient insulin dependent (if having diabetes)?	Category	Y	Yes
				N	No
				U	Unknown
HBA1C	Haemoglobin A1c Level	Patients HbA1c measure defined in percent (%)	Num ###		
RENALFAILURE		Does the patient have renal failure?	Category	Y	Yes

	Presence of Renal Failure			N	No
				U	Unknown
HEPB	Hepatitis B	Does the patient have hepatitis B?	Category	Y	Yes
				N	No
				U	Unknown
HEPC	Hepatitis C	Does the patient have hepatitis C?	Category	Y	Yes
				N	No
				U	Unknown
OTHERLIVER	Other Liver Condition	Does the patient have liver conditions other than hepatitis B or hepatitis C?	Category	Y	Yes
				N	No
				U	Unknown
HIV	HIV	What is the patient's HIV status?	Category	Pos	Positive
				Neg	Negative
				U	Unknown
HIV_DIAGNOSISYEAR	Year HIV Diagnosed	If the patient is HIV-positive, the year they were diagnosed	Num ###		
CD4	CD4 Count	If the patient is HIV-positive, what is their CD4 count at treatment start (cells/μL)?	Num ###		
VIRALLOAD	Viral Load	If the patient is HIV-positive, what is their viral load at treatment start (copies/ml)	Num ###		
ART	Use of Antiretroviral Treatment	If the patient is HIV-positive, are they on antiretroviral treatment?	Category	Y	Yes
				N	No
				U	Unknown
ART_STARTYEAR	Year Antiretroviral Treatment Started	If the patient is on antiretroviral treatment, what year did they start?	Num ###		

ART_REGIMEN	Antiretroviral Treatment Regimen	What is the antiretroviral treatment regimen? List each drug, separated by a comma, using the provided abbreviations with this dictionary.	Char		

PREVIOUS TREATMENT INFORMATION					
Field	**Variable**	**Additional Information**	**Format**	**Category Coding**	**Category Labelling**
PASTTX	Previous Treatment	Has the patient ever received tuberculosis treatment for >30 days?	Category	Y	Yes
				N	No
RECEIVEDFLD	Previous Treatment with First-Line Drugs	If the patient has received previous tuberculosis treatment, was treatment with first-line drugs given for >30 days?	Category	Y	Yes
				N	No
RECEIVEDSLD	Previous Treatment with Second-Line Drugs	If the patient has received previous tuberculosis treatment, was treatment with second-line drugs given for >30 days?	Category	Y	Yes
				N	No
YEARPASTTX1	Year of Most Recent Previous Treatment	The year the patient most recently received previous tuberculosis treatment	Num ###		
REGIMENPASTTX1	Regimen Used for Most Recent Previous Treatment	The drug-regimen given to the patient during the most recent previous tuberculosis treatment. List each drug, separated by a comma, using the provided abbreviations with this dictionary.	Char		
OUTPASTTX1			Category	Cure	Cure

	End-of-Treatment Outcome for Most Recent Previous Treatment	The end-of-treatment outcome recorded for the patient at the end of their most recent previous tuberculosis treatment.		Complete	Completed Treatment
				Fail	Treatment Failure
				Lost	Lost to Follow-up
				U	Unknown
YEARPASTTX2	Year of Second-Most Recent Previous Treatment	The year the patient received previous tuberculosis treatment for their second-most recent treatment episode.	Num ###		
REGIMENPASTTX2	Regimen Used for Second-Most Recent Previous Treatment	The drug-regimen given to the patient during the second-most recent previous tuberculosis treatment. List each drug, separated by a comma, using the provided abbreviations with this dictionary.	Char		
OUTPASTTX2	End-of-Treatment Outcome for Second-Most Recent Previous Treatment	The end-of-treatment outcome recorded for the patient at the end of their second-most recent previous tuberculosis treatment.	Category	Cure	Cure
				Complete	Completed Treatment
				Fail	Treatment Failure
				Lost	Lost to Follow-up
				U	Unknown

