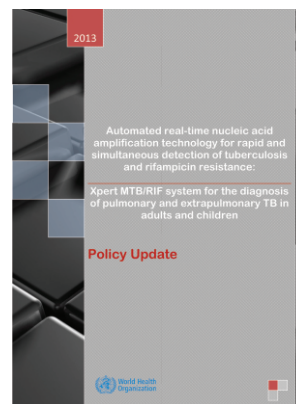




Accelerating access to quality TB diagnosis for pediatric cases in 9 major cities in India

Accurate diagnosis of TB remains an impediment in the management of pediatric TB cases. The diagnosis is complicated because children are unable to expectorate sputum and TB can mimic many other common childhood diseases, including pneumonia, generalized bacterial and viral infections, malnutrition, and respiratory opportunistic infections associated with HIV. Under optimal circumstances, the sensitivity of smear microscopy for the diagnosis of childhood TB remains low. In the absence of bacteriological confirmation, the diagnosis of childhood TB in countries where TB is not endemic is based on a triad of close contact with an infectious patient, a positive tuberculin skin test (TST) result, and abnormalities on a chest radiograph. This criteria, however, has limited application in countries where TB is endemic as most individuals acquire infection and become TST positive during childhood and adolescence. Although growth of *M.tuberculosis* on Lowenstein-Jensen medium is considered to be the gold standard and liquid culture offers the possibility of more sensitive diagnosis of active TB and drug susceptibility, the turnaround time for results on culture tests remains high. These limitation pose challenges in establishing accurate diagnosis of TB in children and add to the potential for both under and over-diagnosis.

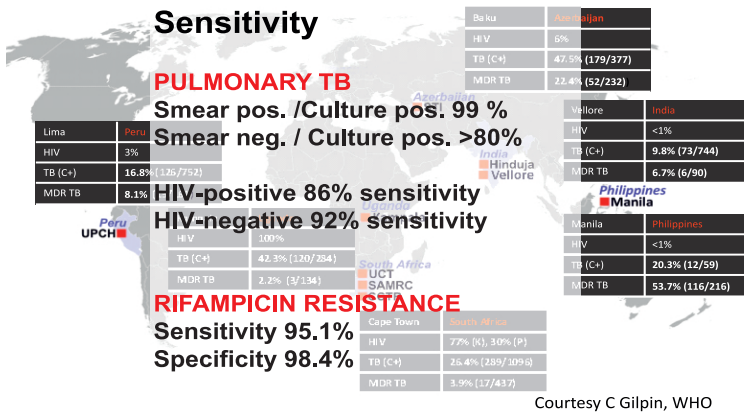
The WHO endorsed, Xpert MTB/RIF® (Cepheid, Sunnyvale, CA, USA), is a cartridge-based fully automated nucleic acid amplification test (CBNAAT) for the diagnosis of TB and rifampicin resistant -TB, suitable for use in disease-endemic countries.



It extracts DNA, concentrates, amplifies, and identifies targeted nucleic acid sequences in the TB genome. Xpert MTB/RIF, is a highly sensitive and specific tool with a quick turn-around time, offers an easy and promising solution in addressing the challenges in the diagnosis of pediatric TB. Recently in the global guidance document released by WHO, it has been recommended that Xpert MTB/RIF may be used rather than conventional microscopy and culture **as the initial diagnostic test in all children presumed to have TB.**

