U.S. Department of Health and Human Services
National Institutes of Health
Office of AIDS Research

Office of AIDS Research Advisory Council
Fifty-Sixth Meeting

February 25, 2021
Virtual
https://videocast.nih.gov/watch=41378

Meeting Minutes

Council Members Present: Dr. Jennifer Kates (Chair), CAPT Mary Glenshaw (Executive Secretary), Dr. Maureen M. Goodenow (Director, Office of AIDS Research), Dr. Tabia K. Henry Akintobi, Dr. Ingrid V. Bassett, Dr. Margaret L. Brandeau, Dr. Tricia H. Burdo, Dr. John J. Chin, Dr. Kathleen L. Collins, Dr. Heidi M. Crane, Ms. Lynda M. Dee, Dr. Veronica Miller, Dr. William G. Powderly, Dr. Ricardo A. Rivero, Dr. Jonah B. Sacha, Dr. Kimberly K. Scarsi, Dr. Bruce R. Schackman, Dr. John W. Sleasman, Dr. Babafemi Taiwo, Dr. Blanton S. Tolbert

***Ex Officio* Members Present:** LTC Julie Ake, Dr. Victoria Davey, Dr. Carl W. Dieffenbach, Dr. Rohan Hazra, RADM Jonathan Mermin

Advisory Council Representatives Present: Dr. Francis Ali-Osman, Dr. Richard E. Chaisson, Dr. Carlos del Rio, Dr. Alan Greenberg

Office of AIDS Research Leadership, Invited Speakers, and Guests Present:
Dr. Christopher P. Austin, Dr. Geetanjali Bansal, Dr. Elisabet Caler, Dr. Nahida Chakhtoura, Dr. J. Rafael Gorospé, RADM Timothy Holtz, Dr. Henry Masur, Dr. Alice Pau, Dr. Bruce Tromberg

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Welcome and Introductions

CAPT Mary Glenshaw, Ph.D., M.P.H., Office of AIDS Research, National Institutes of Health
Jennifer Kates, Ph.D., M.A., M.P.A., Kaiser Family Foundation

Dr. Jennifer Kates welcomed participants to the fifty-sixth meeting of the National Institutes of Health (NIH) Office of AIDS Research Advisory Council (OARAC). A quorum was present. Meeting materials provided to Council members included the agenda, a conflict-of-interest form, and minutes from the fifty-fifth OARAC meeting, held on October 29, 2020.

A motion to accept the minutes of the fifty-fifth OARAC meeting was approved unanimously.

Dr. Kates reviewed the fifty-sixth meeting agenda, noting the inclusion of time for public comments.

Report from the Office of AIDS Research (OAR) Director

Maureen M. Goodenow, Ph.D., OAR, NIH

Dr. Maureen M. Goodenow welcomed attendees and pointed out that OAR and most NIH employees had been teleworking for almost 1 year. She expressed cautious optimism about the trajectory of the COVID-19 pandemic given progress made and recent vaccine distribution efforts but noted that meetings of NIH advisory councils and scientific review panels will be held virtually through at least summer 2021.

Dr. Goodenow memorialized two HIV scientists who had passed away recently, Drs. Catherine Wilfert and John Bartlett. She provided the following updates regarding OARAC membership:

- Terms ending: Dr. Jen Kates, OARAC Chair; three voting members: Drs. Ingrid Bassett, John Chin, and William Powderly; three advisory council representatives—Drs. Richard Chaisson, Alan Greenberg, and Yuan Chang;

- New members: Dr. Francis Ali-Osman, OAR representative from the National Cancer Advisory Board and Dr. Rohan Hazra, *ex officio* member of OARAC; and

- New role: Dr. Blanton Tolbert, acting OARAC chair.

Dr. Goodenow thanked those whose terms were ending and welcomed the new group of advisors. She then commended CAPT Mary Glenshaw, who recently was awarded the U.S. Public Health Service Meritorious Service Medal for her exceptional leadership in working with PEPFAR in sub-Saharan Africa from 2008 to 2019.

In the new Presidential administration, Dr. Francis Collins will continue as the NIH Director; former OARAC member and OARAC Chair Dr. Rochelle Walensky was appointed Director of the Centers for Disease Control and Prevention (CDC). At the time of the meeting, the Senate confirmation process was underway for Dr. Xavier Becerra, nominee for Secretary of the U.S. Department of Health and Human Services (HHS); Dr. Rachel Levine, nominee for Assistant Secretary of Health; and Dr. Vivek Murthy, nominee for U.S. Surgeon General. New leadership among key congressional committees that affect NIH policy includes Senator Patty Murray (D-WA) as the chair of the Senate Committee on Health, Education, Labor and Pensions and the Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies; Representative Rosa DeLauro (D-CT), the chair of the House Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies; and Representative Anna Eshoo (D-CA), the chair of the House Energy Subcommittee on Health.

On January 15, 2021 HHS released the third consecutive 5-year *HIV National Strategic Plan for the United States: A Roadmap to End the Epidemic.* This strategy focuses on four primary goals to end HIV in the United States by 2030; sets indicators to monitor progress, including one related to reducing HIV-related disparities; and builds on HHS collaborations with local, state, federal, and community partners. The 5-year period aligns with the time frame for the NIH's 2021–2025 *Strategic Plan for HIV and HIV-Related Research*, developed by OAR. The National Plan and the NIH Plan both focus on improving outcomes for people with HIV or at risk for HIV acquisition across the lifespan; strengthening dissemination, implementation, and messaging about HIV and HIV research to diverse stakeholders; and increasing capacity and infrastructure for HIV research, prevention, and services.

