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National Institute of Biomedical Imaging and Bioengineering Point-of-Care Technology Research Network: Advancing Precision Medicine

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ABSTRACT To advance the development of point-of-care technology (POCT), the National Institute of Biomedical Imaging and Bioengineering established the POCT Research Network (POCTRN), comprised of Centers that emphasize multidisciplinary partnerships and close facilitation to move technologies from an early stage of development into clinical testing and patient use. This paper describes the POCTRN and the three currently funded Centers as examples of academic-based organizations that support collaborations across disciplines, institutions, and geographic regions to successfully drive innovative solutions from concept to patient care.

INDEX TERMS Point of care technologies, policy.

I. INTRODUCTION

Point-of-Care (POC) is, essentially, the delivery of care wherever the patient may be and a Point-of-Care Technology is defined as a technology that is used for bringing care to the patient rather than taking the patient to care. Realizing the full potential of point-of-care technologies (POCT) represents a critical factor in advancing overall health care by making the predictive, preemptive, preventive, and personalized care of the future accessible to all communities. To advance point-of-care, in 2006 the National Institute of Biomedical Imaging and Bioengineering (NIBIB) proposed a nationwide initiative to create a research network that would build multidisciplinary partnerships and expertise in the development of

integrated systems that address unmet clinical needs at the point-of-care called the Point-of-Care Technologies Research Network (POCTRN).

An April, 2006 workshop “Improving Health Care Accessibility through Point-of-Care Technologies” sponsored by the NIBIB; National Heart, Lung, and Blood Institute (NHLBI); and the National Science Foundation (NSF) assessed the clinical needs and opportunities for use of POCT in primary care, the home, emergency medical services, and in developing countries, and highlighted the state-of-science in sensors and microsystems, low-cost imaging, non-invasive monitoring, and telehealth/informatics. The creation of multidisciplinary partner-

ships was considered a key translational aspect for moving technologies from an early stage of development into clinical testing.

Since 2006, the goal of the POCTRN has been to develop technologies with clinical applications using a network model that enhances complementary strengths and builds multidisciplinary partnerships. To achieve this, each POCTRN Center funded by NIBIB performs or facilitates four core functions:

- Collaborates with physical, biochemical, and computational scientists, and with engineers on exploratory technology development projects.
- Completes clinical needs assessments in areas anticipated to advance the field of point-of-care testing and disseminates this information to the technology development community.
- Provides training to technology developers on clinical issues related to the development of point-of-care devices.
- Provides an adequate administrative structure to ensure that each large complex Center achieves its goals.

The Network also aims to drive the development of POCT through collaborations that simultaneously merge scientific and technological capabilities with clinical need. These collaborative efforts include:

- Utilizing clinical needs to direct technology development.
- Leveraging expertise across Centers to address a range of clinical needs and provide a systems focus.
- Establishing partnerships to create a pipeline from clinical need to field testing of prototype devices.
- Expanding the Network to provide resources to the broader clinical and technology development communities.

An additional objective is to conduct parallel educational activities that advance evidence-based point-of-care practice in critical care, primary outreach and in low-resource environments, including global health care settings.

The Network measures its success through the variety of Center activities:

- Coordination of cross-center communication and collaboration to achieve Network objectives.
- Evaluation and guidance regarding funding of new technology development projects.
- Informing members of individual center activities to leverage resources, expertise, and interests across the Network.
- Implementing mechanisms for center-to-center interactions.
- Development of policies and procedures to be shared across centers.
- Identification of common clinical needs.
- Expertise to develop prototype “systems”.
- Establishment of clinical and industrial partnerships.
- Coordination of education and training programs and other shared practices.
- Community outreach.

- Communication of the Network’s role in advancing point-of-care testing.
- Dissemination of clinical needs information to the technology development community.
- Increased awareness of POCT.
- Outcome studies and parallel funding.

Each awarded Center serves to identify clinical needs in point-of-care testing and communicate those needs to guide device design and appropriate clinical testing early in the development process. Centers also provide resources to both technology development and clinical communities and coordinate activities across their respective areas in the Network.

The NIBIB released the “Point-of-Care Technologies Research Network” solicitation to support specialized centers through a cooperative agreement (U54 mechanism) that covers a spectrum of multidisciplinary and translational research and development activities. The initial funded Centers focused their activities on emerging neurotechnologies, disaster readiness, and advancing point-of-care diagnostics for global health. A second solicitation funded the Centers that are further described in this paper.

II. THE POINT-OF-CARE TECHNOLOGY RESEARCH CENTER IN PRIMARY CARE

The Point of Care Technology Research Center in Primary Care, managed by CIMIT (Consortium for Improving Medicine with Innovation and Technology), is a “center-without-walls” for the rapid transformation of emerging POCT into commercially viable, clinically focused solutions for improving primary health care. CIMIT was founded in 1998 and harnesses the power of multidisciplinary and multi-institutional collaboration to speed the translation of high-impact research into clinical practice and broader dissemination by commercially licensable opportunities.

