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

Office of AIDS Research Advisory Council
Fifty-Second Meeting

October 28, 2019
5601 Fishers Lane, Room 1D13
Rockville, Maryland

Meeting Minutes

Council Members Present: Dr. Jennifer Kates (Chair), Dr. Mary Glenshaw (Executive Secretary), Dr. Maureen M. Goodenow (Director, Office of AIDS Research), Dr. Ingrid V. Bassett, Dr. Tricia H. Burdo, Dr. John J. Chin, Ms. Lynda M. Dee, Dr. Lynne Mofenson, Dr. William G. Powderly, Dr. Kimberly K. Scarsi, Dr. Bruce R. Schackman, Dr. Babafemi Taiwo*, Dr. Charles R. Wira*

***Ex Officio* Members Present:** Dr. Julie A. Ake, Dr. Roy M. Gulick, Dr. Jonathan Mermin, Ms. Sheryl Zwerski

Advisory Council Representatives Present: Dr. Richard E. Chaisson, Dr. Carlos del Rio, Dr. Dianne M. Rausch, Dr. Robert Yarchoan

Invited Speakers and Guests: Dr. Rick Altice, Dr. Valerie Durrant, Dr. Bill G. Kapogiannis, Dr. Nora D. Volkow, Dr. David R. Wilson

Council Members Absent: Ms. Dázon Dixon Diallo, Dr. Scott D. Rhodes

* Participated remotely.

Welcome and Introductions
Jennifer Kates, Ph.D., Kaiser Family Foundation

Dr. Jennifer Kates welcomed participants to the fifty-second meeting of the National Institutes of Health (NIH) Office of AIDS Research Advisory Council (OARAC). Meeting materials provided to Council members included the agenda, a conflict-of-interest form, and minutes from the fifty-first OARAC meeting, held on June 27, 2019. Ms. Lynda Dee moved to accept the draft minutes from the fifty-first OARAC meeting; the motion was seconded by Dr. William Powderly. Members of the Council voted to approve the minutes. Dr. Kates reviewed the fifty-second 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 explained that the NIH HIV/AIDS research program, with the OAR as its coordinator, involves a breadth of activities across agencies, institutions, communities, and other stakeholder groups. The OAR is in the process of finalizing the *FY 2021−2025 NIH Strategic Plan for HIV and HIV-related Research* and is gathering stakeholder feedback to continue to meet the needs of the evolving HIV/AIDS epidemic. NIH's

annual HIV/AIDS budget is developed by OAR, in consultation with NIH Director Dr. Francis Collins and is explicitly tied to the NIH HIV research priorities and the strategic objectives identified in the *NIH Strategic Plan for HIV and HIV-Related Research.* Both the annual Congressional Budget Justification (CJ), which describes the NIH HIV/AIDS budget to Congress, and the annual Professional Judgment Budget (PJ), which estimates the funds needed to fully pursue scientific opportunities leading to an end to the HIV pandemic, have been submitted to Congress and are available online.

Every year, the OAR evaluates projects submitted by NIH Institutes, Centers, and Offices (ICOs) for alignment with NIH's current scientific HIV/AIDS research priorities to respond to its evolving needs; this year, that evaluation further helped initiate *Ending the HIV Epidemic: A Plan for America (EHE)*. The OAR is coordinating the NIH-wide response to *Ending the HIV Epidemic*, which aims to reduce new HIV infections by 75 percent by 2025 and 90 percent in by 2030. To meet the initiative's goals, existing implementation approaches will need to be customized, accelerated, and scaled for uptake in a variety of communities. Dr. Goodenow stressed the importance of ensuring that communities are full partners with researchers and health care providers in developing, implementing, and evaluating *Ending the HIV Epidemic* projects. She reviewed the NIH HIV research priorities and pillars of *Ending the HIV Epidemic*, noting their overlap with the NIH HIV/AIDS research priorities, and outlined OAR's key role in coordinating and tracking EHE-related research activities. Many projects already have been initiated with partner agencies, but funding will increase in fiscal year 2020 to support the full scope of the initiative.

Dr. Goodenow provided an update on the Presidential Advisory Council on HIV/AIDS (PACHA), which in 2019 has increased outreach to communities and will meet next in Washington, D.C., in February 2020. She noted that updates to the Office of Management and Budget on the NIH HIV/AIDS portfolio are continuing, as are community listening sessions across the country. Feedback provided at the listening sessions is helping to develop a framework for *Ending the HIV Epidemic* activities.

Since the last OARAC meeting, Dr. Goodenow has attended numerous conferences, including Southern Solutions, Gathering of 57, U.S. Conference on AIDS, the International AIDS Society (IAS), the Regional Prospective Observational Research in Tuberculosis (RePORT) International Meeting, the International Vaccine Institute, and the 15+ Years of President's Emergency Plan for AIDS Relief (PEPFAR). This year, the OAR has increased its co-sponsorship of workshops with NIH partners, including a workshop on community health workers in the HIV field, sponsored with the National Institute of Nursing Research, and a workshop on HIV-associated comorbidities, coinfections, and complications, sponsored with the National Heart, Lung, and Blood Institute and 19 other ICOs. Dr. Goodenow commented on recurring themes noted in these engagements—such as the importance of patient-centered, multidisciplinary, and community-based approaches—and noted upcoming meetings in which the OAR will participate.