The National Plan is aligned with the goals and priorities of the *Ending the HIV Epidemic: A Plan for America* (EHE) Initiative, which aims to reduce HIV incidence by 90 percent by the year 2030. At a recent meeting of the NIH EHE Working Group hosted by OAR with representatives from additional Institutes, Centers, and Offices (ICOs), attendees agreed that the next phases of the EHE initiative should expand beyond the initial 57 jurisdictions to increase diversity, capacity, and partnerships with additional unrepresented communities; stimulate more innovative, collaborative, and strategic research; and leverage opportunities, networks, infrastructure, and funding resources. This expansion will require innovation and accelerated action through partnerships at multiple levels. In the upcoming weeks, OAR will build on this momentum by welcoming Mr. Harold Philips, the senior HIV advisor at the HHS Office of Infectious Disease and HIV/AIDS Policy and chief operating officer for the EHE Initiative, to the NIH AIDS Executive Committee in March; and by participating in the national EHE meeting in April, which will include a presentation by Dr. Goodenow.

Dr. Goodenow reported on recent HIV research advances. In May 2020, findings from the HIV Prevention Trials Network (HPTN) 083 study were released showing that long-acting injectable cabotegravir is highly effective for the prevention of HIV infection in cisgender men and transgender women who have sex with men. In November 2020, results from HPTN 084, a companion study in cisgender women, showed that cabotegravir is safe and superior to daily oral pre-exposure prophylaxis (PrEP) for preventing HIV acquisition. This research expands options for women around the world to reduce their risk for HIV. HPTN 084 exemplifies the expanded inclusion of women in health research as required by the 21st Century Cures Act, because the clinical research community now knows that efficacy in men does not always translate into efficacy for women or transgender persons. Dr. Goodenow noted that on January 21, the U.S. Food and Drug Administration (FDA) approved Cabenuva, an injectable formulation of cabotegravir and rilpivirine, as a complete regimen administered once a month for the treatment of HIV-1 infection in adults.

Results from two antibody-mediated prevention (AMP) trials were reported in late January at the HIV Research for Prevention (HIVR4P) conference. The AMP trials were large international studies with harmonized protocols for cisgender men and transgender persons who have sex with men and for women. The goal was to examine the safety and efficacy of a manufactured antibody against HIV to protect against HIV acquisition. Results from these studies support the concept that antibodies can be used to prevent HIV acquisition by viruses sensitive to the antibody; however, Dr. Goodenow cautioned these are only the first steps toward developing a new option for PrEP. Current work in this area is focused on the development of more potent antibodies that can be used in combination to increase protection, but additional research is needed in this area.

Dr. Goodenow commented that the NIH HIV funding budget for FY 2021 is $3.09 billion, which is almost $14 million more than FY 2020. Direct NIH HIV funding has increased by $95 million since FY 2018. Dr. Goodenow noted the distribution of resources based on priority areas in FY 2020. Increases since 2018 were allocated to focus on research for vaccines; HIV comorbid neurological and cardiovascular conditions; support for early-stage investigators (ESIs); and EHE projects, diagnostic technologies, research capacity-building through the Research Centers for Minority Institutions (RCMI), and Institutional Development Award (IDeA) programs.

OAR organized and participated in a number of recent meetings. The NIH World AIDS Day virtual event on December 1, 2020, focused on the theme "Science and Community: Working Together to Prepare for the Unexpected." Speakers and panelists shared thoughts on how to build HIV research capacity through the development of infrastructure; how to strengthen the

workforce pipeline; partnerships with community organizations; and increasing support to address diversity, health disparities, and other gaps in research. Drs. Chin, Kates, and Tolbert participated in this event. On December 2, Dr. Goodenow delivered remarks related to NIH research on HIV coinfection with HPV and future directions within the HIV agenda at an Asia-Pacific Economic Cooperation (APEC) Cervical Cancer Technical workshop on the control of human papillomavirus (HPV) in women with HIV. At the December 2–3, 2020, Presidential Advisory Council on HIV/AIDS (PACHA) meeting, topics included addressing the syndemics of HIV, hepatitis, and sexually transmitted infections; a community health centers update on PrEP programming; an update from Dr. Kates on the CDC/HRSA Advisory Committee on HIV, Viral Hepatitis, and Sexually Transmitted Diseases Prevention and Treatment; and an international perspective on COVID-19 and HIV. The next PACHA meeting is March 8–9, 2021, and will include public participation. In addition, it is noted that Dr. Goodenow serves as NIH's representative on the PACHA and is a member of PACHA's Stigma and Disparities Subcommittee. Dr. Goodenow provided remarks at the January 15 NAESM 17th National African American Men Who Have Sex with Men Leadership Conference on Health Disparities and Social Justice; her remarks focused on the NIH HIV/AIDS research program and EHE in the age of COVID-19. Other participants joining her on this panel were Mr. Harold Philips, RADM Jonathan Mermin, and CDR Michelle Sandoval-Rosario. Finally, Dr. Goodenow presented new investigator awards to six early-stage HIV researchers, including the 2021 Bonnie Mathieson Award to Dr. Nathifa Moyo from the University of Oxford, at the virtual International AIDS Society HIVR4P meeting in early February.