Multi-centre FIND Demonstration Studies

9 district, sub-district laboratories and microscopy centers in 6 countries

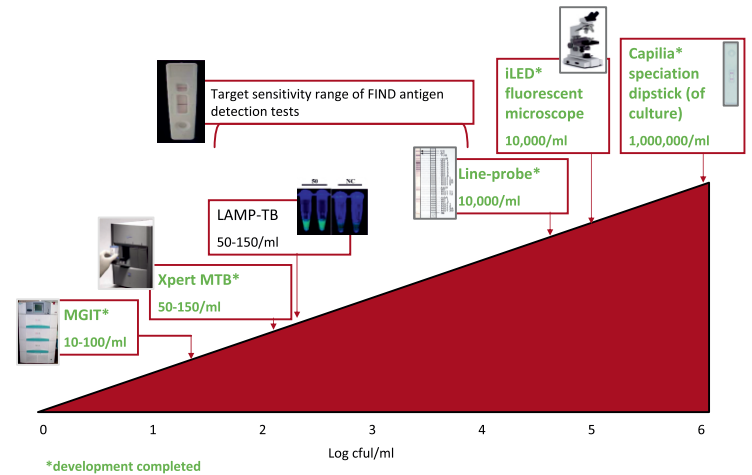


Specimen type	Category (No. of studies, No. of samples)	Pooled sensitivity Median (pooled 95% credible interval)	Pooled specificity Median (pooled 95% credible interval)
Lymph node tissue and aspirates	Xpert MTB/RIF against Reference standard 'Culture' (14 studies, 849 samples)	84.9% (72, 92)	92.5% (80, 97)
	Xpert MTB/RIF against "Composite Reference standard" (5 studies, one unpublished)	83.7% (74, 90)	99.2% (88, 100)
Cerebrospinal fluid	Xpert MTB/RIF against Reference standard 'Culture' (16 studies, 709 samples)	79.5% (62, 90)	98.6% (96, 100)
	Xpert MTB/RIF against "Composite Reference standard" (6 studies, 512 samples)	55.5% (51, 81)	98.8% (95, 100)
Pleural fluid	Xpert MTB/RIF against Reference standard 'Culture' (17 studies, 1385 samples)	43.7% (25, 65)	98.1% (95, 99)
	Xpert MTB/RIF against "Composite Reference standard" (7 studies, 698 samples)	17% (8, 34)	99.9% (94, 100)
Gastric lavage and aspirations	Xpert MTB/RIF against Reference standard 'Culture' (12 studies, 1258 samples)	83.8% (66, 93)	98.1% (92, 100)
	Xpert MTB/RIF against Reference standard 'Culture' (12 studies, 1258 samples)	81.2% (68, 90)	98.1% (87, 100)
Other tissue	Xpert MTB/RIF against Reference standard 'Culture'	81.2% (68, 90)	98.1% (87, 100)

This pediatric TB project represents concerted efforts of RNTCP, FIND, USAID, CDC and NIRT putting in place within a short period, a possible solution to the diagnostic gap. FIND in consultation with RNTCP is implementing this project in Delhi, Hyderabad, Chennai and Kolkata, Nagpur, Surat, Vizag, Agra, Lucknow since April, 2014 with the funding support from USAID and CDC- CoAg.



Sensitivity (cfu/ml) of pulmonary TB tests in portfolio



Under this initiative, FIND has setup high throughput molecular labs at all four sites, catering exclusively to the TB diagnostic needs of pediatric population. These labs provide accurate evidence based same day diagnosis in line with internationally accepted standards of TB care with no cost to patient or provider both in private and public sector. This diagnostic option has been introduced at the existing RNTCP labs for the processing of pediatric specimen types such as sputum, gastric lavage, BAL, induced sputum, lymph node aspirates, etc. for use in Xpert MTB/RIF. Such an effort comes as a big financial relief to poor patients and obviates the necessity to visit private labs and related huge costs.

Any pediatrician both in public and private sector in these 9 cities can either refer their pediatric suspects to these labs or organize transfer of specimen for free of cost testing. The specimen would be tested on the same day and the results communicated to **referring provider** electronically (e-mail and SMS) and at the same time notified to RNTCP under Nikshay.

Project Update

Overall 49,917 pediatric suspects were tested between April '14 to August '16 under this project. A total 55,107 specimens were tested, of which 31512 (57.2%) were non-respiratory specimens. Overall, Xpert gave 49730(99.6%) valid results. Of the 49,917 presumptive TB cases enrolled, 3704 (7.4%), were bacteriologically confirmed. TB detection rates were three fold higher on Xpert as compared to smear microscopy. Further, a total of 323 rifampicin resistant TB cases were detected. The project has demonstrated the feasibility of extending Xpert testing to non-sputum specimens from children with a very high proportion of interpretable results with more than a threefold increase in TB case detection over smear microscopy and detection of significant numbers of rifampicin resistant TB cases. The project has also shown the utility of offering upfront Xpert testing to pediatric presumptive TB and DR-TB patients under programmatic conditions.

We now seek your support to further expand the project coverage and thereby maximize the benefit.

