

## **Request for proposal**

Development of simplified and innovative blood culture system adapted to low level healthcare settings in low- and middle-income countries (LMICs)

### **BACKGROUND**

Bloodstream infections (BSI) have a substantial impact on morbidity and mortality. Blood cultures are the reference method for diagnosis of BSI. Low- and middle-income countries (LMICs) face many challenges when implementing blood cultures, due to financial, logistical, and infrastructure-related constraints. Access to simplified blood culture systems appropriate for use in LMICs has been highlighted as one of the main bottlenecks to addressing antibiotic stewardship, enabling surveillance, and reducing antibiotic microbial resistance (AMR).

Manual methods for blood culturing remain the main method for detection of bloodstream infection in LMICs; however, clinical microbiology capacity is limited and underutilized due to many constraints common to resource limited settings such as short reagent shelf lives, supply chain difficulties and highly skilled labour requirements. The high cost and limited laboratory capacity restrict the use of conventional blood culture methods in LMICs.

Automated systems for blood culture incubation and growth monitoring are used routinely in high-income countries, but they remain costly systems which are not widely available or well adapted for operational constraints that are common for use in LMICs including access to stable power supply and environmental control. As a result, automated blood culture is largely untenable in these locations thereby limiting diagnostic options for clinicians.

Environmentally robust, cost-effective, and easy to use and automated blood culture methods applicable in local/district hospital settings in LMICs are not available at the moment.

### **A RISING NEED IN THE ANTIMICROBIAL RESISTANCE AND COVID-19 CONTEXT**

WHO has highlighted the need for R&D to develop diagnostic solutions to identify bacterial versus viral diseases and support antibiotic stewardship practices at inpatient departments.

Antimicrobial resistance (AMR) is one of the greatest public health challenges of the 21st century. Adequate antibiotic stewardship (AMS) practices to provide the right treatment requires clinical microbiology services with blood culture, pathogen identification (ID) and antimicrobial susceptibility testing (AST). Identifying the cause of infections in patients requiring hospitalization also prevents further development of AMR and can support the development of local clinical guidelines.

Although some progress has been made in the fight against AMR, the unprecedented COVID-19 pandemic may be causing significant setbacks. There is growing concern that many COVID-19 patients are being prescribed inappropriate antibiotics, which may be fueling an increase in drug-resistant infections, particularly in countries lacking antimicrobial stewardship (AMS) programmes and with limited access to diagnostics tools. A concerning study indicated that although 72% of COVID-19 patients received antimicrobial therapies, only 8% had confirmed bacterial/fungal co-infections during hospital admission<sup>1</sup>. With more than 200 million confirmed cases of COVID-19 worldwide, these high rates of inappropriate antibiotic use have worrying implications for the growth of antimicrobial resistance. Without factoring in the effect of COVID-19, the growth of AMR is expected to result in a 25% increase in healthcare costs in low-income countries, versus a 6% increase in high-income countries by 2050<sup>2</sup>. The World Bank estimates that the economic impact of

uncontrolled AMR could result in 24 million people living in extreme poverty by 2030, mainly in low-income countries. COVID-19 has the potential to worsen the effects of AMR beyond these predictions unless urgent action is taken.

To address this AMR crisis, a wider access to blood culture in LMICs is urgently needed, as it is the first step to enable subsequent pathogen identification (ID) and antimicrobial susceptibility testing (AST) for improved antimicrobial stewardship and surveillance.

## PROPOSED SOLUTIONS AND OBJECTIVES

The objective of this Request for Proposals (RFP) is to develop innovative solutions for simplified and improved blood culture technologies to enable use in decentralized district hospitals in LMICs (level 2 facilities).

This RFP aims at gauging interest among manufacturers and institutions working in this field in participating in the development of innovative blood-culture methods applicable in LMICs. The goal is to financially support projects aiming at developing and testing advanced prototypes up to technical feasibility and field demonstration.

