Ref No: NIRT/PROJECT/Insurance/2025-26 Dt.17.11.2025

QUOTATION ENQUIRY

Sealed quotations are invited on behalf of the Director, ICMR- National Institute for Research in Tuberculosis, Chetpet, Chennai-31 from firms regarding clinical trial insurance for 4M kids trial for ICMR – NIRT, Chennai as per details given below.

Sl.No.	Description	Quantity
1.	Clinical trial insurance for 4M kids trial	782 children
Insured Name	ICMR-NATIONAL INSTITUTE FOR RESEARCH IN TUBERCULOSIS	
Study Title	Four-month moxifloxacin containing shorter regimen versus 6 months standard regimen for treatment of drug sensitive TB disease in children aged 1 year to 18 years – open labelled randomized controlled trial (4M kids trial) Version: 2.1 dated 2 May 2025	
Study Subject	782 children	
Study Duration	4.5 years	
Study Site	• Grant Govt. Medical College, Sir JJ Group of hospitals, Mumbai • Rajendra institute of medical sciences, Ranchi • National Institute of Tuberculosis and Respiratory Diseases, New • Delhi • Lady Hardinge Medical College, New Delhi • All India Institute of Medical Sciences, Guwahati • Gauhati Medical College and Hospital, Guwahati • Vanivilas hospital, Bangalore Medical College and Research Institute, • Bangalore • Andhra Medical College, Vishakhapatnam • Institute of Child Health, Madras Medical college, Chennai • ICMR- National Institute For Research In Tuberculosis, Chennai	
	Additional insured; for their respective rights and interest in conducting this trial for named insured a. Investigators b. Ethics Committee members c. Staff and contractual staff involved in the study conduct and analysis of samples d. Head of the clinic e. Head of the institution f. Consultants for the study	
Protocol summary is attached.		

The quotations super scribed as "**Quotation for Clinical trial insurance for 4M kids trial** " addressed to the Director, ICMR-NIRT, Chetpet, Chennai-31(Attention: Administrative Officer - Stores) should be either dropped at the Stores Department at NIRT or sent through Speed Post / Courier or by E-mail (with signature & seal in company letter head to nirtdirector@icmr.gov.in. latest by **08.12.2025 till 03.00 P.M.**

OTHER TERMS & CONDITIONS

1. This is an enquiry & must not be treated as an order.
2. The service provider should submit quotation with GST number only. GST percentage and amount should be shown separately in the quotation.
3. The NIRT Office reserves the right to accept or reject any or all applicants without assigning any reasons.
4. Any decision taken by the Director, NIRT at any point of time in connection with this process shall be final and conclusive and no claim or dispute from any quarter in that regard shall be entertained.
5. No advance payment will be made. The payment will be made on receipt of services availed and satisfactory report of the end users.
6. NIRT, Chennai will not be responsible for any delay for receipt of quotations.
7. NIRT GST No.33AAEAT4818Q1ZZ

17/11/25

ADMINISTRATIVE OFFICER

Four-month moxifloxacin containing shorter regimen versus 6 months standard regimen for treatment of drug sensitive TB disease in children aged 1 year to 18 years - open labelled randomised controlled trial (4M kids study)

