

EXPRESSION OF INTEREST

Date: 6th Oct 2026

ICMR–National Institute for Research in Tuberculosis (NIRT), Chennai, invites Expression of Interest (EoI) from eligible institutions / laboratories under the National Tuberculosis Elimination Programme (NTEP) to participate in the multicentric study titled:

“MTB drug-resistance prediction by targeted next-generation sequencing (tNGS) for TB patients treated with BPaLM regimen under the National Tuberculosis Elimination Program”

The EoI is intended to identify participating sites capable of systematic specimen collection, sample handling, Sequencing, reference test testing and coordination with ICMR-NIRT, Chennai as per the study protocol.

Schedule of EoI

Date of Publication	6 th Oct 2026
Last date of Submission	16 th Oct 2026
Submission mode	Email along with Annexure I

Only shortlisted institutions will be contacted for subsequent steps. ICMR-NIRT reserves the right to modify, withdraw or reissue this EoI, with or without amendments, as deemed necessary by the Competent Authority.

Background

Tuberculosis (TB), including drug-resistant TB, remains a major public health challenge. Timely and comprehensive drug-resistance detection is essential for appropriate treatment selection, particularly for patients receiving Bedaquiline containing regimens such as BPaLM. Conventional phenotypic drug susceptibility testing (pDST) is time-consuming and may have limitations for some drugs, while currently available rapid molecular assays interrogate a limited number of resistance-associated variants. The proposed study evaluates targeted next-generation sequencing (tNGS) as a comprehensive molecular approach for drug-resistance prediction in patients with RR/MDR-TB treated under NTEP.

The study protocol proposes comparison of tNGS results with phenotypic DST, line probe assays and whole-genome sequencing (WGS), with defined procedures for resolution of discordant results.

The study includes ICMR-NIRT, Chennai, as the coordinating institution and proposes capacity building and implementation of tNGS at participating NRL/IRL and other eligible sites. The study protocol specifies targeted sequencing using a 32-plex amplicon approach covering resistance-associated genomic regions, with sequencing and bioinformatic analysis using the designated workflow. The target gene list includes regions associated with resistance to first- and second-line and newer anti-TB drugs, as well as strain typing and NTM speciation targets.

Objectives

Primary Objective

- To determine the clinical utility of targeted NGS in guiding treatment decisions and supporting individualized regimen design in patients treated with the BPaLM regimen.
- To build capacity for performing TB tNGS assays at NRLs, IRLs and participating laboratories.

Secondary Objectives

- To study phylogenetic characteristics, including lineage, heteroresistance, mixed infections and co-infections.
- To evaluate the correlation between NGS-predicted drug resistance and phenotypic DST results.
- To assess the acceptability, feasibility and fidelity of implementing NGS technology in the programme setting.
- To evaluate turnaround time, operational requirements and cost implications of incorporating tNGS into DR-TB diagnostic pathways.

Eligibility Criteria

Institutions applying in response to this EoI should demonstrate:

- Functional linkage with NTEP / State or District TB programme and established DR-TB diagnostic or treatment services.
- Adequate patient volume and capacity to identify and enrol eligible persons aged 14 years and above with microbiologically confirmed RR/MDR-TB being considered for or receiving BPaLM.
- Availability of trained clinical, laboratory and research personnel for specimen collection, documentation and study coordination.

- Facilities for collection, processing, temporary storage and transport of sputum specimens according to the study protocol.
- Availability of appropriate liquid culture facilities, including DST for newer drugs capability; the lab should be certified by NTEP or should have activate EQA program for MGIT DST.
- Availability of appropriate molecular diagnostic facilities, including NAAT/LPA capability.
- Ability to maintain sample identification and linkage using the NIKSHAY ID and study-specific identifiers.
- Commitment to comply with the protocol, ethics requirements, quality assurance procedures, data-management requirements and reporting timelines.
- Institutional Ethics Committee / Institutional Review Board approval or ability to obtain approval before study initiation.