The proposed projects are expected to be completed in 12 months.

**Scope:** We invite proposals for a range of solutions - fully automated, semi-automated or manual approaches appropriate for use in LMICS - that simplify or improve ease of use to support the decentralization of blood culture at the district hospital level, such as but not limited to the following:

- Development and field testing of novel solutions adapted to LMICs for continuously monitored automated blood culture systems capable to process up to ~20-60 bottles simultaneously with modular capability.
- Adaptation or improvement of an existing commercialized solutions to fit the needs in LMICs.
- Development and/or validation of innovative blood collection bottles/vials containing a growth indicator and growth medium.
- Decrease in time to result through improved incubation or agitation systems to enhance growth potentially compatible with commercially available blood culture bottles and media.
- Development of a simple detection system (e.g. optical, mechanical, imaging...) and related signal processing system potentially compatible with commercially available blood culture bottles and media.
- Targeted innovative solutions for pediatric and neonatal populations.

To ensure proposed solutions are appropriate for use in LMICs, it is imperative that technologies address design criteria that support operation in conditions and constraints common in level 2 facilities in LMICs. The indicative operational characteristics (adapted from a published TPP)<sup>3</sup> are listed in the table below and should be used as a guide:

Characteristic	Minimal	Optimal
<b>CONSUMABLES</b>		
<b>Storage conditions of blood culture bottles</b>	12 months at +5°C to 35°C, 70% humidity, including transport stress (48 hours at 50°C); no cold chain required.	>12 months at +5°C to +40°C at 90% humidity & transport stress (72 hours at 50°C); no cold chain required
<b>Shipping conditions of consumables &amp; kit</b>	No cold chain required; tolerance of transport stress for a minimum of 48 hours at 5°C to +40°C. Bottles should have a surface resistant to transport and allow for visual inspection.	No cold chain required; tolerance of transport stress for a minimum of 72 hours at 5°C to +40°C
<b>Waste disposal</b>	Consumables should be able to be disposed of as biohazardous waste as specified by WHO guidelines according to the safe management of waste from health-care activities or per country regulations. Consumables and blood culture bottles should be autoclavable and compatible with incineration for disposal.	
Characteristic	Minimal	Optimal
<b>PROCEDURAL AND OPERATIONAL CHARACTERISTICS</b>		
<b>Ease of use/ complexity</b>	The entire test procedure for system operation after sample collection to result should require a maximum of 2 steps by the user	The entire test procedure for system operation after sample collection to result should require a maximum of 1 step by the user and no additional steps required by user after the sample has been placed into the instrument
<b>Time to result</b>	The proposed solutions should target and demonstrate a time to result comparable or ideally lower than existing reference methods.	
<b>Biosafety</b>	Same as standard blood culture in a closed system	- No need for a biosafety cabinet; basic safety procedures need to be followed (standard PPE)

<b>Operating conditions</b>	<ul style="list-style-type: none"> <li>- Between +10°C to +35°C at 70% humidity and at a max altitude of 2000 meters</li> <li>- Ability to function in a high dust environment, with manual cleaning via standard lab consumable clean wipes or cleaning tool provided with the instrument</li> </ul>	<ul style="list-style-type: none"> <li>- Between +5°C to +40°C at 90% humidity and at a max altitude of 3000 meters</li> <li>- Ability to function in a high dust environment with minimal manual cleaning required by user</li> </ul>
<b>Characteristic</b>	<b>Minimal</b>	<b>Optimal</b>
<b>PLATFORM CONSIDERATIONS (If instrumentation is required)</b>		
<b>Instrument capacity/throughput</b>	Capacity to test at least 40 blood culture bottles per week	Capacity to test at least 40 to 60 blood culture bottles per week, instrument would have the capability to be modular to meet various system capacity needs
<b>Power supply</b>	<ul style="list-style-type: none"> <li>- Able to run off standard electricity and compatible with operation on a back-up power supply</li> <li>- System should have the ability to automatically regulate incoming voltage to provide power with surge and line noise protection to keep equipment working through both low-voltage (i.e., brownout) and high-voltage conditions</li> </ul>	<ul style="list-style-type: none"> <li>- Battery-operated with recharging solution (e.g., solar) and circuit protector lasting up to 3 days of constant use and able to run off standard electricity</li> <li>- Ability of the entire operational system to (e.g. computer, incubator) to be powered by a single solar panel and self-stabilize voltage fluctuations</li> </ul>
<b>Instrument operation during prolonged power outage</b>	Temperature of incubation held over 30°C for more than 4 hours when external temperature is between +10°C to +35°C and held at 35°C if external temperature is > 35°C	Temperature of incubation held over 30°C for more than 8 hours when external temperature is between +5°C to +40°C
<b>Maintenance and calibration</b>	Preventive maintenance should not be needed until after 1 y or 1000 samples; an	Preventive maintenance should not be needed until after 2 y or >5000 samples; an alert should