In late December, OAR released its HIV Stakeholder Outreach and Engagement Report, which covers mid-2018 to early 2020 and summarizes key messages from OAR Listening Sessions and related engagements, including feedback that informed OAR's strategic plan and the NIH HIV research priorities for FY 2021–2025. Dr. Goodenow encouraged members to review the report and noted that stakeholders in every academic setting underscored the critical need to enhance the pipeline of early- and mid-career HIV researchers across disciplines and ensure institutional capacity to conduct cutting-edge science with community relevance. Because of the shift to virtual meetings, OAR hosted eight virtual Listening Sessions in the last quarter of 2020 with colleagues and stakeholders in Nashville, Boston, and West Virginia and participated in a listening session hosted by NIH's Sexual & Gender Minority Research Office. A virtual session is scheduled with Dr. Kimberly Scarsi and colleagues at the University of Nebraska in April 2021. Dr. Goodenow asked OARAC members interested in hosting a listening session to contact OAR.

Dr. Goodenow reminded attendees that OAR assumed oversight and management of the HIVinfo.nih.gov and ClinicalInfo.hiv.gov websites in September 2020. The two new websites continue to offer access to the latest federally approved HIV/AIDS clinical treatment guidelines, as well as other HIV research information, in both English and Spanish. OAR operates a public inquiry response center and disseminates relevant communications via social media and e-blasts. The inquiry response center provides support for the five treatment guidelines panels. This oversight and management transfer to OAR encompassed Phase 1 of the transition is now complete; Phase 2, currently in progress, involves content management, process evaluation, and quality assurance efforts. Later OARAC meetings will include details of website analytics and discussions of future enhancements.

Dr. Goodenow reported that the Vice President and Second Gentleman received their second doses of the COVID-19 vaccine at the NIH Clinical Center in late January 2021; the President and First Lady directly engaged with the NIH by meeting virtually and in person with researchers and NIH staff working to counter the pandemic in February 2021.

Dr. Goodenow commented that the National Institute of Biomedical Imaging and Bioengineering (NIBIB) and the National Center for Advancing Translational Sciences (NCATS) have been leading exciting and significant roles in combatting the COVID-19 pandemic with innovative approaches, some of which may be applicable to HIV. Dr. Goodenow noted that OAR has funded an HIV/AIDS prize as part of NIBIB's Design by Biomedical Undergraduate Teams (DeBUT) challenge, in which undergraduate teams develop technology solutions to unmet health care needs. NCATS' portfolio includes the Clinical and Translational Science Awards (CTSA) Program, which supports a national network of 60 medical research institutions—known as hubs—that work together to improve the translational research process to provide more treatments to more patients more quickly and safely. In FY 2019–2020, 16 CTSA pilot projects focused on HIV. Dr. Goodenow noted that the Directors of NIBIB and NCATS will present to OARAC later in the agenda.

Discussion Highlights

Dr. Tabia Henry Akintobi expressed interest in hosting a virtual listening session, which Dr. Goodenow explained will remain a standing part of OAR activities.

When asked how the change in administration affects the EHE Initiative and NIH's ongoing role, Dr. Goodenow confirmed that budgets for FY 2021 and FY 2022 include resources for EHE. Support for the initiative remains strong. She emphasized the importance of expanding the scope beyond the initial 57 jurisdictions. RADM Mermin added that the new administration has expressed explicit, vocalized support for both EHE and HIV research. Although COVID-19 has disrupted many HIV programmatic activities and much prevention work, RADM Mermin hoped that increased support for the public health system in general after a decline in SARS-CoV-2 infections would include continued resources for EHE. Dr. Kates noted that a recent special issue of *The Lancet* focused on HIV in the United States is framed around the EHE Initiative. Dr. Alan Greenberg commented that the upcoming national EHE meeting will include results of initial Centers for AIDS Research (CFAR) pilot projects.

HIV Antiretroviral and Opportunistic Infections Guidelines Working Groups of OARAC Report Out and Discussion

Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission; Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV; Antiretroviral Agents in Pediatric HIV Infection

J. Rafael Gorospé, M.D., Ph.D., Health Science Administrator, Senior Science Advisor, OAR, NIH

Dr. J. Rafael Gorospé noted that preliminary analysis shows that traffic and utilization of the new guidelines websites remain similar to the same time period from the previous calendar year. Additional data will be shared at the June OARAC meeting. Five of the seven guidelines have posted updates since the October OARAC meeting; no updates have been posted for the Pediatric Opportunistic Infections or Disaster Guidelines.

The major change to the Perinatal Guidelines is a move toward more inclusive language and content to address the care of transgender and nonbinary people who are pregnant or trying to conceive. The Perinatal Guidelines also added a new section about PrEP to reduce the risk of contracting HIV during the periconception, antepartum, and postpartum periods. Changes to antiretroviral (ARV) recommendations in the perinatal guidelines include classifying dolutegravir as Preferred for people who are trying to conceive and those who are pregnant, classifying

lopinavir/ritonavir as Not Recommended Except in Special Circumstances, and classifying tenofovir alafenamide as an alternative ARV based on added data. The Panel has revised language about its recommendations for those who are currently receiving cobicistat-containing ARV regimens to support more informed decision-making in people who are pregnant.