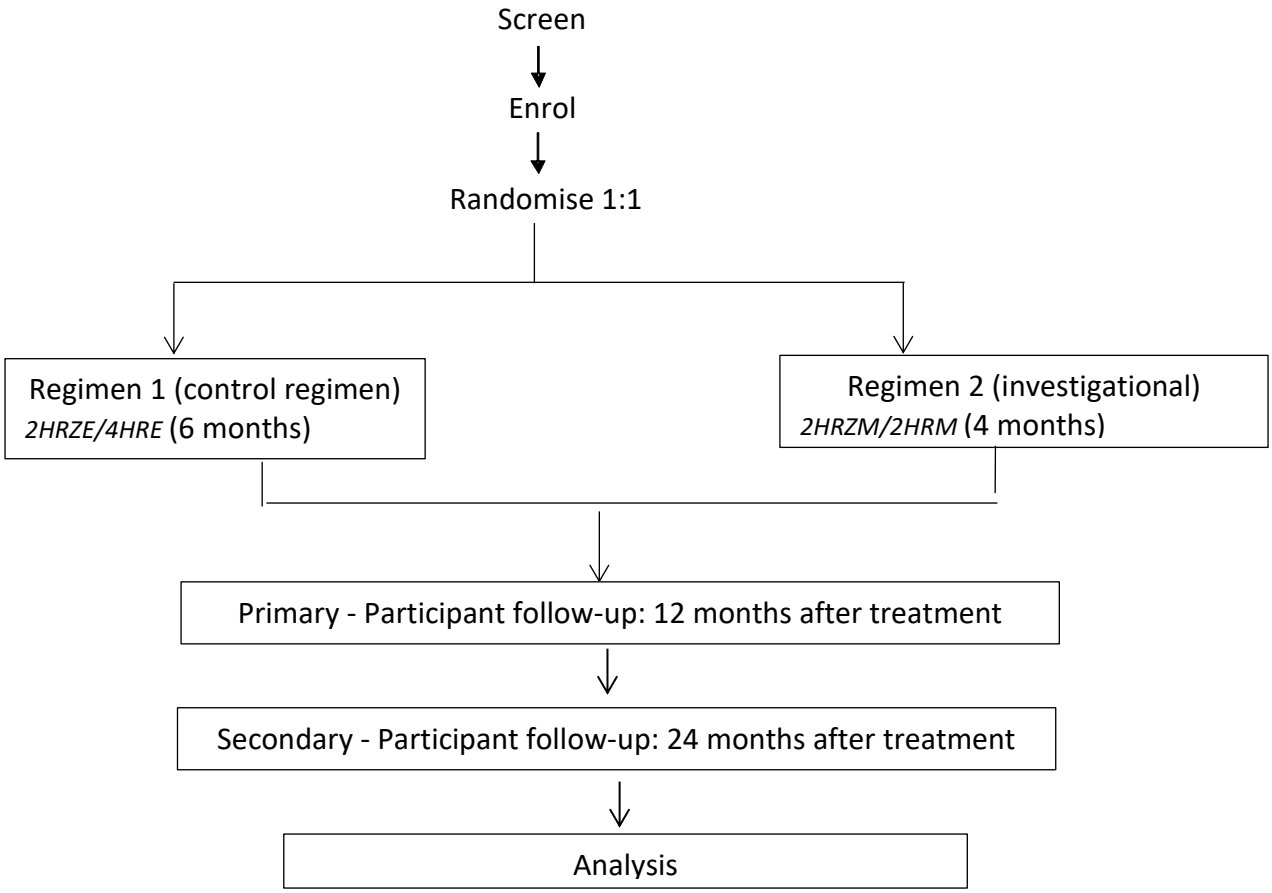
Protocol Summary

Protocol title	Four month moxifloxacin containing shorter regimen versus 6 months standard regimen for treatment of confirmed drug sensitive TB disease in children under 18 years – open labelled randomised controlled trial
Objectives	**Primary Objective**: To determine the efficacy of moxifloxacin containing 4 months regimen (2HRZM/2HRM) for treatment of microbiologically confirmed pulmonary or lymph node drug-susceptible TB in children age 1 to under 18 years in comparison to 6 months of standard treatment (2HRZE/4HRE). **Secondary objective:** • To determine the unfavourable outcome at 24 months post treatment • To determine the adverse drug reactions (ADR) • To characterize moxifloxacin PK parameters in children • To determine the palatability and acceptability of the 4-month moxifloxacin containing daily regimen in children
Study design	Multicentre, randomised, controlled, open-label, 2-arm, phase 3 non-inferiority trial.
Study sites	Guwahati, Mumbai, New Delhi, Ranchi, Chennai, Bangalore, Vishakhapatnam 1. Grant Medical College (GMC) and Sir J.J. Group of Hospitals, Mumbai 2. Rajendra institute of medical sciences, Ranchi 3. National Institute of TB and Respiratory Diseases (NITRD), New Delhi 4. Lady Hardinge College, New Delhi 5. All India Institute of Medical Sciences (AIIMS), Guwahati 6. Gauhati Medical College, Guwahati 7. Vanivilas Hospital and Bangalore Medical College, Bangalore 8. King George Hospital and Andhra Medical College, Vishakapatnam 9. Institute of Child Health, Madras Medical College, Chennai 10. ICMR-National Institute for Research in TB, Chennai
Study population	•Newly diagnosed children or adolescents aged 1 to 18 years with microbiology confirmed drug sensitive pulmonary TB. Microbiological confirmation includes MTB positive from sputum or alternative samples (gastric aspirate, nasopharyngeal aspirate and stool) by CBNAAT (Xpert MTB/RIF or Xpert Ultra or Truenat MTB or MTB Plus) and/or culture. •And no resistance to moxifloxacin, by culture/phenotypic drug susceptibility testing (DST) or Line Probe Assay (LPA)
Outcomes	**Primary outcome** Proportion of participants with unfavourable outcomes at 12 months post treatment completion The primary outcome for efficacy is categorised as: Unfavourable outcomes; a composite of failure, death, reinfection or recurrence Favourable outcome; TB-free survival at 12 months post treatment completion