The specific aims of the Point of Care Technology Research Center in Primary Care are to:

- Apply CIMIT’s innovation model to create clinically-driven point-of-care solutions that address critical areas of unmet need in primary health care.
- Identify and assess unmet primary care needs and develop performance criteria where point-of-care technology solutions would have the highest impact.
- Select and develop the most promising POCT into proof-of-concept prototypes.
- Test and evaluate prototype performance in simulated clinical environments and clinical “living laboratories” relative to clinical performance and implementation criteria.
- Transition prototypes that meet performance specifications into commercially licensable or start-up company opportunities or work with companies to adapt their technologies for use in primary care.
- Train and educate relevant stakeholders – including clinicians, engineers, scientists, students and industry partners – in the innovation process as it applies to meeting health care needs.

- Disseminate “lessons learned” and best practices in innovation methodology and process both nationally and internationally in collaboration with other POCTRN Centers.

A. UNMET NEEDS TARGETED BY THE POINT OF CARE TECHNOLOGY RESEARCH CENTER IN PRIMARY CARE

Primary care providers are at the frontlines of our health care system and serve as the first point of contact for care and as the referral pathway for specialty care. At the same time that the demand for care is increasing with an aging population and an increased burden of chronic disease, the pool of primary care providers is shrinking. This imbalance in supply and demand constrains primary care capacity, limiting access and fragmenting care as patients and families seek out other points of entry, often more expensive and less interconnected, into the health care system.

The introduction of POCT into primary care would increase the capacity of practices to care for more patients by eliminating inefficient testing turnaround delays and the need for post-visit communication of results and recommendations to patients, freeing up clinical time. It is estimated that 55% of a typical primary care physician’s day is spent outside of the examination room, primarily focused on follow-up and documentation of care for patients not physically present [1]. This administrative rework is not only time-consuming, but discontinuous care jeopardizes patient outcomes in that the start of effective therapy may be delayed or, even worse, abnormal results may not be communicated back to the primary care physician from the laboratory or to the patient by the physician, resulting in a serious “failure to diagnose” because of lack of follow-up.

B. SUPPORT FOR INNOVATION BY THE POINT OF CARE TECHNOLOGY RESEARCH CENTER IN PRIMARY CARE

The Center leverages CIMIT’s existing infrastructure. For example, CIMIT has optimized its approach for maximizing potential clinical impact of innovations as a three-stage “find, fund, and facilitate” process that supports development of a pipeline of ideas from early stage proof-of-concept to clinical implementation and commercialization. To support project teams in navigating the Healthcare Innovation Cycle (Fig. 1), the Center uses a variety of integrated methods and processes that are referred to collectively as the “CIMIT Model” of innovation [2]–[4].

Finding significant unmet medical needs and identifying potential clinical collaborators is a critical ingredient in the innovation process and the starting point for the innovation journey. A fundamental tenet of the Center is that innovation must be driven by “clinical pull” and not “technology push.” The Center supports a Needs Assessment core managed by the Massachusetts General Hospital (MGH) John D. Stoeckle Center for Primary Care Innovation. Clinical involvement at all stages of the innovation process is key and so clinical collaborators must be an integral part of all projects funded by the Center.



FIGURE 1. Healthcare innovation cycle.

Funding is awarded on a competitive, peer-review basis once the need has been established. Advancing to the next stage of the cycle, teams design potential solutions based on evaluating a range of technologies or by creating new ones; robust prototypes can then be developed and tested; and evidence is gathered to achieve regulatory approval. Finally, to ensure success, the solution must be broadly disseminated so that it can become a new standard of care.

The POCTRC funds projects in three stages: 1) innovation stage (often called pilot, proof-of concept, or proof-of-principle), 2) acceleration stage (proof-of-value, often called validation), and 3) a clinical adoption/diffusion stage. The Center circulates a Call-for-Proposals for **Innovation Awards** on an annual basis and typically funds 4-6 proposals.

Innovation awards are translational in nature and typically one year in duration, with budgets up to \$100,000 (direct costs) with the objective of scientifically de-risking a novel idea by showing early-stage proof of concept, thereby justifying proceeding on to the proof-of-value stage to generate a viable candidate for further pre-commercial development. To date, the Center has funded 27 Innovation Awards at different levels of maturity across the development pipeline. Seven of these teams are developing multiplexed platform technologies for clinical laboratory testing from small blood samples with results delivered within 15 minutes at the time of the primary care visit.

Projects with the potential for rapid transition to clinical implementation and hand-off to industry within 12-18 months are candidates for CIMIT’s Accelerator Program and/or the program’s healthcare communication course (both are described below). In addition to funding projects that are pre-commercial, the Center also offers a Clinical Adoption and Diffusion Award to assist primary care practices in adopting and adapting commercially available POCT to demonstrate value and speed adoption in the primary care setting. Four Accelerator Awards and two Clinical Adoption and Diffusion Awards have been funded to date.

The percentage of awards to small companies has increased to represent approximately 80% of the award base consistent with the Center’s mission to rapidly advance innovations to impact patient care through commercialization.

Facilitating the journey through the Healthcare Innovation Cycle is never smooth; many challenges are encountered at every point along the cycle. The Center has assembled a team of experts in primary care and laboratory medicine complementing the strong CIMIT network of seasoned experts in translational research to address these challenges.

