TB QUEST

A Quest for Innovations towards Eliminating Tuberculosis

By

INDIA HEALTH FUND
A TATA TRUSTS INITIATIVE

An opportunity to propose innovations that potentiate high impact solutions towards accelerating TB elimination in India

In partnership with

TATA TRUSTS

The Global Fund

DOTS
Pura course, Pakka ilaai

Stop TB Partnership

C-CAMP
Centre for Cellular and Molecular Platforms

About India Health Fund

India Health Fund (IHF), incorporated as Confluence for Health Action and Transformation Foundation (under Section 8 of the Companies Act, 2013), is a collaborative initiative of the *Tata Trusts* and *The Global Fund to Fight AIDS, Tuberculosis and Malaria* to leverage the power of collective impact to catalyze India's fight to end TB by 2025 and Malaria by 2030. India Health Fund aims to strengthen the health ecosystem by bridging the gap between lab to last mile population and translating proof of concepts into impact.

Mission

India Health Fund envisages to be an aggregator of resources from private and public sector, global philanthropic foundations and aid agencies and ensure efficient allocation towards scaling up innovative solutions that catalyze the mission to end Tuberculosis by 2025 and Malaria by 2030.

The Journey So Far

IHF has conducted two rounds of Requests for Proposals and currently has a portfolio of 10 projects. IHF currently partners with a mix of innovators, researchers, not for profit organisations, philanthropic organisations and government agencies. It is also exploring funding partnership with private sector players.

I. Background and Mandate of the TB Quest

Tuberculosis (TB) has been in existence for centuries and continues to be among the top 10 causes of death worldwide claiming nearly 1.5 million lives annually. As per the Global TB Report 2018, India is the hub of the TB epidemic bearing 27% of the global disease burden[1]. The National Strategic Plan 2017-2025 envisions elimination of TB in India by 2025, five years ahead of the global target to end TB by 2030[2]. This goal is undoubtedly a stretch, but by no means impossible. However, achieving this goal calls for innovative 'out of the box' interventions which will require identifying and supporting innovations that can accelerate India's fight to end tuberculosis in a non-linear and sustainable way.

During the plan period, targets for TB are i) 80% reduction in TB incidence (i.e. reduction from 211 per lakh to 43 per lakh) ii) 90% reduction in TB mortality (i.e. reduction from 32 per lakh to 3 per lakh) and iii) 0% patient having catastrophic expenditure due to TB. India's current TB decline rate is however very slow and are unlikely to meet the 2030 Sustainable Development Goals (SDGs) or 2035 End TB targets at this rate. Innovative and comprehensively-deployed interventions are required to dramatically accelerate the rate of decline of TB incidence, to more than 10-15% annually set out by the National TB Control programme.

In alignment with the national efforts, India Health Fund (IHF) has been promoting innovations which potentially address the present gaps and challenges in the TB program. It aims to bring together resources to engender transformative change by supporting innovation that will effectively address the rapidly transforming and complex landscape of TB. IHF's Quest for Innovations towards Eliminating TB' (TB Quest) is a crucial step in this direction.

The TB Quest is thus an ambitious nationwide search for innovators working towards addressing the 'leaky cascade' of TB treatment in India. It aims to support and catalyze innovations to solve key challenges in combating TB in India to help eliminate this ancient disease within the next decade.

---

[1] Global TB Report 2018
[2] https://www.who.int/tb/End_TB_brochure.pdf?ua=1

II. Quest for Innovations towards eliminating TB

The Quest is envisioned as a means to fast-track adoption and scale-up of innovative platforms or practices, which have received prior validation. These innovations will have strong potential to strengthen and transform key aspects of the TB care ecosystem in a non-linear and disruptive manner.

The Quest aims to catalyze solutions by

    i)   Enabling funding support to innovative products or processes
    ii)   Connecting resources for accelerated on-ground adoption, and
    iii)   Engaging stakeholders for sustainability of these efforts

The following activities may be considered for support to facilitate their scale-up at TB unit, block, district and state level.

Product Innovation

- ✓ Clinical validation

- ✓ Beta Prototyping

- ✓ Feasibility Studies

- ✓ Pilot Introduction

    (*additional conditions may apply for this type of investigation/intervention)

Process Innovation

- ✓ Process validation

- ✓ Feasibility Studies

- ✓ Process Demonstration

- ✓ Pilot Introduction

Readiness levels of Proposals can be ascertained from the stages given below:

A) Technology Readiness Level (TRL)

- **TRL 9** – Technology has been applied in its final form and is operational.
- **TRL 8** – Technology is proven and developed but not yet operational or applied anywhere.
- **TRL 7** – Actual system prototype is near completion or ready and has been demonstrated in an operational environment or is at pilot level

TB QUEST
A Quest for Innovations towards Eliminating Tuberculosis

- **TRL 6** – Prototype is being tested in simulated operational environment or in a high-fidelity laboratory environment.
- **TRL 5** – Technology has been put together and can be tested in a simulated environment.
- **TRL 4** – Basic technological components have been integrated to establish that they work together.
- **TRL 3** – Proof of Concept stage / Active R&D has been initiated. This includes analytical studies and laboratory studies to physically validate the analytical predictions of separate elements of the technology.
- **TRL 2** – Technology concept / application formulated
- **TRL 1** – There are paper studies to support the technology's basic properties.