In the Adult and Adolescent Opportunistic Infection Guidelines, the section on coccidioidomycosis has been updated, as have Tables 1, 2, and 4. Additional updates to these guidelines are expected in upcoming weeks.

Three sections, developed jointly with the Perinatal Guidelines Panel, have been added to the Pediatric ARV Guidelines: Maternal HIV Testing and Identification of Perinatal Exposure, ARV Management of Newborns with Perinatal HIV Exposure and Perinatal HIV, and Diagnosis of HIV in Infants and Children. Additional content includes guidance on telemedicine and a new table outlining requirements for in-person versus telemedicine visits. Updates include the section on What to Start and the corresponding table, with recommendations on the use of dispersible dolutegravir tablets in infants and children; guidance on the use of abacavir in infants; and the approval of maraviroc, although it is classified as Not Recommended for first-line treatment in infants and children.

Interim Guidance for COVID-19 and Persons with HIV; Antiretroviral Agents in Adults and Adolescents Living with HIV

Alice K. Pau, Pharm.D., Staff Scientist and Clinical Pharmacist, National Institute of Allergy and Infectious Diseases (NIAID), NIH

Dr. Alice Pau noted that the Interim Guidance for COVID-19 and Persons with HIV was released initially in March 2020 and slightly revised in June, but the first significant update would be published shortly after this meeting. The key update is a review of the emergent epidemiologic data on disease progression of COVID-19 in persons with HIV. Earlier reports showed no difference in clinical outcomes for persons with HIV compared with those without HIV. More recent reports from the United States, United Kingdom, and South Africa showed higher rates of hospitalization, ICU admissions, and mortality in patients with low CD4 counts than adults without HIV. The guidance recommends that all persons with HIV receive the COVID-19 vaccine. COVID-19 patients with and without HIV should be treated similarly. Sections of the guidance regarding children and pregnant women with HIV and COVID-19 have been updated, as well.

The Adult and Adolescent ARV Guidelines Panel released strong recommendations for the use of long-acting injectable cabotegravir and rilpivirine in February 2021. Key considerations include emphasis on the importance of adherence, the necessity of oral “bridging regimens” if interruptions occur, the lack of data on patients who are non-adherent or with history of virologic failure, and the lack of data on use in pregnancy. Another update is anticipated for late spring 2021. Dr. Pau noted that, because cabotegravir and rilpivirine are recommended for optimizing treatment rather than initial therapy, these recommendations will be discussed in the section on optimizing. The spring update will include considerations for substance use and antiretroviral therapy (ART), as well as updates to a number of drug-drug interaction tables based on oral regimens. Other updates in progress include sections on What to Start, Virologic Failure, Poor Immunologic Responses, Adolescents, Women, Tuberculosis, Adverse Reactions, and Cost.

Discussion Highlights

When asked whether the Guidelines support prioritizing people with HIV for the COVID-19 vaccine, Dr. Pau explained that CDC's Advisory Committee on Immunization Practices (ACIP) defines vaccine prioritization, and the Guidelines Panels recommend that individuals with HIV should be prioritized. At the time of the meeting, the CDC list of high-risk individuals for receiving vaccines does not specify individuals with HIV, but does include persons who are immunocompromised. Dr. Kates and RADM Mermin suggested that an advance section of the Guidelines update could be provided to ACIP prior to its upcoming meeting. RADM Mermin added that evidence, although not robust, suggests prioritization. Dr. Kates pointed out the need to communicate such an update to states that do not all follow CDC's recommendations.

OARAC members pointed out that health disparities are strongly associated with COVID-19 risk; thus health equity should be considered in determining vaccine prioritization. Age and health status were other points of vaccine prioritization discussion. Members noted that young otherwise healthy adults with HIV who are virally suppressed are likely at lower risk for poor COVID-19 outcomes than older adults with significant comorbidities and poor socioeconomic conditions. Members agreed that inconsistent and confusing rollout to date made the vaccine less accessible to minorities and older people in many states. A robust discussion of prioritization for vaccination ensued. There were no challenges to the Guidelines Panels recommendation that persons with HIV should be prioritized for COVID-19 vaccination.

OARAC members discussed how to better understand the effects of the COVID-19 pandemic on HIV care, treatment outcomes, and surveillance statistics. RADM Mermin confirmed that this will be an important area of research in coming years; CDC will review all its sources and update its HIV incidence models, but the story will be complex to assemble, confirm, and respond to.

OARAC members commented on the global reach of the Guidelines, recommending a global perspective when considering surveillance and recommendations and commending the Panels for including dolutegravir for those contemplating pregnancy.

