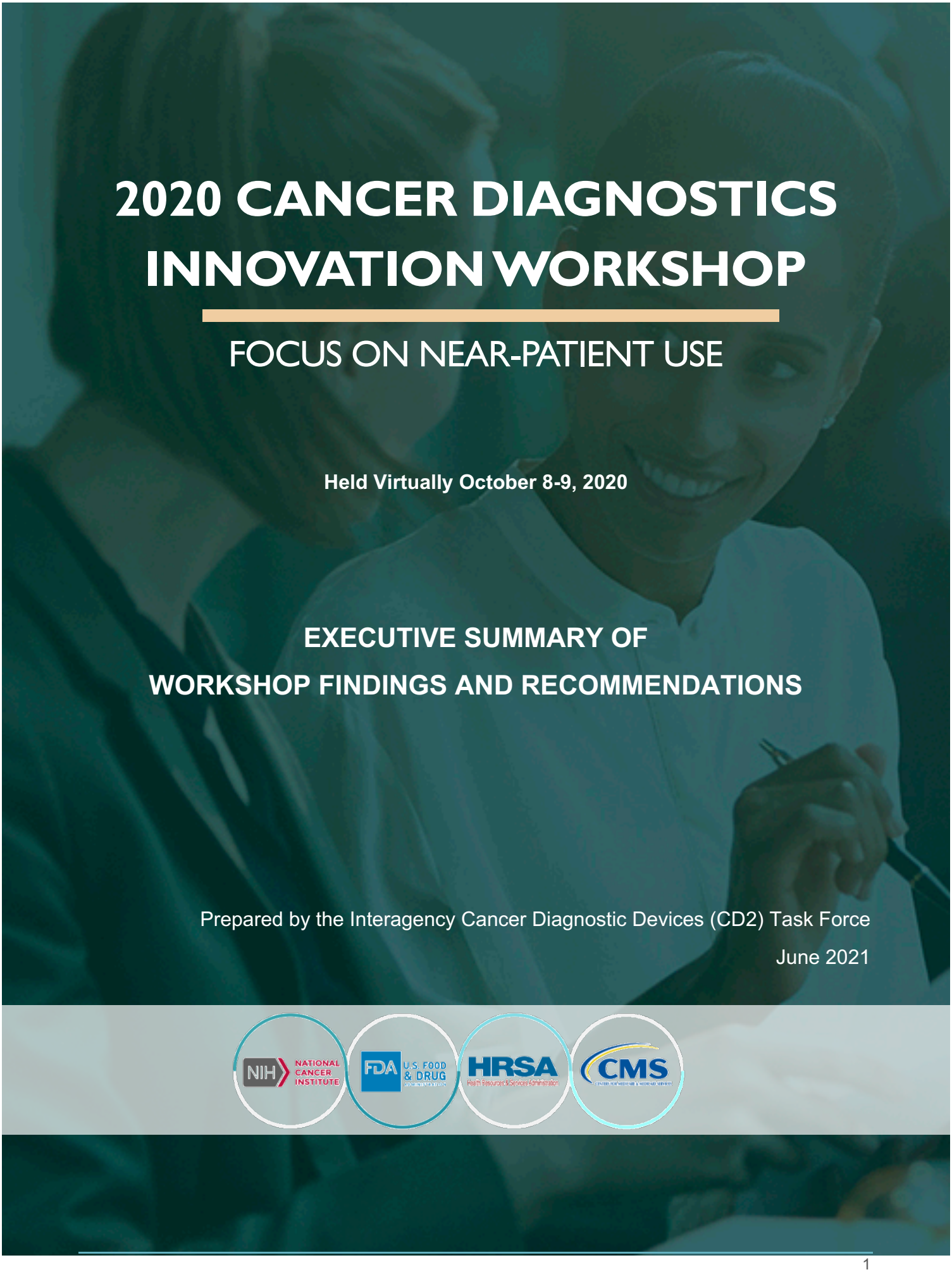

2020 CANCER DIAGNOSTICS INNOVATION WORKSHOP

FOCUS ON NEAR-PATIENT USE

Held Virtually October 8-9, 2020

EXECUTIVE SUMMARY OF WORKSHOP FINDINGS AND RECOMMENDATIONS

Prepared by the Interagency Cancer Diagnostic Devices (CD2) Task Force

June 2021

EXECUTIVE SUMMARY

BRIEF BACKGROUND AND WORKSHOP DESCRIPTION

The National Cancer Institute (NCI), Food and Drug Administration (FDA), Health Resources and Services Administration (HRSA), and Centers for Medicare & Medicaid Services (CMS) partnered in late 2019 to establish the **Interagency Cancer Diagnostic Devices (CD2) Task Force for Near-Patient Use.** For clarity and context, near-patient diagnostics generally refers to a system whereby a sample is analyzed, and the results are delivered in the same location and while the patient is being evaluated. Near-patient diagnostics are often offered at point-of-care (POC) settings (e.g., clinics, pharmacies, homes) where at-home tests may be available with a prescription or purchased over-the-counter (OTC). CD2 is a collaborative effort among four federal partners working together within and across their respective missions to bring more solutions to:

- Detect and diagnose cancer earlier;
- Enhance identification of patients at high risk of developing cancer and surveillance of those at risk of cancer recurrence;
- Improve monitoring of patient response during cancer treatment; and
- Reduce the effect of health disparities and equitably extend the benefits of health care to all populations.

On October 8 - 9, 2020, the CD2 Task Force convened leaders from the public and private sector in a virtual workshop to begin a dialogue on cancer diagnostics for near-patient use (hereafter referred to as the “2020 Cancer Diagnostics Innovation Workshop”). The goal of the 2020 Cancer Diagnostics Innovation Workshop was to identify gaps and opportunities in cancer diagnostics, with a focus on facilitating innovation in cancer screening, surveillance, and early detection for near-patient use with a particular emphasis on addressing critical and unmet needs among geographically isolated, medically underserved, and otherwise vulnerable communities. This is in alignment with the CD2 Task Force goal to lessen cancer disparities by reaching all eligible patients using near-patient screening and diagnostic tools. Given the backdrop of the COVID-19 pandemic that began during the workshop planning period, additional focus was centered on potential testing solutions for OTC and/or at-home tests requiring prescriptions.

More than 70 representatives from academia, industry, and federal agencies (NCI, FDA, HRSA, CMS, Centers for Disease Control and Prevention [CDC], and the National Institute for Standards and Technology [NIST]) participated in the two-day workshop. Throughout the

presentations and interactive breakout discussion groups, participants were asked to identify barriers, challenges, and opportunities related to cancer diagnostics for near-patient use.

Highlights from the workshop included:

- Remarks from NCI, FDA, HRSA, and CMS senior leadership;
- An overview of the state of the science in cervical, bladder, and liver cancer and relevant near-patient testing opportunities;
- An overview of the regulatory framework for cancer diagnostic technologies, including case studies of near-patient diagnostic development and implementation (with examples of colorectal and cervical cancer); and
- Discussion of emergent diagnostic fields, including (but not limited to) liquid biopsies.

This Executive Summary, developed by the members of the CD2 Task Force, provides details of the key issues discussed at the workshop, evaluates the current status of near-patient diagnostics, examines the need for near-patient diagnostics development, and recommends implementation strategies across exemplar cancer types**. Following the challenges and opportunities outlined below, five overarching recommendations and related next steps (a priority list of tasks) are offered for further collaboration among federal and non-federal stakeholder groups. The summary is provided to inform senior leadership at each federal partner agency about important areas that warrant further investment.** A full report of the 2020 Cancer Diagnostics Innovation Workshop is included as an Appendix.

CHALLENGES AND OPPORTUNITIES

Challenge: Higher rates of cancer are found in geographically isolated, medically underserved, and otherwise vulnerable populations, with higher incidence among those who have never been screened or have not been screened in the previous five years. Elevated cancer burden among these populations may be due, in part, to a limited understanding of individual, structural and systemic barriers to care, limited patient access to care and follow-up, individuals' lack of trust in the healthcare system, and the prohibitive cost of healthcare services.

Opportunities:

- Community outreach efforts addressing social needs of patients, including interactions with trusted community health workers (CHWs) and regular community dialogue to increase awareness of near-patient diagnostic tests (e.g., usability, utility, availability) should be a continual part of building support for POC, OTC, and/or at-home tests with prescriptions and patient-centered follow-up care.
- Telehealth-supported modalities, including secure audio, video, and chat communication options, provide opportunities to support bi-directional patient-provider interactions and facilitate cancer screening, testing, and follow-up, as needed. Moreover, technologies that could give objective patient data before, during, and after telehealth visits can bolster shared decision-making between patients and their providers.
- Self-collected, diagnostic sampling devices that are easy to use could enable cancer screenings/tests for some patients who face geographic or other access-to-care barriers. Primary cancer screening test samples using self-collection devices submitted by mail – such as for self-sampling of cervical cells for cytology and human papillomavirus (HPV) testing – are examples of such sampling approaches that were discussed and might be considered for implementation. Leveraging community sites where blood draws and/or bodily fluid (e.g., urine, saliva) collection can be performed (e.g., health clinics, pharmacies) could also be effective. Such testing could be for screening and for ongoing care, such as monitoring patients during treatment (e.g., liquid biopsy).
- Understanding the usability of diagnostic products in a near-patient setting requires a thoughtful understanding of the inter-related patient, provider, and healthcare system context. Importantly, there should be early engagement of clinician and patient

communities in determining the need for diagnostic development and subsequent implementation.

