The Johns Hopkins University Center for Point-of-Care Technologies Research for Sexually Transmitted Diseases
ANNOUNCEMENT OF FUNDING OPPORTUNITY

PART 1. OVERVIEW INFORMATION

1. A. Solicitation Title

IMPROVEMENTS TO RAPID SIMPLE POINT-OF-CARE TESTS (POCT) FOR SEXUALLY TRANSMITTED DISEASES (STDs)

1. B. Purpose

The Johns Hopkins University Center for Point-of-Care Technologies Research for Sexually Transmitted Diseases (the Center) is seeking to facilitate the development of novel detection technologies for Point of Care Tests (POCT). The targets for these POCT are limited to sexually transmitted diseases (STDs). Other infectious diseases will not be considered for this award.

Successful applicants will describe improvements to proposed devices which minimally meet or exceed the current clinically accepted assays (i.e., "gold standard"). The proposed device should have achieved a level of technological maturity equivalent to proof of concept at a minimum. The three technological criteria associated with this domain are development of a prototype(s), supportive experimental results, and institutional IP disclosure. These criteria are derived from the GAITS (Guidance and Impact Tracking System).

Successful applicants will describe the developmental goals of their device with relevance to a "use case". A "use case" is defined by the population of patients who would benefit from the device and the end user needs for which development is intended. For example, a "use case" could be a public health clinic with limited funds available for reimbursement of a test. The end user needs and support for reimbursement cost could vary based on whether the clinic is inside or outside the US.

***In 2022, we especially encourage applications that focus on the detection of syphilis (*Treponema pallidum*), though we will review all applications that fit the solicitation.**

1. C. Minimum Requirements for POCT for STDs

Successful applications will describe the development of tests which minimally meet the criteria in **Table 1**.

Table 1: Description of POCT requirements based on ASSURED criteria[1]

ASSURED criteria[1]	Assay Criteria	Criteria Description
Affordable	Low cost	• "Use case" dependent but not to exceed $30 USD[a]/test
Sensitive	Sensitivity	• Within 90% of current clinically accepted assay
Specific	Specificity	• Within 90% of current clinically accepted assay
User-friendly	Low labor burden/CLIA waivable	• As few manual steps as possible/must be 3 steps or less for CLIA waived test
Robust and rapid	Turn-around time (TAT)	• TAT ≤ 30 min (sample to result)
Equipment-free	Low power reader +no/little sample prep	• "Use case" dependent: Reader (120v to battery operated) / sample prep integrated into reader
Deliverable to those in need	Portable device	• "Use case" dependent: Small bench top to hand held (≤5 lbs.)

[a] United States dollars

Proposed POCT can detect single STDs or multiple STD targets, however, multiplex assays which can detect symptomatically related STDs such as *Chlamydia trachomatis (Ct), Neisseria gonorrhoeae (Ng), Trichomonas vaginalis (Tv),* and *Mycoplasma genitalium (Mg),* are preferred. This solicitation is not limited to the four targets named. Proposals are encouraged which detect STDs other than those listed above, particularly syphilis.

Regardless of the target(s) or platform proposed, proposals should limit the work to tasks that can be completed **within 6 months**.

1. D. Submissions

The solicitation and access to the application are posted on the Center's Point-of-Care Technologies Research Network (POCTRN) funding page.

Expression of Interest (EoIs) applications are required and open to all applicants. EoIs will be evaluated to determine from which applicants full proposals will be invited. Only invited full proposals will be accepted and reviewed.

Expression of Interest forms, invited full proposal forms, and associated PDF files may be accessed at the funding page link noted above. Only electronic submissions will be accepted. Submissions must be time-stamped by the submission system prior to or at the cut-off date and time listed in **Table 2: Key Dates for Application and Anticipated Award Deadlines**. Please note that all deadlines are in Eastern Standard Time (EST) or Eastern Daylight Time (EDT). The Center will not consider proposals which are in the process of submission but not yet submitted prior to the cut-off and not stamped as received in time. Information that is relevant to your organization's intellectual property should be marked "Business Sensitive" or "Proprietary." Classified information or markings such as the word "Sensitive" alone must not be used in any part of the submission.