Updates from the NIH Advisory Council Representatives

AIDS Research Advisory Committee (ARAC)

Richard E. Chaisson, M.D., Professor of Medicine, Epidemiology, and International Health, Johns Hopkins University School of Medicine, Baltimore, MD

Dr. Chaisson provided updates on the most recent ARAC meeting. NIAID received an increase in its HIV/AIDS funding, with a significant proportion of the increase earmarked for EHE projects through CFARs and AIDS Research Centers (ARCs). HIV/AIDS clinical trials networks have been funded through 2027. NIAID already has provided significant support to the EHE Initiative through funds allocated to CFARs and ARCs for implementation science research. Several EHE concept proposals have been put forward for FY 2022 but their awards will depend on identifying new funds. The concepts focus on multidisciplinary treatment approaches, prevention strategies, and epidemiology, all aimed at ending the epidemic. These proposals target research conducted in the 57 priority jurisdictions and require partnerships with local health departments or community organizations, as well as implementation partners, to ensure that solutions address local needs. Dr. Chaisson reiterated that continuation of the EHE plan beyond FY 2021 will depend on sustained support.

The proposed concept focusing on multidisciplinary treatment approaches to end the HIV epidemic aims to use implementation science to develop, implement, and evaluate creative,

multidisciplinary approaches to health care delivery that more effectively engage and retain populations who are underserved or poorly engaged by current HIV treatment programs. The concept related to prevention strategies focuses on research that supports the Diagnose and Prevent pillars of the EHE plan. Research under this concept should focus on reducing both individual risk of acquisition and transmission and population-wide HIV incidence. The third concept aims to respond to underlying changes in the HIV epidemic using cutting-edge epidemiology and data science to enable sustained suppression of HIV and to guide program development and evaluate implementation science interventions to measure success and iteratively plan the next steps. Collaboration among the fields of epidemiology, data science, and implementation science is encouraged in this project. The scope is to identify key populations, risk groups, and contextual factors to understand community and individual HIV vulnerabilities in real time. The project will employ novel methods of data science, artificial intelligence, and machine learning for predictions and increase the speed of and usable knowledge from data. The implementation science program will assemble multidisciplinary teams to build robust and rapidly adaptable evidence-based programs.

National Advisory Council on Drug Abuse (NACDA)

Carlos del Rio, M.D., Department of Global Health, Rollins School of Public Health, Emory University School of Medicine, Atlanta, GA

Dr. Carlos del Rio presented highlights from the last NACDA meeting, particularly focused on a study of viral reservoirs in elite controllers of HIV. Elite controllers, a rare population of individuals whose HIV is controlled below the level of detection without ART, make up about 0.5 percent of the 38 million people living with HIV. The study showed that elite controllers have a lower number of antiretroviral amplification products, distinct viral reservoirs, and a “block and lock” mechanism for controlling viruses. In elite controllers, 45 percent of functioning proviruses reside in “gene deserts”; cells harboring deeply latent HIV genomes are evolutionarily selected. Immune cell therapies that induce a biased integration site profile could be a hope for a functional cure for HIV. Dr. del Rio noted the high levels of interest at the National Institute on Drug Abuse (NIDA) in the impact of substance use disorders on HIV genome integration. He listed several upcoming exploratory studies published by NIDA, an update to NIDA’s AIDS research program website, and an upcoming symposium that will include presentations from awardees of NIDA’s HIV Avant Garde Program.

National Advisory Mental Health Council (NAMHC)

Alan Greenberg, M.D., Chair, Department of Epidemiology and Biostatistics, Milken Institute School of Public Health, The George Washington University, Washington, DC

Dr. Greenberg noted the one major HIV-related issue at the most recent NAMHC meeting, a concept clearance on deciphering neuroimmune dysfunction in HIV utilizing human cell–derived *in vitro* and *in vivo* systems. He pointed out the importance of understanding HIV-associated comorbidities, especially in the area of immune activation and persistent inflammation. The concept focuses on immune dysfunction and the effects on the central nervous system (CNS). Current studies have focused on neuronal death and encephalitis, but new diagnostic and laboratory techniques can facilitate studies in new ways, such as with humanized mouse models and *in vivo* models with human immune cells in the CNS. The purpose of this study is to understand pathophysiological mechanisms of HIV-associated CNS comorbidities by causally linking immune, molecular, cellular, synaptic, and circuit-related processes using human cell–derived *in vitro* and *in vivo* systems.

Discussion Highlights

OARAC members complimented NIAID for its concept highlighting the intersection between epidemiology, data science, and implementation science, which is an insightful perspective that can be applied to both COVID-19 and HIV.

Bioengineering for COVID-19: Rapid Acceleration of Diagnostics (RADx) at Unprecedented Speed and Scale

Bruce J. Tromberg, Ph.D., Director, NIBIB, NIH

Dr. Bruce Tromberg explained that NIBIB works mainly in the areas of engineered biology, synthetic biology, sensors and point-of-care technologies, imaging technologies, and therapeutic devices. Modeling, computation, and machine intelligence are the core components to designs in these areas, particularly to move the technologies toward the future. NIBIB identified three areas which may contribute to the efforts to assuage the COVID-19 pandemic—imaging and artificial intelligence, digital health platforms, and diagnostic test technologies.

