MALARIA QUEST
A quest for innovations towards eliminating malaria

An opportunity to propose innovations that potentiate high impact solutions toward accelerating malaria elimination in India

In partnership with,

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The Global Fund

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ASIA PACIFIC LEADERS MALARIA ALLIANCE

RBM Partnership To End Malaria
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 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 populations and translating proof of concepts into impact.

Mission

India Health Fund envisages to be an aggregator of resources from the 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. Applications from the TB Quest 2019 are currently being assessed. IHF currently partners with a mix of innovators, researchers, not for profit organisations, philanthropic organisations and government agencies. It is also exploring funding partnerships with private sector players who can join hands and create a robust pipeline of products and resources which will help us rapidly advance malaria elimination in India.
I. Background and Mandate of the Malaria Quest

Malaria is one of the most prevalent diseases across the world today having killed nearly 435000 globally in 2017 and affecting nearly 219 million people in the year 2017\(^1\). With the fourth highest burden of malaria in the world and 70\% of the malaria cases in South East Asia, the disease remains a pressing public health challenge for India since ancient times. While 844,558 cases and 194 deaths were reported in India in 2017, the actual burden estimated by the WHO is 9.6 million cases and 16,733 deaths, since data reporting from the private sector is very low in India. Globally the number of cases and deaths have declined substantially over the past decade. In the year 2017 alone, the number of cases in India have dropped by 24\% driven by the steep decline in cases, as much as 80\% in the state of Odisha. While this is encouraging progress toward the goal of ending malaria by 2030, the disease is known for its dramatic resurgence in India during the 1960s, calling for sustained efforts and investments in malaria elimination. Since 2015, the global decline in cases has levelled off and in 2017, most high-burden countries apart from India reported a rise in cases. This is especially concerning since funding trends do not reflect the urgency that these trends signify.

India’s National Vector Borne Disease Control Programme through its National Strategic Plan for Malaria 2017-22 plans to focus on some specific indicators, including ensuring universal coverage of case detection and parasitological diagnosis, strengthening surveillance and case notification and to investigate and classify and respond to cases in all districts, achieve near universal coverage of vector control interventions, provide effective programme management and coordination at all levels to achieve malaria elimination.

To sustain and further accelerate India’s progress towards ending malaria, complex challenges will need to be overcome. Ensuring early detection, correct treatment and preventing further transmission remains the crux of the problem. Hyper-endemic pockets located in forested areas which are difficult to access and conflict-hit, with weak health-care infrastructure and lack of awareness about malaria prevention and management amongst the predominantly tribal populations, have historically hampered malaria control efforts. Tailored solutions to the problems of these regions will be crucial. Wide-spread migration to other regions and states also places the non-endemic areas at risk of outbreaks. For India, strategies such as High Burden, high impact hold good promise since the HBHI strategy aims to tailor the actions needed to tackle malaria in India’s diverse contexts. Managing ‘asymptomatic’ or ‘afebrile’ cases and \(P.\) vivax cases will be crucial as the country progresses toward its malaria elimination goal. Furthermore, given the emerging problem of resistance to anti-malarial drugs as well as insecticides, affordable, safe and effective alternatives are urgently needed. While personal protective measures against malaria exist, these are not universally acceptable or utilised due to various factors.

Aligned with the national efforts, India Health Fund (IHF) aims to promote innovations which potentially address present gaps and challenges as described above. It aims to bring together

resources to engender transformative change by supporting innovations that will effectively address the rapidly transforming and complex challenges posed by malaria. IHF’s Quest for Innovations towards Eliminating Malaria’ (Malaria Quest) is a crucial step in this direction.

The Malaria Quest is thus an ambitious nationwide search for innovators working towards addressing the unconquered frontiers of ending malaria in India. It aims to support and catalyze innovations to solve key challenges in combating malaria in India to help eliminate this ancient disease within the next decade.

II. Quest for Innovations towards Eliminating Malaria

The Quest is envisioned to fast-track adoption and scale-up of innovative platforms, tools or practices which have received prior validation. These innovations will have strong potential to strengthen and transform key aspects of malaria prevention, control and elimination 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 in the public or private healthcare system.