(Note: IHF would ideally consider TRL 6 and above)

B) Process Readiness Level (PRL)

- **PRL 6** – PI (Process Innovation) has been applied in its final form and is operational on limited scale in real life setting (non-project). It is ready to be tested on a large scale at a sub-district level or district level or larger
- **PRL 5** – PI has been proven and deployed in experimental setting (in a few project villages or in a healthcare facility setting) but not applied outside the special project setting
- **PRL 4** – PI has been initiated in experimental setting (in a few project villages or in a healthcare facility setting) but not applied outside the special project setting
- **PRL 3** – PI is developed and being tested in formative studies in the community or healthcare facility and it works but not yet ready for field trial or deployment
- **PRL 2** – PI package has been put together but needs to be tested in small scale in limited environment – few villages or ward of a city.
- **PRL 1** – PI components have been identified based on theory or practical experience or literature. And the package seems workable and synergistic. But not yet tested anywhere.

(Note: IHF would ideally consider PRL 4 and above)

TB QUEST
A Quest for Innovations towards Eliminating Tuberculosis

III. Purpose

The purpose of this Quest is to identify and support innovative products and processes that have demonstrated potential in making a significant difference in the areas mentioned below pertaining to TB elimination.

The innovations can address any of the following:

i) *Bring the 'missing million' TB patients within the purview of care including notification, through innovations to find new cases and ensure care continuum*

ii) *Address gaps in the supply chain of Anti TB drugs and consumables in public and private sector through innovative models and technologies*

iii) *Screening and identification for Latent TB Infection (LTBI) among all identified high risk population groups in India*

iv) *To control infections in settings such as health care facilities, crowded habitations, congregate settings including workplaces where transmission is high*

Funding will be provided to support high-potential innovations that can be leveraged by mainstream operations that ensure scale at the district, state or national level. Awards for funding will be announced after review by an expert panel, as per the applicable terms and conditions.

IV. Program Offerings

i) Milestone based funding for supporting Validation, Clinical Investigation, Beta Prototyping, Feasibility Studies and Pilot Introduction

ii) Collective engagement with global stakeholders of TB and access to the global ecosystem working towards TB elimination

iii) Potential opportunities to present innovations to RNTCP with a clear focus on seamless integration with the National Strategic Plan for elimination of TB by 2025

iv) Hands on mentoring by a committee of experts for guidance on policy and programme, deployment design and methodology, navigating regulatory landscape, understanding national market dynamics and others.

v) Opportunity to receive support from India Health Fund's partners in raising subsequent rounds of funding (subject to due diligence)

V. Qualifications of an Applicant

Applicants can include:

- Companies and limited liability partnerships incorporated in India
- Partnership firms
- Registered Indian non-profit or non-governmental organizations
- Government aided Private/Semi-private/deemed institutions and universities
- Autonomous or semi-autonomous institutions
- Consortiums

VI. Selection Criteria

The Quest invites applications that propose an innovative product or process for addressing any of the problem statements.

Eligibility

1. The innovation should have completed the proof of concept stage and validation stage.
2. Validation data should be readily available for justifying support for next stage.
3. It should be ready for scale-up.
4. Applications must be submitted by registered and incorporated entities.

Co-funding could be considered for supplementing parts of a proposal. However, the applicant should make sure to disclose in case the proposal has been submitted to or a part of it is being funded by another donor agency.

The following fall outside the scope of the Quest and will not be supported by IHF

- Basic science research and development
- Proposals focused on service delivery
- Innovations in the ideation / proof of concept stage/ formative studies
- Incomplete or poorly articulated proposals
- Innovations that fall outside the mandate of the TB Quest 2019
- Applications which propose incremental solutions without a clear innovative element in their proposal

The Quest is a voluntary and discretionary measure in addressing the public health problem of Tuberculosis in India. Therefore, India Health Fund reserves the right to the following:

1. Disqualify proposals that do not meet the requirement of areas of thematic focus stated herein.
2. Disqualify proposals that plagiarizes works by other institutions/organisations.
3. Select or reject proposals strictly based on eligibility criteria.
4. Modify and refine proposals before final selection.
5. Modify budgets based on rationale and justification.
6. Not provide or justify reasons or feedback on rejection of proposals.
7. Verify any information provided by application through different sources.
8. Nullify the Quest at any time owing to any reason.

VII. Project Duration

Proposal should have a maximum time duration of upto 2 years (in case of product centric innovations) and this can be extended to a maximum of 3 years (in case of process centric innovations) with adequate rationale and supporting evidence on case to case basis.

VIII. Tentative Project Budget

Promising proposals will be supported by the India Health Fund with grants of Rupees 50 Lakh or above across the entire duration of the project, contingent on milestones achieved at different stages.

IX. Co-Funding for Proposals

IHF is a strong believer in co-funding as a tool to bring about bigger impact and multiplier effect in the TB ecosystem. The proportion of co-funding and support sought from IHF will be assessed and may vary on a case to case basis.

As an important part of the evaluation process, we request all applicants to keep IHF updated on any co-funding and partnership efforts with reference to the application. We value transparency in the funding process. IHF may be able to extend its support in raising funds for projects.