Table 2: Key Dates for Application and Anticipated Award Deadlines:

Solicitation Release	January 19, 2022
Expression of Interests Due	March 14, 2022, 5 pm EDT
Invitations for Full Fast Track Proposals	April 4, 2022
Full Fast Track Proposals Due	May 16, 2022, 5 pm EDT
Notification of Successful Applicants	July 18, 2022
Review Notification to all Applicants	July 25, 2022
Funds Awarded (anticipated)	Approximately 60 days following notifications of successful

Questions regarding this solicitation may be sent to: POCT-STD@jhuapl.edu up to 48 hours before the submission date and time. Please include the words "**Solicitation POCT4STD**" in the subject line and allow up to 48 hours for responses.

1. E. Sponsoring Organizations

All awards will be contracted by the Johns Hopkins University Applied Physics Laboratory (JHU APL), a member of the Center for Point-of-Care Technologies Research for Sexually Transmitted Diseases (Center for POCTR for STDs).

1. F. Mechanism of Support

The Center will issue one of two types of awards depending upon the receiving entity. A cost no fee contract will be awarded to non-profits and universities, while a fixed costs contract will be issued to commercial and for-profit entities. All sub awards to successful

applicants will use funding from the National Institutes of Health (NIH), National Institute of Biomedical Imaging and Bioengineering (NIBIB), under the authority of the parent grant mechanism administered under the Point-of-Care Technologies Research Network Centers U54. All NIH guidelines, terms, and conditions of award stated in this parent RFA apply to this funding opportunity. Foreign entities may apply to this solicitation as permitted by NIH.

1. G. Funds Available

A total of $150,000 USD is available for sub awards to support improvements to POCT for STDs. The Center may award up to three $50,000 USD sub awards with a period of performance not to exceed six months. A second award for a recipient who successfully completes their first award will be considered, if needed. The amount of total funding available for a recipient in a 12 month period will not exceed $100,000 USD.

1. H. Eligibility

Applications from all sources, including domestic or foreign, public or private, and non-profit or for-profit, will be considered. Awards under this solicitation may be made only to NIH-eligible applicants. Details regarding specific requirements can be found in the NIH Grants Policy Statement Part II: Terms and Conditions of the NIH Grant Awards. Foreign parties (governments, universities, corporations, or individuals) will be screened against the various US government restricted party lists as required by NIH guidelines.

1. I. Solicitation Policies

Please note that secondary subcontracts under this funding program are not permitted. However, proposals that split award funding directly between two institutions are permitted. Each co-applicant institution must submit budget information under the same proposal submission. Proposals accepted for award may be required to provide additional budget information.

Animal studies and human clinical trials may not be proposed under this solicitation. Testing of human clinical samples is only permitted with the use of de-identified clinical materials provided by Johns Hopkins Medical Institutions under their institutional research approved protocols. The need for de-identified clinical material should be noted in the proposal and associated with a specific task. Applicants should contact the Center to discuss use of clinical samples prior to submission of their application.

PART 2. FUNDING OPPORTUNITY DESCRIPTION

2. A. Background

The Johns Hopkins University School of Medicine created the Center for POCTR for STDs (the Center) under an award from the National Institute of Biomedical Imaging and Bioengineering (NIBIB) to coordinate development, clinical evaluation, and reduction to practice of new point-of-care (POC) devices. This Center is a collaboration between the Johns Hopkins University School of Medicine, the Johns Hopkins University Applied Physics Laboratory, the Infectious Diseases Institute at Makerere University College of Health Sciences in Uganda, and Cincinnati Children's Hospital Medical Center. More information about the Center, its members, and the resources available to POCT developers can be found on the Center's website.

The Center's mission is to develop and test the accuracy, acceptability, and optimal implementation of point-of-care tests for sexually transmitted diseases in diverse care delivery contexts both in the United States and in resource-limited settings. Developed technologies are intended to bridge the gap between current biomedical sensors used in

laboratory or research settings and those modified and optimized for use at the bedside, in the clinic, or in a home setting. The Center has conducted a number of needs assessments to understand the particular drivers for the list of requirements for POCT for STDs[2-4].

