Enhancing HIV and TB Diagnosis: Adjunct Technologies for Sample Collection and Processing

Grand Challenges

Request for Proposals

Applications due no later than March 25, 2025, 11:30 a.m. U.S. Pacific Time

Background

Effective diagnostics are the cornerstone of disease management for tuberculosis (TB) and human immunodeficiency virus (HIV), two of the world's most significant infectious diseases. Early and accurate detection is critical for timely treatment initiation, reducing transmission, and improving patient outcomes. However, despite advancements in molecular and lateral flow assay (LFA) diagnostics, major gaps remain in accessibility, affordability, and implementation, particularly in resource-limited settings. Addressing these barriers requires innovative approaches to point-of-care (PoC) diagnostics and supporting technologies that streamline sample collection and sample processing in low-resource environments.

PoC HIV viral load (HIV VL) testing with same-day turnaround times has demonstrated improved clinical outcomes ("Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approac"), yet adoption remains low due to limited market options and technological constraints, as most currently approved tests are either near-PoC or require centralized laboratory processing. ("List of HIV Diagnostic test kits and equipments classified according to the Global Fund Quality Assurance Policy"). A major challenge is the lack of affordable, user-friendly blood collection and sample processing devices that enable robust performance in true PoC settings. Overcoming these challenges is essential for broader adoption of and improved access to life-saving diagnostics for HIV management.

Similarly, TB diagnosis faces significant gaps. Each year, an estimated 10 million people contract TB, yet over 25% go undiagnosed, and fewer than 50% of diagnosed cases utilize a WHO-recommended rapid diagnostic (WRD) (WHO World TB Report 2023). Due to its distinctive cell wall structure and resistance to traditional chemical lysis methods, *Mycobacterium tuberculosis* (MTB) typically requires instrumented mechanical lysis to achieve high sensitivity in molecular diagnostic assays ("New Manual Quantitative Polymerase Chain Reaction Assay Validated on Tongue Swabs Collected and Processed in Uganda Shows Sensitivity That Rivals Sputum-based Molecular

Tuberculosis Diagnostics"). Unlike diseases such as HIV and malaria, there are currently no instrument-free, true PoC molecular diagnostic tools that have adequate performance for detection of TB. While simple tuberculosis lipoarabinomannan (TB LAM) tests represent another unique solution for MTB detection using noninvasive sampling with urine, diagnostic accuracy is modest for PLHIV and otherwise poor. Expanding access to highly accurate testing, particularly in closer proximity to patients, is critical to ending the TB epidemic.

To bridge these diagnostic gaps, developing adjunct technologies for sample collection, lysis, and preparation is essential. Pre-analytical solutions, such as simplified sample collection and stabilization and instrument free sample lysis specifically for TB could enable more reliable and consistent results while reducing reliance on complex laboratory infrastructure. By investing in these supporting technologies, diagnostic platforms can become more accessible, scalable, and effective in reaching underserved populations.

The Challenge

Recent improvements in diagnostic testing have enabled molecular and lateral flow testing to be performed closer to the patient than ever and in some cases at home with a fully consumable test format. The challenge lies in developing solutions upstream to testing that enable easier, more affordable, and self-administered sample collection, sample preparation, and lysis when needed to support innovative PoC tests with faster turnaround times.

Specifically, the objectives of this challenge will be to address one, or all, of the following:

1. **Self-Sample Blood Collection Devices (Phlebotomist-free blood collection)**
    a. Solutions must enable phlebotomist-free collection of at least 1 mL of whole blood with performance comparable to phlebotomist-collected samples. Key parameters include sample quality, volume collected, failure rate, and ease of use.
    b. Solutions must ensure that the sample is stable for at least 24 hours at temperatures up to 40°C and humidity up to 70% without the need for cold chain.
    c. Ideally, the solution should be compatible with serum or plasma generation but must, at minimum, enable robust whole blood collection.
    d. If a design includes a sample collection or container component (e.g., a tube or cup), the storage device must prevent leakage and/or aerosolization of contents during storage and transportation.

e. If a design includes a buffer, it must be compatible with downstream immunoassay or nucleic acid amplification and detection without need for extraction or purification.
f. Solutions developed must be simple enough for use at home by a layperson or by a low-level healthcare worker.