Scope of Work of Participating Sites

- Identify and screen eligible RR/MDR-TB patients according to the study inclusion and exclusion criteria.
- Obtain informed consent and ensure ethical and confidential handling of participant information.
- Collect the required baseline sputum specimens according to the study protocol and diagnostic algorithm.
- Perform routine programme-appropriate rapid molecular testing and LPA, wherever applicable.
- Prepare and transport the designated sample / sputum deposit to ICMR-NIRT or the designated laboratory for tNGS and reference-standard testing.
- Maintain specimen traceability, including NIKSHAY ID, collection date, sample type and relevant laboratory identifiers.
- Provide relevant demographic, clinical, treatment and laboratory information required for the study.
- Facilitate collection of follow-up information required for assessment of clinical utility and treatment outcomes.
- Participate in quality-assurance activities, proficiency assessment, training and monitoring visits as required.

Role of ICMR-NIRT, Chennai – tNGS and Reference Laboratory

ICMR-NIRT, Chennai, will coordinate the central laboratory activities related to targeted sequencing and reference-standard evaluation, in accordance with the approved study protocol. The major activities will include:

- Receipt, accessioning and quality assessment of study specimens / DNA extracts.
- DNA extraction from processed concentrated sputum where applicable, following the study workflow.
- Targeted NGS library preparation and sequencing using the designated tNGS workflow.
- Quality-control assessment at sample, DNA extraction, library preparation, sequencing and bioinformatic stages.
- Bioinformatic analysis and interpretation of sequence data using the designated analysis workflows, including Mykrobe predictor, MTBSeq and the in-house NIRT pipeline as specified in the protocol.
- Prediction of resistance-associated variants, lineage and other genomic characteristics covered by the assay.
- Reference-standard testing and/or coordination of reference testing, including MGIT liquid culture DST, first- and second-line LPA and WGS as specified in the study protocol.
- WGS of resistant samples and a defined proportion of drug-sensitive samples, where applicable, for confirmation and discordant-result resolution.
- Repeat testing and resolution of discordant results according to the predefined study algorithm.
- Generation of laboratory reports and transmission of results to the study team within the agreed timelines.
- Maintenance of laboratory records, sequencing data, quality-control records and appropriate data backup.

Reference-Standard and Comparator Testing

The study protocol specifies comparison of tNGS results with phenotypic and molecular reference/comparator methods. Depending on the study pathway and sample availability, these will include:

- MGIT liquid culture and drug susceptibility testing using the BACTEC MGIT 960 system, with critical concentrations as specified by applicable WHO/NTEP guidance.
- First- and second-line line probe assays.
- Whole-genome sequencing for resistant samples and a defined proportion of drug-sensitive samples.

- Repeat MGIT DST and MIC assessment for specified phenotypically discordant results.
- Repeat / confirmatory testing and sample identity checks for discordant molecular results, as specified in the study protocol.

tNGS Laboratory Workflow

- Raw sputum/processed concentrated sputum generated through the NaLC-NaOH method will be used for DNA extraction, with the additional PBS wash specified in the protocol.
- The Inhouse kit will be used for amplification and Nanopore library preparation kit will be used.
- Inhouse designated bioinformatic pipelines will be used for data analysis and interpretation.
- Dedicated work areas will be maintained for master-mix preparation and library preparation.
- Up to 96 samples may be tested on a flow cell or in two batches of 48 samples, subject to the sequencing workflow.
- The protocol estimates approximately 50 GB of data for a batch of 96 samples; participating laboratories must therefore ensure appropriate data transfer, storage and backup arrangements.
- Where sequencing data are insufficient for one or more genes, repeat testing will be undertaken using a freshly collected specimen, preferably a morning specimen. Culture will also be subjected to tNGS if the load is very low.

Quality Assurance

A comprehensive quality-assurance framework will be implemented across the specimen, molecular, sequencing and reference-testing workflow. The study protocol specifies quality checks at each major step.

- Assessment of specimen quality and quantity and DNA quality and quantity.
- Quantification and normalization during library preparation, including Qubit-based quality checks where applicable.
- Negative control, such as a water-only control, during DNA extraction / relevant processing batches.
- Reference genomic DNA, such as *M. tuberculosis* H37Rv or *M. bovis* BCG, for library preparation and sequencing quality control.
- Duplicate testing of selected samples within the same or different runs to assess reproducibility.
- Assessment of sequence assembly, coverage and variant calling using more than one analytical pipeline.
- Monitoring of invalid, failed and insufficient data runs and appropriate repeat testing.

