ICMR - National Institute for Research in Tuberculosis (Indian Council of Medical Research)

invites Expression of Interest (EoI)

"To undertake a Multi-centric Parallel arm Randomized Clinical trial to improve treatment outcomes among persons with drug sensitive pulmonary TB treated with 4 or 6 months of High dose Rifampicin containing regimens with or without Levofloxacin (PRaCTISe-HR)"

Invitation of Expression of Interest

ICMR–National Institute for Research in Tuberculosis, Chennai is pleased to invite Expressions of Interest (EoI) from interested clinical trial sites and ICMR Indian Clinical Trial and Education Network (INTENT) centres for the purpose of collaborating and conducting a Multi-centric Parallel arm Randomized Clinical trial to improve treatment outcomes among persons with drug sensitive pulmonary TB treated with 4 or 6 months of High dose Rifampicin containing regimens with or without Levofloxacin (PRaCTISe-HR).

Schedule of EoI:

- Date of Publication: 24 April 2025
- Last date of submission: 18 May 2025

Interested applicants may submit required information through the link available at the end of this document. Please note that only shortlisted centres will be contacted for subsequent steps. The selected researchers shall be invited to join the research team and shall collaborate to roll out the clinical trial, which will be coordinated by ICMR-National Institute for Research in Tuberculosis, Chennai. The protocol has been reviewed critically and approved by the Project Review Committee of Indian Council of Medical Research and the project implementation shall be reviewed by ICMR and an independent expert committee.
ICMR reserves the right to cancel this EoI and/or reissue it with or without amendments, without incurring any liability or obligation and without assigning any reason therefor. ICMR reserves the right to amend or add further details to the EoI as deemed necessary by the Competent Authority, which will be duly notified.

Background

Despite wide implementation of highly efficacious regimen, Tuberculosis (TB) treatment success rate is 88% throughout the world. In India among patients who were initiated on treatment the success rate ranges from 85 to 88% for the past 10 years and death rate reported is 3.9 % for the year 2022 [1]. Studies have shown that about 5-10% will have recurrent TB (treatment failure of the first treatment, relapse, or treatment after being lost to follow-up)[2]. Most patients do recur within 6 months of treatment cessation with sensitive bacilli and are repeatedly treated with same line of treatment as new case. Moreover, patients with recurrent TB are more at risk of having drug resistant TB[3]. Moreover, data on TB recurrence rate among patients initiated on daily regimen is currently limited.

High dose Rifampicin: A recently conducted clinical trial from ICMR-NIRT[4] and systematic reviews[5-8] published in recent years have documented that high-dose rifampicin is efficacious, and safe than the conventional 10 mg dosage. Studies have also documented that High dose rifampicin containing regimen result in prevention of drug resistance, which is a highly desirable property of an anti-TB regimen[9]. Even though high-doses of Rifampicin are found safe and beneficial, with respect to culture conversion, its impact on treatment outcomes and long-term recurrence free survival is unclear. Evidences highlight the need for effective strategies to improve treatment outcomes and reduce TB recurrence in India and Use of high-dosage RMP in reducing relapse

rates remains to be explored in clinical studies.

Researchers have always been interested in two specific aspects of treatment – shortening of TB treatment and aborting drug resistance and recurrences using additional drugs or optimizing the drug dosages.

The current ICMR call is being proposed to evaluate two strategies tried in order to reduce recurrences

1. Usage of High dose Rifampicin given either for 2 months or for 6 months along with other first line anti-TB drugs.

2. Addition of a Fluoroquinolone along with high dose rifampicin to reduce the treatment duration from 6 months to 4 months.

Objectives

ICMR invites EOI to select institutions that will participate in the conduct of an ICMR-funded trial which will address the following research questions:

1. Primary Objective

To determine the recurrence-free survival among persons with drug sensitive (new or previously treated) pulmonary Tuberculosis aged above 14 years treated with High dose Rifampicin containing regimens with or without Levofloxacin at 18 months post randomization.

- Efficacy Comparison 1: High dose rifampicin for 2 or 6 months vs Standard of care – (superiority Design)
- Efficacy Comparison 2: High dose Rifampicin along with levofloxacin for 4 months vs Standard of care (Non-inferiority design)

2. Secondary Objectives:

1. To estimate the proportion of PTB patients with grade 3/4 adverse drug reactions
2. To determine the treatment response at end of treatment

Trial Design: A multicenter parallel arm randomized clinical trial.

Target Population: Persons with Symptomatic drug sensitive (new and previously treated) pulmonary TB aged > 14 years of age with sputum smear and or CBNAAT positive.

Scope of work

- Selected institutions will conduct the said clinical trial at their institutions, ensuring compliance to ethical requirements and good clinical practices.
- Overall trial coordination and trial monitoring will be the responsibility of ICMR-NIRT, Chennai

Eligibility Criteria:

Institutes interested in submitting an Expression of Interest (EoI) should provide information regarding the following parameters

1. **Proven experience:** The applicant must have demonstrated experience in conducting late-phase clinical trials in Tuberculosis, both in-facility as well as community-based trials. This includes a history of successfully managing and executing such trials, with verifiable outcomes. Experience in conduct of regulation-compliant clinical trials is desirable.

2. **Access to facilities and resources:** The applicant must have access to necessary facilities, equipment, and resources required to conduct comprehensive clinical evaluations. This includes, but is not restricted to, clinical trial infrastructure (for e.g., three-room strategy, Investigational Product management facilities, etc.), availability of experienced GCP-certified human resources, availability of Standard Operating Procedures, laboratory facilities for TB related diagnostics, medical care facilities (for SAE/AE management), clinical trial data management resources, DHR-registered Institutional Ethics Committee and any other resource essential for the successful execution of the trial

3. **Access to adequate number of cases/ study participants:** The applicant should demonstrate capacity to enroll eligible study participants from health facilities and community.