Late stage projects that are scientifically and technically de-risked and have well-understood market channels, but require further development and investment of money and/or business development expertise to attract interest from an entrepreneur or commercial entity to achieve initial market penetration, may be candidates for facilitation by mentors from the Center's Accelerator Program, serial entrepreneurs who are former founders or CEOs of MedTech companies and who have an intimate understanding of the medical device and diagnostic markets. These seasoned executives join projects essentially full-time to drive them to commercial success by working with project teams to develop and execute a complete plan that includes a "go-to-market" strategy as well as market, competitive, financial and intellectual property analysis.

Funded teams may also participate in a 10-week Healthcare Commercialization CRAASH (Commercialization Results Accelerator to Advance Solutions in Healthcare) course, taught by industry veterans and based on decades of experience from the Coulter Foundation, Massachusetts Institute of Technology (MIT), Yale, and CIMIT. The program formalizes development of a tested business model through the process of validating business hypotheses. Teams receive 1:1 mentoring from successful healthcare entrepreneurs and group coaching from commercialization experts and investors.

Other core resources include CIMIT's virtual collaboration platform (CoLab), a Systems Engineering Core, a Clinical Validation Core, an Education Core and a medical device interoperability program.

CIMIT CoLab®—the Virtual Collaboration Platform is a synthesis of best-in-class, secure, cloud-based tools with functionality designed to allow users to manage the activities of the Center, and to support teams through the Healthcare Innovation Cycle. CoLab was used by the POCTRN to develop a web portal for easy access to information common to all Centers [5], including events, solicitations, clinical needs assessment, and prior awards.

The Systems Engineering Core was developed based upon the recognition that new POCT do not exist in isolation; rather, they exist within ecosystems of other technologies and systems, and these systems influence their likelihood of success or failure and their effectiveness. NIBIB and Center leadership convened a workshop in 2013 to explore the future of point of care testing and technologies. Proceedings were published on behalf of the Network and three Centers [6].

The Clinical Validation Core provides a range of services, including clinical samples for testing, bench validation in a laboratory setting, and clinical trials in the MGH Ambulatory

Practice of the Future (APF), as well as other primary care settings. As an example, the APF in collaboration with the MGH Clinical Laboratories published the results of a pilot study of implementation of a point-of-care testing satellite laboratory in a primary care practice. Findings demonstrated high patient/provider satisfaction, increased efficiency, and financial viability of the model [7], [8].

The Education Core offers a series of monthly webinars. Webinars are recorded, archived and available as podcasts [9].

The Medical Device "Plug-and-Play" (MD PnP) Program [10], led by Dr. Julian Goldman, is an important resource for the Center relative to the definition of device requirements and performance standards. The program was established to lead the development and adoption of open standards and related technologies to facilitate widespread clinical use of medical device data and network-based medical device integration.

III. CENTER FOR FUTURE TECHNOLOGIES IN CANCER CARE (CFTCC)

The Center for Future Technologies in Cancer Care (CFTCC) is located at Boston University (BU). The CFTCC comprises several cores that work together to identify clinical needs, assess new technologies, build prototypes and educate stakeholders. The Center focuses on a range of technologies for deployment along the continuum of care to improve early detection, enhance the lives of patients in care, monitor survivors, and support caretakers.

The specific aims of the CFTCC are to:

- Enable and foster clinician/engineer partnerships.
- Perform clinical needs assessments and impact analysis.
- Fabricate alpha prototypes in the Alpha Prototyping Core Facility for Center stakeholders.
- Make fully functional prototypes for clinical testing in conjunction with the Fraunhofer Center for Manufacturing Innovation's (FCMI) Beta Prototyping Facilities.
- Provide training and networking opportunities for Center stakeholders.
- Promote POCT for cancer nationally and internationally.

We have built an integrated multidisciplinary team consisting of engineers, clinicians, public health practitioners, and technology transfer experts. This team evaluates technologies in various stages of development for their suitability across a range of primary care and non-traditional healthcare settings. Development, commercialization, and deployment of POC treatments for cancer has the potential to reduce healthcare costs by catching more cancers at earlier stages of progression, enabling treatment outside of specialized cancer centers, and monitoring at-risk patients remotely through mobile health strategies.

A. CENTER MISSION, ORGANIZATION, AND RESOURCES

Moving cancer treatments out of specialized centers and into local clinics or home care could significantly lower healthcare costs in many settings. Often patients have to travel long distances to receive treatments at cancer centers, or make

repeated trips for monitoring over many months. In low-resource settings in the developing world, there may not be any options for cancer treatment. Surgical treatments carry infection risks, and in many places there are not enough surgeons to treat all of the patients in need.

Technologies like targeted ultrasound and light-based treatments could allow providers with less specialized training to treat more patients for less money. Tools for monitoring chemotherapy patients at home between treatments could eliminate travel and office visits. Mobile health strategies for collecting data about high-risk populations could lead to new interventions to directly impact cancer screening rates.

The Center focuses on the identification, prototyping, and early clinical assessment of innovative POCT for the treatment, screening, diagnosis, and monitoring of a range of cancers. A major aspect of this effort involves assessing early stage technologies in terms of clinical needs, market demands, setting appropriateness, and commercialization strategies (Fig. 2).