X. Evaluation Criteria

The applications will be evaluated on the following parameters:

- Relevance of Technology or Process Innovation proposed
- Validation so far
- Transformative value

- Simplicity and Feasibility to Scale
- Financial Sustainability
- Alignment to policy goals and/or commercial ecosystem
- Organizational strength
- Partnership

XI. Timeline and Process Flow for Applications

Call for Applications –	8th February 2019
The Applicant will be required to submit an online application following registration on *https://ihf.innovatealpha.org/login* Only the applications submitted online will be accepted for further evaluation. No e-mail or hard copy will be entertained	
Webinars by IHF for prospective applicants	(i) Week of 25th February, 2019* (ii) Week of 18th March, 2019*
*(*Exact date and time along with more information will be available on IHF website by the third week of February 2019)*	
Application Deadline	8th April, 2019
- Window for submission of applications closes - The applicant will be required to submit an online application following registration on the website. - The applications should be submitted well in time without waiting for the last date to avoid any last-minute technical difficulties. Applicants can save drafts of the application before final submission. - Only the applications submitted online will be accepted for further evaluation. No e-mail or hard copy application will be entertained. - Preliminary assessments and compliance checks would be conducted on all completed applications. Incomplete applications may not be processed for further evaluation.	
Preliminary screening for eligibility checks and appropriateness for further evaluation of application	End April, 2019
All applications will be screened for eligibility checks and appropriateness for further evaluation of the application	
Short-list announcement	First Week of May, 2019
Communication to short-listed applicants for an in-person presentation	

TB QUEST
A Quest for Innovations towards Eliminating Tuberculosis

In-person presentation to an Expert Panel	End May/Early June, 2019
• Short-listed applicants will be required to submit further information and supporting documentation as may be relevant by logging into their registered account, prior to attending the in-person presentation to the Expert Panel. • Short-listed applicants to conduct their final presentation and pitch to an expert panel.	
Final announcement of selected applicants	July, 2019
• List of selected innovations will be announced	
Award Letter and start of Project	Timeline is Subject to Due-Diligence
• Due diligence and audit of the awardee will be conducted by the India Health Fund. Satisfactory completion of the same is mandatory for the issuance of final Award letter.	

TB QUEST
A Quest for Innovations towards Eliminating Tuberculosis

XII. Problem Statements

Problem Statement 1

Bring the 'missing million' TB patients within the purview of care including notification, through innovations to find new cases and ensure care continuum.

Background

India bears the highest burden of TB in the world and is among the top contributors of the diagnostic gap between the estimated and detected TB patients. According to the recent WHO Global TB report 2018, while 1.9 million TB patients were reported, the actual disease burden is estimated to be 2.7 million implying that the treatment status and outcome of almost a million TB cases remains unknown[3]. The situation is grimmer for patients with MDR-TB where an abysmal 22% of the overall estimated number of cases are reported.

The problem of the 'missing million' can pose a serious challenge in achieving the global and national End TB targets. A majority of these missing cases seek treatment in the private sector which is largely fragmented, lacks notification and adequate patient follow up mechanisms. The missing TB patients often go untreated or treated inadequately. Most of them maybe lost in between various private and public sector healthcare providers. This not only impacts the health and wellbeing of individuals but also contributes to the spread of TB amongst the patients' close contacts. Every untreated patient can potentially infect up to 10-15 new people in their lifetime[4]. Identifying and bringing these missing patients into the national programme's fold is thus critical in ensuring that all patients are supported and cured in a timely manner and further infection transmission is prevented.

Two approaches in TB case finding have been globally recommended to intensify the search for the 'missing million'- i) Active case finding is a community-based approach among high risk groups using tests, examinations or procedures that can be rapidly applied, whereas ii) Enhanced case finding is geared toward ensuring identification and detection of presumptive TB patients among those who are already seeking healthcare for any other disease[5]. Evidence, both global and in the Indian context, indicates an urgent need for innovations in these approaches to enhance the national TB programme's capacity to bring the missing million within its' fold[6,7].

---

[3] Global tuberculosis report 2018. Geneva: World Health Organization; 2018 Retrieved from
http://www.who.int/tb/publications/global_report/en/

[4] Tuberculosis factsheet. World Health Organization; 2018. Retrieved from http://www.who.int/news-room/fact-sheets/detail/tuberculosis

[5] Florian Marx and Grant Theron, Intensifying tuberculosis case finding – opportunities, challenges and open questions, SACEMA quarterly, March 15, 2018. Retrieved from
http://sacemaquarterly.com/tuberculosis/intensifying-tuberculosis-case-finding-opportunities-challenges-and-open-questions.html

[6] ibid

Intensifying TB case finding is among the top priorities of India's National Strategic Plan (NSP) for TB elimination over the next 5 years[8]. The NSP has listed out vulnerable population groups among urban, rural and tribal areas. In this context, the national TB programme aims to achieve 100% coverage of active case finding among these population groups by the year 2020.

Scope of Innovation

Proposed innovations could be directed towards enhancing the efficiency of TB case finding. The technology or process innovations may address one or more of the following challenges:

1. **Enhancing and/or complementing the existing capacities of the program by increasing the sensitivity, specificity and rapidity of TB detection tests (including MDR TB) in an institutional and/or community setting, with special focus on paediatric and extra-pulmonary TB patients**
   - Lack of reliable and sensitive point-of-care testing for TB leads to false negatives (missed cases), delays in detection and loss to follow-ups. Testing systems with sensitivity and specificity which are 15%-20% better than existing platforms will play a transformative role in existing case finding strategies.
   - Lack of uniformity in diagnostic test protocols in the private sector.
   - The sensitivity, specificity and efficiency of present diagnostic technologies may not cater to detection in paediatric patients or among patients unable to provide adequate sample for testing. This is also a challenge in patients with extra pulmonary tuberculosis where the sample is not only difficult to obtain but can be extracted in very limited quantity at any point of time. In such cases, platforms enabling broad/alternate sample-based testing are urgently required.
   - The processing and interpretation of present diagnostic technologies are technician dependent, thus prone to misdiagnosis and misinterpretation leading to false negatives slipping out of the system. Given the lack of trained staff particularly in the rural settings, technological innovations that help automate/ validate the diagnostic test findings can help address this challenge.
   - Transfer and storage of sputum samples makes it prone to contamination and requires un-interrupted refrigeration to maintain integrity of the samples which is challenging and cost intensive in ACF activities particularly in remote areas[9].