- Maintenance of complete batch records, run records, QC records and corrective-action documentation.

Proposed Discordant-Result Resolution

- GeneXpert versus LPA: tNGS result will be considered final as specified in the study protocol.
- LPA versus tNGS: tNGS result will be considered final after confirmation of sample identity / mislabelling and repeat sampling where required.
- GeneXpert versus tNGS: WGS result will be considered final after confirmation of sample identity / repeat sample where required.
- MGIT-DST versus WGS: phenotypic and genotypic results will be compared; repeat MGIT testing and MIC assessment will be performed for discordant drugs as specified at ICMR-NIRT.

Data Management and Reporting

- Baseline demographic, clinical, treatment and diagnostic information will be recorded according to the study protocol.
- NIKSHAY ID will be recorded separately to facilitate subsequent linkage with treatment outcomes.
- tNGS, WGS, LPA and phenotypic DST results will be linked using study-specific identifiers.
- Turnaround time, testing cost, infrastructure requirements and operational feasibility will be documented.
- Laboratory results will be reported to the designated study team through the agreed secure reporting mechanism.
- Genomic data and participant information will be anonymized / de-identified and maintained confidentially.

Expected Deliverables

- Generation of reliable tNGS results for enrolled RR/MDR-TB participants.
- Reference-standard and comparator DST results for study samples, where applicable.
- Assessment of agreement between tNGS-predicted resistance and phenotypic / molecular reference results.
- Resolution and documentation of discordant results.
- Assessment of turnaround time, feasibility and cost of tNGS implementation.
- Capacity building and technical support for participating laboratories.
- Generation of a curated dataset suitable for clinical utility, diagnostic-performance and implementation analyses.

**Infrastructure and Capability Assessment – Information to be Submitted by Applicant Sites:
Annexure 1 to be completed**

Domain	Required capability / information
Patient volume	Average number of RR/MDR-TB patients/Samples managed / month.
Specimen collection	Facility and trained staff for sputum collection and sample processing.
Molecular diagnostics	Availability of NAAT, GeneXpert/Truenat and LPA facilities.
Culture/DST	Availability of MGIT culture/DST and established linkage to a reference laboratory.
Cold chain	Availability of 2–8°C, –20°C and/or –80°C storage as required.
Biosafety	Availability of appropriate BSL-2/BSL-3 facilities and SOPs.
Sequencing	Existing NGS platform / facility, if available; details of sequencing infrastructure and data storage.
Bioinformatics (Optional)	Availability of suitable computing, secure data transfer and trained personnel.
Quality assurance	Internal QC, EQA/proficiency testing and documentation systems.
Human resources	Clinical, microbiology, molecular biology, sequencing and data-management personnel.
Regulatory	IEC/IRB status and estimated timeline for approval.
Programme linkage	Linkage with NTEP / DR-TB centre / CoE and sample referral mechanism.

Other details required: As per Annexure 1

Review and Selection Process

- Initial screening of EoI submissions for completeness and eligibility.
- Technical review of laboratory, clinical, sample-volume and quality-assurance capabilities.

- Shortlisting based on study requirements, geographic/programmatic representation, sample availability and laboratory readiness.
- Site assessment / virtual or physical feasibility assessment, where required.
- Final selection and communication to shortlisted institutions by the Competent Authority.

Important Points for Submission

- Applicants should provide complete and accurate information against every item in the EoI.
- The applicant should clearly describe its current laboratory infrastructure and not include facilities that are only proposed unless clearly identified as such.
- Participation will be subject to institutional approvals, study-specific training, quality requirements and execution of the required study/collaboration documentation.
- The selected sites will be expected to comply with the approved protocol, SOPs, biosafety requirements, confidentiality requirements and reporting timelines.