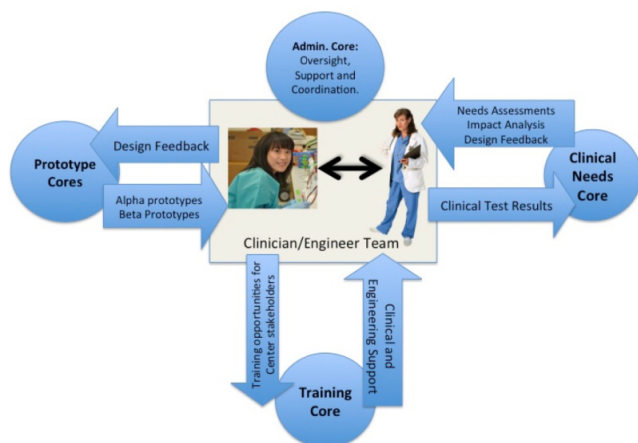


FIGURE 2. Overall center organization.

The Center comprises an Administrative Core, a Clinical Needs Assessment and Impact Analysis Core, a Training Core, and a Prototype Development and Testing Core divided into two parts, the Alpha and Beta Cores, which are both available to Center stakeholders, depending on the stage of technology development. The team evaluates technologies in various stages of development for their suitability across a range of primary care and non-traditional healthcare settings.

An important part of the POCT design process is to move ideas from the lab bench into user-friendly formats. While presentations and drawings can be useful tools in communicating ideas, having a prototype device that a potential end user, manufacturer, or investor can hold in their hands is much more valuable. The alpha prototype in the design phase is a critical time to work out potential bugs or incompatibilities in the system before large scale investments are made in beta prototypes.

The CFTCC Alpha Core prototyping lab on the BU campus enables researchers (from industry, academia, and medicine) from all across the country to build rapid prototypes of their

devices. The Alpha Core houses basic equipment for the prototyping of microfluidic and paperfluidic devices. Parts can be prototyped using standard photolithography and PDMS processing with the assistance of Core staff. Core staff will also make and ship small (less than 10) batches of parts to investigators working on translating benchtop assays into microscale platforms.

The Core can laser cut, hot emboss, and heat seal thermoplastic devices with microscale features. Other prototyping capabilities include xurography (cutter-plotter), wax printing, and reagent spotting on plastic and paper devices. 3D printing is also available. The Core staff helps investigators plan prototyping activities to best suit their experimental designs. Finally, the Core staff can work with developers of mobile applications to design user interfaces.

The Beta Prototyping Core is housed at the Fraunhofer Center for Manufacturing Innovation in Brookline, MA, which is co-located with the BU campus. The Beta Core is tasked with fabricating prototypes that can be used in pre-clinical and feasibility testing. The design of these work-like prototypes is often iterative and involves clinical and engineering collaborators. The FCMI team has expertise in optical device design (endoscopic tools), microfluidic chip fabrication, assay development, and instrumentation. Investigators with funded CFTCC prototype projects are screened for fit with the Beta Core capabilities. Often projects transition from the lab to the Beta Core after a year of Center funding. The Training Core leads the CFTCC efforts in outreach to the wider community of technology developers, researchers, clinicians, and patients and their advocates. Programs include seminars, workshops, and trainings aimed at promoting POCT and transfer of those technologies out of the lab. Educating test and device developers about regulatory requirements, reimbursements, planning for human subjects research, and managing intellectual property concerns are missions of the Core. All training activities are live streamed and archived [11].

The Clinical Needs Assessment (CNA) Core works in conjunction with the Dana Farber Cancer Institute to carry out and disseminate survey research aimed at determining where and when POCT could make the most impact in patient care.

B. CENTER SUCCESSES TO DATE AND FUTURE PLANS

Over the last four years, the CFTCC has funded 17 prototyping projects, three fellowships, and several small exploratory projects in our Alpha Prototyping Core. The vast majority of these projects have secured follow on funding from federal and private sources. Three new ventures have been started. The reach of the Center is national with projects at BU, the University of California Davis, the University of California Berkeley, Massachusetts General Hospital (MGH), the University of Texas Austin, Michigan State University, the University of Arizona, and the Massachusetts Institute of Technology (MIT).

The CFTCC conducts an open call for new projects in the fall of each year to fund 3-7 prototyping projects. Projects

are reviewed externally, ranked, and then matched to Center capabilities. After one year, if projects have met their proposed milestones, they are encouraged to apply for follow-on funding for specific translational activities. Projects may also be referred to the Beta Core and receive in-kind services from that Core to develop or enhance a prototype device.

These projects include several point-of-care tests for the early detection of cancer or monitoring of disease [12]–[17], mobile health applications to coordinate care and patient outreach [18], [19], and devices and tools to enable minimally invasive testing at lower level care facilities including in primary care [20].

The Beta Prototyping Core has completed prototypes for researchers at the University of Arizona, MIT, BU, and for industry. Prototypes include a wearable device for breast cancer chemotherapy monitoring, microfluidic sample preparation modules, and an instrument to fabricate hydrogel reagents for high-throughput point-of-care screening tests.

A specific focus of the Center is on identifying clinical needs in high disease burden populations and funding new technologies that address those needs. The CNA Core published a survey study conducted to determine the preferences for POCT in cancer screening among primary care clinicians [21]. The CNA also worked with an international group of scientists and clinicians working on point-of-care devices to identify barriers to translation in low resource settings and, in particular, West Africa [22].