DISEASE CHARACTERISTICS					
Field	**Variable**	**Additional Information**	**Format**	**Category Coding**	**Category Labelling**
DISEASE_SITE	Site of Tuberculosis Disease	The site of tuberculosis disease diagnosed in the patient	Category	PTB	
				EPTB	
				Both	
EXTRAPULM_SITE	Primary Site of Extrapulmonary Tuberculosis	If extrapulmonary tuberculosis is diagnosed, the primary site affected	Category	Miliary	Miliary TB
				Genital	Genitourinary TB
				CNS	Central Nervous System TB
				Periton	TB Peritonitis
				Pericar	TB Pericarditis
				Lymph	TB Lymphadenitis
				Pleural	Pleural TB
				GI	Gastrointestinal TB
				Bone	Bone TB
				Joint	Joint TB
				Other	Other
CAVITATION_BASE	Lung Cavitation	Was there presence of lung cavitation on chest x-ray at treatment start?	Category	Y	Yes
				N	No
				U	Unknown
BILATERAL_BASE	Bilateral Disease	Was there presence of bilateral disease on chest x-ray at treatment start?	Category	Y	Yes
				N	No
				U	Unknown
AFB_BASE			Category	Pos	Positive

	Acid-Fast Bacilli Smear Result	What was the patient's acid-fast bacilli smear result (taken up to 1 month after treatment start)? Consider all samples taken over this time frame and consider positive if any were positive (i.e. scanty or greater).		Neg	Negative
				Contam	Contaminated
				ND	Not Done
CULTURE_BASE	Sputum Culture Result	What was the patient's sputum culture result (take up to 1 month after treatment start)? Consider all samples taken over this frame and consider positive if any were positive.	Category	Pos	Positive
				Neg	Negative
				Contam	Contaminated
				ND	Not Done
CULTUREMEDIA	Culture Media Used	If culture was done, what media was used for the result reported?	Category	Solid	Solid Media
				Liquid	Liquid Media

GENOTYPIC DST					
Field	**Variable**	**Additional Information**	**Format**	**Category Coding**	**Category Labelling**
XPERT_BASE	Gene Xpert Used	Was Gene Xpert used for diagnosis?	Category	Y	Yes
				N	No
DATE_XPERT	Date of Gene Xpert	Date of Gene Xpert used for diagnosis <mm/dd/yy>	Date		
XPERT_RIFRESULT_BASE	Gene Xpert Rifampicin Resistance Result	What was the result for rifampicin resistance on Gene Xpert?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
FIRSTLINE_LPA_BASE	First-Line LPA Used		Category	Y	Yes

		Was first-line LPA used after TB diagnosis?		N	No
DATE_FIRSTLINE_LPA	Date of First-Line LPA	Date of first-line LPA used after TB diagnosis <mm/dd/yy>	Date		
FIRSTLINE_LPA_H_BASE	First-Line LPA Isoniazid Resistance Result	What was the result for isoniazid resistance on first-line LPA?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
FIRSTLINE_LPA_R_BASE	First-Line LPA Rifampicin Resistance Result	What was the result for rifampicin resistance on first-line LPA?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
SECONDLINE_LPA_BASE	Second-Line LPA Used	Was second-line LPA performed after TB diagnosis?	Category	Y	Yes
				N	No
DATE_SECONDLINE_LPA	Date of Second-Line LPA	Date of second-line LPA used after TB diagnosis <mm/dd/yy>	Date		
SECONDLINE_LPA_SLI_BASE	Second-Line LPA Second-Line Injectable Resistance Result	What was the result for second-line injectable resistance on second-line LPA?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
SECONDLINE_LPA_FQ_BASE	Second-Line LPA Fluoroquinolone Resistance Result	What was the result for fluoroquinolone resistance on second-line LPA?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated

PHENOTYPIC DST					
Field	**Variable**	**Additional Information**	**Format**	**Category Coding**	**Category Labelling**
PHENODST	Phenotypic DST Done	Was phenotypic DST performed?	Category	Y	Yes
				N	No
DATE_PHENODST	Date of Phenotypic DST	Date of phenotypic DST done after TB diagnosis <mm/dd/yy>	Date		
DST_H_BASE	Isoniazid Resistance Result	What was the result for isoniazid resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_HIGHH_BASE	High-Level Isoniazid Resistance Result	What was the result for high-level isoniazid resistance (MIC >2 μg/ml) on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_R_BASE	Rifampicin Resistance Result	What was the result for rifampicin resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_E_BASE	Ethambutol Resistance Result	What was the result for ethambutol resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_Z_BASE	Pyrazinamide Resistance Result	What was the result for pyrazinamide resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_AM_BASE	Amikacin Resistance Result	What was the result for amikacin resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible

				Contam	Contaminated
				ND	Not Done
DST_KM_BASE	Kanamycin Resistance Result	What was the result for kanamycin resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_CM_BASE	Capreomycin Resistance Result	What was the result for capreomycin resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_OFX_BASE	Ofloxacin Resistance Result	What was the result for ofloxacin resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_CFX_BASE	Ciprofloxacin Resistance Result	What was the result for ciprofloxacin resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_MFX_BASE	Moxifloxacin Resistance Result	What was the result for moxifloxacin resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_LFX_BASE	Levofloxacin Resistance Result	What was the result for levofloxacin resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_S_BASE	Streptomycin Resistance Result	What was the result for streptomycin resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated

				ND	Not Done
DST_ETOPTO_BASE	Ethionamide / Prothionamide Resistance Result	What was the result for ethionamide / prothionamide resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_CSTRD_BASE	Cycloserine / Terizidone Resistance Result	What was the result for cycloserine / terizidone resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_PAS_BASE	Para-Amino-Salicylic Acid Resistance Result	What was the result for para-amino-salicylic acid resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_LZD_BASE	Linezolid Resistance Result	What was the result for linezolid resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_CFZ_BASE	Clofazimine Resistance Result	What was the result for clofazimine resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_BDQ_BASE	Bedaquiline Resistance Result	What was the result for bedaquiline resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done
DST_DLM_BASE	Delamanid Resistance Result	What was the result for delamanid resistance on phenotypic DST?	Category	R	Resistant
				S	Susceptible
				Contam	Contaminated
				ND	Not Done

FOLLOW-UP DST AND ACQUIRED DRUG RESISTANCE					
Field	**Variable**	**Additional Information**	**Format**	**Category Coding**	**Category Labelling**
FOLLOWUP_DST	Follow-up DST Performed	Was there follow-up DST performed?	Category	Y	Yes
				N	No
FOLLOWUPDST1_DATE	Date of First Follow-up DST	Date of first follow-up DST <mm/dd/yy>	Date		
FOLLOWUPDST_RES1	Resistant Isolates on First Follow-up DST	List newly discovered resistances not found on baseline DST. If none discovered, list "no change in DST." List each drug, separated by a comma, using the provided abbreviations with this dictionary.	Char		
FOLLOWUPDST_SUS1	Susceptible Isolates on First Follow-up DST	List newly discovered susceptible drugs not found on baseline DST. If none discovered, list "no change in DST." List each drug, separated by a comma, using the provided abbreviations with this dictionary.	Char		
ACQUIRED_RESISTANCE	Acquired Drug Resistance	List the drugs that the strain was shown to acquire resistance to during any follow-up DST (defined as previously identified susceptibility and subsequent resistance on follow-up DST). List each drug, separated by a comma, using the provided abbreviations with this dictionary.	Char		

REGIMEN INFORMATION					
Field	**Variable**	**Additional Information**	**Format**	**Category Coding**	**Category Labelling**
STARTINGREGIMENTYPE	Regimen Type at Start of Treatment	List the starting regimen type: short (intended duration 9-11 months) or long (intended duration ≥18 months)	Category	Short	Short Regimen
				Long	Long Regimen
TXSTART_DATE	Treatment Start Date	Date of second-line drug initiation in this treatment episode <mm/dd/yy>	Date		
INITIAL_REGIMEN	Starting Treatment Regimen	List the drugs the patient is on at the start of treatment. List each drug, separated by a comma, using the provided abbreviations with this dictionary.	Char		
TWOMONTH_REGIMEN	Treatment Regimen at Month Two	List the drugs the patient is on at month two of treatment. List each drug, separated by a comma, using the provided abbreviations with this dictionary.	Char		
SIXMONTH_REGIMEN	Treatment Regimen at Month Six	List the drugs the patient is on at month six of treatment. List each drug, separated by a comma, using the provided abbreviations with this dictionary.	Char		
TWELVEMONTH_REGIMEN	Treatment Regimen at Month Twelve	List the drugs the patient is on at month twelve of treatment.	Char		