Contact for Further Details

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Annexure 1

A. Institution & NTEP Linkage

- 1. Name of Institution, Department/Laboratory, State and District**
- 2. Name, designation, official email and contact number of the Principal Investigator/Site Investigator**
- 3. What is your institution's linkage with NTEP?**
 - State/District TB Programme
 - DR-TB Centre
 - NRL
 - IRL
 - Centre of Excellence
 - Other
- 4. Does your institution provide DR-TB diagnostic/treatment services and manage patients receiving or being considered for BPaLM?**
 - Yes / No
- 5. Is your institution linked with NIKSHAY, and can NIKSHAY IDs be linked with study-specific identifiers?**
 - Yes / No / Partially

B. Patient Volume & Recruitment

- 6. Average number of RR/MDR-TB patients managed per month**
 - Numeric
- 7. Average number of BPaLM patients managed per month**
 - Numeric
- 8. Estimated number of eligible RR/MDR-TB participants/samples that your institution can contribute to this study per month**
 - Numeric
- 9. Does your institution have adequate patient/sample volume to recruit participants aged ≥ 14 years with microbiologically confirmed RR/MDR-TB?**
 - Yes / No

C. Specimen Collection & Transport

- 10. Does your institution have trained staff and facilities for sputum collection, processing, temporary storage and specimen traceability?**

- Yes / No / Partially

11. Is there an established system for transporting specimens to ICMR-NIRT/designated laboratory, and what is the usual collection-to-dispatch time?

- Yes / No
- <24 h / 24–48 h / >48 h

12. Can your site provide the required demographic, clinical, treatment and laboratory information and facilitate follow-up information?

- Yes / No / Partially

D. Molecular Diagnostic & Culture/DST Capacity

13. Which molecular diagnostic facilities are available at your institution?

- GeneXpert
- Truenat
- First-line LPA
- Second-line LPA
- Other NAAT

14. Is MGIT liquid culture and phenotypic DST available at your institution? If yes, specify the platform and approximate monthly DST volume.

- Yes / No
- Platform: MGIT/MIC
- **monthly DST volume**

15. Is your laboratory NTEP-certified for MGIT DST or participating in an active EQA/proficiency-testing programme?

- NTEP certified
- Active EQA
- Both
- Neither

16. Does your laboratory perform DST for newer anti-TB drugs? If yes, please specify the drugs.

- Yes / No
 - list of drugs
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E. Infrastructure & Biosafety

17. What specimen storage facilities are available?

- 2–8°C
- –20°C
- –80°C
- Temperature monitoring available

18. What biosafety facilities are available for TB laboratory activities?

- BSL-2
- BSL-3
- Both
- Other

19. Are appropriate biosafety SOPs and laboratory workflows implemented at your institution?

- Yes / No / Partially

F. Sequencing & Bioinformatics

20. Does your institution have an NGS facility? If yes, specify the platform, instrument and current sequencing capacity.

- Yes / No
- Platform, instrument and current sequencing capacity.

21. Is adequate infrastructure available for sequencing-related activities and data storage?

- Yes / No / Partially

22. Is in-house bioinformatics capability available, including trained personnel and secure data transfer/storage?

- Yes / No / Partially

G. Quality Assurance & Human Resources

23. Does your laboratory have documented SOPs, internal QC, EQA/proficiency testing and a CAPA/documentation system?

- Yes / No / Partially

24. Please provide the availability of key personnel for the study: clinical, microbiology, molecular biology, sequencing and data management.

- Available / Partially available / Not available for each category

25. Is your institution willing to participate in study-specific training, proficiency assessment, QA activities and monitoring visits?

- Yes / No

H. Ethics, Regulatory & Programme Readiness

26. What is the current status of your Institutional Ethics Committee/IRB approval?

- Approval available
- Application submitted
- Approval to be obtained
- Not available

27. Is your institution able to comply with the study protocol, informed-consent/ethical requirements, confidentiality, biosafety and data-management requirements?

- Yes / No

28. Is there an established linkage with the NTEP/DR-TB Centre/CoE for patient referral, sample referral and treatment/follow-up information?

- Yes / No / Partially

I. Overall Readiness & Commitment

29. What is your institution's overall readiness to participate, and what support/challenges should be considered?

- Fully ready
- Ready with minor support
- Requires additional support
- Not currently ready
- **Please specify major challenges and support required:** Paragraph

Declaration and commitment to participate

I certify that the information provided is complete and accurate and represents the current status of our institution/Laboratory. I confirm our willingness to comply with the approved study protocol, SOPs, biosafety, quality-assurance, confidentiality, data-management and reporting requirements, subject to institutional approvals and final selection by ICMR-NIRT/competent authority.

I Agree

Name of authorized applicant

Designation

Date