---

[7] An Action Framework for Higher and Earlier TB Case Detection, Background document for DOTS Expansion Working Group Meeting, STOP TB partnership, Geneva, 13-14 October 2009. Retrieved from http://www.stoptb.org/assets/documents/global/awards/tbreach/Achieving%20higher%20case%20detection.pdf

[8] National Strategic Plan for TB elimination 2017-25. Retrieved from https://tbcindia.gov.in/

[9] Y. Pang, J. Du, Z.Y. Zhang, X.C. Ou, Q. Li, H.Xia, *et al.* **The feasibility of sputum transportation system in China: effect of sputum storage on the mycobacterial detection**, Biomed Environ Sci, 27 (2014), pp. 982-986

- MDR-TB case identification at the healthcare centre can take weeks under the present mechanism. This may contribute to the 'leaky cascade' of TB care right at the case finding stage.

2. **Rapid and manifold increase in case finding and notification through technological & process innovations for detecting presumptive TB cases:**
   - Specific population sub-groups[10] in urban, rural and tribal areas remain under served by existing ACF strategies due to their unique set of challenges. Identification of sub-groups within these high-risk populations which should be screened for active tuberculosis can help prioritize and allocate limited resources for case finding initiatives. This includes screening of people with clinical manifestations (chest symptomatic), prone to occupational hazards for TB (e.g. silicosis) and contact tracing (domestic and community-level). Patients with extra pulmonary tuberculosis and those who belong to the pediatric age groups could also be a focus.
   - Presumptive patients are lost to referrals before as well as after being identified and enrolled in the public or private healthcare systems. The high patient volumes in a largely fragmented private sector may be a barrier to an integrated referral system.
   - Robust intra-referral chains are lacking that streamline linkages of presumptive TB patients from the broader health system and other vertical programmes such as NCDs, HIV, Maternal health, ICDS, school health programmes, with the RNTCP. As a result, patients and beneficiaries under these programmes who might be presumptive TB patients as well are completely missed or identified at a later stage.

---

[10] These sub-groups include urban slums, industrial workers, migrant labourers, hard-to-reach villages and tribal regions, malnourished population and people in congregate settings such as prisons and shelters.

TB QUEST
A Quest for Innovations towards Eliminating Tuberculosis

Problem Statement 2

Address gaps in the supply chain of Anti TB drugs and consumables in public and private sector through innovative models and technologies

Background

National TB programmes in many parts of the world struggle with drug shortages and stock-outs which lead to delays in treatment initiation and lapses. A supply chain audit by the Global Fund to Fight AIDS, Tuberculosis and Malaria of country-level supply chains found lapses in intra-country coordination among multiple stakeholders, inadequate oversight, a lack of forecasting and reliable data regarding stocks and patient demand among other problems. The Fund conducted this review in fifteen countries across Asia and Africa, including India. The report notes that along with 'tactical' improvements in supply chains and allied areas, improving drug supply chains will entail systemic improvements[11]. The report noted that weak supply chains were much more likely to cause lapses in compliance and adherence, a critical problem that cannot be ignored in the TB treatment regimen.. India's National Strategic Plan for TB elimination 2017-25 has acknowledged ensuring streamlined and uninterrupted supply of quality Anti TB drugs as a core priority area.

Presently, the Revised National Tuberculosis Control Programme (RNTCP) routes its procurement of first line and second line drugs through two channels. World Bank supported procurement is done through an agency selected by the MoHFW while procurement under the Global Fund to Fight AIDS, Tuberculosis and Malaria is done through the Global Drug Facility of the Stop TB partnership[12]. At the central level, the procurement, supply chain and logistics is managed by the Central TB division with support from a supply chain management and logistics agency[13].

Over the years the RNTCP has made considerable progress towards streamlining the country's complex TB drug supply chain, including the recently launched Nikshay Aushadhi portal. However, continued efforts are needed to rationalize processes including drug forecasting and procurement, implement effective logistics management information systems and building human resource capacities at various levels to effectively plan and execute the supply chain.

The NSP 2017-25 document and Joint TB Monitoring Mission (2015) report also highlight some operational challenges such as inadequate storage infrastructure at state and district levels; lack of uniformity in packing and distribution of second line drugs and lack of an efficient and robust ICT platform for managing and streamlining drug supply chain.