		List each drug, separated by a comma, using the provided abbreviations with this dictionary.			
EIGHTENNMONTH_REGIMEN	Treatment Regimen at Month Eighteen	List the drugs the patient is on at month eighteen of treatment. List each drug, separated by a comma, using the provided abbreviations with this dictionary.	Char		
END_REGIMEN	Treatment Regimen at End of Treatment	List the drugs the patient is on at the end of treatment. List each drug, separated by a comma, using the provided abbreviations with this dictionary.	Char		
TXEND_DATE	Treatment End Date	Date treatment ended in this treatment episode <mm/dd/yy>	Date		
REGIMENDURATION_CHANGE	Intended Duration of Regimen Changed	If the patient started on a short regimen, did they switch to a long regimen?	Category	Y	Yes
				N	No

TREATMENT INFORMATION					
Field	**Variable**	**Additional Information**	**Format**	**Category Coding**	**Category Labelling**
BDQ_DURATION	Bedaquiline Duration	If the patient received bedaquiline, the total number of days the patient received it.	Num ###		
DLM_DURATION	Delamanid Duration	If the patient received delamanid, the total number of days the patient received it.	Num ###		
PA_DURATION	Pretomanid Duration	If the patient received pretomanid, the total number of days the patient received it.	Num ###		
INJ_DURATION	Injectable Duration	If the patient received an injectable, the total number of days the patient received it.	Num ###		
TXDUR_MONTHS	Treatment Duration		Num ###		
DOT	Directly Observed Therapy	Was directly observed therapy used?	Category	Y	Yes
				N	No
DOT_TYPE	Type of Directly Observed Therapy	State the type of directly observed therapy used. Virtual includes methods such as video.	Category	Comm	Community
				Hosp	Hospital
				Pharm	Pharmacy
				Virtual	Virtual
DOT_FREQUENCY	Frequency of DOT Visits	How many days per week is DOT provided to the patient (range 1-7 days)	Num ###		

SURGERY AND HOSPITALIZATION INFORMATION					
Field	**Variable**	**Additional Information**	**Format**	**Category Coding**	**Category Labelling**
SURGERY	Lung Resection Surgery	Did the patient have lung resection surgery related to MDR/RR-TB?	Category	Y	Yes
				N	No
				U	Unknown
SURGTYPE	Type of Lung Resection Surgery	What was the type of lung resection surgery?		Lobe	Lobectomy
				Pneu	Pneumonectomy
				Wedge	Wedge Resection
				Other	Other
				U	Unknown
SURG_DATE	Date of Surgery	What was the date of surgery?	Date		
HOSP	Hospitalization	Was the patient hospitalized at any point during treatment?	Category	Y	Yes
				N	No
				U	Unknown
HOSPEPISODES	Number of Hospitalization Episodes	What is the total number of hospitalization episodes during treatment?	Num ###		
HOSPDUR_DAYS	Total Hospitalization Duration	What is the total duration of hospitalization during treatment?	Num ###		

ADVERSE EVENT INFORMATION					
Field	**Variable**	**Additional Information**	**Format**	**Category Coding**	**Category Labelling**
AE	Adverse Event Occurred		Category	Y	Yes
				N	No