Dr. Goodenow reminded attendees that the next iteration of the *NIH Strategic Plan for HIV and HIV-related Research* will cover 5 years (previous versions covered 2 years each), noting OAR's new staff members are key to implementing the strategic plan. She outlined the meeting's agenda and commented that OAR hopes to maximize the engagement with OARAC by gathering suggestions for future meeting agenda items, shifting focus areas, and identifying how OARAC can provide guidance most effectively to OAR.

Discussion Highlights

Dr. Goodenow clarified that additional PACHA members have been nominated, but the confirmation process takes time. She explained that the current roster includes representation from diverse ethnic and cultural backgrounds. Regarding the IAS meeting, Dr. Goodenow confirmed that the planning committee for IAS 2020 is developing plans that will allow attendees to participate in activities scheduled in both San Francisco and Oakland, CA, such as scheduling noncompeting plenaries, allowing for travel time, and planning pop-up events for those who do not travel between sites. Attendees requested that other agencies provide updates at the next OARAC meeting on their plans related to the *Ending the HIV Epidemic* initative.

When asked about data on early-stage investigators (ESIs), Dr. Goodenow explained that the final 2019 data will be reviewed to determine what percentage of ESI funds had been awarded to investigators in the HIV field; she recommended that OARAC comment on the appropriate proportion. Participants emphasized the importance of creating implementation research opportunities for ESIs.

Dr. Goodenow noted that the OAR plans to review clinical trial networks and cohort studies this year, adding that HIV research has led to the formation of clinical trials networks across the NIH, which help community stakeholders participate. Participants pointed out that all clinical trials networks have ESI programs. Participants discussed the opportunities presented by modification of a funding opportunity announcement (FOA) for the clinical trials networks to support increased implementation science and work with partner organizations.

When asked whether community partners participate in listening sessions, Dr. Goodenow explained that many Centers for AIDS Research (CFAR) have hosted the OAR-led sessions and have included their constituencies and community advisory boards; they also generally invite other community members to participate. In addition, OAR has conducted several listening sessions directly with community-based activists, service providers, organizations, and implementing agencies in several key jurisdictions. More listening sessions in new settings with wide cross sections of stakeholders are planned for Fiscal Year 2020.

The Science of Drug Addiction and HIV
Nora D. Volkow, M.D., Director, National Institute on Drug Abuse (NIDA), NIH

Dr. Nora Volkow explained that, although HIV incidence is decreasing in the general population, it is increasing among people who inject drugs. She described the evolution of the opioid epidemic, noting that the majority of deaths now are from fentanyl overdose. Injection, which delivers a greater quantity of a drug to the brain quickly and intensifies the rewarding effects, often is a favored delivery method, but because many communities do not have syringe-exchange programs, HIV can spread among people who inject drugs. Dr. Volkow asked the attendees to consider what is required for healthcare professionals to implement practices known to be effective, pointing out that useful addiction-related medications—such as methadone, buprenorphine, and naltrexone—are available but not used. Treatment with medications for opioid use disorder can lead to HIV prevention, because medications control the urges to both take the drug and engage in risky behavior that can result in HIV infection. Additionally, treatment for opioid use disorder may increase the likelihood that a person with HIV will receive treatment.

The challenges of treating opioid use disorders with medication include implementation—initiating and sustaining people on opioid treatment medications or antiretroviral therapy (ART)—and accessing coverage for treatment. Dr. Volkow noted that the United States offers some of the best access to treatment in the world, yet only a fraction of the people who require treatment are covered. Methadone clinics are not widespread, and patients with drug addictions often find complying with complex treatment and medication regimens to be difficult. NIDA has partnered with pharmaceutical companies to develop extended-release formulations for the known effective medications, which would decrease the complexity of treatment. Additionally, researchers are looking for alternative medication targets.

Many implementation science initiatives are trying to bring screening and treatment of opioid use disorder into the health care system and integrate the treatment of these disorders with infectious diseases or other comorbidities, including HIV. NIDA staff are working further to bring these interventions into justice settings (e.g., jails and prisons), despite the fact that stigma often is associated with administering agonist medications. Naltrexone provides a significant benefit in viral suppression among incarcerated people with HIV and those who inject drugs. This approach works both for retaining people in treatment and on medication and for improving HIV outcomes. The number of people who are virally suppressed decreases as a function of time when someone is released from prison or jail. Dr. Volkow noted that many people might be treated for HIV while in prison or jail, but upon release, they do not have insurance, and minimal follow-up care is provided. From the implementation science perspective, current models of care must be identified and interventions must be developed to ensure that someone who leaves jail or prison will be able to continue receiving ART and follow-up care.

Dr. Volkow discussed the effects of release from prison related to viral load and opioid use. She described studies conducted in other countries that have integrated models of care, in which a system navigator ensures that the person continues to receive antiretroviral drugs and medications to treat opioid use disorder. Providers offer psychosocial counseling and ART for patients with any level of CD4 counts. Dr. Volkow noted the need to address socioeconomic factors, adding that loneliness and isolation lead to risky behaviors that might result in addiction or infection. Providing models of care that include meaningful social interactions for people is valuable for both prevention and recovery. The four priorities at NIDA that parallel the NIH HIV/AIDS research priorities are to: (1) prevent transmission of HIV among people who use drugs; (2) have a basic understanding of the effects of drugs, how they influence behavior, and the interaction of HIV with drugs in the brain and other physiological systems; (3) consider comorbidities associated with substance misuse and HIV; and (4) accelerate scientific discoveries and opportunities for innovation in HIV/AIDS and substance use research.