Product Innovation

✓ Validation*  
✓ Beta Prototyping  
✓ Feasibility Studies  
✓ Pilot Introduction

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

Process Innovation

✓ Process validation  
✓ Feasibility Studies

India Health Fund will not fund projects based solely on field implementation of Behaviour Change Communication (BCC), advocacy, community engagement and other areas or interventions which are based on improving community or administrative awareness and participation.
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
- **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 settings (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 an 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 on a small scale in a 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)*
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 malaria elimination.

The innovations can address any of the following problem statements:

i) Innovative Technologies to Strengthen Surveillance to provide accurate estimates of Disease burden and Data-Based-Decision Making and Risk-Prediction from the public and private sector

ii) Developing innovative methods of vector control and personal protection for enhancing or complementing current strategies

iii) Improving logistical modalities and quality assurance for malaria consumables

iv) Consistently detecting and diagnosing cases of malaria, both in high and low endemicity regions

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. Why technological innovations are required in Malaria

Malaria has many challenges specific to it. As a vector-borne disease, malaria occurs after the trio of vector-parasite-victim is completed, and hence has multiple variables which need to be addressed. Moreover, controlling and preventing the growth and spread of mosquitoes is a challenge unique to vector-borne diseases, of which malaria is the most widely prevalent. In India, most malaria hotspots occur in remote areas where conventional health systems struggle to reach affected populations. Technological innovations which can supplant or supplement human efforts and facilitate greater access will be valuable for tackling malaria.

On another note, significant challenges face India and the world as some regions are heading towards elimination, while others still face high caseloads and challenges in reducing malaria prevalence. Globally, caseloads have increased or plateaued in the past two years. Resistance to conventional vector control measures, the skill shortages and lack of capacity in some domains such as entomology, the challenge of creating additional diagnostic tools which can support and eventually replace labour-intensive microscopy, and the need for decision-makers to access data for rapid decision-making all rank high among the malaria innovation needs for India.

To strengthen programme implementation, new tools are necessary. Tools facilitating rapid, Point of Care (PoC) and accurate diagnosis, case mapping, more accurate entomological analyses, and rapid data transfer for decision-making will all help speed up the path to malaria elimination.
Despite the incentives given to start-ups through government initiatives, health-based startups and innovators face the unique challenge of having to make products which need to be point-of-care, resilient under tough and low-resource circumstances, and yet be of high accuracy and quality. Innovators often do not have access to the necessary domain expertise for creating technically sound products which meets the health program’s expectations. One of IHF’s mandates is to fund and provide mentorship to such technological innovations and the Malaria Quest is one of our approaches to widen our reach to the best innovators working within the malaria domain which can quickly transform the malaria landscape.

V. Program Offerings

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

ii) Collective engagement with global stakeholders and ecosystem engaged in the malaria elimination space

iii) Potential opportunities to present innovations to government/private partners with a clear focus on seamless integration with the national malaria elimination efforts

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)
VI. 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

VII. 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. The project should be ready for scale-up, which signifies that the innovation should be in a stage where it can be deployed in a field area for validation and testing.
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 if 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
- Basic research related to insecticides, drugs or vaccines
- Incomplete or poorly articulated proposals
- Innovations that fall outside the mandate of the Malaria 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 malaria 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 work 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.

VIII. Project Duration

The proposal could have a time duration of up to 2 years, however, if they vary significantly from this timeline, project durations will need to be supported with an adequate, coherent rationale and supporting evidence for justifying the duration.

IX. Tentative Project Budget

Promising proposals will be supported by the India Health Fund with grants or funding during the entire duration of the project, contingent on milestones achieved at different stages. The quantum of funding will be contingent on the project and its mandate.