The need to develop sensitive, specific, and more easily available POC technologies for diagnosing sexually transmitted diseases is critical. These infections are particularly problematic in women. Most STDs in women are asymptomatic and only detected through routine screening or when women present themselves for testing after being notified of infection in sexual partners or because they perceive themselves to be at risk. Five of the top ten reportable diseases to the Centers for Disease Control and Prevention (CDC) in the United States are STDs[5]. Chronic on going infections with these organisms may eventually lead to more serious conditions such as pelvic inflammatory disease and sterility.

2. B. Operational Environments and End User Preferences

POCT have been proposed for various settings. It is important that developers have a "use case" in mind when they are proposing a POCT. The optimal test characteristics for different operating environments vary.[2,4,8] **Table 3** shows possible operating environments where POCT would be beneficial and the characteristics associated with these settings.

Table 3: POCT Operational Environment and Characteristics Associated with Each

Operational Environment	Average Patient Visit Time (Hours)	Preferred Power Choices	Storage of Assay Reagents
Emergency Department (ED)	4<	120V (commercial power)	Cold storage possible to -20° C
Urgent Care Clinic or Community Clinic (UC)	1>	120V (commercial power)	Highly variable: Cold storage possible to 4° C, -20° C or none
Home Care (HT)	0.25 (suggested)	Non-commercial power such as batteries (rechargeable)	Reliable cold storage below 4° C may not be possible
Low Resource Setting Clinic (LRS)	2> Varies widely	Batteries but not rechargeable (due to lack of consistent commercial power)	No reliable cold storage

It should be noted that the users (the people conducting the POC tests) may be significantly different in each of these operational environments and may include medical doctors, other trained health professionals, or lay people without medical backgrounds. In some cases, the patients would be expected to self-collect a sample and/or run the tests themselves[6,7].

2. C. Research Objectives

While the types of POC technologies considered will include both novel detection technologies and novel enabling technologies, this solicitation is seeking primarily to provide "tactical" funding to develop or improve on novel detection technologies. Detection technologies are defined as technologies in which the device is able to identify and discriminate the infectious agent using a clinically relevant sample. Enabling technologies are defined as technologies which can be used with currently available diagnostic rapid tests to improve and simplify sample preparation or rapid development of new specific reagents (antibodies, aptamers, etc.) for use in existing detectors with potential to be transferred into a health care setting or home use.

"Tactical" funding is directed to a critical experiment(s) which, if successful, would 1) provide preliminary data, 2) enable first demonstration, 3) verify proof of principle/concept or 4) complete a seedling effort to enable organizations to seek additional funding for more robust technology development. These awards are narrow in scope, but should open the path to more robust and detailed development or integration of detection and/or enabling technology.

2. D. Infectious Targets

Preference in this solicitation is given to tests which definitively diagnose syphilis or discriminate syndromically related treatable STDs such as *Chlamydia trachomatis (Ct)*, *Trichomonas vaginalis (Tv), Neisseria gonorrhoeae (Ng)*, or *Mycoplasma genitalium (Mg)*. These organisms are listed as examples only. Other organisms that cause STDs (with the exclusion of Zika virus) and are treatable infections will be considered. Assays which can detect active Syphilis infections are particularly of interest.

Detection can be achieved by:

a) Detecting genetic or protein-based components of the organism
   Or
b) Detecting combinations of general optical or electrical characteristics which can be determined to be unique to the organism
   Or
c) Detecting surrogate markers as long as the clinical significance of the surrogate marker is well established

Comparative measures of sensitivity will vary by organism[9]. However, for *Chlamydia*, a successful technology would be expected to achieve an analytic detection of less than 1,000 elementary bodies/mL when presented in relevant diluents, which include phosphate buffered saline, DEPC treated water, or TRIS borate buffer. If required for the success of the detection technology, protocols for sample concentration must be included as part of the assay protocol.