Discussion Highlights

Attendees commented that people participating in syringe service programs regularly are more likely to get into medication-assisted treatment/therapy and more likely to stop using drugs, leading to a decrease in HIV and hepatitis C infection rates. Dr. Volkow agreed that such known strategies remain underutilized. For example, the maximum dose for buprenorphine is lower than the ideal dose; other versions are not covered by insurance. Additionally, most treatment programs provide only one medication and offer no choice.

Participants encouraged linking evidence to policy and collaborating with other agencies. Dr. Volkow commented on current efforts, including participation in the Helping to End Addiction Long-term^{SM} Initiative, or NIH HEAL Initiative^{SM}, and the launch of a collaboration with jails and

prisons to gather evidence on the effectiveness of integrated care models. She emphasized the need to determine how to present science eloquently so policymakers cannot ignore it.

Attendees suggested that OAR's requirement for an HIV-related outcome in all studies may reduce the ability to study related issues, such as opioid use or Hepatitis C. Drs. Goodenow and Volkow agreed that more integrated approaches are needed.

A participant asked about barriers at the federal level to establishing syringe-exchange programs. Dr. Volkow responded that most of the problematic barriers are found at the state level, adding that treatment in prisons and jails similarly is determined by the state and not by the federal government.

Dr. Jonathan Mermin outlined the participation of the Centers for Disease Control and Prevention (CDC) in the *Ending the HIV Epidemic* Initiative and commented on the challenges associated with collaboration across agencies.

When asked about the lack of interventions for methamphetamine, Dr. Volkow agreed on its dangers but noted that an effective treatment has not been identified. She pointed out that methamphetamine use increases sexual drive and desire, which contributes to the HIV epidemic, and commented on the difficulty of addressing the impulsive and high-risk behaviors that are common among people who use drugs.

In response to a suggestion from an OARAC member, Dr. Kates planned to arrange for updates on OAR's cost-sharing arrangements at the next OARAC meeting.

Implementation Science and Accelerating HIV Prevention and Treatment in Key Populations Who Use Drugs
Rick Altice, M.D., M.A. Director of Clinical and Community Research, Professor of Medicine, Yale University

Dr. Rick Altice explained that evidence-based interventions to prevent HIV transmission in people who inject drugs are known, usually with approximately 50 to 60 percent efficacy with regard to prevention, but the issue is with scalability and implementation. He emphasized that without implementation science, evidence-based practices take many years to develop and implement; many are never successfully implemented. Frameworks must address multiple levels, such as policies and human resources. Implementation strategies require active facilitation or coaching at multiple levels to accelerate the process. Using an implementation science framework provides a heuristic to move the process forward; key factors to consider when choosing a framework include the evidence available, the context, and the facilitation. The installation process requires conducting a landscape analysis to identify resources available and define strengths and weaknesses. The next step is implementing the strategy, so after the initial implementation, a process evaluation can be conducted to ensure that the practice follows the plans, is integrated into standard practices, and is operationalized and funded adequately into the future.

Multiple stakeholders are contributing to create a multilevel framework model that can be adjusted to individual needs. Dr. Altice described the need to move implementation science frameworks to the mobile space where many relationships now are sustained, as well as into health care culture and developments at the policy level.

In terms of efficacy, Dr. Altice referred attendees to Dr. Volkow's list of effective medications but cautioned that treatment options must be meaningful to patients and stakeholders. For example, injectable interventions could be helpful for people leaving criminal justice settings, but a provider for the treatment must be available. Treatment strategies must consider patients' preferences, as well, but successful treatment has secondary benefits across the entire cascade for prevention.

Implementation frameworks for opioid agonist therapies must account for sites where treatment might be implemented. Dr. Altice noted a treatment hub structure and added that the World Health Organization mandates coverage of 40 percent or higher to prevent an HIV epidemic among people who inject drugs. In the United States, coverage is 11 percent overall and very geographically constrained, leading to the evolution of specialty services. Facilitation processes are available to expand and improve addiction treatment to increase the number of patients on treatment within specialized settings, such as hub-and-spoke models to stabilize people in decentralized locations. He noted that with the current advanced treatment strategies, most patients do not need significant intervention to be successful. However, the current challenges of moving implementation into the primary care setting include determining which health care professionals are willing to provide treatment. In some countries, care is provided in pharmacies; the Governor of California recently declared an intent to make pre-exposure prophylaxis (PrEP) available in pharmacies, but many other bottlenecks in the complex U.S. health care system restrict access to treatment.