	Not assessable **Secondary outcomes** 1. Proportion of participants with TB-free survival at 24 months post treatment completion 2. To determine the adverse drug reactions (ADR) in both groups 3. To characterize moxifloxacin PK parameters in children 4. To determine the palatability and acceptability of the 4-month moxifloxacin containing daily regimen in children
Sample size	Primary endpoint rate: The primary efficacy analysis, based on the per-protocol 95% data from Turkova A et al, indicates that the unfavourable outcome rate with the standard 6-Month regimen as well as 4-Month shorter regimen was 7.3% [44/602]. The inferiority margin was set at 5.5% ($\delta = 0.55$) Type-1 error, $\alpha = 0.025$ [One-sided test of 2.5%] Power: 80% (type 2 error, $\beta = 0.20$) Proportion of enrolled patients who might be late exclusions due to ineligibility criteria and deemed 'not assessable' or 'loss to follow-up' : 10% With the above assumptions, the minimum required Paediatric TB cases per arm will be 391, and the total required sample size for the trial will be 782 Paediatric TB cases.
Study regimen	Regimen 1 (control regimen): 2HRZE/4HRE (duration 6 months) Eight weeks (2 months) of daily treatment with isoniazid (H), rifampicin (R), pyrazinamide (Z), ethambutol (E), followed by 16 weeks (4 months) of daily treatment with isoniazid, ethambutol and rifampicin Regimen 2 (investigational regimen): 2HRZM/2HRM (duration 4 months) Eight weeks (2 months) of daily treatment with isoniazid (H), rifampicin (R), pyrazinamide (Z), and moxifloxacin (M) followed by 8 weeks of daily treatment with isoniazid, rifampicin, and moxifloxacin daily
Eligibility criteria	**Inclusion:** a. Parent or guardian is willing and able to provide written informed consent for potential participant's study participation; in addition, when applicable potential participant is willing and able to provide assent for study participation. b. At enrolment, age 1 years less than 18 years of age c. At enrolment, diagnosed with confirmed Pulmonary (including pleural effusion) TB disease (PTB) or confirmed lymph node (extra-thoracic and/or intrathoracic) TB disease, defined as participants with microbiological confirmation with or without signs and symptoms of TB disease. • Microbiological confirmation includes MTB positive by NAAT (approved by central TB division for use in children) and/or culture and no resistance to quinolones by culture/phenotypic DST and/or LPA from; o lymph node aspirate or FNAC o sputum or alternative samples (gastric aspirate, nasopharyngeal aspirate and stool)