The Training Core has posted the assembled multimedia resources from all major outreach projects conducted during the past 4 years. The CFTCC website [23] serves as a valuable resource for new funding opportunities for cancer researchers interested in POCT, and for test and device developers interested in applications in cancer care.

We have hosted and co-hosted a semi-annual course called Cancer Care for Engineers and Scientists and workshops focusing on regulatory issues in addition to day-long science symposia. In 2016, the course “New Directions in Cancer Care for Nonspecialists: Immunotherapy and Resistance to Therapy” was well attended both in person and virtually. This workshop was a full-day meeting for clinicians, engineers, and scientists to come together and learn about a very exciting new topic in cancer care.

The Alpha Prototyping Core hosts annual Hack-a-thon events each October at the BU Engineering Product Innovation Center (EPIC). EPIC staff help participating teams fabricate alpha prototypes during the event. The resulting projects are presented by the teams via short videos describing their work. These videos are available on the CFTCC website [24]. In addition to the competition, this event continues to raise awareness of the Center and its resources in the field of cancer care technologies.

The Alpha Prototyping Core also participated in the CAMTech: Global Cancer Innovation Hack-a-thon in the spring of 2016, and winners of this event were awarded Alpha Core time to generate their first prototype units for testing. Several of the hackathon participants are also working

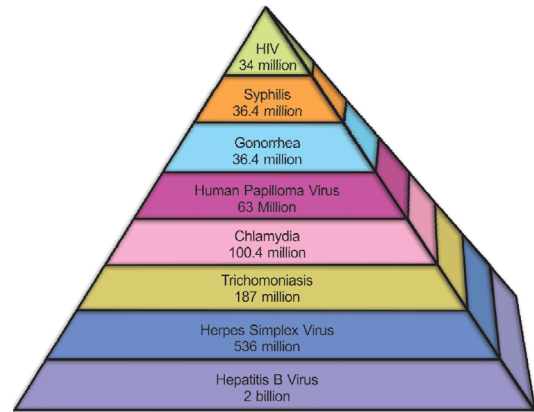


FIGURE 3. Global estimates of STDs.

with the Clinical Needs Assessment Core to identify market opportunities for their new technologies.

IV. CENTER FOR EXCELLENCE FOR THE DEVELOPMENT AND TESTING OF POINT OF CARE TESTS (POCT) FOR SEXUALLY TRANSMITTED DISEASES (STDs)

There are over 110 million prevalent STDs/year and 19.7 million incident STDs in the U.S./year [25], with new estimates of health care costs at \$15.6 billion [26]. Costs for chlamydial infections are estimated at \$516.7 million; gonorrhea, \$162.1 million; hepatitis, \$50.7 million; HIV, \$12.6 billion; human papillomavirus, \$1.7 billion, herpes simplex virus (HSV-2), \$540 million; syphilis, \$39.3 million; and trichomonas infections, \$24.0 million. Global estimates of STD prevalence are astounding. Fig. 3 shows relative world prevalence. Point-of-care tests have great potential to significantly play a role in addressing the epidemics of STDs in resource constrained and poor countries. Stigma, privacy and confidentiality issues unique to STD on top of issues of health inequity and health disparities in populations make STDs optimal for POCT, as well as home care tests or over-the-counter tests (OTC) [27].

A. CENTER MISSION, ORGANIZATION, AND RESOURCES

Our mission is to drive the development of appropriate POCT through collaborations that merge scientific and technological capabilities with clinical need. The long-term goals of our Center are to address the epidemics of Sexually Transmitted Diseases (STDs) in the U.S. and in resource-poor settings by development and better use of POCT, so as to address health inequity and to improve the sexual health of individuals.

The Center is organized in the following manner:

1. An administrative structure to ensure that the large, complex Center achieves its goals in a timely manner. To ensure each functioning component works smoothly together and integrates with other Centers in the NIBIB POCTRN, our administrative component functions to accelerate a smooth transition along a pipeline from developmental prototype assays through in-house and

pilot testing. In this coordinated manner, we can assist with the logical development of point-of-care assays that are proven to have sufficient scientific merit and can progress towards eventual clinical trials and FDA submission.

2. A clinical needs assessments and health impact assessments component for clinicians, end-users, and other appropriate stakeholders, in order to advance and inform the field of point-of-care testing design, development, and utilization by disseminating this information to the technology development community [28], [29].
3. A collaboration component staffed with physical scientists, biochemical scientists, computational scientists, and systems engineers providing support for exploratory technology for prototype development projects and industry for testing of more mature POCT in beta and pilot evaluations to insure a logical progression of assays along a pipeline from the concept stage to the clinical testing stage (Fig. 4).
4. A clinical evaluation component for very mature point-of-care assays by providing real world testing in clinics worldwide inclusive of resource-poor countries. In this way, we both enhance use of POCT in these settings such as emergency departments, home testing, as well as advance end-user familiarity, clinical acceptance, and ultimately the use of such tests, resulting in measureable improved health outcomes especially for those settings experiencing health disparities and inequities.
5. A developer training component to provide training across all career levels about clinical and process issues as well as needs related to the development of point-of-care devices in an iterative fashion, as well as to provide training for scientists in resource-poor settings and education of relevant stakeholders on the development and potential impact of POCT.
6. A subject matter expertise review component emphasizing clinical drivers of technology progression for introducing new or expanding existing point-of-care STD technologies, through design assistance (study, instrument, assay) and operational feedback iterated to permit spiral development and allow for project off ramps in a “go no-go” manner, such that we insure that deliverables for each project are met.