---

[11] The Global Fund to Fight AIDS, Tuberculosis and Malaria's In-country supply chain processes:
https://www.theglobalfund.org/media/6363/oig_gf-oig-17-008_report_en.pdf?u=636727911240000000
[12] Frequently Asked Questions (FAQs) on Procurement & Supply Chain Management under RNTCP:
https://tbcindia.gov.in/showfile.php?lid=3107
[13] Standard Operating Procedures manual for State Drug Stores, Page 1:
https://tbcindia.gov.in/showfile.php?lid=3153

Furthermore, experts have outlined the challenges in the national TB supply chain[14] such as long lead times due to inaccurate forecasts and delays in procurements; weak distribution infrastructure and transport mechanism beyond the state and district levels and lack of capacity for inventory management or consumption tracking.

Scope of Innovation

To plug some of these existing gaps in the system innovations can address;

1. **An efficient demand forecasting mechanism for the national TB programme**
   - It is essential for the TB programme to take stock of their need and their potential demand from the manufacturers. Lack of quality information/data about the currently enrolled patients undergoing treatment with RNTCP and actual drug utilization trends is a key barrier to this exercise.
   - Data on patient volumes across TB variants and resistance strains is lacking which makes it difficult to accurately predict drug procurement requirements.
   - Second Line Drugs for MDR-TB have a relatively shorter shelf life of 24 months. Procurement and distribution delays lead to a loss of more than 6 months of their effective shelf-life.

2. **Tracking of drug supply chain, especially in the private sector**
   - The drug flow from manufacturer to the end consumer i.e. the patient currently follows multiple and intersecting pathways. This is especially a challenge in the private sector distribution network. This makes it difficult for the programme officials and policymakers to identify the specific points where intervention is needed to streamline the supply chain.
   - Making fixed dose combination drugs accessible from the public distribution network to patients being treated in the private sector through reliable private sector drug distribution networks (eg corporate pharmacies, private chemists) is another challenge.

3. **Logistics management information systems with special focus on private sector**
   - There is a lack of an effective and seamless ICT platform for reporting and tracking real time information on drug stocks, expiry dates and potential stock-outs. Such a system can also help rationalize the drug distribution to minimize the need and resources required for storage. Innovations in the logistics management system through technology may overcome this challenge.

4. **Last mile delivery of drugs in hard to reach areas**
   - As the JMM report noted, transport of drugs in remote and hard-to-reach areas is inefficient. Innovations in drug logistics supply are needed to overcome this challenge.

---

[14] https://www.nap.edu/read/13243/chapter/9#110

TB QUEST
A Quest for Innovations towards Eliminating Tuberculosis

5. **Integration of variety of drug packaging into the government's storage and transportation infrastructure.**
   - Certain forms of TB require different dosage requirements, which become difficult to standardize in the presence of ever-changing packaging formats by the manufacturer.
   - New bio-safe packaging/layering or storage options that can increase the shelf life of SLDs and prevent leaks and spills
   - Indicators depicting transport, storage and maintenance conditions (e.g. temperature, humidity etc.) to estimate efficacy of drug from distribution centres to patient site.

Problem Statement 3

Screening and identification of Latent TB Infection (LTBI) among all identified high risk population groups in India*

Background

Latent TB Infection (LTBI) is a condition where people are infected with the TB bacilli but do not have any of the symptoms associated with TB. Approximately 40%[15] of the Indian population possesses LTBI ranging from 9% to 80%[16] in various population groups. The lifetime risk of LTBI developing into active TB is 5- 10% however pre-disposing conditions such as suppressed immunity in cases of HIV, diabetes, malnutrition or pediatric patients, multiply the risk of patient with LTBI developing active or full-blown TB. Identifying LTBI and providing prophylactic treatment to these patients is an effective TB control strategy since it reduces the risk of progression to active disease.

WHO recommends that national programmes contextualize LTBI protocols according to disease burden and availability of resources. However, LTBI screening and prophylaxis is strongly recommended for people living with HIV and child contacts of all TB patients[17]. Till date, LTBI management is a strategy employed largely in the developed world where majority of TB burden is due to reactivation of latent TB. Given the pressing need to identify, treat and monitor the huge burden of active TB, preventive treatment for TB has remained a low priority strategy in most high burden countries including India[18].

In line with the latest WHO recommendations and recent evidence[19], India aims to prioritise screening for LTBI among select high risk groups, as a part of the intensified national strategic plan for TB elimination 2017-2025. These high-risk groups include: People living with HIV, children in contact with Pulmonary TB patients, patients with silicosis, clinically indicated high risk patients for e.g. patients on immunosuppressants and high-risk adult contacts of pulmonary TB patients. The RNTCP aims to rapidly expand coverage of preventive therapy for patients with LTBI from 10% in 2015 to 95% by 2025 among the specified risk groups. Experts have called for an evidence-based policy for LTBI management relevant to the Indian context[20].

---

[15] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4429378/

[16] http://medind.nic.in/ibr/t12/i1/ibrt12i1p1.pdf

[17] Latent TB Infection : Updated and consolidated guidelines for programmatic management, WHO 2018 https://www.who.int/tb/publications/2018/latent-tuberculosis-infection/en/

[18] Moonan PK, Nair SA, Agarwal R, *et al* Tuberculosis preventive treatment: the next chapter of tuberculosis elimination in India *BMJ Global Health* 2018;**3:**e001135. https://gh.bmj.com/content/3/5/e001135

[19] Houben R, Menzies NA, Sumner T, *et al*, Feasibility of achieving the 2025 WHO global tuberculosis targets in South Africa, China, and India: a combined analysis of 11 mathematical models. Lancet Glob Health 2016;**4**: e806–e815.doi:10.1016/S2214-109X (16)30199-1

[20] https://www.sciencedirect.com/science/article/pii/S0019570718303159?via%3Dihub

TB QUEST
A Quest for Innovations towards Eliminating Tuberculosis

Scope of Innovation

Proposed innovations could be directed towards addressing the following challenges:

1. Identification of simple, sensitive and cost-effective diagnostic tools for identifying latent TB infections
2. Identification of the sub-set of patients within the high-risk populations which are more likely to be latently infected with TB bacterium
3. Identification of the subset of LTBI positive patients which are more likely to progress to active tuberculosis and need to be enrolled for prophylactic treatment as per RNTCP guidelines.