	<p>alert should be included to indicate when</p> <p>maintenance is needed; should be able to be calibrated remotely, or no calibration should be needed</p>	<p>be included to indicate when maintenance is needed; should be able to be calibrated remotely, or no calibration should be needed</p>
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Proposed solutions should be designed to be compatible with various systems/approaches for downstream pathogen ID and AST. Depending on provider performance and usability feedback, there is potential for further collaboration of partners selected under this RFP for broader collaboration and integration with bacterial identification and antibiotic susceptibility rapid point-of-care test methodologies.

**BENEFITS OF WORKING WITH FIND**

FIND is an international non-profit organization that enables the development and delivery of much-needed diagnostic tests for poverty-related diseases. FIND acts as a bridge between experts in technology development, policy, and clinical care, reducing barriers to innovation and effective implementation of diagnostic solutions in low- and middle-income countries. FIND fosters global health product development partnerships, engaging in active collaboration with over 150 partners, including health ministries, bilateral and multilateral organizations, research and academic institutes, commercial partners, private-public partnerships, NGOs and over 80 clinical trial sites. In addition to addressing market entry barriers for diagnostics, FIND supports the appropriate use of diagnostics in many countries through training programmes, quality assurance programmes, and laboratory strengthening work.

FIND intends to catalyse the development of simplified blood culture solutions by establishing the right partnerships and providing assistance and resources in areas such as R&D, product validation, regulatory & clinical affairs, manufacturing, quality systems and processes. Through this RFP, FIND will be supporting R&D activities as a first step to implementation of simplified blood culture solutions at low level healthcare settings in LMICs. FIND may also provide implementation support at a later stage by working closely with national ministries of health in LMICs, as well as assistance/guidance on the WHO endorsement process and/or other international regulatory bodies.

As part of this initiative, FIND is also conducting a market and landscape analysis of blood culture technologies in LMICs in partnership with external consultancies, the learnings from which will be available in Q3 2021 and can be shared with our selected development partner. The market landscape is expected to provide further understanding of the current AMR diagnostics supply tools, future needs, and forecasts at Level 2 laboratories in LMICs.

## WHO IS INVITED TO RESPOND TO THIS RFP?

This Request for Proposal (RFP) is for **manual and automated blood culture system manufacturers, blood culture media producers, and developers & manufacturers of innovative technologies for bacterial enrichment/isolation** interested in receiving financial support for developing innovative automated/semi-automated blood culture systems to be deployed in LMICs.

Academic-industry partnerships are welcome to apply as well as academic institutions with a clear commercialization plan and/or manufacturing partners.

### *Support provided:*

We expect to be able to support 1-3 projects. An envelope of \$0.5M to \$1.5M USD per project will be available depending on individual projects overall budget and scope.