X. Co-Funding for Proposals

IHF is a strong believer in co-funding as a tool to bring about bigger impact and a multiplier effect in the malaria 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.
### Quest Timelines

<table>
<thead>
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<th>Dates</th>
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<tbody>
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<td>Launch of Malaria Quest</td>
<td>July 8, 2019</td>
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<td>Webinar 1</td>
<td>July last week</td>
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<td>Webinar 2</td>
<td>August third week</td>
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<td>Applications close</td>
<td>September 2, 2019</td>
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<td>Pre-screening &amp; primary evaluation</td>
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<td>Notification to shortlisted candidates</td>
<td>October 30, 2019</td>
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<td>Final evaluation presentations</td>
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<td>Declaration of results</td>
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<td>December 2019</td>
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<td>January 2020</td>
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<td>February 2020</td>
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XII. Problem Statements

Problem Statement 1

Innovative Technologies to Strengthen Surveillance: Accurate Estimate of Disease burden, Data-Based-Decision Making and Risk-Prediction from the public and private sector

Background

The World Malaria Report 2017 identified India as one of the countries with ‘weak’ surveillance systems, while acknowledging its progress in reducing the malaria burden\(^2\). Strengthening India’s malaria surveillance capacity is fundamental for accurately assessing and accelerating the country’s success in its’ efforts to eliminate the disease\(^3\). Ensuring rigorous surveillance is critical on various fronts- patient (incidence, mortality, treatment outcomes), vector, parasite, service delivery and utilisation, and predicting epidemic outbreaks\(^4\). Surveillance needs also vary by different levels of endemicity. For example, government officials and programme managers in highly endemic areas require aggregated population level data while patient surveillance in areas with low endemicity needs individual case- based tracking and follow-up.

The latest World Health Organization (WHO) Global Technical Strategy for Malaria identifies surveillance as an intervention that encompasses the tracking of the disease burden, programmatic responses and acting based upon the received data. The strategy document also strongly recommends prioritizing investments in surveillance tools and strategies including entomological surveillance, drug efficacy surveillance, surveillance of cases and management among others.

Improving surveillance for Malaria is also one of the top recommendations of the Tribal Health Report of the MoHFW and the Ministry of Tribal Affairs released in 2017\(^5\). Most malaria hotspots in India are situated in areas inhabited by tribal communities and are often inaccessible by conventional means of transport. This makes the development of a low-cost, feasible and effective surveillance system critical for the future, especially as malaria control initiatives are scaled up and as the country aims to reduce parasite incidence and ultimately achieve elimination. This will ensure that all elements of malaria diagnosis and management including mass screening, diagnosis, treatment, an abnormal spurt in cases, drug resistance etc are recorded and decisions are taken based upon this evidence.

Challenges

‘Missing’ cases and deaths: Gaps exist in routine data recording and reporting leading to under-estimation of malaria cases and deaths. Several factors contribute to this such as data loss resulting from paper-based reporting and human errors, lack of trained healthcare staff for

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\(^2\) World Malaria Report 2018, World Health Organisation  
\(^3\) Ghosh SK, Rahi M. Malaria elimination in India—The way forward. J Vector Borne Dis 2019;56:32-40  
\(^4\) Global Technical Strategy for Malaria 2016-2030, World Health Organisation  
\(^5\) Report of the Expert Committee for Tribal Health in India, Ministry of Health and Family Welfare and Ministry of Tribal Affairs, Government of India
surveillance activities in remote areas and referral loss at various levels of healthcare from screening to treatment and subsequent follow-up.

Vulnerable/High-risk populations: Specifically, case notification and surveillance of some high-risk populations such as migrants, children under 5 years of age, pregnant women are major challenges. Surveillance of existing and emergent drug resistance patterns is also a critical gap area. Developing tools or strategies which can monitor these vulnerable populations is essential.

Decision-making support to programmes: Government programme officials require accurate and timely field level data for efficient programme planning including resource allocation, supply forecasting and allocation, and micro-planning of activities. Currently such tools and solutions to support decision-making at various levels of the public healthcare system are lacking.

Tracking vector population and trends: Accurate vector surveillance is critical in planning and adapting malaria control/elimination strategies. This includes measuring and tracking seasonal changes in vector density, identification of new species and changing vector behaviours such as resting and biting. However, most techniques currently used for vector identification and research such as mosquito traps are complex, time consuming and require highly trained specialists. Furthermore, lack of trained entomologists in the country is a major barrier to effective vector surveillance.