4. **Multidisciplinary team:** The applicant should form a team including investigators from all the required domains

Applicants are required to submit required information through the link available at the end of this document. Only those entities that meet these eligibility criteria will be considered for the subsequent stages of the EoI evaluation process.

Review Process

The process for reviewing the Expression of Interest (EoI) submissions will involve the following steps:

1. **Initial Screening by ICMR:** The EoI documents will be evaluated and shortlisted by a team at the Indian Council of Medical Research / ICMR-NIRT. During this initial phase, the ICMR team will screen the applications for completeness and accuracy of information. Each application will be screened independently, irrespective of the number of applications submitted by a single ICMR-INTENT centre.

2. **Short listing of Applicants:** Applications that meet the eligibility criteria will be reviewed by independent experts based on the information submitted by applicants and shortlisted for further consideration by the Competent Authority of ICMR.

3. **Further steps:** Selected centres for the trial will be informed about their selection and further procedures regarding the trial.

Important Points for Submitting the Expression of Interest (EoI):
Your submission must thoroughly address each specific question outlined in the application form. Provide clear, concise, and detailed responses that demonstrate your understanding and alignment with the EoI requirements. Adherence to these points will be critical in the evaluation of your EoI. Please ensure that your submission is complete and aligned with the objectives.

The EOI can be submitted through ONLINE MODE ONLY by the Principal Investigator on behalf of the proposed team. Interested parties should fill out the form at the below link and submit an Expression of Interest (EOI) as per the ***Annexure I*** in PDF format.

Application Link: https://forms.gle/XtMyaj7cU7GjuGRK7

Timelines:

Milestone	**Date**
Release of Call	24/04/2025
End of Call	18/05/2025
Shortlisting of EOI applications	30/05/2025
Investigators meeting and SOP Finalization	1st week of June, 2025

For any queries related to the call, please contact:

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35mg/kg vs 10mg/kg Rifampicin in pulmonary TB: A phase IIb randomized controlled trial. Open Forum Infect Dis 2024 ; 11(3):

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ANNEXURE I

A. EOI Application

S.No	General Information	
1	Name and address of the Medical College/ Hospital/ Research Institute/ other facility where the clinical trial will be conducted	
1a	Type of Organization	Government/ Private/ Non-Government Organization
2	Name of the Principal Investigator with Designation and Qualification	
2a	Phone number and email id of the Principal Investigator	
3	Details of Co-Investigators: Name, Designation and Qualification	1. .. 2. ..
4	Research Team (<500 words) Summarize and justify the composition of the research team, based on the expertise of the individual team members in conducting the trial.	
5	Does the investigator and/or site staff have experience in conducting clinical trials?	1. Yes 2. No
5a	If yes, Please attach list of research activities for investigator and/or site staff for the last 5 years, including indication, phase of study, type of TB (e.g., DS/MDR/XDR), current study status (closed/ongoing), and number of participants	
5b	Collaboration with ICMR or contribution to ICMR activities in last 5 years (maximum 250 words).	
6	Incidence of TB in your TU/District/State	1. DS TB (New): ____ 2. DS TB (Previously treated): _____ 3. HIV-TB : _____
7	How many drug sensitive TB cases are diagnosed in your Institution or hospital every year? Note adult's vs children	1. Adults _____ 2. Children >14 y ___
8	How many drug sensitive pulmonary TB cases could be enrolled in the trial in a month?	
	Site Infrastructure and Facility	
9	Is your college / institution attached with Laboratory facility	Bacteriology: Yes /No Biochemistry: Yes /No

		Hematology: Yes/ No
9a	If no, Is it attached with any external lab and its distance from site	
9b	Does the local laboratory perform sputum smears, mycobacterial cultures and drug susceptibility testing?	1. Yes 2. No
10	Availability of Chest X-ray facility	1. Yes 2. No
11	Is there an In-Patient facility for TB patients available on site/close to the site? If yes, provide details below (name, address, distance from site)	
12	Does the site have a registered (DHR/CDSCO) local IEC to oversee the trial?	1. Yes 2. No
13	If no, which ethics committee is the site/institution attached to?	
14	Does the site have storage facility (both for CRFs and Drugs)	1. Yes 2. No
15	Name and Signature of the person providing the details	

B. Single file CV of PI and team members (with each CV limited to a max of one page)

Please provide a single file CV of the PI and other key investigators from each identified area. Each CV should include:

a. Academic and professional qualifications
b. Current position and affiliation
c. Up to five most relevant previous research grants
d. Up to five most relevant previous publications
e. Experience in undertaking projects on Tuberculosis

C. Endorsement letter from the head of the Organization with the following commitments

i. I agree to conduct the trial in accordance with the clinical trial protocol.

ii. I agree to personally supervise the trial at my site and will report all adverse events and serious adverse events as per regulatory requirements and Good Clinical Practice.

iii. I agree to ensure that the study team assisting in the conduct of the trial are suitable, qualified and experienced.

iv. I agree to inform all the trial participants that the drugs are being used for investigational purposes and ensure the requirements relating to obtaining informed consent and IEC review and approval specified in the NDCT Rules, 2019 guidelines are met

v. I agree to maintain adequate and accurate records and I will fully cooperate with any trail related audit conducted by authorized representatives of the sponsors and ethics committee.

vi. I agree to assure security and maintain confidentiality of all the trail related data

Name of the Principal Investigator **Signature and date**

Name of the Head of the Institution: **Signature and date**