Applicant : National Center for Tuberculosis and Lung Diseases, Georgia

Project title : Capacity Building for Diagnostic and Clinical Management of MDR and XDR Tuberculosis in Civil and Penitentiary Sector in Georgia in the context of new anti-TB drugs implementation and Surveillance of X/MDR-TB Transmission in Georgia

Overall objective	The overall goal of the proposed project is to strengthen the fight against X/MDR TB at the National Level through capacity building of TB Program in Georgia in Diagnostic and Clinical Management of MDR and XDR Tuberculosis in Civilian and Penitentiary sectors within context of new treatment protocol implementation			
	Intervention logic	**Objectively verifiable indicators of achievement**	**Sources and means of verification**	**Risks and assumptions**
Specific objectives	***Specific Objective 1:*** *To strengthen the National Reference Laboratory capacity in phenotypic and genotypic susceptibility testing for second-line drugs including new drugs as Bedaquiline, Linezolid and Delamanid.*	1. By the end of the project 100% of Culture positive Rifampicin resistant TB (RR-TB) cases receive phenotypic and genotypic susceptibility testing for second-line drugs including new drugs as Bedaquiline, Linezolid and Delamanid; 2. 3 staff of NCTLD have completed the training at selected NRL.	National Reference laboratory electronica data base; National TB electronic data base.	The language is a barrier for a correct appropriation of training: Trainees must be fluent in English.
	Specific Objective 2: *To strengthen the National TB Program capacity in clinical management and effective treatment observance of drug resistant TB patients countrywide including the penitentiary sector.*	1. Treatment success rate of X/MDR TB patients increase to 55% from 46% at baseline (2012 cohort) 2. Loss to follow-up among X/MDR TB patients decrease to 25% from 34% at baseline (2012 cohort)	National TB Electornic data base/TB Registry;	The language is a barrier for a correct appropriation of training: Trainees must be fluent in English.
	Specific Objective3: To *acquire evidence based data about primary resistance transmission indexes by Identifying hot spots of MDR and XDR-TB transmission within Tbilisi.*	100% of MDR cases with HIV, HCV and or Diabetes co-morbities within Tbilisi area and their contacts to have performed genotyping in order to List the evidence based clusters of strains from laboratory data, linked by genotype and geographical patterns and its putative transmission setting.	Edition of agregated data from database in final report: the list of identified clusters with hypothesis of transmission events.	Considering the delay from TB infection to disease, by the time frame of the project, clusters of transmission identified at end of project will not be exhaustive. However, the clusters will be stored and can be used any time.

Expected result(s)	*1.1 NRL has an HR capacity to perform drug susceptibility testing for the full profile of second line drugs including Bedaquiline, Linezolid and Moxifloxacin using MGIT technology and performs the genotypic MTBDRsl test;* *1.2 Every Rifampicin Resistant (RR) and or MDR TB patient receives second line DST performed on liquid media using MGIT at diagnosis and during treatment follow-up and MTBDRsl test;* *1.3 Country is conducting routine drug resistance surveillance for all second line drugs including new TB drugs;* *1.4 Treatment regimens are fully individualized more rapidly and exclude empiric regimens while using new TB drugs;*	1. 3 **Microbiologists** can perform phenotypic and genotypic susceptibility testing for second-line drugs including new drugs as Bedaquiline, Linezolid and Delamanid. 2. Phenotypic and genotypic susceptibility are available for **50 MDR-TB** isolates 3. Accuracy of Drug Susceptibility patterns and interpretation of 50 MDR-TB isolates at end of training shows **98% concordance** of phenotypic and genotypic Drug Suceptibility testing between trainers and trainees on the 50 MDR-TB processed isolates. 4. **100%** of Culture positive Rifampicin resistant TB (RR-TB) cases receive phenotypic and genotypic **susceptibility testing for second-line drugs** including Bedaquiline, Linezolid and Moxifloxacin using MGIT technology and genotypic MTBDRsl test;	Recorded raw data from MGIT system and MTBDRsl strips; EQA panel readout; Training certificates; National TB Electornic data base/TB Registry;	Trainees must be experienced in mycobacteriology in order to correctly interpret readouts.
	2.1. TB Medical personnel countrywide possess the state of the art knowledge of managing MDR and XDR TB patients including management of adverse events/reactions by international and in-country trainings; 2.2 X/MDR-TB treatment success rate is increased, while loss to follow-up rate is decreased through establishing patient therapeutic education tool, improving patient treatment adherence and tolerance of treatment	1. **2 Georgian TB doctors** to be trained abroad for 3 months each 2. **200 doctors** to be trained in-country by the 2 doctors in case management and psychosocial support 3. **8 web** conferences conducted between France and Georgia to discuss difficult to treat MDR cases 4. **100% of managable Adverse Events (AEs) or Serious Adverse Events (SAEs)**adequately managed 5**. 100% of recommendation** from French Mission report conducted by Esther are addressed.	Training certificates; In country training participant attendance logs/training assessment sheets; Web conference Screenshots, SAE and Monthly AE reports/tracking logs International expert program evaluation report	Adverse events encountered during training do not encompass all potential ones.
	Result 3.1: *NCTLD has a collection of genotypic data of MDR-TB, XDR-TB strains and geographic information from the related infected patient*	1) 100% of notified MDR and XDR TB strains with HIV, HCV and diabetes co-morbidities within Tbilisi area are sent at National Reference Laboratory at NCTLD for genotyping; 2) Of these 100% cases is documented with geographical patient information. 3) Genotypic resistance conferring mutations to new drugs in phenotypically resistant strains are identified.	Raw data from electrophoresis gels at laboratory. List of putative resistance conferring mutations to new drugs.	The increasing number of resistant strains may exceed NCTLD laboratory HR ressources capabilities.