Risk identification and prediction: The malaria programme’s activities such as number of cases detected, coverage and utilisation of personal protection equipment and impact of vector control efforts, directly impact disease trends. Malaria trends also have a strong association with climatic factors such as changes in rainfall, temperature, humidity and floods. Additionally, changes in human activity in the form of migration, construction, deforestation and lifestyle can increase the probability of a future outbreak.

Scope for Innovations

- Affordable and feasible solutions that can easily integrate within the government’s malaria control programme and help streamline data collection and timely reporting of all malaria cases and deaths, with a focus on vulnerable/neglected population groups (described in the challenges section)

- Tools that can help translate surveillance data in real-time into actionable insights for programme managers such as identification of clusters of high prevalence, sudden changes in trends, coverage/utilisation of malaria treatment and prevention services etc. Such tools should support analysis, interpretation and usage of routine surveillance data according to the stage of malaria elimination and the regional endemicity.

- Dynamic demand forecasting mechanisms for drugs and consumables and efficient allocation/re-allocation of resources amongst various levels of endemicity to prevent shortages or expiry.

- Innovative tools/approaches that can help simplify vector surveillance activities such as devices to identify vector species and count.
• Risk prediction surveillance systems that are equipped to constantly monitor, collate and analyse multiple types of data related to the patient, weather, changes in physical environment, vectors, logistic supply etc. to predict, avert and effectively manage potential outbreaks.

• Mapping and quantifying certain changes in the parasite such as HRP-2 deletions, sensitivity of current diagnostic tests and highlighting any major gaps arising from them.

• Mapping anomalies and changes in vector behaviour, resistance or treatment failures to provide real-time data and burden of important events (e.g.: Mechanisms to map and identify the burden of certain important phenomena such as resistance or presence of anomalies such as PfHRP-II deletions.)
Problem statement 2

Developing innovative methods of vector control and personal protection for enhancing or complementing current strategies

Integrated vector management has proven to be a widely successful strategy in controlling Malaria transmission. Techniques for vector control and personal protection include obstructing the life cycle of Malarial vectors at various stages including use of larvicides, biological control using Gambusia fish, control of adult populations using approaches such as Indoor residual sprays and space sprays.⁶

Recently, however, resistance to nearly all classes of currently known insecticides, namely, pyrethroids, organophosphates, carbamates and organochlorines has been documented with increasing intensity. Many of these products are now increasingly inefficacious in multiple countries. The WHO has reported some resistance to most of these classes in nearly sixty countries.⁷ Another WHO review in 49 countries showed that most of these insecticides had become inefficacious in at least some locations across the world.⁸ Domestically, India has a varied scenario regarding insecticide resistance. A study in Gadchiroli, Maharashtra showed that A. culicifacies demonstrated resistance to most insecticide classes, while other studies show a more varied scenario. This is a particularly alarming phenomenon since few other methods of vector control (VC) exist.⁹,¹⁰

The sole reliance of vector control on chemicals can prove to be harmful in the longer run as resistance will inevitably develop for these products sooner or later. Moreover, these mechanisms are not useful in some key geographical circumstances since they can be deployed only through specific mechanisms such as Indoor residual spraying or through LLINs.

On the other hand, while vector control measures are effective in reducing vector density around household surroundings, mobility of people to various settings in and around them makes personal protection necessary. In hilly areas, forests, and even in urban areas, there are many opportunities for mosquitoes to bite humans when they venture out of houses. In many tribal areas, people often sleep outside the house or near farms or forests, making them even more vulnerable to bites. Even if all vector control measures such as IRS, larvicidal measures and physical barriers are in place, mosquitoes will still find opportunities to bite humans. Similarly,

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Manual of Integrated vector management: NVBDCP
⁷ https://www.who.int/Malaria/publications/atoz/who-ir-framework-2017-presentation-eng.pdf?ua=1
Framework for a national plan for monitoring and management of insecticide resistance in Malaria vectors
⁸ http://apps.who.int/iris/bitstream/handle/10665/250677/9789241511157-eng.pdf?sequence=1
Test procedures for insecticide resistance monitoring in Malaria vector mosquitoes
⁹ http://www.jvbd.org/article.asp?issn=0972-9062;year=2017;volume=54;issue=2;spage=111;epage=130;aulast=Raghavendra: Temporo-spatial distribution of insecticide-resistance in Indian malaria vectors in the last quarter-century: Need for regular resistance monitoring and management
Status of insecticide resistance in An. culicifacies in Gadchiroli (Maharashtra) India.
multiple other challenges such as improper design of houses which allow easy entry and resting of mosquitoes and frequent visits by people outside their homes complicates personal protection measures and different biting times of various sub-species of mosquitoes makes personal protection a complicated endeavour.