Dr. Altice commented that reaching persons in jails and prisons is the "final frontier." The key to most successful evidence-based facilitation processes is understanding the customer and fixing the problems specific to that situation. He provided an example of how medication-assisted treatment was introduced in Ukraine over time, where progress was hindered by patients' negative attitudes toward treatment and providers who did not agree with the treatment protocols mandated by the Global Fund. Using evidence, Dr. Altice's team was able to boost the retention rates by increasing the amount of methadone delivered over a specific period of time. Buprenorphine was the preferred treatment, particularly when delivered outside the addiction treatment setting, which was unique to this location. Dr. Altice's team drew on promising practices to develop home-grown innovations, such as a pilot buprenorphine prescription program and "take-home" dosing. When a challenge was issued throughout the country, groups that did not take any steps to answer the challenge had very low implementation fidelity, indicating a lack of interest in the work. The areas with the strongest increases in program implementation had a strong program lead willing to make changes to follow promising practices. Regarding HIV treatment as prevention, Dr. Altice emphasized that implementation policies indicate that no "one size fits all" strategy is possible. He explained that a differentiated care model for people who inject drugs is not currently available, despite the overlap of injection drug use with HIV and hepatitis C incidence. However, many behavioral interventions are known to be effective along the continuum of care.

Dr. Altice noted that many laws criminalize behaviors associated with HIV risk—for example, laws against homosexuality and drug use in Asia. Such structures concentrate people who use drugs and people who have HIV into stigmatized groups, including in prisons and jails. The proportion of people with HIV in the United States is much higher in prisons than in the general population. Eastern Europe and Central Asia are the only places in the world where HIV incidence and mortality are increasing because of the high-risk environment, laws, and lack of effective HIV treatment, which amplify the disease. The 12-month period after incarceration is a high-risk time for HIV transmission and therefore a time that should be targeted for intervention, including by providing methadone treatment before release from prison and establishing

linkages to care after release. Dr. Altice noted factors affecting virus levels and treatment retention among those released from prison, commenting that a long-term investment is needed because HIV is a chronic disease. He also described efforts to develop longer-acting treatments, such as implants, to increase retention.

Dr. Altice discussed sexualized drug use as more common among men who have sex with men (MSM) and transgender women than other populations. Amphetamines—with stimulants or as polypharmacy drugs—promote riskier sex, increasing HIV transmission opportunities, but also deplete serotonin, which can lead to increased suicidality several days after drug use. Dr. Altice suggested PrEP on demand as a possible strategy to decrease HIV transmission because drug use often occurs on weekends. He emphasized that many HIV prevention and treatment tools are available and can be scaled up adequately with the use of implementation science strategies to move the field forward.

Discussion Highlights

When asked whether implementation science can be introduced earlier in the translational journey, Dr. Altice explained the strategy of hybrid implementation trials to determine the most effective tools. He reiterated the importance of studying patient preference to increase retention.

Dr. Altice commented on several collaborations with pharmaceutical companies to determine which people might prefer various treatment options and develop decision aids to help patients make informed choices.

When asked about a decrease in usage rates, Dr. Altice explained that many people use drugs less often as they age. He predicted that the data would show another increase in drug use, driven by different factors, in line with the currently identifiable increase in hepatitis C rates. Dr. Altice stressed the need to use radical approaches in implementing treatment, referring to the scale-up challenge in Ukraine.

Updates to the U.S. Department of Health and Human Services (HHS) HIV/AIDS Treatment and Prevention Guidelines from the Working Groups of the OARAC
Roy "Trip" Gulick, M.D., M.P.H., Chief, Division of Infectious Diseases, Weill Cornell Medicine

Bill G. Kapogiannis, M.D., Medical Officer, Eunice Kennedy Shriver *National Institute of Child Health and Human Development, NIH*

Dr. Trip Gulick reminded attendees that the HIV treatment guidelines working groups are overseen by OARAC and suggestions from members are welcome. He reminded Council members of the history, structure, and revision process of the guidelines panels, explaining that the guidelines were conceived in 1996—the year the first three HIV protease inhibitors were approved—to provide evidence-based guidance to clinicians on the safe and effective use of ART; Dr. Gulick stressed that the goal remains the same today. He explained the update process, noting that the guidelines generally are updated once or twice per year, but an important safety update may prompt the panels to release a notice sooner than the next planned update. He further outlined the working groups' membership and representation, which includes community members and participants representing government agencies.

The latest revision of the Adult and Adolescent ARV guidelines, published on July 10, 2019, included three important updates. The substance use and HIV section was broadened to include substances in addition to opioids, with a focus on the impact on ART. A new section

addresses challenges related to transgender populations and HIV and includes information on strategies, drug–drug interactions, interpretation of laboratory parameters, and specific comorbidities related to hormone therapy and ART. The HIV-2 coinfection section now includes clinical trial data with recommendations to start ART for all patients and expanded recommendations to integrate therapy. Another revision is expected to be published in December 2019 or January 2020. Key updates for that revision include revised recommendations for lipid and glucose monitoring and a complete revision to the "treatment as prevention" section based on the evidence of using ART to achieve virologic suppression and consequent prevention of HIV transmission to sexual partners. Additional updates include newly approved regimens, updated language, and expansion and updates of several other sections, as well as a new section on the association of ART with weight gain.

Updates to the opportunistic infection guidelines since July 1, 2019, reflect new information on diagnostics, therapeutics, pharmacology, drug resistance, and drug regimens. Further recommendations on the treatment known as 1HP are pending further discussion with CDC. Other updates include language edits, revised information about immunizations and treatment for histoplasmosis, and new recommendations regarding *Cryptosporidium* and *Microsporidia*.