Other acceptable measures of sensitivity would be technologies that achieve a sensitivity ≥ 90% when compared to the current clinical reference standard. For *Chlamydia*, the current accepted clinical reference standard is a vaginal or urine nucleic acid amplification test (NAAT), according to the CDC[10]. The developed test must show high specificity of the organism compared to expected confounding or commensal organisms. For the example of *Chlamydia trachomatis*, the technology would be expected to differentiate between *C. trachomatis, C. pneumoniae* and *C. psittaci.* Similarly, an assay for *Neisseria gonorrhoeae* should not detect non-pathogenic Neisseria, such as *N. subflava, N. cinnerea, N. lactamica,* etc. Another measure of specificity is a technology that achieves ≥ 97% specificity compared to the current clinical reference standard. It is expected that the pre-clinical development will include testing of the diagnostic assay versus known dilutions of cultured organisms in order to determine the limit of detection (LOD).

Evaluation of detection technologies under consideration for award will include an assessment of the following technology performance metrics[8,9]:

- Achieves an analytic detection of low numbers of target STD. This value will vary according to the STD selected for detection. For example, Ct infections tend to present with low numbers of elementary bodies (EB<1000) shed during an infection while Ng infections tend to present with numbers significantly higher (>5000).

- Achieves a sensitivity ≥ 90% when compared to the current clinically accepted assay

(also referred to as a “gold standard” assay).

- Demonstrates greater specificity to the target organism compared to expected confounding or commensal organisms.

- Demonstrates a detection time from sample collection to result in 30 minutes or less in a relevant operational setting (ED, UC, LRS, or HT).

- Demonstrates successful implementation by an inexperienced user, such as a non-laboratorian, with or without training. If intended to be CLIA waived, the test should not include more than 3 steps (exclusive of sample acquisition).

- Must be prepared for storage at room temperature (18-40^{o}C) or 4^{o}C for at least 6 months.

- Assay answer /readout must preferably not be subjective unless the end user is located in a resource-limited setting.

- Tests include all necessary controls for quality assurance and assay performance.

2. D.1.) Other General Notes about the Research Objectives

- Proposals that describe component systems which have not been integrated or breadboard systems with preliminary results are eligible under this solicitation but applicants must describe specifically how they intend to reach the developmental level required to participate in testing of clinical samples in future years.

- Proposals using component-based systems where some of the components are already in use in food, medical, or environmental markets should emphasize which components are under development and which are novel developments.

- The development award can be used to modify an existing laboratory developed test for use in an urgent care clinic or home market.

- Batched assays which can be developed for single use assays are acceptable under this proposal.

- Size, weight, and storage conditions of assay reagents are not restricted for entry into clinical evaluation.

- All devices must work with standard power (120V) or batteries with the exception of LRS environments where standard non-rechargeable batteries are preferred.

2. D.2.) Further Details about Successful Test Characteristics

- Multiplex detection technologies are desired which can discriminate *Chlamydia* from other important STDs including *Neisseria* spp., *Trichomonas* spp., *Staphylococcus* spp., *Acinetobacte*r spp., and *Candida albicans*. Additional infections of interest to distinguish include *Treponema pallidum*, *Haemophilus ducreyi*, and Herpes Simplex virus (HSV).

- Protocols for use of the detection technologies should be written to accommodate users with at least an 8th grade reading level. Protocols should include all sample processing steps especially if sample concentration is necessary for successful detection. Protocols may be supplemented by up to one day of training for inexperienced users.

- Assay readout must be easy to read using a visual color change readout (subjective manual read of visual color change permitted in LRS only), digital, or graphic formats. Tests must include controls for interpretation of positive and negative values and a control for verification of assay performance. There are no requirements regarding the final size or packaging of the device at completion of funding.

2. E. Review Criteria

All reviewers and Center staff with access to proposals have completed conflict of interest and non-disclosure agreements ensuring confidentiality of the proposals.

2. E.1. Expressions of Interest

EOIs submitted by the deadline **(Table 2)** will be evaluated by Center staff for the following criteria:

- Has achieved a maturity level of "Proof of Concept" or above based on the GAITS criteria
    - development of a prototype(s)
    - supportive experimental results
    - institutional IP disclosure
- Meets or exceeds ASSURED criteria
- The importance and number of STD(s) species detected
- Innovation /novelty of the approach

EOIs determined to meet the requirements outlined in this solicitation will be recommended for full proposals in order to elaborate on the proposed POCT solution.