	• Signs and symptoms include: - Persistent fever for > 2 weeks without a known cause - Persistent cough for > 2 weeks - Weight loss of 5% or more or failure to gain weight in last 3 months despite adequate nutrition - With or without contact with PTB in last 2 years - Chest Xray suggestive of TB (hilar or paratracheal lymphadenopathy with or without parenchymal involvement and fibro-cavitary lesions) d. Eligible to be started on standard first-line drug-susceptible TB regimen in view of TB disease e. HIV negative f. Alanine aminotransferase (ALT) within normal range (less than or equal to 2.5 times the upper limit of normal); Total bilirubin less than or equal to 2.5 times the upper limit of normal g. Willingness to be followed up for 2 years **Exclusion:** a. Children diagnosed with Drug resistant TB (DR-TB): resistant to isoniazid, rifampicin, pyrazinamide, ethambutol, and/or fluoroquinolones. b. Clinically diagnosed TB disease (presumed TB) c. Extrapulmonary TB requiring more than 6 months regimen (central nervous system and/or bones and/or joints, and/or miliary TB, and/or pericardial TB and/or TB of the GI tract and/or renal TB or disseminated TB) d. Hepatic or renal disease as evidenced by clinical or biochemical abnormalities e. Known allergy or intolerance to any of the study drugs or drugs in the same class as the study drugs f. Prolonged QT syndrome (QTcF> 440 ms or bundle branch block or heart block on ECG) g. Seizure disorder h. Pregnancy or lactation i. Any known contraindication to taking anti-TB drugs j. Evidence of significant medical condition which in the judgement of the Investigator ***Late excluders:*** Enrolled participants who are subsequently determined to have resistance to quinolones by LPA or DST. They will be withdrawn from the study and would be referred to NTEP to continue appropriate ATT.
Screening assessments	**Clinical evaluation** 1. Demographic details and a detailed clinical history including history of previous treatment for TB 2. Details of present complaints and past medical history 3. Menstrual history for female participants attained menarche. **Laboratory evaluation** 1. Potential participants will undergo the following: chest radiograph (CXR), and respiratory samples or alternate samples (gastric aspirate, expectorated or induced sputum, NPA or stool) for CBNAAT and culture. All CBNAAT positive samples will be

	sent for culture and will undergo LPA or phenotypic DST for moxifloxacin resistance screening. 2. Paediatric Electrocardiograph for 4 month regimen arm 3. Urine Gravindex test for female patients of child bearing age to rule out pregnancy 4. Haemogram consisting of total and differential white cell counts, red blood cell count, haemoglobin estimation and platelet count. 5. Serum biochemical tests for estimating urea, creatinine, bilirubin, alanine and aspartate transaminase, and alkaline phosphatase. 6. ELISA test for HIV antibodies, if not done earlier within the past 3 months.
Follow-up	**Follow-up during treatment** During the treatment phase the patients will be followed every month **Follow-up post- treatment** During post-treatment, the patients will be followed up every month until 6 months post-treatment, thereafter every 3 months until 18 months.
Study duration	Recruitment, training of staff: 1 month Duration of enrolment: 6 months Duration of treatment: 4 or 6 months Follow-up period : 24 months from treatment completion Data analysis and report generation : 2 month Total study duration: 4 to 4.2 years



Appendix:

Definition of outcome measures

1. **Treatment failed**

   A patient whose treatment regimen needed to be terminated or permanently changed to a new regimen or treatment strategy

2. **Cured**

   A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment, who completed treatment as recommended, without evidence of MTB and no evidence of failure

3. **Treatment completion**

   Participants who have successfully completed either the 4 month regimen or 6 month regimen and whose outcome does not meet the definition for cure or treatment failure. These participants who at the end of the follow-up period are clinically without symptoms/signs of ongoing active TB and are unable to produce a sputum specimen

4. **Status at 12 months (primary outcome) and 18 months (secondary outcome) post-treatment**

   Each participant will be classified into one of the following 3 outcome categories of Favourable Outcome, Unfavourable Outcome or Not Assessable (loss to follow up)

   Favourable Outcome (treatment success) meeting any one of the following and not classified as having an unfavourable outcome:

   • Participants who at the end of the follow-up period (12 months and 18 months after treatment completion) are clinically without symptoms/signs of ongoing active TB and produce a sputum / gastric lavage specimen that is without evidence of M. tuberculosis (Cured)

   • Participants who at the end of the follow-up period are clinically without symptoms/signs of ongoing active TB and are unable to produce a sputum specimen (treatment completed)

   Unfavourable Outcome (absence of cure) meeting any one or more of the following:

   • A participant whose treatment regimen needed to be terminated or permanently changed to a new regimen or treatment strategy.