Dr. Bill Kapogiannis noted that the pediatric ARV guidelines panel includes a new nonvoting observer—from the Australasia Society for HIV, Viral Hepatitis, and Sexual Health Medicine—as the Society considers adopting the pediatric ARV guidelines. The pediatric ARV guidelines were updated in full in April 2019; Dr. Kapogiannis reviewed the updates, which were outlined during the previous OARAC meeting. He noted that the pediatric opportunistic infection guidelines are published in sections as needed; three new sections were published since the last meeting, primarily reflecting new vaccines. Additionally, three edits resulted from revisions by the authors. Finally, the section on varicella-zoster virus has moved into CDC clearance. Dr. Kapogiannis requested nominations for members to co-chair the panel.

The next revision of the perinatal HIV treatment guidelines will be published in December 2019 and will include recommendations on reproductive options for couples in which one or both partners are living with HIV to recognize the "undetectable equals untransmittable" (U=U) concept, additional recommendations for those who have not achieved viral suppression or when suppression status is unknown, and the use of ART during pregnancy. The guidelines now recommend dolutegravir for all pregnant women, regardless of their trimester, and as an alternative for women trying to conceive; the panel strongly recommends supporting the use of dolutegravir with appropriate counseling to enable patient-centered decisions made jointly by women and their health care providers.

Discussion Highlights

An OARAC member indicated that the most recent update to the opportunistic infection guidelines included an error introduced during CDC's review and requested an explanation of the need for an external review after the experts on the guidelines panels have made their recommendations. Dr. Alice Pau, the Executive Secretary of the Adult and Adolescent ARV Guidelines Working Group, explained that some of the HIV treatment guidelines panels are independent, but others are cosponsored by several agencies. Dr. Mermin commented that, in general, a CDC review is appropriate and not necessarily a problem; he added that this incident needs to be discussed further. Dr. Kates suggested that OARAC needs to better understand the differences between the review processes among the five panels.

The members asked for clarifications regarding issues relevant to U=U for which data are lacking, including the frequency of viral load testing and the transmission method. Dr. Gulick explained that although the guidelines panels can make recommendations only about proven information, the panels sometimes are willing to reflect expert opinion. In this case, the guidelines likely will recommend that those who want to demonstrate durable suppression to partners might benefit from more frequent viral load testing.

Participants encouraged more diversity on the panels and a better definition of OARAC's role in the process.

Attendees recommended a more rapid update of the Adult and Adolescent ARV Guidelines regarding treatment as prevention or U=U, noting the urgency felt by the community on this issue. Dr. Gulick and OARAC members discussed whether the urgency of this issue directly affects people to the extent that a safety statement should be published prior to the planned update of the guidelines in December 2019 or January 2020. The expedited alerts usually are succinct and might lose impact if published more frequently. The OARAC moved to emphasize the urgency of this issue and encouraged the panel to publish its update in December 2019, rather than January 2020, and requested a more detailed explanation of the update process at a future meeting. The Guidelines representatives agreed to incorporate these recommendations in their plans.

Updates from the NIH Advisory Council Representatives

AIDS Research Advisory Committee (ARAC)
Richard Chaisson, M.D., Professor of Medicine, Epidemiology, and International Health, Johns Hopkins School of Medicine

Dr. Richard Chaisson noted that the National Institute of Allergy and Infectious Diseases (NIAID) interim financial plan includes a payline at the 10th percentile for established investigators and the 14th percentile for new investigators, although competing research initiatives could be cut by as much as 20 percent. The overall success rate at NIAID is about 20 percent. The NIH has awarded $6 million in supplemental funding through CFARs and AIDS Research Centers for *Ending the HIV Epidemic*; recipients met in Chicago the week of the OARAC meeting to plan implementation of the initiative. Clinical trials network applicants had been encouraged to add an attachment to their applications focusing on research for the *Ending the HIV Epidemic* initiative; the timeline for network recompetition has been adjusted accordingly.

One concept proposal reviewed at the meeting is titled Digital Limited Interaction Trials in Epidemiology (D-LITE), which assesses the feasibility of establishing online cohorts to study HIV risk behavior and outcomes. This proposal was approved with modifications based on discussions with the ARAC about the inclusion of women and people who use drugs. Additional approved concept proposals focus on natural killer cells; long-acting treatments for HIV and HIV co-infections; novel therapeutics directed to intracellular HIV targets; immunity, prevention, and treatment in transgender people; and engineering immunity through vaccines. Two programs were renewed: (1) the Integrated Preclinical AIDS Vaccine Development Program (IPCAVD), and (2) its complementary program, Preclinical and Translational Support for HIV and Other Candidate Agents (PTVDS), which provides the materials. The single concept that was not approved was a proposal for studying the footprints of successful postexposure prophylaxis

(PEP); the ARAC indicated that the failure of PEP was so rare that this was not a particularly promising area of research.

National Advisory Mental Health Council (NAMHC)
Dianne M. Rausch, Ph.D., Director, Division of AIDS Research, National Institute of Mental Health (NIMH), NIH

Dr. Dianne Rausch reviewed two new initiatives presented to the NAMHC. Dr. Rausch reminded attendees that adolescents regularly have much poorer outcomes along the care cascade than adults. A differentiated care approach focuses resources on those who need them most and when they need them, because individuals differ in the level of intervention at which they thrive. Advancing Differentiated Care Approaches for Adolescents Living with HIV would search for new strategies to allow decision points for those who need differing levels of care. Dr. Rausch emphasized that the NIMH prioritizes creating strategies that address the developmental context of adolescents.