	Result 3.2: *Database on DR-TB circulating strains with geographic and temporal information about strains onset is built.*	1 (one) database is rolled out and filled in with the collection of acquired data (genotypes of isolates and geographical information from related patients)	Electronic edition of database in intermediate and final reports.	indicated social places may be limited to address of living; not extended to social places of TB patients.
	Result 3.3: *The monitoring of the transmission is improved.*	Transmission route have been identified for 100 cases. List of putative resistance conferring mutations to new drugs for 50% of strains phenotypically resistant to BDQ, Linezolid or Delamanid on year 3 (year 1 and 2 will be dedicated to capacities implementation).	intermediate and final reports includes endpoints: countrywide distribution of clusters, list of clusters sorted by size, density of clusters.	no risk identified
Activities	***Activity 1.1.1:*** *Training of 3 Georgian microbiologist in Europe: 2 for 1.5 months twice for phenotypic and genotypic drug susceptibility testing for new anti-TB drugs and one - 3 months twice for phenotypic and genotypic second-line drug susceptibility testing*			Daily routine workload of trainers may limit the time for training.
	Activity 1.1.2: *Support for phenotypic and genotypic second-line drug susceptibility testing*			no risk identified
	Activity 1.1.3: *Capacity building for phenotypic and genotypic second-line drug susceptibility testing : in-country training led by the trained Georgian microbiologist*			Heavy daily routine workload of trainers and trainees may limit the time to spend for training.
	Activity 1.1.4: *Evaluation of the capacity building in laboratory tools for 2nd line DST MGIT system, including Bedaquiline and MTBDRsl*			no risk identified
	Activity 2.2.1: *Capacity building in adverse drug event clinical management and therapeutic education : training of 2 Georgian clinicians abroad.*			The language is a barrier for a correct appropriation of training: Trainees must be fluent in English.
	Activity 2.2.2: *Capacity building in adverse drug event clinical management and therapeutic education : in-country training led by International experts (part of this activity to be guaranteed through a consultancy channel)*			The language is a barrier for a correct appropriation of training: Trainees must be fluent in English.
	Activity 2.2.3: *Capacity building in managing difficult to treat MDR-TB cases through regular online communication exchanges.*			The language is a barrier for a correct understanding: Trainees must be fluent in English.
	Activity 2.2.4 *_In-country trainings for 200 doctors led by the two Georgian trained clinicians*			no risk identified
	Activity 3.1.1: *Data acquisition: prospective collection of MDR-TB and XDR-TB (with co-morbidities)isolates and related patients information: geographical and temporal data of patients at onset; laboratory MIRU-VNTR patterns of related isolates, and whole genome sequences of clustered strains.*			Too many strains to process for the only trained laboratory specialists at NCTLD.
	Activity 3.2.1: *Develop and roll out database to store geographical/temporal and genotypic information of DR-TB circulating strains.*			no risk identified
	Activity 3.3.1: *Data analysis: query database to spot clusters of transmission events, its frequencies and countrywide distribution; Release putative resistant conferring mutations to new drugs.*			The short timeframe of the project, compared to the physiopathology of TB, do not allow to capture all transmission events.
				Preconditions