Challenges:

Lack of Vector control mechanisms for outdoor biting

Vectors in India show diversity in their breeding sites. While the species *Anopheles culicifacies* and *Anopheles stephensi* breed in relatively clean stagnant water, the species *Anopheles fluviatilis* breeds in slow-moving streams of water, more commonly seen in hilly regions such as the Northeast and Odisha, where it proves to be challenging to control due to their remoteness and due to the challenging geographical circumstances. In such a scenario, devising tailored strategies, some of which can be physical interventions for controlling vector resting and growth need to be explored.\(^1\)

Over-reliance on chemical vector control measures and insecticide resistance

Chemical vector control measures invariably face the threat of resistance, and while emergence of resistance can be delayed through the cyclic use of insecticides, this has never been practiced in India. Also, other methods of vector control should be explored. Moreover, in rural areas, modes such as IRS and LLINs meet with some limitations of usability and IRS sometimes does not occur in some homes due to resistance from local communities and their refusal to allow IRS personnel to spray within their homes. In such a scenario, other methods of preventing mosquito biting inside the house need to be explored.

Challenges in personal protection:

Protecting people outside houses against exophilic biting: Personal protection products need to account for many integral factors such as livelihoods, the daily lifestyles, habits and even the beliefs of local communities using these measures, and most importantly, the constraints and restrictions that many tribal communities live in. Using bed nets is impossible if individuals are sleeping on farms or are in forests during times when mosquito bites occur.

Behavioural limitations which reduce effectiveness of existing personal protection measures:

India has had a problem in achieving universal coverage, especially in terms of resupply of LLINs once the earlier batches have exhausted their use. While distribution networks have managed to provide the first supply of LLINs to underserved areas and have achieved last-mile coverage, replacement after the end of the LLINs' lifecycle remains a problem.\(^2\) Multiple behavioural

\(^1\)https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4216505/

Environmental management through sluice gated bed-dam: a revived strategy for the control of *Anopheles fluviatilis* breeding in streams

\(^2\)https://Malariajournal.biomedcentral.com/articles/10.1186/s12936-017-2117-0

Monitoring of LLIN coverage versus utilization
factors were reported by users including feeling suffocated, being unable to sleep within LLINs during warm weather, sleeping on farms and places where using LLINs is difficult were reasons given for non-usage of LLINs by some patients. A recent study by Raghavendra et al. (2017) noted that the household level coverage of LLINs was inadequate to cover the entire household. Multiple people or sections of people in the household remained uncovered. The controlled, single-channel availability of LLINs remained a problem.

Multiple socio-economic factors such as the family size, gender ratios and customs determine LLIN use. Adolescents do not sleep besides parents and hence, separate bed nets are usually required for them. Another point necessary to note is that many-a-times, residents in tribal areas may sleep near bonfires in the winter without using bed nets, leaving them vulnerable to biting. Hence, the most effective current tool for personal protection is rendered ineffective due to behavioural factors.

Unavailability of currently available personal protection tools in rural areas: While there are few scientifically validated products in the market, personal protection products are widely sold across commercial channels, including electricity-based emanators, coils, topical applicants among others. However, they are unsuitable for many malaria endemic areas due to a lack of electricity, unreliable supply-chain channels and prohibitive prices. Innovations within this area should account and address behavioural factors which limit adherence to personal protection measures. Innovations which can utilize newer personal protection measures or can create novel mechanisms of personal protection from mosquitoes can be devised.

