Using the Best Laboratory Science to Advance Public Health:

A Report of the Advisory Committee to the Director, Laboratory Workgroup

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Issue: *CDC laboratories need to use best laboratory science advances to protect public health – advances that often originate in academia, small companies, or major instrument manufacturers. These advances include new instrument platforms, new diagnostic tests, and new laboratory diagnostic technologies. At the same time, CDC should be promoting testing that can be readily performed on commonly available instrument platforms and using diagnostic technologies that are readily available to private and public health partner laboratories.*

Questions: *How can CDC ensure that it stays at the forefront of laboratory technology and laboratory science advances that benefit public health? At the same time, what could CDC do better to promote testing on commonly available instrument platforms and to better use diagnostic technologies that are readily available to private and public health partner laboratories?*

Review

The Laboratory Workgroup (LW) of the Advisory Committee to the Director (ACD) met virtually on Friday September 15, 2023. The LW members heard from two external guests: Dr. Bruce Tromberg, National Institute of Biomedical Imaging and Bioengineering, NIH, and leader of the Rapid Acceleration of Diagnostics (RADx®) Program, and Mr. Rodney Wallace, Director of the Biomedical Advanced Research and Development Authority (BARDA)'s Detection, Diagnostics and Devices Infrastructure Division. The LW also heard from two subject matter experts from CDC: Dr. Ren Salerno, Director, CDC Division of Laboratory Systems and Dr. Duncan MacCannell, Director, CDC Office of Advanced Molecular Detection.

Overview

The LW believes that CDC should take advantage of the scientific and technological expertise available in the external laboratory sector. Actions to address this challenge should occur at the national level, and internally at CDC. At the national level, CDC should assert leadership by convening representatives of all sectors of the laboratory industry, including diagnostic manufacturers, commercial and academic laboratories, and health-related federal agencies, to develop and plan for a coordinated response to biological emergencies. The plan should detail the roles and responsibilities of developing and deploying testing methods for emerging pathogens, using the unique skills and resources of each sector. In parallel, CDC should explore use of communication and contracting processes modeled on those used at other federal agencies to work with a broad range of potential partners, including academic experts and industry, in responding to the health needs of the nation. The Laboratory Workgroup understands that implementing these recommendations will require policy changes at the level of the Department of Health and Human Services, as well as the appropriation of funds to support the activities.

Current situation: The CDC does not take full advantage of the scientific expertise and technological advances available outside government.

Here are three examples of opportunities to improve partnerships with the private sector:

Example 1: **Use of outdated tests**. During the mpox outbreak of 2022, public health laboratories within the Laboratory Response Network (LRN) used a molecular test that was developed by CDC in 2002, when the US was concerned about potential use of variola virus as a bioterror weapon. The PCR test detected non-variola orthopoxviruses, including monkeypox virus, but had not been adapted to contemporary specimen collection devices, automated nucleic acid extraction instruments, nor use on high throughput PCR platforms. These practical limitations severely reduced the number of diagnostic tests that public health laboratories could perform. To address this gap, CDC reached agreement with five commercial laboratories to rapidly adapt the CDC test to the high throughput level needed to detect the virus, and thereby limit the spread of the monkeypox virus. Had the outdated LRN methods been modernized prior to the mpox disease outbreak, the delay to broad availability of testing in the public health system would have been minimized.

Example 2: Poor turnaround time for diagnostic test results. The CDC is the national public health reference laboratory and is expected to maintain diagnostic tests for rare pathogens. Members of the Laboratory Workgroup are aware of reports of long delays in the receipt of results for some rare pathogen tests. Other laboratories have the capability to conduct these tests, but there is no pathway for their engagement in this service.