		Did the patient permanently stop a drug in response to an adverse event during treatment?		U	Unknown
AE1_DATE	Date of First Adverse event	What was the date of the permanent discontinuation of the drug(s)?	Date		
AE1_DRUG	Drug Responsible for First Adverse Event	List the drugs permanently stopped in response to the first adverse event. List each drug, separated by a comma, using the provided abbreviations with this dictionary.	Char		
AE1_GRADE	Grade of First Adverse Event	What was the grade of the first adverse event?	Num ###		
AE1_SYSTEMORGAN	System / Organ Class Affected by First Adverse Event	Which system / organ classes were affected by the first adverse event? List each system / organ class, separated by a comma, using the list provided with this dictionary.	Char		
AE2_DATE	Date of Second Adverse event	What was the date of the permanent discontinuation of the drug(s)?	Date		
AE2_DRUG	Drug Responsible for Second Adverse Event	List the drugs permanently stopped in response to the second adverse event. List each drug, separated by a comma, using the provided abbreviations with this dictionary.	Char		
AE2_GRADE	Grade of Second Adverse Event	What was the grade of the second adverse event?	Num ###		
AE2_SYSTEMORGAN	System / Organ Class Affected by Second Adverse Event	Which system / organ classes were affected by the second adverse event?	Char		

		List each system / organ class, separated by a comma, using the list provided with this dictionary.			
AE3_DATE	Date of Third Adverse event	What was the date of the permanent discontinuation of the drug(s)?	Date		
AE3_DRUG	Drug Responsible for Third Adverse Event	List the drugs permanently stopped in response to the third adverse event. List each drug, separated by a comma, using the provided abbreviations with this dictionary.	Char		
AE3_GRADE	Grade of Third Adverse Event	What was the grade of the third adverse event?	Num ###		
AE3_SYSTEMORGAN	System / Organ Class Affected by Third Adverse Event	Which system / organ classes were affected by the third adverse event? List each system / organ class, separated by a comma, using the list provided with this dictionary.	Char		

FOLLOW-UP MICROBIOLOGY RESULTS					
Field	**Variable**	**Additional Information**	**Format**	**Category Coding**	**Category Labelling**
CULTURE_MONTH2	Culture Result Month 2	What is the culture result for the sputum sample tested during month 2?	Category	Pos	Positive
				Neg	Negative
				Contam	Contaminated
				ND	Not Done
CULTURE_MONTH4	Culture Result Month 4	What is the culture result for the sputum sample tested during month 4?	Category	Pos	Positive
				Neg	Negative
				Contam	Contaminated
				ND	Not Done

CULTURE_MONTH6	Culture Result Month 6	What is the culture result for the sputum sample tested during month 6?	Category	Pos	Positive
				Neg	Negative
				Contam	Contaminated
				ND	Not Done
CULTURE_MONTH8	Culture Result Month 8	What is the culture result for the sputum sample tested during month 8?	Category	Pos	Positive
				Neg	Negative
				Contam	Contaminated
				ND	Not Done
CULTURE_MONTH10	Culture Result Month 10	What is the culture result for the sputum sample tested during month 10?	Category	Pos	Positive
				Neg	Negative
				Contam	Contaminated
				ND	Not Done
CULTURE_MONTH12	Culture Result Month 12	What is the culture result for the sputum sample tested during month 12?	Category	Pos	Positive
				Neg	Negative
				Contam	Contaminated
				ND	Not Done
CULTURE_MONTH14	Culture Result Month 14	What is the culture result for the sputum sample tested during month 14?	Category	Pos	Positive
				Neg	Negative
				Contam	Contaminated
				ND	Not Done
CULTURE_MONTH16	Culture Result Month 16	What is the culture result for the sputum sample tested during month 16?	Category	Pos	Positive
				Neg	Negative
				Contam	Contaminated
				ND	Not Done
CULTURE_MONTH18	Culture Result Month 18	What is the culture result for the sputum sample tested during month 18?	Category	Pos	Positive
				Neg	Negative
				Contam	Contaminated
				ND	Not Done
CULTURE_MONTH20			Category	Pos	Positive