Scope of innovations in vector control and personal protection

- Innovative methods of vector control which can avoid the problem of development of resistance to chemical insecticides.
- Innovative methods of insecticide resistance management and rotation
- Vector control measures which will work in challenging geographical circumstances such as slow-moving streams and hilly areas where conventional methods are not effective.
- Modes of innovations which can control vector populations through novel mechanisms which have not been utilized in current vector control programs.
- Modes of vector control which are eco-friendlier since current VC strategies have a collateral effect on other insects.
- Technologies or products which can prevent exophilic biting in forests, farms and in hilly areas where people often travel outside homes during biting hours.
- Technologies which can prevent entry of mosquitoes into houses or not allow resting of mosquitoes in houses.
- Innovations or products which can circumvent behavioural and geographical limitations such as high temperatures and outdoor sleeping where currently effective tools such as LLINs cannot be utilized.
• Developing methods of personal protection which utilize other modes of repelling or targeting vectors apart from chemical insecticides.

• User-friendly and effective tools of personal protection which can withstand the multiple problems that affect personal protection products.
Problem statement 3

Improving logistical modalities and quality assurance for malaria consumables

Since malaria is present in some of the poorest and most inaccessible areas of India, while also leading to outbreaks in rural and urban areas, building robust supply chains becomes a critical area of intervention. With multiple challenges such as poor road connectivity, villages or tribal hamlets which takes hours to reach by foot, the threat of conflicts in some areas affected by malaria and the unfeasible nature of deploying additional manpower in all these scenarios makes malaria supply chains a major challenge.13

For instance, many malaria endemic areas in Odisha, Chhattisgarh, Maharashtra and especially the North East are either dense forests where road connectivity is frequently disrupted due to rains, have villages based deep within forests or atop hills where no vehicles can reach or are likely to reach in the near future. Often, even routine healthcare supplies including IFA tablets, ORS sachets and the simplest necessities are also unavailable due to their inaccessibility.

On the flipside, certain areas within India are now well placed to proceed towards elimination, and in such cases, using similar programmes and supply chains may not be an optimal use of resources.

Challenges:

Inaccessibility to malaria endemic areas affecting timely delivery of malaria consumables

Many areas that are affected by malaria are inaccessible due to being in remote areas where roads or conventional modes of transport do not reach. Moreover, in some areas, seasonal problems such as rains and flooding leads to some areas being inaccessible. Malaria transmission is high during the rainy season, and health workers inaccessible areas find it particularly challenging to ensure seamless supply of consumables for diagnosing and treating malaria.

Ensuring quality of consumables for adequate program impact

A major problem pointed out by the WHO is the presence of fake drugs within the system, especially in India, leading to poor treatment outcomes for many patients. Moreover, a large proportion of substandard drugs comprise of ACTs, which is a grave threat since sub-therapeutic doses of ACTs can rapidly lead to resistance among malarial parasites.14 Moreover, WHO estimates suggest that the proportion of substandard drugs could be as high as 50% of the total supplies, which could seriously jeopardize treatment regimens for patients, especially those prescribed ACTs. Point-of-care testing devices which can detect the quality of drugs and

14 http://theconversation.com/fake-drugs-are-one-reason-malaria-still-kills-so-many-92712: Fake drugs are one reason malaria still kills so many
innovations in tamper-proof or unique packaging which makes it easier to identify genuine products from fake ones would be a valuable intervention in this domain.

While the supply chain of malaria consumables has improved, the unique geographic distribution of malaria endemic areas makes it particularly challenging to design dynamic and end-to-end supply chains and ensuring year-round supply of consumables since deploying supplies to such areas remains a challenge. Devising mechanisms which can accurately forecast supply, ensure its quality and track utilization are necessary for keeping a track of elimination efforts.

**Scope of Innovations:**

- Solutions which can ensure timely, safe and easier delivery of malaria consumables even in challenging or hard-to-reach areas or facilitating rapid supply of malaria consumables from one area to another wherever needed.

- Tools for point-of-care testing of quality of malaria consumables, especially drugs, which are critical for the quality treatment of malaria and preventing resistance due to counterfeit or substandard drugs.