   • A participant after treatment completion (either 4 months or 6 months), has sputum that is positive for M. tuberculosis (culture positive).

   • Participants who had a positive culture for M. tuberculosis during treatment.

   • Absence of clinical cure:
     - Participants who at the end of treatment period (4 months or 6 months) continue to have symptoms/signs of ongoing active TB with or without microbiological confirmation
     - Participants receiving any extension of treatment beyond that permitted by the protocol

   • Participants who die from any cause before starting treatment or during the course of treatment

   • Participants re-infected with a new strain of *M. tuberculosis*, demonstrated to be different from that identified at study entry through genotyping methods

Not assessable - Loss to follow up (meeting any one or more of the following and not already classified as having an unsuccessful or successful outcome)
•Participants failing to complete treatment and not assessable at the end of the follow-up period.
•Participants who completed assigned treatment but do not complete follow-up
•Participants who die during the follow-up phase (>/= 15 days after completion of study treatment)

Reasons for the change include:
• no clinical response and/or microbiological confirmation with newer strain during treatment ;
• Adverse drug reactions; or
• evidence of additional drug resistance to medicines in the regimen.

Serial cultures (where applicable), radiological clearance and weight gain will be taken into consideration while assessing outcomes and management of the patient.

Table: Schedule of visit

Visit	V0	V1	V2[#]	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14	V15	V16
4 month	**BL**	**T1**	**T2**	**T3**	**T4**	**PT1**	**PT2**	**PT3**	**PT4**	**PT5**	**PT6**	**PT9**	**PT12**	**PT15**	**PT18**	**PT21**	**PT24[$]**
Informed Consent[@]	√																
Clinical Evaluation	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
CBNAAT	√																
Sputum smear and MGIT	√		√		√								√				√
Urine Pregnancy Test[£]	√																
ECG	√	√	√	√	√												
LFT (1ml)*	√																
RFT (1ml)*	√																
Haematology (2ml)*	√																
Chest X-Ray	√		√		√								√				√
USS abdomen	√																
ELISA for HIV*	√																
Adverse drug reaction monitoring		√	√	√	√												
Acceptability and palatability**		√	√	√	√												

BL baseline, T treatment, PT post treatment *[@]Assent required where applicable; [#]Interim review at end of intensive phase*At baseline there after based on requirement; [£]where applicable*

Visit	V0	V1	V2[#]	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14	V15	V16	V17	V18
6 month	**BL**	**T1**	**T2**	**T3**	**T4**	**T5**	**T6**	**PT1**	**PT2**	**PT3**	**PT4**	**PT5**	**PT6**	**PT9**	**PT12**	**PT15**	**PT18**	**PT21**	**PT24[$]**
Informed Consent[@]	√																		
Clinical Evaluation	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
CBNAAT	√																		
Sputum smear and MGIT	√		√				√								√				√
Urine Pregnancy Test[£]	√																		
LFT (1ml)*	√																		
RFT (1ml)*	√																		
Haematology (2ml)*	√																		
Chest X-Ray	√		√				√								√				√
USS Abdomen	√																		
ELISA for HIV*	√																		
Adverse drug reaction monitoring		√	√	√	√	√	√												
Acceptability and palatability**		√	√	√	√	√	√												

BL baseline, T treatment, PT post treatment [@]*Assent required where applicable;* [#]*Interim review at end of intensive phase**At baseline there after based on requirement;* [£]*where applicable*