Challenge: Screening and early near-patient testing for HPV have had a positive impact on cervical cancer detection. However, there are other cancer types where screening and early detection are still challenging. For instance, hepatocellular carcinoma (HCC) represents the fastest rising cause of cancer-related death in the U.S, despite the availability of several emerging therapeutic options as well as known risk factors such as a cirrhosis and chronic hepatitis from viral infection. HCC remains difficult to manage in part due to the late stage at which it is detected and the increasing prevalence of non-alcoholic steatohepatitis in the United States. Bladder cancer is easily treatable when it has not yet transitioned into the muscle tissue (i.e., non-muscle invasive). Recurrence rates after first detection and treatment of the non-muscle invasive phenotype are high, with absolute number of cases having increased more than 50% in the last 20 years. There has also been a subsequent increase in deaths from the muscle-invasive phenotype.

Opportunities:

- There is an urgent need for tests capable of detecting HCC earlier. Further, better performing assays for monitoring and more granular stratification of patients with non-alcoholic fatty liver disease, nonalcoholic steatohepatitis (NASH), and cirrhosis would benefit the broader national strategy towards reducing the incidence and impact of HCC.
- Assays that enable early detection and offer alternative noninvasive methods for frequent surveillance of bladder cancer are critically needed. There are novel urine-based biomarkers under development, which – if proven successful – could offer an opportunity to explore an OTC option for such testing.

Challenge: Bringing a diagnostic test to the market for POC, OTC, and/or at-home tests with prescriptions can be a complex endeavor; these tests require a manufacturer to design and develop the technology to meet the needs of the near-patient setting. This process also includes considerable technical, regulatory, financial, and managerial challenges. These challenges must be addressed from the outset and should be systematically assessed during initial development. For example, a developer may have a robust biomarker and the ability to engineer a portable device that could be used to measure that marker. After development of the device, it may be realized that a robust biomarker and portable tool are not of value if they can only be used by highly skilled personnel or only available to those with the financial resources to purchase it. Thus, additional early considerations for developers include ease of use, affordability, and user-friendly ways to transmit data to a healthcare provider.

Opportunities:

- To promote near-patient devices, manufacturers need to better understand and have support for navigating the regulatory process and reimbursement fee structure. Possibilities include a roadmap for developing the evidence needed to support product development, marketing, and adoption. The research community could explore risk mitigation tools that consider the scope of the disease, potential for benefit, how to sustain best practices and, where appropriate, patient preferences, to ensure a net positive effect on patient outcomes. Although there would be additional consideration depending on the specific cancer type, manufacturers of near-patient tests could readily apply this roadmap to their own needs.
- Additional dialogue is needed to address the challenge of lowering both developmental and patients' costs for these tests. In addition, although there may be financial disincentives for developing tests for pediatric cancers, rare malignancies, and aggressive cancers, more attention is needed in these areas.
- It is also important to encourage and participate in creating consensus guidelines by standards developing organizations. This work may include assessment and development of appropriate specifications for accuracy and precision of platforms for specific near-patient uses as well as standardization of data across different platforms. As a result, increased accuracy of the tests would lead to higher confidence across the medical community for the near-patient tests.

A CALL TO ACTION: RECOMMENDATIONS AND NEXT STEPS

The following **recommendations (priority list of tasks)** provide potential ways in which federal partners can move forward with identifying diagnostics and near-patient tests targeted to community needs; accelerating research and development of tests for specific near-patient purposes; initiating training/education that may best apply to the translation or implementation of near-patient diagnostics; and creating pilot funding opportunities to support these activities. Suggestions for the organizations that should lead the initiatives are included, as relevant.