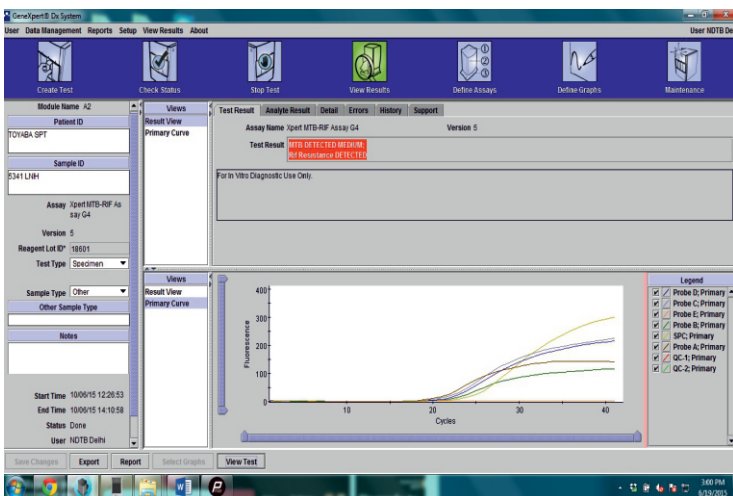
How to engage in the project

1. Refer the paediatric suspect or the suspect specimen to the below mentioned project site
2. Specimen transportation costs are covered under the project at a standard rate
3. Specimen to be accompanied by a duly filled standard lab request form (Annexure 1) with contact number and mail id of referring provider.
4. Test results will be communicated to through SMS/or E-Mail within 12 working hours of specimen receipt
5. If TB is diagnosed the case can opt for free of cost treatment under RNTCP or opt for private treatment

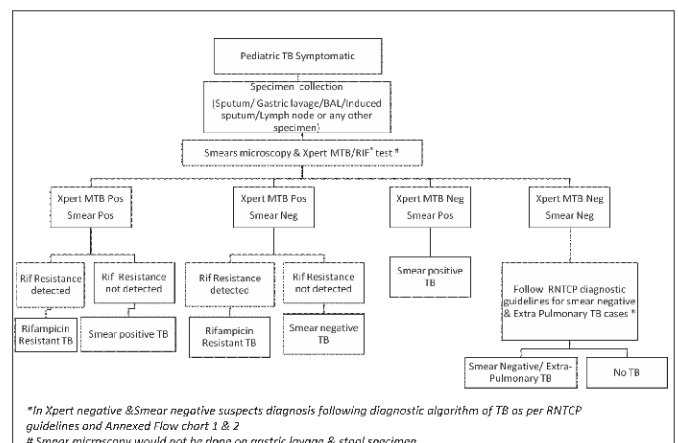
Project site contact details IRL Guwahati, Assam
Guwahati Medical College
Narakasur Hill Top
Guwahati-32, Assam

Contact Details: Mrs. Anita Ghosh: 8876159403
Ms. Lekhika Pathak: 8486648408
Mr. Ridip Ch. Sarma: 8876565599

Example of GeneXpert Test results



Diagnostic Algorithm



RNTCP Request for Culture and Drug Sensitivity Testing Annexure I
(Required for Culture and DST laboratory to conduct testing; please send copy to District TB Officer)

Patient information		Molecular TB/DST result	LAB NO:	Date of Receiving								
Patient Name:		Test: <input type="checkbox"/> Line Probe Assay (LPA) <input type="checkbox"/> CBNAAT Test validity: <input type="checkbox"/> Valid <input type="checkbox"/> Invalid										
Patient Address with landmark		M. Tuberculosis: <input type="checkbox"/> Detected <input type="checkbox"/> NOT detected Rifampicin: <input type="checkbox"/> Resistant <input type="checkbox"/> Sensitive <input type="checkbox"/> Not Available Isoniazid: <input type="checkbox"/> Resistant <input type="checkbox"/> Sensitive <input type="checkbox"/> Not Available										
Patient Mobile No. or other Contact No		Notes										
Age:	Sex: Male <input type="checkbox"/> Female <input type="checkbox"/>	Date tested: _____ Reported by (Name & Signature): _____										
Date of collection		Sample 1: _____ Sample 2: _____										
Type of Specimen		Lj/ Liquid Culture results										
Name referring facility (PHI/DMC/Other):		Date received	Specimen	Specimen No.	Smear result	Neg	Pos	1-19 col	+	++	+++	Contaminated
District			A									
HIV Status : Known : +ve/-ve Unknown			B									
Past History of ATT : Yes/No		Notes:										
Reason for Testing		Result Date:		Reported by (Name & Signature):								
DIAGNOSIS		Lj/ Liquid culture DST Results: (Note: 'S' if susceptible, 'R' if resistant)										
<input type="checkbox"/> Failure <input type="checkbox"/> Re-treatment case S+ at 4 th month <input type="checkbox"/> Contact of known MDR TB case <input type="checkbox"/> S+ at diagnosis, re-treatment case <input type="checkbox"/> Any follow up S+ <input type="checkbox"/> S- at diagnosis, re-treatment case <input type="checkbox"/> HIV TB case <input type="checkbox"/> Presumptive EP-TB <input type="checkbox"/> PLHIV Presumptive TB <input type="checkbox"/> Presumptive Pediatric TB <input type="checkbox"/> Enhanced case finding		Date DST Initiated	Specimen No	S	H	R	E	Z	Km	Ofx	Eto	Other
RNTCP TB Reg No. and Type Cat		Result Date:		Reported by (Name & Signature):								