To discuss further,

- Measures to prevent spread of airborne infection in health facilities are lacking. In this scenario, screening among healthcare providers is crucial and needs to be explored since studies suggest that 43% of the TB care providers in India have LTBI[21].
- There are no conclusive tests to determine LTBI. The diagnosis is based on testing for prior exposure to the infection and absence of active TB symptoms.
    - Mantoux Tuberculin Skin Test (TST) and interferon-gamma release assays (IGRA) such as the QuantiFERON-TB Gold are the two tests that help identify prior exposure to Mtb and thus utilized to detect LTBI. Newer tests are also available including C-Tb test to detect LTBI.
    - If either of tests show positive results in a patient, chest X-rays are needed to rule out active disease before determining the treatment.
    - Given the complex triage approach, mechanisms that can support healthcare providers to accurately judge the presence or absence of LTBI based on these factors can help streamline treatment initiation for LTBI.
- Furthermore, both the tests are unable to accurately differentiate active TB from latent TB. Specificity of TST is also low among BCG vaccinated individuals resulting in false positives. While the IGRA tests have a higher specificity (BCG vaccination status does not impact test results), they are more expensive, complex with limited availability. Hence TST continues to be the first choice for testing LTBI in resource poor settings.
- In immunocompromised patients, sensitivity of these tests and ability to predict progression to active disease is low[22].
- More specific, sensitive, reliable and cost-effective tests that utilize other forms of sample such as blood or urine thus need to be demonstrated in the Indian context.

---

[21] Nasreen S, Shiloh M, Malvankar-Mehta MS (2016) Prevalence of Latent Tuberculosis among Health Care Workers in High Burden Countries: A Systematic Review and Meta-Analysis. PLoS ONE 11(10): e0164034. https://doi.org/10.1371/journal.pone.0164034

[22] Pai M, Rodrigues C. Management of latent tuberculosis infection: An evidence-based approach. Lung India [serial online] 2015 [cited 2018 Nov 27];32:205-7. Available from: http://www.lungindia.com/text.asp?2015/32/3/205/156210

TB QUEST
A Quest for Innovations towards Eliminating Tuberculosis

- In India feasibility, impact and cost-effectiveness of implementing LTBI screening protocols among identified high-risk groups at scale is yet to be conclusively determined. There is a need to demonstrate an effective, targeted and contextually relevant LTBI screening protocol for India to help establish future pathways and guidelines catering to those living with LTBI.
- Effective testing protocols for latent TB need to also address the vast epidemiological and programmatic differences that exist in the TB scenario in India[23].

[Note: Deliberations are presently underway to strengthen the pathways for management of LTBI under the national TB program. LTBI cases identified by projects supported by IHF through this quest can potentially be linked to RNTCP for initiating management.]

---

[23] Moonan PK, Nair SA, Agarwal R*, et al* Tuberculosis preventive treatment: the next chapter of tuberculosis elimination in India *BMJ Global Health* 2018;**3:**e001135. https://gh.bmj.com/content/3/5/e001135

TB QUEST
A Quest for Innovations towards Eliminating Tuberculosis

Problem Statement 4

To control infections in settings such as health care facilities, crowded habitations, congregate settings where transmission is high.

Background

Globally, transmission of tuberculosis by droplet infection is a major concern. Studies show that nearly 43% of India's healthcare workers are latently infected with the tuberculosis bacterium[24]. The prevalence of tuberculosis was found to be lower among medical students, about 6.9%, but went up to 97 per cent among all types of healthcare workers

Infection control is one of the core strategies in stopping TB transmission. It can be applied at various levels including at the source of the infection, by changing the physical environment and protecting the population groups at risk of exposure. RNTCP's airborne infection control guidelines provide protocols to mitigate risk factors across three main control areas [25]:

Administrative- These are to identify persons with respiratory symptoms, separate them into appropriate environment, fast track the movement of patients through the healthcare facility to reduce exposure time to others.

Environmental- This includes ensuring mechanisms for effective ventilation, either through natural or mechanical means.

Personal protective equipment- This is for use by persons in high risk settings or procedures.

Airborne infection control methods range from strengthening infection control strategies at the managerial and administrative level of hospitals, training healthcare workers for infection control, disseminating critical information about TB infection and epidemiology at strategic locations in healthcare facilities and making infrastructural changes to healthcare facilities to facilitate better patient flow, and implementing strategies.