Example 3. Not keeping up with advances that bring testing closer to the patient. Much of the focus on test development at CDC has been on traditional approaches to testing, i.e., FDA-approved and laboratory developed tests performed in a CLIA-licensed laboratory setting. However, the commercial laboratory industry, because of technological advances, is embracing newer approaches that bring testing closer to the patient. In this approach, the analytical process performed for, or by, a patient is outside of the traditional clinical laboratory using a CLIA-waived or over-the-counter test. Additionally, changes in specimen collection are finding their way into mainstream laboratory testing, including decentralized testing in non-traditional settings, self-collection, and home collection of clinical specimens. Already, public health practices have begun to incorporate these concepts. CDC could be thinking more broadly around ways to incorporate such strategies into the public health response. Commercial laboratories have been exploring and implementing these novel concepts for some time, and the diagnostics industry is making more complex testing available in the Clinical Laboratory Improvement Amendments (CLIA)-waived and near-patient space. The development and implementation of such strategies could be supported by insights from commercial laboratories and in-vitro device manufacturers, broadening approaches to emergency laboratory response. Reporting results of notifiable conditions to appropriate public health authorities from these non-traditional testing venues will need to be addressed.

What are the challenges to enhancing public-private partnerships at CDC?

CDC Engagement Practices. CDC employees told the LW that they generally engage private companies through formal processes such as published requests for information (RFIs). The process may be complex, lengthy, and onerous, limiting the more spontaneous, partner-driven collaborative approach

that enhances productivity in the private and academic sectors. By contrast, other US Government programs, such as RADx, BARDA, and the Department of Energy, have processes that permit rapid engagement of experts from inside and outside industry without compromising the integrity of procurement.

Inadequate resources to support continuing scientific advancement at CDC: The LRN, which consists of about 130 government-run laboratories, depends on sufficient, sustained, and uninterrupted funding to maintain even baseline capability for institutions within the network. Currently, there are no advanced hospital, or commercial laboratories which, as members of the LRN, could infuse new capabilities into the network. Scientific advances in the LRN are therefore dependent on the lead member (CDC) having the will, expertise, and financial resources to continually incorporate scientific progress. CDC has not been able to do this in recent years, even though there has been an increase in the frequency of biological threats.

Cultural norms: Private industry has a profit-motive and may only invest in new products or services where there is an expected financial return, or added customer value. At the same time, the motive to increase the client-base in private laboratories can also drive improvements in service, including non-burdensome processes for sample submission and appropriate turnaround times for test results that support patient care and outbreak recognition alike. CDC officials understandably want to avoid the perception that the government is favoring one company or technology over another without adequate justification and an appropriate process.

Are there pre-existing models of public-private partnerships that CDC could adopt?

There are at least three examples where federal government agencies have developed relationships with private industry with the aim of supporting scientific advances to benefit public health.

National Institutes of Health (NIH)-RADx®: The NIH launched the RADx® initiative to speed innovation in the development, commercialization, and implementation of technologies for COVID-19 testing. The RADx initiative was a national call for scientists and organizations to bring their innovative ideas for new COVID-19 testing approaches and strategies. Funded projects included new applications of existing technologies that make tests easier to use, easier to access, and more accurate. Beyond the pandemic, RADx has also provided funding to accelerate validation, regulatory authorization, and commercialization of innovative point-of-care (POC) tests for hepatitis C virus RNA (HCV RNA) detection and quantitation, as well as tests for mpox. Through RADx, NIH employees engage with private industry more effectively and rapidly than through standard processes. Other NIH groups, such as the Antibacterial Resistance Leadership Group, also regularly work with private industry.
https://arlg.org/
https://www.nih.gov/research-training/medical-research-initiatives/radx/radx-programs and
https://www.nibib.nih.gov/covid-19/radx-tech-program/ITAP

BARDA: BARDA, like CDC, is an agency of the U.S. Department of Health and Human Services (HHS). Its mission is to prepare for and respond to public health emergencies, protecting the public against pandemic influenza, emerging infectious diseases, and chemical, biological, radiological, and nuclear accidents and threats. BARDA acts as a bridge between the Federal Government and the biomedical

industry, working to promote and advance the research and the development of various drugs, therapies, vaccines, tests, and diagnostic tools and medical devices necessary to respond to a pandemic or epidemic. BARDA is a component of the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) and has processes that permit engagement of experts inside and outside industry while maintaining the independence of its procurement processes. https://www.excedr.com/blog/barda-funding-guide.