Dr. Rausch explained that mood disorders, cognitive dysfunction, and many other mental health factors can affect risk behavior and increase the probability of HIV infection. Additionally, such mental health conditions can affect someone after HIV infection; the physical effects of HIV—such as inflammation, dysbiosis, and drug toxicities—can increase psychological or social disruption. The NIMH is interested in understanding the mechanisms of pathways related to mood disorders—including chronic inflammation, immunosuppression, gut–brain axis dysfunction, and adverse psychological factors—in the hopes of developing novel interventions for people living with HIV. Dr. Rausch explained that the initiative, Mood Disorders in People Living with HIV: Mechanisms and Pathways, is written broadly to encompass the many factors that can affect mood disorders.

Dr. Rausch reminded attendees that the *Ending the HIV Epidemic* initiative supplements were awarded to NIH CFARs and ARCs to support implementation science and create opportunities to collaborate. Although not all the sites that received supplements are in areas with a disproportionate burden of HIV, Dr. Rausch emphasized the importance of using existing sites to build a strong foundation for the initiative. She listed some of the many areas that could be addressed under the initiative, noting the broad range of topics covered by the supplements.

National Cancer Advisory Board (NCAB)
Robert Yarchoan, M.D., Director, Office of HIV and AIDS Malignancy, National Cancer Institute (NCI), NIH

Dr. Robert Yarchoan focused on the activities of the NCI Board of Scientific Advisors (BSA), which has an *ad hoc* subcommittee on HIV and AIDS malignancies and infrastructures for obtaining biospecimens from people with HIV. He explained that cancer is now the leading cause of death in people with HIV. AIDS-defining cancer has continued to be a problem, particularly in low- and middle-income countries, as well as in the United States; non-AIDS-defining cancers are becoming more important, as well, depending on the age of the patient. A working group to the subcommittee discussed the feasibility of a vaccine for Kaposi's sarcoma-associated herpesvirus (KSHV), given that KSHV infection is more prevalent in low- and middle-income countries and in MSM in the United States. The working group could not reach a decision and recommended a symposium to continue the discussion.

The working group discussed ways to obtain biospecimens from patients who go on to develop HIV-associated cancers or other cancers. These cancers are low in frequency, so the working

group proposed linking various cohorts into one virtual cohort to obtain the specimens. The group also recommended promoting investigator-initiated research that combines people working on HIV and AIDS malignancies with those working on other malignancies, which would promote cross-fertilization. These recommendations were accepted by the BSA and are now being considered by the NCI.

Dr. Yarchoan discussed a request for applications for the program titled U.S. and Low- and Middle-Income Country HIV-Associated Research Centers, which now is entering Phase 3. The goals include accelerating scientific knowledge about HIV-associated cancers, continuing to develop research capacity in low- and middle-income countries, supporting collaborations between U.S. investigators and low- and middle-income country investigators, and fostering early-career investigators interested in AIDS- and HIV-associated malignancies. Partnerships are between U.S. and low- and middle-income country investigators; the next phase is open to all investigators, not only to those who received grants in the first two phases. This program uses a U54 mechanism and includes research projects in a topic area, as well as supporting cores. In Phase 3, the networks are envisioned as larger and based in institutions in one or more low- and middle-income countries. Applications that include multiple principal investigators (PIs) must include at least one PI from the United States and one from a low- or middle-income country who have worked together previously, but teams can include new collaborations, as well. Dr. Yarchoan noted the emphasis on supporting the development of junior investigators. This program likely will support five or six networks for 5 years. Dr. Yarchoan commented that previous phases have been highly successful in expanding this field to engage investigators from Africa, South America, and other geographic areas in this research.

Discussion Highlights

Dr. Yarchoan commented on the difficulty of including people with HIV in clinical trials for common cancers but noted that progress is ongoing. Attendees pointed to the Anal Cancer High-Grade Squamous Intraepithelial Lesions (HSIL) Outcomes Research (ANCHOR) study as an example of success and suggested a similar trial for cervical cancer.

OARAC members requested a future update on the NIH initiative to find cures for HIV and sickle cell disease.

Report Out from the HIV Strategic Plan Working Group
Dianne M. Rausch, Ph.D., Director, Division of AIDS Research, NIMH, NIH

As the working group chair, Dr. Rausch explained the process used to develop the *NIH Strategic Plan for HIV and HIV-Related Research.* The OAR is a mandated office with the responsibility for coordinating scientific, budgetary, legislative, and policy components of the NIH HIV research agenda for HIV/AIDS. The Office is charged with identifying research priorities and developing a budget, which must be transparent and informed by stakeholder input. The CJ and PJ are part of the mandated budget process, as is the Strategic Plan, which ensures that available funds are allocated appropriately. Information on the progress of the portfolio is gathered through the NIH AIDS Executive Committee, which includes representatives from all ICOs that receive HIV/AIDS funding, and the OARAC. Community input was gathered through requests for information (RFIs) and listening sessions.