	Culture Result Month 20	What is the culture result for the sputum sample tested during month 20?		Neg	Negative
				Contam	Contaminated
				ND	Not Done
CULTURE_MONTH22	Culture Result Month 22	What is the culture result for the sputum sample tested during month 22?	Category	Pos	Positive
				Neg	Negative
				Contam	Contaminated
				ND	Not Done
CULTURE_MONTH24	Culture Result Month 24	What is the culture result for the sputum sample tested during month 24?	Category	Pos	Positive
				Neg	Negative
				Contam	Contaminated
				ND	Not Done

TREATMENT OUTCOME INFORMATION					
Field	**Variable**	**Additional Information**	**Format**	**Category Coding**	**Category Labelling**
OUTCOME_DEFINITION	End-of-Treatment Outcome Definition	Specify the guideline year the outcome definition follows—this is preferably the 2013 guidelines, but can follow 2005 guidelines if not available.	Category	WHO2013	2013 Definitions
				WHO2005	2005 Definitions
OUTCOME	End-of-Treatment Outcome	End of treatment outcome assigned to the patient, following the outcome year specified above.	Category	Cure	Cure
				Complete	Treatment Complete
				Fail	Treatment Failure
				Death	Death
				LTFU	Loss to Follow-Up

CULTURECONV	Culture Conversion	Did the patient culture convert (defined as two consecutive negative cultures taken at least 28 days apart)? If the patient was culture negative at baseline, list as BaseNeg.	Category	Y	Yes
				N	No
				BaseNeg	Baseline Negative
CULTURECONV_DATE	Date of Culture Conversion	If the patient culture converted, what was the date of conversion (defined as the date of the first of the two consecutive negative cultures)?	Date		
TWOCONV	Culture Conversion by Month Two	If exact date of conversion is unknown, did culture conversion occur before the end of month two?	Category	Y	Yes
				N	No
				U	Unknown
SIXCONV	Culture Conversion by Month Six	If exact date of conversion is unknown, did culture conversion occur before the end of month six?	Category	Y	Yes
				N	No
				U	Unknown
CULTUREREV	Culture Reversion	If patient converted or was culture negative at baseline, was there culture reversion (defined as two consecutive positive cultures taken at least 28 days apart)?	Category	Y	Yes
				N	No
				U	Unknown
CULTUREREV_DATE	Date of Culture Reversion	If patient had culture reversion, what was the date of reversion (defined as the date of the first of the two consecutive positive cultures)?	Date		
RELAPSE_MONITORING	Post-Treatment Relapse Monitoring	Was post-treatment monitoring for relapse performed?	Category	Y	Yes
				N	No

RELAPSE_FOLLOWUP_DUR	Duration of Relapse Monitoring	What was the duration of relapse monitoring, in months?	Num ###		
RELAPSE_OUTCOME	Occurrence of Relapse	Did the patient experience relapse?	Category	Y	Yes
				N	No
RELAPSE_DATE	Date of Relapse	What was the date of the relapse episode?	Date		
RELAPSE_REINFECT	Relapse or Reinfection	If resources permitted, was this classified as a true relapse or as a reinfection?	Category	Relapse	Relapse
				Reinfect	Reinfection
				U	Unknown

Annex 2. Drug Abbreviations, System/Organ Classes, and End-of-Treatment Outcome Definitions

Tuberculosis Drug Name / Drug Class	**Abbreviation**
Isoniazid	H
Rifampicin	R
Ethambutol	E
Pyrazinamide	Z
High Dose Isoniazid	HighH
Streptomycin	S
Rifabutin	Rfb
Amikacin	Am
Capreomycin	Cm
Kanamycin	Km
Ofloxacin	Ofx
Ciprofloxacin	Cfx
Moxifloxacin	Mfx
Levofloxacin	Lfx
Gatifloxacin	Gfx

Sparfloxacin	Sfx
Ethionamide	Eto
Prothionamide	Pto
Cycloserine	Cs
Terizidone	Trd
Para-Aminosalicylic Acid	PAS
Linezolid	Lzd
Clofazimine	Cfz
Amoxicillin and Clavulanic Acid	AmxClv
Imipenem-Cilastatin	Ipm
Meropenem	Mpm
Bedaquiline	Bdq
Delamanid	Dlm
Pretomanid	Pa
Perchlozone	Pcz
Thioacetazone	T
Rifapentine	Rpt
Second Line Injectables	SLI
Fluoroquinolones	FQ