1. **Diagnostic design targeted to community needs.** To address health disparities and health equity, near-patient diagnostic product use requires consideration of patient-centered care, local/community setting resources, and the healthcare system to incorporate information into product design and usability testing. It is important to engage underserved and medically vulnerable communities – and the providers that serve them – throughout the design and implementation process. Ideally, near-patient tests should be easy to use and interpret; appropriate for the intended purpose (e.g., assay performance vs. clinical utility); and affordable.

   Next steps:

   - **Listening sessions/virtual workshops.** HRSA, in collaboration with other CD2 Task Force partners, could host listening sessions/virtual workshops. Patient, provider, and community input could inform POC and OTC prescription device design. Stakeholder input could also inform targeted technical assistance, training, and integration into clinical workflows. Study designs may include early detection and dissemination plans. This information could inform new patient-centered workflow algorithms that integrate POC/OTC with prescription tests and follow-up care, including access to treatment. Experts from CDC would be asked to participate in these activities.

     In addition, NCI should explore the creation of opportunities (e.g., funding opportunities, contract awards) that encourage human-centered design principles and community-engaged research. Support, guidance, and training for studies validating new tests/technologies with subsequent usability testing could be performed. Patients from target populations should be invited to join these studies. Federal partners could identify new – and leverage existing – strategies and collaborations (e.g., the NIH's Citizen Science Initiative, CMS and HRSA outreach efforts) to engage the patient and advocacy community before studies begin.

2. **Emphasize technology development** with specific clinical focus to facilitate development of tests that are clinically accurate in detecting biomarkers known to be highly correlated to disease states. To improve upon cancer-specific biomarker types, additional work is needed on accurate measurement, reliability, and validity.

   Next Steps:

   - **Public-Private Partnership Workshop.** The CD2 Task Force could host a follow-up workshop focused on bridging both biomarker experts and assay developers around a small set of predefined indications with robust markers. The workshop outcomes would address feasible solutions and drive further pilot studies, grant supplements, or contract-based mechanisms for accelerated translation.

   - **Regulatory and Reimbursement Workshop.** The CD2 Task Force could host a follow-up workshop featuring NCI-funded researchers or other developers, government regulatory and insurance representatives, and private payers focused on sharing information on educational resources relevant to obtaining regulatory approval or clearance for near-patient devices, available standards, technical requirements, and coverage and reimbursement of these devices. Such educational resources and guidance documents should also be published with open access for test developers.

3. **Support education and training on the use of near-patient tests with more emphasis on outreach and telehealth activities.** CHWs, patient advocates, and peer educators are needed to bridge the formal and informal healthcare systems, working collaboratively with geographically isolated and medically underserved communities that may have a lack of trust in the healthcare system. In addition, CHW training on post-screening procedures can help patients with follow-up questions and concerns. Furthermore, expanded broadband access and use of telehealth modalities can support shared decision-making and patient-centered communication about options for follow-up referrals.

   Next Steps:

   - **Support Learning.** HRSA, in collaboration with other federal partners, could facilitate learning sessions with its network of telehealth subject matter experts to further define best practices in support of POC/OTC tests to improve cancer-related screening and test outcomes.

   - **Education.** The CD2 Task Force, in collaboration with patient and community groups, other HHS agencies, and their respective Offices of Minority Health, could develop culturally sensitive educational materials and outreach implementation strategies to promote the acceptance and use of near-patient diagnostic devices and tool development.

- **Training.** The CD2 Task Force, in collaboration with other stakeholders, could develop specialized training for implementation and evaluation of the educational materials.
- **Funding Opportunities.** NCI could explore the creation of research funding opportunities to support related activities.

4. **Implement a recommendation roadmap for the scientific, clinical, and patient community.** Creating a web-based roadmap that stakeholders (e.g., patients, providers, developers) can use to understand/navigate the testing needs of underserved communities and the development process is important. The roadmap could include logistics, diagnostic guidelines, implementation, and other relevant issues as they relate to cancer diagnostic devices for near-patient use, especially in the context of underserved populations.

   Next Steps:

   - **Community Resource/Interactive Website.** NCI, in coordination with the other federal partners, could develop a community resource (interactive website) for research investigators/companies considering potential diagnostic devices or tests. Such a resource/website could provide step-by-step information on relevant issues as they relate to cancer diagnostic devices for near-patient use and links to any relevant documents and existing materials. Technical assistance for cancer diagnostic developers is an important consideration.
   - **Workshops.** The CD2 Task Force could host a follow-up workshop on bridging diagnostic development and community engagement at the onset of both development and testing in a formalized process.