Center resources include:

1. Diagnostic expertise and advice for developers of POCT for STDs, including guidance and the ability to provide clinical de-identified specimens in limited numbers to new developers.
2. The ability to advertise solicitations for funding opportunities in the form of small grants for the development of POCT for STDs.
3. Conducting and providing needs assessments with clinicians and patients and follow-up training for indus-

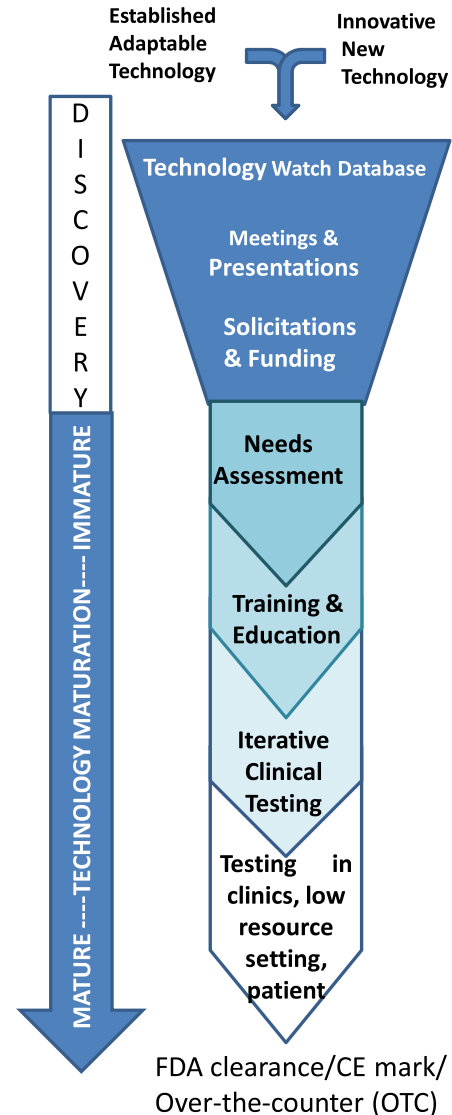


FIGURE 4. Center pipeline.

try for the sage development of POCT for STDs that can be accurate, timely, and simple.

4. A laboratory facility to beta test point-of-care assays, using our archived de-identified clinical samples.
5. The capacity to assist clinical sites in the collection and testing of preclinical trial assays in an early stage of maturity to guide their further refinement.
6. Access to testing sites in places outside the clinic, such as the Internet, the emergency department, and foreign countries.

B. CENTER SUCCESSES TO DATE

1. Emergency Department- We have conducted studies in busy high-volume emergency department (ED) settings to evaluate performance and feasibility of integrating FDA-approved POCT for STDs into clinical practice, with a focus on patient self-testing and use of tablet-

based kiosks. We developed and optimized a kiosk-based platform for obtaining consent for HIV testing in the ED, and integrated that method into practice. We evaluated an FDA-cleared point-of-care test for *Trichomonas vaginalis* (TV), demonstrating high level of patient and provider acceptability of self-testing with tablet-guided facilitation, and showed excellent performance of the assay and high level of patient and provider concordance (98%), wherein the patient self-collected the vaginal sample, processed the sample following kiosk directions, and interpreted their own results.

2. Needs Assessments Component- Although development of POCT has been evolving for decades, the belief of “if you build it, they will use it” has been a critical barrier to the commercialization and adoption of these technologies. We have conducted key informant interviews, focus group sessions among practitioners specializing in STD diagnosis and testing, STD POCT researchers, laboratorians and developers, and patient end-users to determine what an ideal POCT would look like with regard to setting, user requirements, device performance (sensitivity and specificity), and device usability in terms of complexity and time requirement [28]–[30]. We have extended our needs to Adolescent Medicine clinicians, OB-GYNs, HIV providers, and primary care clinicians practicing in FQHCs who are required by the new Affordable Care Act to provide STD screening, diagnosis and treatment services.
3. Training Component- While new technologies have been moving laboratory science into ever more exciting and amazing methods of disease detection, these new technologies still require a high level of laboratory skill and expensive equipment and reagents. Our Training Component is embedded in the STD/HIV Prevention Training Center at Johns Hopkins University (JHU). The training center has endeavored to educate STD point-of-care technology stakeholders about issues associated with developing diagnostics that will be practical, affordable, cost-effective, and still profitable to the developers [31].
4. Development of POCT within the Center
 - A. At the Baltimore Campus of the University of Maryland, the Center project with Professor Chris D. Geddes is developing low cost, ultra rapid, sensitive assays for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, to test them clinically, and then to commercialize the technology using the Microwave Accelerated Metal Enhanced Technology (MAMEF) [32].
 - B. At Johns Hopkins Whitaker School of Engineering, a team led by Professor Tza-Huei Wang and his JHU BioMEMS Group is developing a microfluidic device for delivering a low-cost and mobile nucleic acid amplification test (NAAT) for STD detection. Dr. Dong Jin Shin and colleagues developed a bioanalytic platform based on the principles of droplet magnetofluidics for

the detection of *Chlamydia trachomatis* with performances comparable to standard-of-care NAAT tests.