There is ample evidence from the developed countries that altering the physical environment can help reduce spread of TB. A smaller study in Nigeria found evidence of infection reduction when health workers were trained and when stringent environmental, personal, managerial and administrative measures were instituted. The study noted that implementing such systems along with using effective infection control tools was critical[26]. However, replicating the success of infection control in high burden and largely resource poor settings continues to be a challenge. Some settings unique to Indian cities and metropolises such as ill-designed infrastructure projects including Slum Rehabilitation Authority (SRA) housing, congregate settings such as hospitals and other health care facilities, the inevitable contact

---

[24] Latent TB noted in nearly half of India's healthcare workers. https://www.scidev.net/asia-pacific/tb/news/latent-tb-india-health-workers.html

[25] Guidelines on airborne infection control in healthcare and other settings. April 2010 (Provisional)

[26] Building and Strengthening Infection Control Strategies to Prevent Tuberculosis — Nigeria, 2015 https://www.cdc.gov/mmwr/volumes/65/wr/mm6510a3.htm

SS TB QUEST
A Quest for Innovations towards Eliminating Tuberculosis

with crowds in large settings such as train stations and bus terminals, prisons, refugee camps are some of the major infection sites. Technologies and process innovations which can reduce infections in such setting can be particularly meaningful.

Scope of innovations

Innovations can aim at addressing one or more of the following challenges:

1. Conditions that help reduce the bacterial load in the environment in congregate settings, healthcare facilities, means of transport and households.
    a. Facility based protocols or guidelines to improve patient flow, expedite identification and treatment of TB patients and thus prevent spread of infection.
    b. Handheld or handsfree fever/symptom detectors or other detection mechanisms can flag potentially infected patients and quarantine them for further screening.
    c. Replicable and affordable designs for buildings to help reform or renovate into well ventilated and healthier homes and congregate settings like slum rehabilitation authority buildings, slum areas and areas with high population density and footfalls.
    d. Affordable and acceptable personal protective equipment such as particulate respirators and surgical masks which can be easily used by patients and those around them.
    e. Easy to install and low-cost mechanical ventilation devices.

2. Bacteriostatic and bactericidal technologies which significantly reduce infection risks:
    a. Low cost technologies (such as UV germicidal irradiation, microfilms or electrostatic charges) which can disinfect congregate spaces.
    b. Innovations need to address operational challenges in deploying these technologies within the limitations of existing building structures and lack of trained manpower to perform maintenance or repairs.

3. Broad-based health systems innovations which are transformative in nature for reducing infections
    a. Systems, software or programs which can map patients, a dashboard for identifying high density areas, individual case data (linking to Nikshay or other relevant government portals). Such systems can potentially be linked to schemes such as DOTS, PMJAY or Nikshay which can create a database and map of addresses which can help identify high density areas and recommend screening drives or warrant infrastructural changes to government authorities.

XIII. Frequently Asked Questions

1. **What does the Quest support?**

   Quest for Innovations towards Eliminating Tuberculosis – supports innovative post proof of innovations which have reached TRL-6 or beyond for products; or PRL-4 or beyond for processes. Such innovations should be in any one or more domains addressed by the problem statements.

   Products should have crossed proof of concept and reached TRL-5 or beyond (where TRL defines the Technology Readiness Level and TRL 5 describes that the Technology has been put together and can be tested in a simulated environment)

2. **Can an applicant submit more than one application for different innovations?**

   Yes, the applicant can submit multiple applications within the domain framework as mentioned for Q1.

3. **What should be the grant size of the individual project proposal?**

   IHF does not suggest any grant size for any project submitted in the TB Quest. The financial ask should be realistic and in alignment with the proposed work. The decision to approve the grant request; the periodicity and the conditions of the disbursements lies wholly with IHF.

4. **Can an applicant's proposal address more than one problem statement?**

   It is possible that the applicant's proposed innovation addresses aspects which are covered in more than one problem statement. In such case the applicant may mention in the application the specific aspects within the problem statements that the application addresses. However, while applying, ONLY ONE problem statement should be selected which, according to the applicant, most closely aligns to the proposal.

5. **If the proposal fits more than one problem statement, should I make separate submissions of the same proposal?**

   No, you have to submit the proposal only <u>once</u> while selecting the problem statement which most <u>closely aligns</u> to your proposed innovation. However, in the proposal mention the other problem statements that your innovation can potentially address.

6. **How many projects will be selected for support per problem statement?**

IHF does not want to limit the number of applications selected under individual problem statements. Final decision on proposals will be purely assessed on merit.

7. **What is TRL-6?**

TRL-6 refers to the level when your Prototype is being tested in simulated operational environment or in a high-fidelity laboratory environment.

For more information on the different TRLs, please see below:

- **TRL 9** – Technology has been applied in its final form and is operational.
- **TRL 8** – Technology is proven and developed but not yet operational or applied anywhere.
- **TRL 7** – Actual system prototype is near completion or ready and has been demonstrated in an operational environment or is at pilot level
- **TRL 6** – Prototype is being tested in simulated operational environment or in a high-fidelity laboratory environment.
- **TRL 5** – Technology has been put together and can be tested in a simulated environment.
- **TRL 4** – Basic technological components have been integrated to establish that they work together.
- **TRL 3** – Proof of Concept stage / Active R&D has been initiated. This includes analytical studies and laboratory studies to physically validate the analytical predictions of separate elements of the technology.
- **TRL 2** – Technology concept / application formulated
- **TRL 1** – There are paper studies to support the technology's basic properties.