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15 [https://gh.bmj.com/content/3/4/e000725](https://gh.bmj.com/content/3/4/e000725): Field detection devices for screening the quality of medicines: a systematic review
Problem Statement 4

Consistently detecting and diagnosing cases of malaria, both in high and low endemicity regions

Background:

The World Malaria Report 2018 published by the World Health Organization noted that an estimated 276 million rapid diagnostic tests (RDTs) were sold globally in 2017. In the same year, 245 million RDTs were distributed by NMPs. Most RDTs (66%) were tests that detected *P. falciparum* only and were supplied to sub-Saharan Africa\(^\text{16}\). Despite this, an increase in the number of malaria cases were reported in some areas. Thus, to curtail the spread of malaria and its related morbidities it is imperative to prioritise the timely diagnosis of malaria both at the patient and program levels.

In contrast to global trends, India saw a sharp decline of malaria to historically low levels in the last two years. Further, while some states like Odisha have recorded a decline as high as 80%, this has not been observed uniformly across all states in India. A high endemic state poses a potential threat to other low-endemic areas and thus the need for continued detection of cases and bringing them into purview of treatment becomes an urgency. Keeping levels low and preventing a resurgence of malaria will be a challenge.

An overview of present diagnostic tests and its challenges\(^\text{17}\)

There are numerous diagnostic options available, however there is a need to continuously evolve these methods in the face of newer challenges posed by the parasite and at the implementation level.

**Microscopy:** This is the mainstay of malaria diagnosis against which new diagnostic tests are measured to detect *Plasmodium* parasites in blood smears. The sensitivity of microscopy is 50-100 parasites per microliter of blood; thus it misses samples with a lower parasite load. The bottlenecks in its use at the PoC also include a rapid decline in skills among microscopy professionals, e.g.: inadequate blood smears preparation and inability to manually identify parasites in low parasitaemia samples. Missing cases of malaria due to low sensitivity could be dangerous in rural areas where this could lead to patients being left untreated\(^\text{18,19}\).

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\(^\text{16}\) [https://apps.who.int/iris/bitstream/handle/10665/275867/9789241565653-eng.pdf?ua=1](https://apps.who.int/iris/bitstream/handle/10665/275867/9789241565653-eng.pdf?ua=1)


\(^\text{19}\) [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6194647/Anaemia and malaria](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6194647/Anaemia and malaria)
Rapid diagnostic tests (RDTs): These tests are based on detection of parasite antigens and they
work well as point-of-care devices. Some drawbacks of RDTs include a lower sensitivity of
detection of malaria compared to microscopy, problems with identifying non-falciparum
species, and false negatives due to *P. falciparum* strains that have lost the PfHRP2 gene.

Mixed Infections: Studies have confirmed that the pattern of Malarial infections in India is
changing. Identifying mixed infections is a challenge with the present platforms\(^\text{20,21,22}\).

Genetic Diversity of the parasite: Odisha, which showed that the conventional Rapid diagnostic
Tests (RDTs), based on Histidine rich Protein-II for diagnosis had extremely low sensitivity, since
some strains of *Plasmodium falciparum* show HRP2 deletions and render the test to be
ineffective in diagnosing Malaria. Rapid diagnostic kits and point-of-care diagnostics will now
need to account for these variations.

Increase in parasite drug resistance: Presumptive treatment by using Fixed Dose Combinations
(FDCs) of ACTs and focusing on a clinical cure vs radical cures is essential. Drug resistance due
to mismanagement of drug surveillance is a critical danger that needs to be tackled through
better diagnosis, case detection and accurate and appropriate treatment.

Scope of Innovation:

To overcome these challenges, innovative solutions along with the existing tools and strategies
are the need of the hour.

Proposed innovations could be directed towards strengthening of either the outreach and/or
the efficiency of detecting malaria.

1. **Enhancing the outreach strategies in detecting malaria**

   - The challenges of detecting malaria cases in high endemic areas is very different from
     those in low endemic areas. The sensitivity and specificity of the tools aside, the
     strategies employed to reach the target communities and deliver the tests will be
different too. The economies of scale which apply in high endemic areas might not work
in communities at the margins of elimination, thus having fewer cases or in areas with
scattered tribal communities. Low numbers, however, also need to be dealt with as they
risk a resurgence. The tools and strategies for such areas need to be relevant to the
communities being served to optimize the use of available technical and human
resource.