- C. Collaboration with the Cincinnati Children’s site provides access to a population of adolescent patients seeking primary, urgent, and emergency care at a large, urban, tertiary care academic medical center. They have demonstrated the acceptability and effectiveness of self-testing for STDs among women using a point-of-care STD test; the benefits of women learning their STD results at the time of testing; and the acceptability of self-collected vaginal swabs from women for STDs, which allows women greater access to self-testing [33]. We demonstrated that using privacy shelters, as well as use of a health van is an acceptable setting to men and women to collect genital samples for STD testing. POC testing resulted in improved antibiotic stewardship.
5. STD testing outside the Clinic via Internet Recruitment [34]
 - A. We have successfully translated our internet recruitment STD screening program called IWTK into public health practice, which allows a participant to collect a sample at home and mail it to the Center laboratory for testing with modernization of the site to be HIPAA compliant and results accessed through a secure login with password protection so that the participant can obtain his/her results in a secure manner online [35].
 - B. Trichomonas Home POC Test. Our website developers revised the IWTK site to allow female participants to access a link to the home test research study for trichomonas (TV). A questionnaire assessed acceptability and experience of the process for women participants. The accuracy of the home test was compared to the gold-standard mail-in molecular test for TV. One of the key findings was that over 80% of the participants would test themselves at home for TV if the rapid TV test were available over-the-counter.
 - C. HIV Home POC Test- A new study has begun to increase HIV screening in adolescents, women and men with health inequity, in Blacks, and especially in men who have sex with men (MSM), by promoting direct outreach to persons through the Internet and smart phones by a) the ability to order a self HIV test for performance at home and b) providing a coupon on the IWTK website for a free HIV test at participating clinics, based on participant zip code.
6. STD Testing in Resource-Limited Settings- Given the significant burden of STDs in sub-Saharan Africa (SSA), we established a site at the Infectious Diseases Institute (IDI) at Makerere University College of Health Sciences in Kampala, Uganda. We have focused our efforts on syphilis detection particularly in pregnant women, who have a prevalence of syphilis from 1 to 8% across SSA [36]. Rapid treponemal

lateral flow assays can be used to diagnose patients at the point-of-care. Both the Trinity and SD Bio-line tests met the WHO standard for accuracy (>85% sensitivity; >95% specificity) against the sequential algorithm. The IDI POC STD site has also screened more than 15,000 pregnant women as part of a clinical trial to improve syphilis partner notification, testing, and treatment (NCT02262390). Asymptomatic STD infections are being measured in HIV-infected key populations.

Finally, the technology exploration component (Filling the Development Pipeline and Integration and Facilitation of Technology Development) works to seek out novel technologies and encourage their interaction with the Center [37]. Up to three sub awards at \$50,000 each are awarded per year from this component through open solicitations. Targeted funding is provided to organizations developing POCT. The purpose of these tactical awards is to support key studies which will help them win larger awards toward commercial development of POCT.

V. CONCLUSIONS

Solving many of today's unmet medical needs requires new models for successfully transforming healthcare. The Point-of-Care Technologies Research Network represents a new partnership-based model that supports and facilitates collaborations across disciplines, institutions, and geographic regions to successfully drive innovative solutions from concept to patient care. The three Centers within the Network focus on commercially viable, point-of-care solutions for improving primary health care, the diagnosis and treatment of cancer, and the diagnosis of sexually transmitted diseases. As a Network, Centers provide resources to both technology development and clinical communities and coordinate activities with other Centers. In this way, expertise, Core resources, project support, and educational events are shared across Centers, a process that is facilitated by frequent communication among Center directors and program managers as well as the development of common policies and procedures across Centers.

Built on the success of this NIBIB initiative, future trans-NIH activities that focus on the advancement of multiplexed and multi-use POCT will serve to enhance multidisciplinary partnerships and Center-Center synergies while supporting further development of integrated systems to address unmet health care needs.

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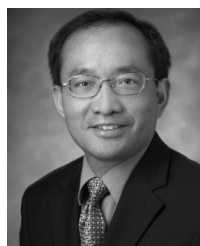


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CHRIS D. GEDDES is a Tenured Professor with the University of Maryland Baltimore County and the Head of the Institute of Fluorescence founded by Dr. Geddes in 2001. With an array of internationally known scientists as members, the Institute of Fluorescence boasts hundreds of person-years of fluorescence experience.