Department of Energy (DoE): DoE operates multiple laboratories and facilities that conduct technology transfer through partnerships with industry, universities, and non-profit organizations. One example is the Strategic Partnerships Projects. In this initiative DoE national laboratories are available to conduct work for other federal agencies and non-federal customers on a 100% reimbursable basis. This work uses laboratory personnel and facilities, pertains to the mission of the laboratory, does not conflict or interfere with the achievement of DoE program objectives, does not place the laboratory in direct competition with the domestic private sector, and does not create a potential future burden on DoE resources. Justifications for this program include: (1) DoE laboratories represent a national scientific asset and, under appropriate conditions, this resource should be made available to U.S. industry and universities to strengthen their technology base and improve their international competitiveness and (2) research and development (R&D) interactions between DOE laboratories and industry help transfer technology developed by the laboratories, thus aiding the further development and commercialization of laboratory technologies by industry. https://science.osti.gov/lp/Strategic-Partnership-Projects

Here are examples of situations where external partnerships have already advanced CDC's public health mission.

It is important to note that CDC has already developed productive relationships with academia and private industry. Some examples include:

- In 2018, CDC's Division of Laboratory Systems developed a memorandum of understanding (MOU) with several professional societies, the American Clinical Laboratory Association (ACLA), the Association of Public Health Laboratories (APHL), and the Council of State and Territorial Epidemiologists (CSTE), to support surge testing from public health laboratories to commercial laboratories in biological emergencies. In 2022, an expanded MOU with six professional laboratory industry organizations, plus CSTE, CDC and FDA was signed to have broader applications, and to be more encompassing.
- In 2021, CDC's Advanced Molecular Detection program established the SARS-CoV-2 Sequencing for Public Health Emergency Response, Epidemiology and Surveillance (SPHERES) to coordinate SARS-CoV-2 sequencing. The SPHERES collaboration includes scientists from clinical and public health laboratories, academic institutions, and the private sector. https://www.cdc.gov/coronavirus/2019-ncov/variants/spheres.html
- Despite starting with an outdated test, in 2022, the CDC was able to quickly reach agreement with five commercial laboratories to provide high throughput testing for mpox disease by adapting the monkeypox virus assay that the CDC had developed. The agreement, which did not provide funding to support testing, did include a requirement for reporting results to CDC.

- In 2022, CDC funded five Pathogen Genomic Centers of Excellence which are collaborations between U.S. public health agencies and academic institutions. https://www.cdc.gov/amd/whats-new/PGCOE-announcement.html
- The LW was made aware that the CDC, focusing in the area of guideline development, is already working with RADx and an industry partner in a project aimed at Hepatitis C virus elimination.

Here are examples of situations where further development of external partnerships could have advanced CDC's public health mission.

- The CDC's failed COVID-19 diagnostic test development in early 2020 illustrates the risk of having a national single point of failure. In future outbreaks, a decentralized model of test development, including clinical or commercial laboratories would provide redundancy if one laboratory experiences a failure. This approach for shared responsibility for test development was made as Recommendation 8 in the previous LW Report (Review of the Shortcomings of CDC's First COVID-19 Test and Recommendations for the Policies, Practices, and Systems to Mitigate Future Issues) and is included again, here, as it would require CDC developing stronger relationships with both public and private external partners.

- CDC's at-times delayed responses for reference testing of rare or esoteric pathogens raises the question of whether developing a regional public/private network of advanced reference laboratory experts in particular disease areas, e.g., rare tick-borne diseases, would allow CDC to more effectively invest its scarce resources elsewhere. This approach could improve the turn-around time and quality of responses for patients suffering from rare infectious diseases potentially enabling treatment in a time frame that could mitigate morbidity, mortality and/or spread to other people. This approach was made as Recommendation 9 in the previous LW Report and is included again, here, as it would require CDC developing stronger relationships with external partners.

What is the value of a coordinated strategy for laboratory preparedness?