5. **Identify one or two cancer indications for expanding the diagnostic portfolio available to providers/patients.** Several small, targeted funding initiatives could be built out for near-patient test use at home with a prescription or in community-based clinics. Additional targeted funding could address surveillance for survivors of non-invasive bladder cancer, broad scale screening for hepatitis C virus-positive individuals, specific markers of NASH-driven HCC, or other risk assessment strategies. Additional funding could also address methods for expanding the umbrella of recently approved liquid biopsy assays (e.g., robust sample collection tools for methods/assays based on targeted next generation sequencing [NGS]).

   Next Steps:

   - **Exploratory Research Studies.** Pilot research studies from existing NCI-funded grantees, Small Business Innovation Research (SBIR) contract solicitation, and/or Notice of Special Interest connected to later-stage NCI programs (e.g., Academic-Industrial partnerships program, Innovative Molecular Analysis Technologies program,

SBIR and Small Business Technology Transfer programs) could be used to integrate and amplify novel urine biomarkers of bladder cancer phenotypes with readily accessible POC or OTC tests with prescriptions for at-home testing platforms.

- The National Institutes of Health (NIH) Rapid Acceleration of Diagnostics (RADx) initiative provided a replicable model of how to bring POC and OTC testing rapidly to market (i.e., from bench to bedside). To date, almost 20 diagnostic products (and an additional 12 in the pipeline) have come from the projects funded by this program (some had prior EUAs and some were directly obtained due to the RADx support). Further, the program has put 125 million COVID-19 tests onto the market since April 2020 and spurred development of a myriad of new technologies. These include handheld polymerase chain reaction devices, loop-mediated amplification tests, paper-based diagnostics, rapid lateral flow assay antigen tests, smartphone readers, NGS, and machine-learning-assisted diagnostics. The program stayed within the boundaries of NIH policy and federal regulation for research and development acquisitions while simultaneously moving these products forward within months. While diagnostics for cancer may not have the same urgency compared to a pandemic, certain aspects of the program could be applied for cancer diagnostics development including the following:
    - Rapid but comprehensive review process;
    - Milestone-based project management approach with fail-fast model;
    - Analytical and clinical validation and testing clinical utility in POC or at-home setting; and
    - Guidance for regulatory approval support for scale-up manufacturing, commercialization, and implementation.

  The infrastructure built for the RADx initiative remains in place. Further, lessons have been learned relating to the process, but also for refining it moving forward for other initiatives. This could be modeled to translate a suite of early/mid-stage cancer testing platforms for near-patient use, albeit in a smaller, more resource-targeted form.

- **Standards.** More efficient transfer of new near-patient use tests into patient care requires that greater standardization of measurement methods and data management be established. The CD2 Task Force could identify and lead coordinating activities among standards organizations (such as the Clinical and Laboratory Standards Institute and NIST) and the public/private sector. This effort would ensure that all stakeholders involved are performing and interpreting test/diagnostic results consistently and accurately. Setting standards for accuracy is critical for all tests, but false positives and false negatives have particularly serious consequences with cancer tests. Areas of importance for quality assurance, reliability, and reproducibility include the standardization of specimen collection, handling, storage, and analysis; evaluation of the analytical and clinical performance of the final diagnostic test; and meeting

regulatory requirements. An opportunity exists for the CD2 Task Force to identify and lead coordinating activities among standards organizations and the public/private sectors.

CONCLUSION

Advances in technology have led to the possible expansion of diagnostic tests and tools designed for use in the homes of patients as part of primary care. Near-patient diagnostics have many advantages, including reduction of total costs, improved patient access to care, and rapid diagnosis. As a result, effective treatment options can be discussed with patients, timely clinical decisions made, and follow-up care coordination can be streamlined.

While progress has been made in the field of near-patient diagnostic testing, the possibility to bring additional tools to more patients is complex. Considerations of cancer type; appropriate biomarkers that can be measured at POC/at home; best practices for communicating with diverse populations; available biomarkers; knowledge of existing healthcare delivery systems, regulation, cost, and coverage; integration of patient-centered design; and many other aspects all contribute to the complexity and challenges of the diagnostic testing process.

The 2020 Cancer Diagnostics Innovation Workshop was a first-of-its-kind effort to identify and define multilevel factors, barriers, and innovative solutions to cancer diagnostics for near-patient use. Workshop participants identified critical gaps and opportunities for moving timely and effective near-patient cancer diagnostics forward in a collaborative manner. Well resourced, coordinated, and collaborative efforts across the federal partners and other key stakeholders will be needed to advance and implement near-patient cancer tests and achieve improved health outcomes for all.