He has extensive experience in fluorescence spectroscopy, particularly in fluorescence sensing and metal-fluorophore interactions, publishing over 250 peer-reviewed papers (has an h-index of 40), and 30 books. He is internationally known in fluorescence and plasmonics and his laboratory is widely credited with the development of the metal-enhanced fluorescence and related plasmon-fluorescence technologies, securing in excess of U.S. \$25 million in recent years to pursue his research aspirations. He is the Editor-in-Chief of the *Journal of Fluorescence* and the Founding Editor-in-Chief of *Who's Who in Fluorescence*, *Annual Reviews in Fluorescence*, and *Annual Reviews in Plasmonics* volumes. In addition, due to the labs' pioneering efforts in the fields of metallic nanoparticle-fluorophore interactions, he launched a *Plasmonics* (Springer) in 2005, which is a leading journal in the field today. He was a Permanent Member of the NIH's EBIT R01 Study Section (2007-2012) and chaired the NIH's Analytical and BioAnalytical SBIR Study Section from 2004 to 2009. He is a fellow of both the Royal Society of Chemistry and the Institute of Physics. He holds over 100 patents in the fields of fluorescence and plasmonics.

Dr. Geddes' research group has developed a platform technology for the ultrafast and ultrasensitive detection of clinical analytes. The new technology combines the use of Metal-Enhanced Fluorescence (MEF) to amplify fluorescence signatures up to a million fold, with the use of low power microwaves. The resultant technology, Microwave-Accelerated Metal-Enhanced Fluorescence (MAMEF), when applied to antigen, antibody or protein detection, can be applied to STD identification without the need for time consuming laboratory processing and amplification, such as by real-time PCR. He utilizes his MAMEF technology with the Hopkins POC STD Center.



LEA WIDDICE is an Assistant Professor of Pediatrics at the Cincinnati Children's Hospital Medical Center and the University of Cincinnati College of Medicine. Her research interests include adolescent reproductive health and sexually transmitted infections. She completed medical school at the University of Washington, Seattle, her pediatrics training at the Floating Hospital for Children, Tufts Medical Center, and her adolescent medicine fellowship at the University of California

at San Francisco. Upon completion of fellowship, she joined as a faculty member at the Cincinnati Children's Hospital Medical Center, Division of Adolescent Medicine. Her current research efforts focus on human papillomavirus epidemiology and HPV vaccination immunogenicity and delivery.

Before attending medical school, she worked in the biotechnology industry in the manufacturing and research and development of both point-of-care and ELISA diagnostic tests. For this grant, she conducts studies of self-administered vaginal and male swab collection and testing for sexually transmitted infections using point-of-care test devices in clinical settings involving adolescent men and women. In addition, she assists co-investigators in needs assessment for sexually transmitted infection diagnostic tests and in developing a reliable scoring system for point-of-care test devices.



JOANY JACKMAN received the B.A. degree in American studies from Brandeis University, the B.S. degree in biological sciences from the University of Connecticut, and the Ph.D. degree from the Program in Cell and Molecular Biology, University of Vermont.

Dr. Jackman began working in the area of infectious diseases with the U.S. Army Medical Research Institute of Infectious Diseases in 1997. The focus of this work was to develop

novel methods of rapid pathogen identification and diagnosis of infection using mass spectrometry and microarray methodologies. She joined the Johns Hopkins University Applied Physics Laboratory in 2000, where she has continued her work in rapid pathogen identification and advises in biocontainment facility design and operations. In 2003, she received the Christopher Columbus Homeland Security Award in the area of emergency response.

Dr. Jackman is developing methods to analyze breath for novel markers of infection. This technology uses proteins and lipids secreted by the host in response to pathogens in the lungs to detect signs of infection prior to the appearance of symptoms. The technique is non-invasive and rapid. Analysis is carried out using mass spectrometry of exhaled breath. Both the pattern of secreted proteins and the chronology of their production are used to identify infected individuals prior to the appearance of signs and symptoms. In 2005, she received the Invention of the Year from the Johns Hopkins University Applied Physics Laboratory for her work in breath diagnostics.

During the past eight years, she has participated in technology reviews with the Department of Defense such as Joint Program Executive Office and other military agencies and conducted technology reviews and testing for DARPA. She is a Sigma Xi Distinguished Lecturer where she provides presentations on agroterrorism, biothreat detection, breath as a diagnostic, and the history of bioterrorism. In addition, she has been an active member of the Maryland Fire Rescue Service in the Washington area and is certified to the level of EMT-B and Firefighter II.



RISHI A. MATHURA serves as the Scientific Program Specialist with the National Institute of Biomedical Imaging and Bioengineering.



TIFFANI BAILEY LASH serves as a Program Director/Health Scientist Administrator with the National Institutes of Health. She manages the research portfolios for the Biosensors, Platform Technologies, and mHealth programs with the National Institute of Biomedical Imaging and Bioengineering (NIBIB). She is also the Program Director of the NIBIB Point of Care Technologies Research Network, consisting of three centers charged with developing point-of-care diagnostic

technologies through collaborative efforts that merge scientific and technological capabilities with clinical need.

She received the Ph.D. degree in physical chemistry from North Carolina State University via a collaboration between the Department of Chemistry and the Department of Chemical and Biomolecular Engineering. Prior to her current position, she worked within the NIH's science policy administration. During that time, she worked at the National Institute of General Medical Sciences and the National Heart Lung and Blood Institute, as well as the NIH Office of the Director. She has been selected as a Science Policy Fellow for both the American Association for the Advancement of Science and the National Academy of Engineering. She also has a background in small business innovation and intellectual property. Her interdisciplinary research interests include microfluidics, biopolymers with controlled molecular architecture, and biosensor technologies.