NIBIB collaborated with the NIH Office of the Director to establish several types of RADx programs and leads the RADx Tech and RADx ATP branches. Dr. Tromberg emphasized that the RADx efforts are highly collaborative across a number of organizations. NIBIB was able to leverage and expand its existing network, allowing the Institute to quickly review and fund concepts, test and validate new technologies, and provide expert guidance. The RADx operation was designed around the concept of an innovation funnel. The initial call for applications from the community resulted in 750 applications; 140 of those underwent an intensive evaluation and review process. In Phase 2, 27 projects remain and already are contributing to testing efforts through personalized tests, high-throughput laboratory tests, and laboratory products.

The speed and scale of COVID-19 projects has had a cumulative impact, reducing the device approval timeline from 5–6 years to several months. NIBIB supported approximately 150 companies in Phase 1 and Phase 2; Dr. Tromberg anticipated that more than 2.5 million COVID-19 diagnostic tests per day would be conducted by March 2021.

NIBIB supports a validation core—managed by Emory University and The Georgia Institute of Technology—which has evaluated approximately 60 projects for feasibility, particularly focusing on the performance gap between rapid antigen tests and polymerase chain reaction (PCR) tests. Some new technologies were known to be in development in laboratories but had not yet reached the marketplace; by de-risking and investing in these projects, NIBIB was able to speed up their translation to the marketplace. Dr. Tromberg described the example of pooled PCR tests, which allows for the rapid isolation of close contacts.

The clinical studies core, based at the University of Massachusetts, focuses on the real-world clinical applications of each type of test. One example is a project to determine how many sequential lateral flow assays are required to equal the performance of a PCR test. A single test might not capture infection, but infection will be shown in tests conducted over multiple days. This core is working with CDC to determine whether at-home approaches can help break the chain of transmission.

The deployment core, centered at Consortia for Improving Medicine with Innovation and Technology at Massachusetts General Hospital, is working to create playbooks and develop end-to-end solutions. The major product for this core is a website—whentotest.org—with a

calculator that provides information on how to structure testing for organizations of specific sizes.

To facilitate these projects, NIBIB has supported digital health platforms and apps that can instruct individuals in how to take the test, link to electronic health records (EHRs), facilitate digital contact tracing, provide proof of health status, etc. Within the app-based format, lateral flow assays can be read with a machine-learning approach to help the user determine whether a test is positive or negative.

Dr. Tromberg emphasized that the most significant initial step in this effort was leveraging and expanding an existing network, which allowed the introduction of new processes to provide funds to awardees quickly. This effort highlighted the urgent need for new purpose-driven technology given the insufficiency of off-the-shelf solutions. Bioengineering and technology development communities engaged with a nontraditional partner—public health and policy communities—to achieve success in this effort, suggesting opportunities for future collaboration. Several ongoing challenges remain. Given the $1 billion investment, NIBIB must ensure that these technologies are leveraged for other diseases and future pathogens. Regulatory and reimbursement systems are not ready for population-level screening, surveillance, and prevention efforts.

Dr. Tromberg emphasized that the RADx process will be embedded permanently in NIBIB's structure—it is a demonstrated mechanism for rapid acceleration and dissemination to the rest of the NIH and beyond.

COVID-19 Across the Translational Science Spectrum: Implications for HIV Research

Christopher P. Austin, M.D., Director, NCATS, NIH

Dr. Christopher Austin explained NCATS' activities in response to COVID-19 and potential strategies for emerging infectious diseases in the future. He emphasized that NCATS took an unprecedented open and collaboration-based approach to COVID-19 and focused on existing programs and infrastructure. Dr. Austin pointed out that if NCATS and the NIH were able to work with unprecedented urgency and scale on the COVID-19 pandemic, all patients with other diseases are owed the same speed and efficiency of translation.

The COVID-19 OpenData Portal, an online data resource, launched in May 2020 to openly and quickly share COVID-19-related drug discovery data and experiments for all approved drugs. NCATS worked with many collaborators to develop a variety of assays across a wide range of viral targets. All data were made available within a week of completion. Dr. Austin noted that in addition to high levels of interest from internal researchers, external groups have asked to add their data to the system, suggesting that such data sharing may become more standard.

An app called CURE ID has been in development for the past several years, aimed at capturing clinicians' real-world experience with neglected tropical diseases and allowing users to discuss the diseases and potential treatments in real time. CURE ID was rapidly pivoted to COVID-19 in its early months, which was very important as a real-time, ICU provider–friendly platform. Multiple partners now are helping to expand CURE ID. Dr. Austin stressed that this is another example of rapid progress as a result of radical sharing.

For the COVID-19 Serosurvey, NCATS gathered a representative population sample and analyzed those individuals for a variety of antibodies to determine how many asymptomatic people had been infected with SARS-CoV-2. Two longitudinal follow-ups at 4 and 8 months are

planned. For every person with identified COVID-19, five other individuals were infected but not symptomatic or diagnosed.

A similar effort was conducted with the National COVID Cohort Collaborative (N3C). In the early days of the pandemic, gathering information on its demographics was difficult. NCATS and the CTSA program had been working for several years to develop an informatics platform to share EHR data in a centralized, secure location housed at NCATS. Dr. Austin emphasized that the N3C was possible because it was built on 3 years of infrastructure-building. He pointed out that although the data enclave currently is focused on COVID-19, if a large number of institutions apply this system, it could become a disease-agnostic platform. Unique aspects of the N3C platform include its scope, harmonized data, collaborative analytics, and centralized and secure nature.