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\(^\text{21}\) [https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0193046] : Malaria diagnosis by PCR revealed differential distribution of mono and mixed species infections by *Plasmodium falciparum* and *P. vivax* in India

\(^\text{22}\) [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5863947/#pone.0193046.ref060] : Malaria diagnosis by PCR revealed differential distribution of mono and mixed species infections by *Plasmodium falciparum* and *P. vivax* in India
• Private sector reporting is as important as the engagement of non-certified community healers where most of the patients might be treated. Mapping stakeholders and bringing them within the structured diagnostic system is a challenge that needs redressal.

• Biomarker based identification of susceptible individuals before they are infected is a preventive strategy to keep a tab on the numbers contracting malaria.

• Identification of asymptomatic cases of *P. falciparum* which sub-clinically undergo haemolysis of red blood cells and leads to a worsening of anaemia among patients and identification of latent/dormant malaria, many of which could be *P. vivax*, is important not just to improve disease outcomes for the individual but to also curtail the reservoir of disease in the community.

2. **Enhancing or complementing the existing capabilities of the program by increasing the sensitivity, specificity and rapidity of the malaria detection test**

• Development of better, more robust non-invasive or minimally invasive, accurate (sensitive and specific), rapid, cost-effective, robust, point-of-care testing which can account for species variations.

• Good quality blood sample collection and transportation tools might augment efficiencies of present diagnostic tools.

• Besides the need for developing a powerful alternative to microscopy, the ability of microscopy to diagnose needs to be enhanced through innovations.

• Identifying low parasitaemia and mixed infections will be important to identify the so far undetected reservoir of malaria parasite. About 51% of India’s cases are caused by *Plasmodium vivax* and nearly 13% of infections are now caused by mixed species infections, which lead to more severe manifestations of the disease than mono infections. Uncommon co-infections such as *P. malariae* and *P. falciparum* and a higher rate of *P. vivax* and *P. falciparum* co-infections were found in some endemic areas across India.

• Identification of different blood stages of the parasite may translate to initiation of preventive intervention before the patient becomes symptomatic or before the infection progresses to full-blown clinical malaria.

• Detecting hypnozoites within liver cells is an additional necessity, especially for progressing towards elimination, detecting and treating dormant malaria is essential.

• Immunological markers to detect haemolytic anaemia caused by malaria.

• Fever diagnosis is a concept which needs to be developed further within the health systems, it can be extended for diseases extending to scrub typhus, brucellosis and others which may be manifesting itself within patients but remaining undiagnosed since they are lesser known.
• Tests accounting for LDH & HRP-II deletions and going beyond Aldolase-PfHRP tests which have poor sensitivity.

• Limited studies have shown the advantages of protein-based RDTs. These strongly promote the use of high sensitivity proteomics techniques to find new biomarkers for low parasitaemia in *P. vivax* infected individuals, biomarkers for severe disease, as well as the development of protein arrays for detecting immune signatures in asymptomatic individuals. In addition, metabolomics presents an unexplored avenue for the specific detection of *P. vivax* infections and disease severity.

• The tests should involve detection of parasite antigens that are non-polymorphic, as antigens that can evolve rapidly by acquisition of polymorphic mutations will become more difficult to detect in diagnostic devices as the parasite may evolve to evade diagnosis.

3. **Detection of anti-malarial resistance among infected patients**

   Newer tools are needed to manage artemisinin resistance in *P. falciparum* and chloroquine-resistant *P. vivax*. A robust and early detection test for the active and early infections can streamline treatments and diagnosis of multiple similar pathologies.
XIII. Frequently Asked Questions

1. What does the Quest support?

Quest for Innovations towards Eliminating Malaria 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 Malaria 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 must submit the proposal only once while selecting the problem statement which most closely aligns 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
- **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 anywhere.

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

Yes, consortia 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, must be a 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.

10. **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.

11. **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. 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 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.
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 may be 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.