2. E.2. Full Proposals

All full proposals will be evaluated by at least three independent scientific reviewers who are external to the Center. Full proposals will be evaluated based on the following criteria:

- Scientific and technical merit
- Potential to apply technology to common STDs using multiplex diagnostic testing
- The ability to fulfill the specific research objectives as stated above
- Significance and relevance to the mission of the Center
- Pre-analytical efficiency and rapid analytical speed of assay using laboratory strains
- Sensitivity and specificity compared to gold standard assay results
- Limit of detection (LOD)
- Storage conditions not lower than 4^{o}C
- Appropriate quality assurance provision (e.g., assay and device controls, within performance/calibration controls for devices)
- Appropriately scoped to the amount of funding and period of performance requirements
- Competence and experience of the investigative team

- Bioengineering and research environment in which the work will be performed
- Suitability for use in near-patient applications in ED, UC, LRS, or HT
- Incorporation of testing principles or assay improvements that can achieve proof of feasibility or a higher maturity level within **the next two years**
- Plan for effective evaluation of the diagnostic method using archived clinical samples

2. F. General Award Information

A technology monitor from JHU APL will meet with successful awardees monthly to review progress and achievement of critical milestones and deliverables. As required by NIBIB, our Center will track the progress of awards using the GAITS platform.

The GAITS platform is based on the Healthcare Innovation Cycle (Figure 1) and structures work packages in deliverables and milestones.

Figure 1: GAITS Healthcare Innovation Cycle

It is important to note that a single $50,000 USD award is not expected to address all of the maturity levels or all of the domains shown above especially since proposals should have achieved at least technological (technical readiness level) TRL 3 by the time of application (proof of concept).

A second six month award for technologies that are successful in their first period of performance will be considered if needed. The first award must be completed before a second award can be negotiated; however, it is permitted to apply for a second award in anticipation of completing the first award by the time the new proposal is reviewed.

PART 3: APPLICATION PROCESS

3. A. General Application Information

All applicants are eligible to submit Expressions of Interest through the Center's POCTRN funding page. EoI applications must be submitted on or before the date and time listed in **Table 2**. Optional questions are indicated as such and answering optional questions does not affect the preference given to any submission.

If invited for a full proposal, the applicant must fill out and submit the Full Proposal form by the date and time listed in **Table 2**.

3. B. Points of Contact

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APPENDIX I: Literature Cited

1. Peeling RW, et al “Rapid tests for sexually transmitted infections (STIs): the way forward. “ Sex Transm Infect. 2006. 82 Suppl 5:v1-6

2. Jackman, J et al. ”Minding the Gap: An approach to determine critical drivers in the development of Point of Care diagnostics.” Point Care. 2012. 11(2):130-139.

3. Hsieh Y-H. et al. “Perceptions on Point-of-Care Tests for Sexually Transmitted Infections - Comparison between Frontline Clinicians and Professionals in Industry. Point Care. 2012 .11(2):126-129.

4. Rompalo, A.M. et al. “Point-of-care tests for sexually transmissible infections: what do 'end users' want?” *Sexual health*. 2013.10(6): 541-5.

5. Braverman P. K.”Sexually transmitted diseases in adolescents.” Med Clin North Am. 2000 84(4):869-89, vi-vii

6. Huppert JS, Hesse EA, Bernard MC, Bates JR, Gaydos CA**,** Kahn JA. Accuracy and trust of self-testing for bacterial vaginosis. J Adolesc Health. 2012 Oct;51(4):400-5. Epub 2012 Mar 21.

7. Jenkins WD, Weis R, Campbell P, Barnes M, Barnes P, Gaydos C. Comparative effectiveness of two self-collected sample kit distribution systems for chlamydia screening on a university campus. Sex Transm Infect. 2012 Mar 7. [Epub ahead of print].

8 . Hsieh Yu H. et al “What qualities are most important to making a point of care test desirable for clinicians and others offering sexually transmitted infection testing?” PLoS One. 2011. 6(4):e19263.

9. Vickerman P. et al. Sensitivity requirements for the point of care diagnosis of Chlamydia trachomatis and Neisseria gonorrhoeae in women. Sex Transm Infect. 2003. 79(5):363-7.

10. www.cdc.gov/std/chlamydia/stdfact-chlamydia-detailed.htm (accessed 15 Jan 2019).