NCATS pivoted its tissue chip program to develop a multicellular human-based microfluidic platform. Some existing lung chips were able to be pivoted rapidly to use for studying COVID-19 therapeutics. The lung chip incorporates both the immune system and viruses; Dr. Austin noted that the major challenge was finding a biosafety level 3 facility that could conduct the studies.

NCATS was able to pivot another resource, CTSA's Trial Innovation Network, to randomized controlled trials aimed at determining whether convalescent plasma is an effective treatment for COVID-19 and, if so, when and in whom. NCATS is approaching its enrollment target and working with the FDA to identify criteria for authorizing use of convalescent plasma.

For the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) program, the government worked together with the private sector and other partners in unprecedented ways. ACTIV identified areas needed to address the pandemic—preclinical research, therapeutics, clinical trials, and vaccine—and arranged for public–private partnerships to work in these areas. Dr. Austin provided examples of activities in each area of ACTIV. He noted that recruitment has been a problem in all trials, because most COVID-19 patients were previously well and often not in a health system. NCATS established a connection to CVS Pharmacy to identify participants, particularly for outpatient trials. Dr. Austin emphasized that this is an opportunity for the kind of real-world studies that meet the patient where they are, which is a strategy that HIV researchers have been working to implement, as well. He noted the success of recruitment through CVS pharmacies. Half of the patients contacted were from underrepresented minorities; more than a quarter of those contacted then went to the ACTIV-2 website and explored signing up for the trial. CVS has a new Clinical Trial Services initiative that could be applicable to other diseases and conditions—such as rare diseases—particularly those that make travel difficult.

Dr. Austin has been involved in a government-university-industry roundtable that includes leaders across these institutions in both life and physical sciences. He noted that, as the fields converge, this group has facilitated many interesting interactions and abilities to leverage expertise across fields.

Dr. Austin commented on what he has learned throughout the process of addressing COVID-19, particularly that moving from fundamental discovery to research and vaccines can be accomplished much more quickly than has historically occurred. The urgency of COVID-19—felt by everyone in the research ecosystem—reflects the urgency that patients with untreatable diseases always have felt. Recalculating the risk-benefit ratio to address the urgency of the pandemic has led to a proactive willingness to share information. Dr. Austin suggested that this cycle could be self-reinforcing—increased efficiencies lead to increase productivity, which has the potential to increase the return on investment despite sharing credit and profits. Although

many of the conditions, regulatory and policy exemptions, and additional funding likely will not continue without active steps by participants in all sectors, Dr. Austin suggested that leaders in the field could proactively educate policymakers about the conditions needed to make such successes possible for other diseases. He emphasized that if this level of effort is not applied to other diseases, those in the field are admitting that the lives of patients with COVID-19 have more value than the lives of those with other diseases.

Discussion Highlights

When asked what barriers remain to implementing true community-based clinical trials for HIV similar to those achieved through remote consenting and the NIH-CVS partnership, Dr. Austin commented that, except for complex inpatient studies, academic health centers are not the ideal place for trials. Community hospitals have had the most success in recruiting because they are located where patients live, patients are comfortable going to them, and fewer competing studies are occurring there. Additionally, patients have expressed hesitation about visiting large academic centers because of COVID-19. The NIH as a whole has begun to consider whether its traditional research network needs to change to adjust to these challenges.

Dr. Tromberg commented on how to maintain the momentum of this crisis response, pointing out that this process has shown that the pressures and outcomes of the innovation funnel can be changed to move technology—which progresses continuously even in the absence of a crisis—out of the laboratory more quickly and efficiently. He added that government can play an important role in de-risking and accelerating development even under non-pandemic conditions.

In response to a question about the unsustainable pace of pandemic research and the uncertain level of research outside of academic centers, Dr. Austin explained that academic sites will remain hubs and can send representatives to more distant sites to build the infrastructure needed to extend research into communities. Similarly, a foundation must be built to sustain an increased pace of research beyond the pandemic, including securing additional funding and training additional clinical staff. OARAC members pointed out that communities and trainees need to be assured that funding and career paths will be available in the long-term, especially because COVID-19 likely will continue to be relevant. Dr. Austin noted that CTSA sites have been participating in community engagement research for many years; this foundation of established trust was critical to the success of the COVID-19 efforts. Dr. Tromberg commented that he sees the most potential for long-term impact in the collaborations formed during this response. The pace of delivering funding to investigators was unprecedented and helped move purpose-driven solutions into implementation and deployment. Dr. Austin added that quality is not inconsistent with speed, but the authority to move quickly is required.

In response to a comment about the different needs of vaccine and therapeutic trials at academic or community sites, Dr. Austin agreed that the model used would not work for all studies.

OARAC members encouraged the research community to take the time to properly evaluate the successes and challenges of the COVID-19 response and use the lessons to both prepare for the next pandemic and make progress on reducing the long translational gap.

When asked if the technologies developed to address COVID-19 can be applied in other areas, Dr. Tromberg noted that the innovation funnel is used widely in entrepreneurial programs, but NIBIB was able to reduce it to practice in a new way, providing intensive review and management throughout the process. Dr. Austin added that the ACTIV program used the same

model. Dr. Kates pointed out that siloed funding is a significant challenge to research advancement, but the COVID-19 effort has provided proof of concept that now may be applied in many areas.