Dr. Rausch explained that the Plan's strategic objectives are to: (1) advance research to end the epidemic and improve the health of people with, at risk for, or affected by HIV across the lifespan; (2) ensure that the NIH HIV research program remains responsive to emerging

scientific priorities and discoveries; (3) promote dissemination and implementation of research discoveries; and (4) build research infrastructure capacity to enhance sustainability of HIV research discovery and implementation. Responses to the RFIs emphasized the importance of recruitment and training of new investigators, partnerships and research collaborations, and accommodation of the increasingly multidisciplinary nature of HIV research. Additionally, respondents confirmed that NIH's priorities are relevant but recommended a clear assessment of projects for alignment with the priorities. OAR-led listening sessions with the community provide a transparent forum for a diverse set of stakeholders to communicate with the OAR and the NIH and can provide suggestions for new initiatives.

The OAR will collaborate with NIH ICOs and stakeholders to manage dedicated HIV/AIDS research efficiently and harness emerging scientific priorities, with the hopes of expanding these collaborations and linking HIV research to broader initiatives; for example, a link to the 21st Century Cures Act will encompass research policies related to the inclusion of minorities and women and the focus on health across the lifespan. Additionally, the Strategic Plan aligns with the goals of the *National HIV/AIDS Strategy for the United States.*

The working group stressed the importance of including sexual and gender minority populations, newborns, children, adolescents, women, and racial and ethnic minorities. Group members requested updated data points from the OAR and suggested an increased emphasis on stigma, clarification of socio-structural determinants of health, and increased accountability and transparency in monitoring NIH's performance. The Strategic Plan has been submitted to NIH Director Francis Collins and is expected to be released to the public soon.

Discussion Highlights

Dr. Rausch clarified the process for adapting the plan to emerging science and confirmed that retention in care is included in the plan. Dr. Kates requested that the plan be distributed to OARAC members when ready.

Updates from the Tribal Health Research Office (THRO)
David R. Wilson, Ph.D., Director, THRO, NIH

Dr. David Wilson explained that American Indian tribes are considered sovereign nations—treaties with the federal government stipulate that the United States government would provide health services and education to native communities as a government-to-government relationship. Each of the 573 federally recognized tribes has its own government structure, most of which are very different from each other. THRO's primary function is to coordinate tribal health research across the entire NIH, which it accomplishes through the NIH Tribal Advisory Committee (TAC) and the Tribal Health Research Coordinating Council. The TAC includes representatives from each Indian Health Service (IHS) service area who provide recommendations to help guide NIH's investment in tribal communities. The Tribal Health Research Coordinating Council comprises members appointed by ICO directors to catalyze ideas, training, initiatives, and career development.

This year, THRO—in consultation with tribal nations and NIH coordinating committees—developed the first *NIH Strategic Plan for Tribal Health Research*. Another important document developed this year was the first *American Indian/Alaska Native (AI/AN) Research Portfolio* to illuminate how the NIH is spending its investment to address tribal health research. Dr. Wilson stressed that assessing the research portfolio is only the beginning of an ongoing process.

THRO collaborated with the NIH, HHS, and Substance Abuse and Mental Health Services Administration (SAMHSA) on a tribal consultation on the opioid crisis in Indian Country. Dr. Wilson noted that this consultation was an opportunity to better demonstrate to tribes the difference between health research conducted by the NIH and health care provided by the IHS. THRO developed a searchable tool to provide tribal communities access to NIH data; tribal communities can use this tool to identify gaps in research in their community and address them with their tribal epicenters. Summer students from tribal nations coded the data, providing them with internship experience that helped the communities as well.

Dr. Wilson described a workshop on genetic research and the informational brochure that resulted, which explains how genetic research can benefit tribal communities. Other THRO publications explain privacy issues and emphasize the importance of considering community impact when conducting research with tribal communities. The TAC wrote a paper outlining issues to consider regarding participation in direct-to-consumer ancestry testing kits, including how a participant's data may be used by secondary researchers.

THRO helped arrange Navajo participation in the Environmental influences on Child Health Outcomes (ECHO) program. Navajo Nation contains a number of open uranium mines, so understanding the long- and short-term effects and potential connection to increases in cancer incidence is important. THRO was able to clarify how the data are stored and accessed, as well as the ethics obligations held by the grantee.

Dr. Wilson outlined the current efforts at THRO and emphasized the importance of engaging communities and identifying priorities, which may differ between tribal leaders. Dr. Wilson commented on the unique model of customer-owner health care services run by the Alaska Native Consortium and described a meeting in South Dakota, during which weather affected the original plans for the event but led to fruitful community connections in a more casual setting.

THRO helps to bring important conversational topics to tribal communities, such as intellectual property, which was discussed in a webinar at the National Congress of American Indians. Additionally, THRO brought NIH's data sharing and data management policy to the communities to gather information on tribes' privacy and security needs. THRO now is developing a network of training opportunities across the NIH to allow students to try multiple ICOs to find the right fit. Participating students learned about the role of Congress in funding science and had the opportunity to meet with Native American members of Congress. Dr. Wilson noted the intent to build a sustainable pathway for trainees through regional training hubs, which prepare high school students for the rigors of biomedical research at the NIH. Additionally, THRO is working to build relationships with tribal epicenter directors to facilitate trusted research partnerships.

Dr. Wilson pointed out that tribal communities have some of the highest rates of HIV transmission among MSM; working with IHS funding at the tribal epicenters could provide an opportunity for OAR to address HIV transmission in native communities. An important consideration would be how to shape funding opportunity announcements to allow the epicenters to assume the role of primary investigator rather than requiring partnership with an academic institution. Dr. Wilson emphasized the importance of ensuring that urban Indians—who can be hard to identify but are a vulnerable population—are served well in terms of reducing HIV transmission. He recommended developing a pilot project with epicenters that could be scaled up and form the basis for long-term relationships.