Drug Name / Drug Class of Antiretroviral Therapy	**Abbreviation**
Nucleoside/Nucleotide Reverse Transcriptase Inhibitor	NRTI
Abacavir	ABC
Didanosine	ddl
Emtricitabine	3TC
Stavudine	d4T
Tenofovir alafenamide	TAF
Tenofovir disoproxil fumarate	TDF

Zidovudine	AZT or ZDV
Non-nucleoside Reverse Transcriptase Inhibitor	NNRTI
Delaviridine	DLV
Efavirenz	EFV
Etavirine	ETR
Nevirapine	NVP
Rilpivirine	RPV
Protease Inhibitor	PI
Amprenavir	AMV
Atazanavir	ATV
Darunavir	DRV
Fosamprenavir	FPV
Indinavir	IDV
Lopinavir + ritonavir	LPV/r
Nelfinavir	NFV
Saquinavir	SQV
Tipranavir	TPV
Fusion Inhibitor	FI
Enfuviritide	ENF or T-20
CCR5 Antagonist	CCR5
Maraviroc	MVC
Integrase Inhibitor	II
Bictegravir	BIC
Dolutegravir	DTG
Elvitegravir	EVG
Raltegravir	RAL

SYSTEM/ORGAN CLASS

Blood and lymphatic system disorders
Cardiac disorders
Congenital, familial and genetic disorders
Ear and labyrinth disorders
Endocrine disorders
Eye disorders
Gastrointestinal disorders
General disorders and administration site conditions
Hepatobiliary disorders
Immune system disorders
Infections and infestations
Injury, poisoning and procedural complications
Investigations
Metabolism and nutrition disorders
Musculoskeletal and connective tissue disorders
Neoplasms benign, malignant and unspecified (incl cysts and polyps)
Nervous system disorders
Pregnancy, puerperium and perinatal conditions
Psychiatric disorders
Renal and urinary disorders
Reproductive system and breast disorders
Respiratory, thoracic and mediastinal disorders
Skin and subcutaneous tissue disorders
Social circumstances
Surgical and medical procedures
Vascular disorders

WHO 2013 Outcome Definitions (Preferred)	
Outcome	**Definition**
Cure	Treatment completed as recommended by the national policy without evidence of failure AND three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase (or Month 8 if no intensive phase).
Complete	Treatment completed as recommended by the national policy without evidence of failure BUT no record that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase (or Month 8 if no intensive phase).
Failure	Treatment terminated or need for permanent regimen change of at least two anti-TB drugs because of: (1) lack of conversion by the end of the intensive phase, or (2) bacteriological reversion in the continuation phase after conversion to negative, or (3) evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs, or (4) adverse drug reactions.
Death	A patient who dies for any reason during the course of treatment
Lost to Follow-up	A patient whose treatment was interrupted for 2 consecutive months or more.

WHO 2005 (Laserson) Outcome Definitions (if 2013 not possible)	
Outcome	**Definition**
Cure	Completed treatment according to programme protocol and has at least five consecutive negative cultures from samples collected at least 30 days apart in the final 12 months of treatment. If only one positive culture is reported during that time, and there is no concomitant clinical evidence of deterioration, a patient may still be considered cured, provided that this positive culture is followed by a minimum of three consecutive negative cultures taken at least 30 days apart.
Complete	Completed treatment according to programme protocol but does not meet the definition for cure because of lack of bacteriological results (i.e. fewer than five cultures were performed in the final 12 months of treatment).
Failure	Treatment will be considered to have failed if two or more of the five cultures recorded in the final 12 months of therapy are positive, or if any one of the final three cultures is positive. (Treatment will also be considered to have failed if a clinical decision has been made to terminate treatment early because of poor clinical or radiological response or adverse events).
Death	A patient who dies for any reason during the course of MDR/RR-TB treatment
Lost to Follow-up	A patient whose treatment was interrupted for two or more consecutive months for any reason without medical approval.