ESI Taskforce Report Out

Elisabet Caler, Ph.D., Health Science Administrator, Senior Science Advisor, OAR, NIH

Dr. Caler reported on the ESI Taskforce, which analyzed the success of ESIs in HIV research in accordance with the directives of the 21st Century Cures Act, as well as in response to feedback from OAR listening sessions about the lack of opportunities for ESIs. The ESI Taskforce identified HIV ESI awards between 2015 and 2020, compared them to the overall NIH awards trend since the publication of the OD Next Generation Researchers Initiative (NGRI), and plans to design a sustainable framework to promote or enhance support of HIV ESIs. This work aligns with Goal 4 of the OAR strategic mission, which aims to build human resource and infrastructure capacity to enhance the sustainability of the HIV research workforce.

The Taskforce examined NIH data, incorporated information from the Office of Portfolio Analysis, gathered input from OAR listening sessions, and evaluated variables from a number of other sources. Dr. Caler emphasized that all the data presented in this meeting is publicly available through the NIH RePORTER. After the NGRI initiative in 2017, the number of overall NIH awards to ESIs increased by about 40 percent. However, the proportion of HIV awardees are a small subset of the overall NIH awardees and have actually decreased in later years post NGRI. Although the increases in the HIV budget are small compared to the NIH overall budget, Dr. Caler commented that this trend still is disappointing. The Taskforce determined that a greater proportion of ESI R01 awardees had received a previous K award than those who had not, indicating that the K award mechanism, although competitive and demanding, is working as designed, as a path to more substantial grants. The Taskforce is conducting further analyses to identify the differences between these pools of applicants..

Dr. Caler outlined actions and future steps to support Early Stage Investigators. The Taskforce is deepening its analysis of the transition to R01 awards and the research topics covered. A series of activities will continue the Taskforce's efforts, including listening sessions and engaging with ICOs. Thus far, the Taskforce actively sought potential meritorious ESI applications that were not funded but could increase the junior investigator pipeline. ICOs were asked to submit ESI applications that met the criteria, resulting in a partnership with five ICOs to provide full or partial funding to nine meritorious applications, raising the number of funded ESI HIV applications by 25 percent in FY20. Seven of these awards were made to female principal investigators. This effort established a precedent for a partnership mechanism; efforts are ongoing to incentivize ICOs to fund applications in key priority areas. Planned activities for 2021 include continuing partnerships with ICOs, ESI listening sessions, an expert panel consultation, and an ESI symposium. Dr. Caler welcomed input from OARAC on listening session topics, examples of success, and opportunities for enhancing support and engagement of a diverse ESI workforce.

Discussion Highlights

OARAC members stressed the importance of this topic and commented on other metrics that could be assessed, many of which the Taskforce already has studied but were not presented publicly. Dr. Caler confirmed that the expert panels will include a highly diverse group of seasoned investigators to gain insight into strong approaches to support new HIV investigators.

Participants suggested also assessing nontraditional awards in addition to R01-equivalent awards.

Participants discussed the need to extend or supplement funding for ESIs whose responsibilities or timelines were affected by the pandemic, which could have a significant effect on their careers. Dr. Caler commented that a year is probably not long enough to determine how many HIV ESI researchers have switched to other COVID or other infectious diseases in the wake of the pandemic, but evaluating and planning for these pipeline issues will be important in upcoming years.

Dr. Goodenow challenged members to consider the ideal pipeline for ESIs and the metrics that should be used to assess their success. Dr. Caler invited OARAC members to continue to provide their input to the Taskforce going forward.

Public Comment

Jennifer Kates, Ph.D., Kaiser Family Foundation

Mr. John Meade, Senior Program Manager for Policy at AVAC: Global Advocacy for HIV Prevention and a member of the Research Work Group of the Federal AIDS Policy Partnership, commented on the importance of increasing diversity efforts to recruit ESIs who represent Black, Indigenous, and other people of color, who are disproportionately at risk for HIV/AIDS. The Work Group strongly supports efforts by the NIH to increase and amplify the leadership of ESIs from disproportionately affected communities. Mr. Meade suggested convening a federal interagency task force to review current efforts to increase diversity and strategize about ways to increase outreach and improve diversity in the future.

Closing Remarks and Adjournment

Maureen M. Goodenow, Ph.D., OAR, NIH
Jennifer Kates, Ph.D., Kaiser Family Foundation

Dr. Goodenow thanked the Council members and speakers, especially departing members, and reminded attendees that the June 24, 2021, meeting will be virtual.

Dr. Kates added her thanks, particularly to Dr. Goodenow and CAPT Glenshaw, and adjourned the meeting at 4:20 p.m. EST.

Certification

I hereby certify that, to the best of my knowledge, the foregoing summary minutes are accurate and complete.

Blanton Tolbert Digitally signed by Blanton Tolbert
Date: 2021.07.20 21:57:36 -04'00'

Blanton Tolbert, Ph.D.
Acting Chair, OARAC

Date

Mary Glenshaw -S Digitally signed by Mary Glenshaw -S
Date: 2021.07.19 13:48:15 -04'00'

CAPT Mary Glenshaw, Ph.D., M.P.H.
Executive Secretary, OARAC

Date