भारतीय आयुर्विज्ञान अनुसंधान परिषद
स्वास्थ्य अनुसंधान विभाग, स्वास्थ्य एवं परिवार
कल्याण मंत्रालय, भारत सरकार

Indian Council of Medical Research
Department of Health Research, Ministry of Health
and Family Welfare, Government of India

Date: 22/09/2022

Expression of Interest (EOI) for "Development of In Vitro Diagnostic (IVD) Kits against drug resistant *Salmonella enterica* Infections"

The Indian Council of Medical Research, New Delhi, invites Expression of Interest (EOI) through web-portal from the experienced R&D companies/Institutions/In-vitro Diagnostic (IVD) kit manufacturers for development of diagnostic kits for diagnosis of drug resistant *Salmonella Typhi* Infections

BACKGROUND

Enteric fever, commonly known as typhoid fever, is a significant global public health problem, particularly concentrated in South Asia, with India bearing a high burden of the disease. It is estimated that there are 11-21 million cases of enteric fever worldwide each year, resulting in 120,000-160,000 deaths. Due to lack of proper diagnosis & heterogeneity of disease, the exact burden of disease is unclear but extrapolation of regional data estimates 586 cases per 100,000 person-years typhoid/paratyphoid incidence in India.

Antibiotics have been effective in treating enteric fever; however, the escalating global antimicrobial resistance has complicated the situation. *Salmonella enterica* serovar Typhi (*S. Typhi*), the bacterium responsible for typhoid fever, has developed resistance to multiple antibiotics, including three first-line agents. Multidrug-resistant strains are prevalent in parts of Asia and Africa. In Sindh, Pakistan, extensively drug-resistant *S. Typhi* has emerged, which is resistant to fluoroquinolones and third-generation cephalosporins, leaving only a few antibiotic options, such as azithromycin and costly intravenous carbapenem drugs.

The disease can be effectively treated with antibiotics, however escalating global antimicrobial resistance, including the emergence and spread of multidrug resistant variants of *Salmonella enterica* serovar Typhi (*S. Typhi*) has worsened the situation. To prevent the further spread of resistant *S. Typhi* it is imperative to identify antibiotic susceptibility testing for individual patients before commencing antibiotic therapy.

A related variant, *Salmonella enterica* serovar Paratyphi (*S. Paratyphi*), also causes enteric fever and affects approximately 3.4 million people annually, resulting in 19.1 thousand deaths in

comparison to 10.9 million cases and 116.8 thousand deaths by *S. Typhi*. While the morbidity and mortality of *S. Typhi* make it a greater public health concern, the increasing prevalence of *S. Paratyphi* in certain regions necessitates a next-generation diagnostic test capable of detecting both *S. Typhi* and *S. Paratyphi*. Moreover, clinical syndromes caused by the two serovars are indistinguishable, making it crucial to differentiate between them before starting antibiotic therapy due to their different antibiotic susceptibility profiles.

SCOPE

Rapid diagnostics and accurate diagnostics are crucial for early detection, appropriate treatment, and effective disease management. Improved disease diagnostics will support the government in guiding interventions program efforts to prevent the diseases.

The existing typhoid diagnostic tests, such as the Widal test, TUBEX, Typhidot, and Test-It (KIT), have shown sub-optimal sensitivity and specificity, leading to challenges in accurately identifying typhoid cases at the point of care (POC). Consequently, healthcare professionals often resort to empiric treatment with antibiotics, which can contribute to the overuse of antibiotics and the emergence of antibiotic-resistant strains of *S. Typhi* and other bacteria.

The most widely used RDT is the Widal test which has low performance (sensitivity range, 57%–74%; specificity range, 43%–83%) as reported in many studies. The performance of other typhoid RDTs, like TUBEX (average sensitivity of 78% and a specificity of 87%), Typhidot (average sensitivity of 84% and a specificity of 79%), and Test-It (KIT) (average sensitivity of 69% and a specificity of 90%) is also sub-optimal. To have a meaningful impact on the overuse of antibiotics that has contributed to the emergence of resistance in *S.* Typhi and other bacteria, an improved typhoid POC test needs to be used. To combat these issues, there is an urgent need for indigenously developed, improved typhoid POC tests that offer higher sensitivity and specificity. Such tests would enable healthcare professionals to promptly and accurately diagnose typhoid, leading to more appropriate and targeted treatment, which in turn, could result in better patient outcomes and reduced antibiotic misuse.