The COVID-19 pandemic clearly indicated that all laboratory sectors played an essential role in providing diagnostic or surveillance testing, and no one sector, acting alone, could support the unprecedented needs. There was, however, confusion on the part of federal and state executive leadership regarding what testing resources were available, what the capacity was and at what stage of the pandemic each sector was best used. Additionally, the laboratory sectors did not coordinate effectively, working mostly independently of each other and sometimes at cross-purposes when competing for supplies. To improve the response to the next biological emergency, there is a critical need to develop, formalize and exercise the concept of a national laboratory system in which all partners understand their roles and responsibilities, and act in a coordinated fashion during biological emergencies.

As the premier public health laboratory, it is both logical and essential that CDC take the lead in organizing the health-related federal agencies and all sectors of the laboratory and diagnostics manufacturing industries to develop a role-based plan for managing the next biological emergency. The first step in developing that plan must be to make building and maintaining external relationships of prime importance to CDC.

Recommendations

1. **CDC should explore the feasibility of developing formal partnerships with other federal scientific agencies to take advantage of their pre-existing relationships with private industry**. Given the current funding climate, it is neither realistic, nor efficient to suggest that CDC duplicate the work of RADx, BARDA or the DoE. Each of these agencies has a different mission and focus, although, in some areas, their missions overlap with that of CDC. However, if CDC can develop a close, role-based, formal partnership with each of these entities, CDC could become an integral part of the evaluation and field deployment process for new technologies that benefit public health. This new relationship could promote advocacy for funding to support evaluation and deployment roles for CDC.

2. **CDC should make working with the private sector an accepted approach to ensuring that CDC stays at the forefront of laboratory technology**. To do this, CDC should investigate and adopt processes in use at other federal agencies that do not interfere with the integrity of government procurement. CDC should also investigate ways to openly collaborate, share information, receive feedback, and incentivize diagnostics development with commercial entities that routinely develop and manufacture tests, including laboratory instruments. Creating a routine and ongoing process for open collaborative development with these commercial partners would ensure that relationships and processes are in place for working to develop, implement, and scale diagnostic technologies when the need becomes urgent (e.g., outbreak of an emerging pathogen). Having on-going interactions will help CDC use diagnostic technologies that are readily available in private and public health partner laboratories. As examples: CDC could offer to provide technical expertise and specimens, or synthetic control material, to selected laboratories when a new pathogen emerges to speed test development; CDC could make industry aware of what the public health needs for testing in specific areas are so that industry can fill these gaps; CDC could offer exchange fellowships for scientists with an industry background to work in assay development at CDC for a period and, vice versa, CDC scientists could work in industry.

3. **CDC should consider making testing for rare or esoteric diseases available in non-CDC public health laboratories and large academic reference laboratories**. CDC should consider issuing a request for information to assess interest from large US clinical reference laboratories in CDC funding a number of regional reference Centers of Excellence in diagnosis of rare infectious diseases. This approach would have advantages of accessing external scientific expertise in test development, reducing the burden on CDC while, at the same time, providing redundancy for access to rare diagnostic tests, improving test submission processes and shortening the turn-

around-time to results. This type of relationship needs to take into account that CDC currently provides free testing; costs must be reasonable and there must be a path for those without means of payment to receive tests for free.

4. **CDC should take the leadership role in convening representatives of all laboratory sectors in the US, as well as leadership from federal agencies with a health and preparedness role. The task of this group would be to develop and exercise a living plan for coordinating the functions of the agencies and laboratory sectors during biological emergencies.** It is critical that CDC cultivate a coordinated, role-based laboratory-response system through facilitated discussion and collaboration with public health, industry, academia, and other partners that span local, state, and federal levels. The new CDC Center for Laboratory Systems and Response is the appropriate leader of this activity.

5. **CDC should consider always including external subject matter experts (SMEs) in the laboratory sciences as members on relevant CDC Advisory Committees and Boards of Scientific Counselors.** These areas of expertise could include clinical diagnostics, commercial laboratories and the diagnostic manufacturing industry. This inclusion could achieve several positive outcomes: (1) availability of expertise on the quality management culture of external clinical and commercial laboratories, (2) partnership building with external SMEs who can help develop and invigorate a collaborative system-based culture at CDC, and (3) promotion of awareness, in the private laboratory community, of public health needs that private industry may be able to contribute to.