## TIMELINES

The **deadline to respond to the RFP is 11:59pm CET, 26 July 2021.**

## PARTNER SELECTION PROCESS

Proposals will be assessed, and partners selected, through a systematic process designed to be objective, independent, and transparent to ensure that the most suitable developers are selected, and potential conflicts of interest are avoided. Proposals will be assessed by a FIND internal and external panel of expert reviewers.

The evaluation of proposals will be conducted over a 3-week period following the closure of the RFP. Selected applicants will be notified and invited to participate in a teleconference call to present their proposal. Proposals selected for funding negotiations will then engage with FIND, who will follow its own procedures for due diligence, contracting, and monitoring. We anticipate funding awards and contract execution by October 2021. Studies will run for 1 year after contract execution (expected Q4 2021 to Q4 2022) and no longer than December 2022.

Applications will be assessed on their proposed commercial plan to ensure sufficient experience and capacity to deliver on the stated objectives. Applicant's will be assessed based on the following criteria:

- Fit of the proposed solution with the TPP presented in Table 1
- Product development capabilities of the organization
- Manufacturing expertise/capacity
- Strength of team
- Distribution capacity
- Quality and regulatory strength
- Technology readiness and time to market
- Clinical evaluation plan
- Projected cost in relation with milestones and realistic timeline to delivery in the 12-month period
- Interest and presence in LMICs markets

## HOW TO APPLY AND PROPOSAL REQUIREMENTS

Submit proposals via the [FIND's Technology Scouting Submission Webform](#). Please select 'AMR' as the 'Disease Area' and 'RFP: Simplified blood culture' as the 'Disease Area Subtype' and proceed with the online submission. Please also upload a proposal in a PowerPoint format using the submission template provided as guidance.

The PowerPoint proposal should contain no more than 20 slides and include the following information:

- Presentation of the company/institution and previous experience in the field
- Description of the proposed technical solution,
- Description of downstream ID and AST solutions that are compatible with the proposed simplified blood culture solution
- Commercial strategy in the blood culture field as well as presence in LMICs
- Current and expected manufacturing capability/capacity
- Clinical evaluation and regulatory approval preliminary plan
- Expected timelines and key milestones and deliverables for the project duration
- Detailed financial support required to achieve the primary objectives.
- Any other support FIND could offer that would be beneficial for the project success (field testing, usability studies and feedback...)

FIND intends to use the information on technologies submitted in response to this RFP to update the community's understanding of the blood culture technology pipeline. All tests submitted to this EOI will automatically be included in the blood culture and bacteria identification technologies pipeline tracker which may be published on FIND's website. If you do **not** want your product to be included, please mention it in the application.

## QUESTIONS AND FURTHER INFORMATION

**Please contact:** [bloodculture\\_RFP@finddx.org](mailto:bloodculture_RFP@finddx.org)

Questions will be accepted and responded to expediently while the RFP remains open.

### *References:*

1. Rawson TM, Moore LSP, Zhu N, et al. Bacterial and fungal co-infection in individuals with coronavirus: A rapid review to support COVID-19 antimicrobial prescribing. Clin Infect Dis 2020.
2. World Bank. Drug-Resistant Infections: A Threat to Our Economic Future. Washington, DC, 2017.
3. Dailey, P. Defining System Requirements for Simplified Blood Culture to Enable Widespread Use in Resource-Limited Settings. [Diagnostics \(Basel\)](#). 2019 Mar; 9(1): 10.

## APPENDIX 1: GOVERNANCE, ELIGIBILITY, AND PARTNER EXPECTATIONS

This RFP will be executed **according to FIND governance, policies and procedures**. These are summarized below; full details can be found on the [FIND website](#).

### **Low- and middle-income country access and quality**

Applicants are expected to commit to:

- Abiding by the FIND [global access policy](#).
- Submitting a product to WHO prequalification programme and/or stringent regulatory authority, as relevant.
- Establishing and sustaining the highest IVD quality standards, in particular during production scale-up.
- Undertaking activities in LMICs to support market introduction and access (e.g., customization of supporting materials, local registration, sales, and distribution activities).