The Indian Council of Medical Research (ICMR) is inviting Expression of Interest (EOI) from research institutes and companies possessing a track record and demonstrated expertise in developing products within the specified domain. Submissions that present validated proof of concept or inventive ideas with evident potential for real-world application are sought through this EOI platform. Prospective candidates meeting the eligibility criteria are strongly urged to submit their proposals. Priority consideration will be given to diagnostic products that are at an advanced stage of development. ICMR is prepared to extend a grant-in-aid over a duration of 18-24 months, with the overarching aim of achieving a tangible product by the conclusion of this time frame.

ICMR invites EOIs proposals that address the below-mentioned research question:

Priority Research Question
Develop novel multiplex rapid, (near) point of care affordable diagnostic tests for detection of *Salmonella enterica* serovar Typhi & Paratyphi and detection of antimicrobial susceptibility for surveillance and clinical purpose.

OBJECTIVE

Development of diagnostic kits for diagnosis of drug resistant *Salmonella enterica* infections detecting following:

- Typhoid fever caused by *Salmonella enterica* serovar Typhi.
- Paratyphoid fever caused by *Salmonella enterica* serovar Paratyphi.
- Differentiation between these two serovars
- Detection of drug susceptibility and resistance
- Resistance gene panel covering gene targets leading to detection of resistance against drugs such as Azithromycin (acrB) and Cefitriaxone (CTX-M, SHV). Mutations resulting in MDR Typhi (TEM, cat, sul & dfrA, gyrA & parC) are to be considered.
- High sensitivity and specificity as cross-reactions with non-typhoidal Salmonella are common

ELIGIBILITY

The proposals can be submitted by:

1. Public, private, NGOs, academia and research institutions, including medical colleges, universities, engineering colleges etc.
2. Proposals with proof of concept or ideas with potential for translation are invited for development.
3. Preference will be given to proposals that emphasize collaborations between academia and industry. These collaborations should include a partner with expertise in diagnosis, like a medical college, and another partner working on creating a kit or assay. The second partner could be from engineering institute, start-up, or the industry with demonstrated previous experience of diagnostic development.

IMPORTANT TERMS & CONDITIONS

1. The applicant should demonstrate well-established expertise and proven proficiencies in the realm of diagnostic development.
2. ICMR will concentrate on proposals that explore innovative diagnostic markers, including gene targets associated with multidrug resistance. These markers should offer both high sensitivity and specificity.
3. ICMR will be providing a grant-in-aid for a period of 18-24months with the expected outcome of a product by the end of tenure. A mid project 9-month progress report will be mandatory to assess deliverables progress

When and how to submit a proposal:

The full-length research (detailed) proposal should be submitted through online mode only on https://forms.gle/hkrGUDpLD9fiweW77 and no proposal in physical/hard copy/email is to be submitted.

Submission link
https://forms.gle/hkrGUDpLD9fiweW77

Review process:

The EOI documents for 'Development of In Vitro Diagnostic (IVD) Kits against drug resistant Salmonella enterica Infections' will be evaluated and shortlisted by the Indian Council of Medical Research (ICMR). The ICMR team will screen the applications for technical accuracy and eligibility. The shortlisted teams will then collaborate to develop a detailed proposal, under the guidance of ICMR Hqrs. The proposal will be evaluated based on factors such as proposed plan, feasibility of implementation of plan, data management capabilities, prior experience of diagnostic development, established relationship with a commercial company. The feasibility and suitability of integration of the proposed methodology in the final proposal to be developed under the guidance of ICMR Hqrs shall also be considered while shortlisting the EOI. The shortlisted teams will be invited to collaborate to develop a detailed proposal under the guidance of ICMR. An independent committee will review the final proposal for consideration for funding. Please note that only shortlisted PIs will be contacted.