8. **What is PRL-4?**

PRL-4 refers to a process innovation which has been initiated in experimental setting but has not been applied outside the special project setting

- **PRL 6** – PI (process Innovation) has been applied in its final form and is operational on limited scale in real life setting (non-project). It is ready to be tested on a large scale at a sub-district level or district level or larger
- **PRL 5** – PI has been proven and deployed in experimental setting (in a few project villages or in a healthcare facility setting) but not applied outside the special project settings
- **PRL 4** – PI has been initiated in experimental setting (in a few project villages or in a healthcare facility setting) but not applied outside the special project setting
- **PRL 3** – PI is developed and being tested in formative studies in the community or healthcare facility and it works but not yet ready for field trial or deployment

SS TB QUEST
A Quest for Innovations towards Eliminating Tuberculosis

- **PRL 2** – PI package has been put together but needs to be tested in small scale in limited environment – few villages or ward of city
- **PRL 1** – PI components have been identified based on theory or practical experience or literature. And the package seems workable and synergistic. But not yet tested any where.

9. **Can consortiums apply for funding through the Quest?**

Yes, consortium can apply, however, it's important that the roles of the Consortium participants is clearly pre-defined. At least one entity, which proposes to receive the grant money, has to be registered/incorporated organization in India.

10. **Can an international agency be part of the consortium?**

Yes, an international agency can be part of the consortium.

11. **Can an applicant apply simultaneously for multiple funding for the same project?**
The applicant should declare at the time of application and then before receiving the grant if the same application has been submitted for support or is currently receiving support from any other donor. They should also justify why the applicant is seeking multiple avenues of funding for the same project.

12. **For what purposes can the funding provided be utilized?**

The Quest is meant for post proof-of-concept innovations (at or above TRL-6) that need to be scaled. Funding can therefore, be utilized for clinical testing design study and its outcomes, manpower, consumables, equipment, and project related travel. Funding can also be utilized for publication of project findings, additional patent filings and for seeking regulatory approvals strictly associated with the project work. The funding should be solely restricted to work within the focus areas mentioned.

13. **Can I edit my application if I want to make changes to my proposal or my particulars after I've made the submission?**

No, you cannot edit your proposal after you have made the submission.

14. **What does due diligence entail?**

The Due Diligence includes a holistic evaluation of the applicant organisation and the proposal. It will cover aspects, including but not limited to, technical feasibility and rationality, progress of clinical study, financial assessment and refinement of business model. It will also include reflecting on the long term vision, goal and intermediary outcomes envisaged in the proposal, project implementation plan and competence of the applicant.

TB QUEST
A Quest for Innovations towards Eliminating Tuberculosis

Due diligence may require multiple iterations between IHF and its expert panel, external independent auditors who may be hired to assist in the process and applicants. Awards will be announced purely on merit basis and after satisfying the rigorous due diligence process. Mere satisfactory completion of due diligence does not entitle an applicant for funding and support

15. **Will an applicant be eligible to receive funding from India Health Fund upon selection?**

    Yes, an applicant will be eligible for funding upon final selection but the final decision on awarding funding will be taken after due diligence as described for Q 5.

16. **Can an applicant find other funding partners for additional funding?**

    Yes, the selected applicants can find other funding partners. However, IHF must be informed about such efforts if it is for the same project.

17. **Whether funding provided pursuant to the Quest will be in collaboration with other prevalent government initiatives?**

    The Quest will complement government initiatives and not duplicate/overlap with them. Further, India Health Fund is independent from ongoing government initiatives.

18. **How many applicants are expected to be finalised?**

    The number of applicants finalised has not been pre-determined.

19. **Who will undertake the evaluations?**

    The evaluations will be undertaken by a panel of experts in the field relevant to the project, and by the IHF team.

20. **How can an applicant submit queries?**

    Please submit queries via email to contact@indiahealthfund.org

21. **Why didn't a project idea get accepted?**

    If a proposal did not fit the problem statements or the applicant did not satisfactorily comply by the eligibility criteria set out by IHF, or for any other conflicting issues etc. then the application maybe rejected. We encourage applicants to apply in subsequent programs aligning proposals with the focus area stated.

22. **Where can I get more clarity on the quest and what it entails?**

India Health Fund will be organizing two webinars as well to further clarify queries that the potential applicant may have. The dates and time will be made available on IHF website as per the schedule mentioned in the timelines. If you have additional queries then you may send the questions on *contact@indiahealthfund.org* so that the facilitator may take it up during the course of the webinar. Additional options for live chat/posting queries during the webinar will be shared subsequently.

If you are unable to attend the webinars, you may reach out to us on *contact@indiahealthfund.org*. Furthermore, post every webinar we will update the FAQs listed on the website.

23. **Can an organization which is getting registered soon apply?**

Applicant organizations will have to produce relevant supporting documents if they are shortlisted. A shortlisted application will only be processed when all documents that are asked for are submitted. Without these documents, applications will be rejected.

24. **Is it possible to apply in languages other than English?**

The Quest will be accepting applications only in English. However, if applicable, you can submit supporting documents in a vernacular language while giving us a translated copy in English of the same.

25. **Information related to Intellectual Property and Information Access**

IHF works towards saving human lives as its highest priority and this will be the guiding philosophy for promoting solutions towards the achieving the goal. Therefore, IHF encourages applicants to share knowledge, processes and solutions that emerge from the project for benefit of society and accelerate the same in times of crisis.

IHF emphasizes that the project outcomes be published in an open access peer reviewed journal. It is urged that the successful applicant disseminates about development of the solutions and solutions with a wider audience and stakeholders. The ownership of intellectual property will be a discussed post selection between the recipient organisation and IHF.

***