2. **Sample Collection for MTB**
    a. Solutions must enable collection of reproducibly consistent specimen biomass that does not require pipetting.
    b. If a design includes a sample collection or container component (e.g., a tube or cup), the storage device must prevent leakage and/or aerosolization of contents during storage and transportation.
    c. If a design includes a buffer, it must be compatible with downstream lysis and nucleic acid amplification and detection without need for extraction or purification.
    d. Samples must be stable for up to 72 hours at temperatures up to 40°C and humidity up to 70% without the need for cold chain.
    e. Solutions must be safe for administration and simple enough for home use by a layperson or low-level healthcare worker.

3. **Sample Preparation Devices (Instrument-free sample processing) for HIV detection**
    a. Sample preparation solutions could include single or multiple sample processing aspects such as sample clean up, filtration, plasma/serum generation, analyte concentration, etc.
    b. If sample preparation is integrated with sample collection, the processing step (e.g., plasma/serum separation) should be seamless and included in the collection workflow.
    c. If sample preparation includes stabilization, specifically for RNA targets, solutions should enable sample stabilization for at least 24 hours or more at temperatures up to 40°C and humidity up to 70% without the need for cold chain. The samples must also meet performance equivalence to fresh samples (**TSS 1** - Human immunodeficiency virus (HIV) rapid diagnostic tests for professional and/or self-testing).
    d. Ideally, no additional instruments should be required to complete the steps. However, if any are necessary, they must be compact, easily transportable, battery-powered, and cost-effective (under $50 USD).
    e. The solution must be simple and safe enough to be performed at home by a lay user or by a low-level health care worker.

4. **Sample Lysis Devices (Instrument-free lysis) for TB lysis**
    a. Novel devices must demonstrate feasibility of MTB cell inactivation (by standard biosafety analysis protocols) and lysis (as compared to mechanical lysis via bead beating or sonication) without the need for a reusable instrument. ("New Manual Quantitative Polymerase Chain Reaction Assay Validated on Tongue Swabs Collected and Processed in Uganda Shows Sensitivity That Rivals Sputum-based Molecular Tuberculosis Diagnostics").
    b. The solution must break open the MTB cells (>50% lysis efficiency compared to mechanical lysis via bead beating or sonication) without damaging target DNA.
    c. The resulting lysate must be stable for up to 72 hours at temperatures up to 40°C and humidity up to 70% without the need for cold chain.
    d. Ideally, no additional instruments should be required to complete the steps. However, if any are necessary, they must be compact, easily transportable, battery-powered, and cost-effective (under $50 USD).
    e. The solution must be simple and safe enough to be performed at home by a lay user or by a low-level health care worker.

5. **Sample Clean up and Analyte Concentration**
    a. Pre analytical solutions to improve analyte quality for improved assay performance including but not limited to sample clean up, analyte concentration, and interference removal.
    b. The solution must demonstrate equivalence with laboratory sample clean up methods and analyte concentration kits.

Evaluation Criteria:

- Feasibility and innovation in meeting collection, processing, and/or lysis requirements.
- Cost-effectiveness and scalability.
- Analytical performance and validation data as per published guidelines.
- Alignment with decentralized or PoC needs as per published guidelines.
- Product shelf life at ambient temperature, and transportation stability in target LMIC countries as suggested by Global Fund Priority Country List.

Eligibility Criteria

This initiative is open to nonprofit organizations, for-profit companies, international organizations, government agencies, and academic institutions. We particularly encourage applications involving projects led by women or from women-led organizations and applications from institutions based in low- and middle-income countries.

Funding Level

We will consider proposals for awards of $100,000 to $250,000 USD for each project, with a grant term of up to 2 years. Application budgets should be commensurate with the scope of work proposed. Indirect costs will be considered and should be included in the budget for the up to the grant amount awarded (subject to the Gates Foundation's indirect cost policy).