Tentative Timeline

Activities	Date
Release of Call	22.09.2023
Last date for submission of EOI	30.10.2023
Shortlisting of EOIs	15.11.2023
Proposal development workshop	2nd week of December 2023
Submission of a full proposal	31.01.2023

In case of any query, you may contact the following official:

Dr. Kamini Walia,
Scientist G
ECD Division, ICMR Headquarters,
V Ramalingaswami Bhawan, Ansari Nagar, New Delhi-110029
Email: *icmr.amrdx@gmail.com*

Points to be kept in mind while submitting the EOI:

1. The EOI must address the specific research question that is mentioned in the call text.
2. Collaborative, multi-centre, interdisciplinary, innovative research initiatives from the applicant will be encouraged.
3. Descriptive studies, systematic reviews and secondary data analysis will not be considered
4. Should focus on outcomes that are translatable.
5. Evaluation of the development of indigenous technologies and solutions relevant to the Indian context may be prioritized
6. Foreign collaboration is not allowed under the call.

Only shortlisted PIs will be contacted

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Format of Expression of Interest (EOI) to be submitted

A. **Name of the Senior Researcher (Principal Investigator):**
B. **Name of the institute:**
C. **Address with email id and phone no. of PI**
D. **Type of Organization:**
   - Government
   - Private
   - Non-Government Organization

E. **A brief description (maximum 500 words) of track record of the applicant research group and institute** (Summarise and justify the composition of the research team, based on the expertise of the individual team members in designing and implementing the project. Also, highlight the skill set and expertise the members shall bring to the research team that shall be constituted by the ICMR Hqrs for the development of final protocol and research project implementation)

F. **List of publications in last 7 years (since 01-01-2017)**
   In prescribed format (Annexure-I) for Principal Investigators (PIs) and Co-Principal Investigators (CoPIs) proposed for study. Publications where s/he was the First/last/ corresponding author, should be included. Highlight impact of each publication e.g. inclusion in policy/protocol/programme or being cited in patents/commercialization of results etc.

G. **List of research projects undertaken in last 5 years (since 01-01-2019)**
   In the prescribed format (Annexure- II)

H. **List of patents, technologies, products commercialized** (Annexure-III)

I. **Collaboration with ICMR or contribution to ICMR activities in last 5 years** (maximum 250 words).

J. **Briefly describe how the proposal will contribute to objectives and activities of ICMR** (maximum 200 words)

K. **Research Team**
   Summarize and justify the composition of the proposed research team, based on the expertise of the individual team members in designing and implementing the project. Also, highlight the skill set and expertise the members shall bring to the research team.

L. **Illustrative Budget outline (additional to the 2-page limit).**

In this EOI, provide an estimated budget outline (no budget justification required at this stage) under the following headings: staff, recurring contingency, data management, travel and equipment.

M. One-page CV of the principal investigator and other key investigators (additional to the 2-page limit).

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

- Academic and professional qualifications
- Current position and affiliation
- Up to five most relevant previous research grants
- Upto five most relevant previous publications

……. ……..

(Signature) (Signature with seal)

Principal Investigator **VC/Dean/Principal/Director/Secretary of the University/College/Institute /NGO**

Date ……

Annexure-I (list of publication since 01-01-2017)

Title of publication in AMA style	Impact factor of journal	Name of policy/programme/ protocol document or patent/commercialization of products where cited.

Annexure-II (list of projects since 01-01-2019)

Short title of the project	Primary objective(in brief)	Type of study (e.g. RCT /Prevalence/Lab-based)	Sample size	Grant amount	Time period

Annexure-III (list of granted patents/commercialized products since 01-01-2017)

Intellectual Property	Application Number	Title/ Technology or Project to which the invention is related	Status (Filed/Granted)
Patent			
Trademark			
IndustrialDesign			