Discussion Highlights

When asked about opportunities for CFARs and non-CFAR investigators to partner with tribes, Dr. Goodenow noted that the OAR received numerous applications for supplements and funded about two-thirds of them, but they still are waiting for the main portion of the funding for the initiative, which will be provided in subsequent fiscal years. Dr. Mermin added that Cherokee Nation spans one of the targeted jurisdictions for the *Ending the HIV Epidemic* initiative and noted the importance of mental health treatment as directly related to HIV care. Dr. Wilson planned to meet with representatives from the Office of Behavioral and Social Sciences Research the day after the OARAC meeting.

Dr. Wilson explained that THRO is working with the Office of Data Science Strategy to provide internships to students to conduct real-time data analysis at the epicenters and provide useful reports to the community, particularly because the epicenters have large amounts of data without the capacity to analyze them. Dr. Goodenow commented that other groups have expressed interest in developing their capacity to be PIs, so developing ideas for capacity building could be useful.

Dr. Wilson mentioned that the NIH is partnering with the CDC to hold the first traditional medicine summit, which will convene the largest collection of traditional healers ever assembled to discuss best practices and reinvigorate the community's use of traditional medicine. Additionally, a partnership with Centers for Medicare & Medicaid Services will assess how to reimburse for traditional medicine. OARAC members suggested looking to low- and middle-income countries for a blueprint in building capacity.

AIDS and Related Research Study Section Reorganization: Update and Evaluation
Valerie Durrant, Ph.D., Director, Division of AIDS, Behavioral and Population Sciences, Center for Scientific Review (CSR), NIH

Dr. Valerie Durrant explained that CSR reviews about 75 percent of NIH grant applications; the rest are reviewed by individual ICOs. CSR emphasizes reviewing applications in a fair, timely, and expert way that is free of inappropriate influences. Transparency is one of CSR's core principles. Most HIV-related research is reviewed in the AIDS and AIDS-Related Research Integrated Review Group (IRG), which has a uniquely quick pace of review that requires a different review structure and reviews only of applications with direct relevance to HIV.

Dr. Durrant outlined the history of the IRG, explaining that its recent reorganization aimed to adjust the IRG's alignment with the most relevant science context. The focus areas of the new groups reflect the shift in priority from acute disease to chronic infection, with a recognition of the interdisciplinary nature of the current field, particularly in translating research to treatment and public health. CSR has implemented an elaborate process to ensure that the study sections are identifying the highest-quality research and supporting the NIH mission, as well as a review every 5 years to keep the study sections focused on current science.

Since the reorganization, each new study section has met three times. Most are receiving 60 to 85 applications, which seem to be successfully focused within the new thematic areas. An additional marker of success is the reduction in the use of Special Emphasis Panels (SEPs), which previously were required often to review applications that did not fit the previous section's focus areas. Success can be measured by the proportion of applications from ESIs; increases suggest that the reorganization reduced the areas of science that ESIs might consider outdated. Since the reorganization, reviewers are being used more efficiently, leading to a higher quality of reviewers. Additionally, applications with the highest scores show a diversity of topics, demonstrating that the full scope of the study sections is represented.

Next steps include continuing to transition reviewers to panels that best fit their expertise and increasing transparency by revising application guidelines to include more specificity. Stakeholder input currently is being collected, with surveys scheduled to be distributed soon.

Discussion Highlights

Dr. Durrant clarified that study section member conflicts of interest are reviewed in SEPs, noting that although there is no formal evaluation structure for conflicts of interest, the expectations are clear and written into the best practices. Reviewers and the platform for the review have been evaluated for appropriateness as well.

In response to a question about how grants funded by these study sections affect the field, Dr. Durrant explained that CSR studies publication and citation rates, noting which grants resulted in no publications, but cautioned that the lag time is significant. She emphasized that peer review is a human process, so it is subjective, and requested suggestions for groups to compare to better assess success.

When cautioned about the differences between human subjects research and basic science research, particularly in the expertise required on the review panels, Dr. Durrant explained that the group is attentive to the issue and working to ensure that mixed reviews support the science.

Dr. Durrant clarified that the population science study section receives too many applications, so CSR is reviewing the overlaps between topic areas to determine whether the boundaries can be refined.

Public Comment
Jennifer Kates, Ph.D., Kaiser Family Foundation

Dr. Kates stated that no written public comments had been received.

Closing Remarks/Adjournment
Maureen M. Goodenow, Ph.D., OAR, NIH
Jennifer Kates, Ph.D., Kaiser Family Foundation

Dr. Goodenow thanked the Council members, guidelines working groups, and speakers. She outlined future meetings and plans to celebrate World AIDS Day (December 2, 2019) and recognized OAR's Piper Brown, who plans to retire at the end of the year.

Dr. Kates expressed her thanks for the opportunity to represent distinct perspectives on the OARAC and adjourned the meeting at 4:06 p.m. EDT

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

- S -	2 / 27 / 20
Jennifer Kates, Ph.D. Chair, OARAC	Date

- S -	2 / 27 / 20
CAPT Mary Glenshaw, Ph.D., M.P.H. Executive Secretary, OARAC	Date