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

# Office of AIDS Research Advisory Council Fiftieth Meeting

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

### **Meeting Minutes**

Council Members Present: Dr. Charles Wira (Chair), Dr. Jay Radke (Executive Secretary), Dr. Tricia H. Burdo, Dr. David D. Celentano,\* Dr. John J. Chin, Dr. Elizabeth Connick, Ms. Linda M. Dee, Ms. Dázon Dixon Diallo, Dr. Jennifer Kates, Dr. Lynne M. Mofenson, Dr. William G. Powderly, Dr. Scott D. Rhodes, Dr. Kimberly K. Scarsi, Dr. Bruce R. Schackman, Dr. Babafemi Taiwo

**Ad Hoc Members Present:** Dr. Heidi M. Crane,\* Dr. David M. Smith,\* Dr. Ingrid V. Bassett, Dr. Margaret L. Brandeau, Dr. Maureen M. Goodenow (Director, Office of AIDS Research)

*Ex Officio* Members Present: Dr. Julie Ake, Dr. James M. Anderson, Dr. John Brooks, Dr. Roy M. Gulick, Dr. Victoria J. Davey, Dr. Sarah Read

**Advisory Council Representatives Present:** Dr. Richard E. Chaisson, Dr. Carlos del Rio, Dr. Alan E. Greenberg, Dr. Robert Yarchoan

**Invited Speakers and Guests:** Dr. Kendall J. Bryant, Dr. Patrice Desvigne-Nickens, Dr. David Goff, Dr. Bill G. Kapogiannis, Dr. Helene Langevin, Dr. Carl Schmid

Council Members Absent: Dr. Jonah B. Sacha, Dr. Blanton S. Tolbert

\* Participated remotely.

#### **Welcome and Meeting Overview**

Charles Wira, Ph.D., Geisel School of Medicine at Dartmouth

Dr. Charles Wira welcomed participants to the fiftieth 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 forty-ninth OARAC meeting, held on November 15, 2018. Dr. Lynne Mofenson moved to accept the draft minutes from the forty-ninth OARAC meeting; the motion was seconded by Dr. Scott Rhodes. Members of the Council voted to approve the minutes. Dr. Wira reviewed the fiftieth meeting agenda, noting the inclusion of time for public comments.

# Report of the Office of AIDS Research (OAR) Director

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

Dr. Maureen Goodenow welcomed attendees and noted new Institute and Center Directors Dr. Helene Langevin of the National Center for Complementary and Integrative Health (NCCIH), Dr.

Bruce Tromberg of the National Institute of Biomedical Imaging and Bioengineering (NIBIB), and Dr. Noni Byrnes of the Center for Scientific Review (CSR). Dr. Goodenow additionally commented on the new and changing staff at OAR. Donna Adderly will be retiring after 30 years at the OAR. Carlo Johnson will be the new Supervisory Budget Analyst. The new deputy director of OAR is Dr. Timothy Holtz, who will begin at OAR in June.

Dr. Goodenow explained that the OAR produces two budget documents each year. The Congressional Justification (CJ) Budget, an annual report to Congress that justifies the President's budget for NIH HIV research and the OAR, recently was approved and is posted on OAR's website. The Professional Judgment (PJ) Budget estimates the amounts necessary to conduct all appropriate AIDS activities and optimally fill the NIH research agenda, without regard for the likelihood of receiving these funds. The PJ Budget recently was submitted to the Office of Management and Budget (OMB) and Congress with a fiscal year (FY) 2020 request that was 15 percent greater than the FY 2019 estimated budget for NIH's HIV/AIDS portfolio. This increase would be distributed across OAR's research priorities, with 30 percent dedicated to efforts under the "Reducing the Incidence" area to focus on preventing new infections.

The NIH Strategic Plan for HIV and HIV-Related Research is transitioning to a 5-year cycle for FY 2021–2025; OAR will assemble a OARAC/NAEC working group to provide input on the development of that plan. Additional input on NIH's HIV research priorities currently is being gathered through a request for information (RFI), with stakeholder engagement sessions planned throughout the United States. The priorities may be shifted after input from the community.

Dr. Goodenow reviewed the research portfolio in relation to the current scientific priorities and demonstrated that the broad categories designated in the priorities can be divided into more detailed areas, such as vaccine and nonvaccine spending under the "Reducing the Incidence" category. She noted that, for FY 2019, the NIH already had approved for HIV research a \$45 million increase above the FY 2018 budget; these funds are focused on vaccine research and comorbidities, particularly neurological and cardiovascular complications of HIV infection.

In addition to the initiatives discussed, OAR reviews the research portfolio annually. When projects nearing completion are determined to be no longer aligned with current priorities, their dollars are moved to a strategic fund for which all Institutes, Centers, and Offices (ICOs) with HIV research agendas can compete. As new projects receive support from the strategic fund, the research areas emphasized by OAR shift over time. Since this process was instituted in 2015, the percentage of projects aligning with the priorities has increased from 83 percent of the NIH HIV portfolio to more than 95 percent in 2019.

Dr. Goodenow explained the Ending the HIV Epidemic initiative, a collaborative national response announced during the President's 2019 State of the Union address that aims to reduce new infections by 75 percent in the next 5 years and 90 percent in the next 10 years. The four key strategies are rapid diagnosis and treatment, protection of those at risk, rapid response to growing clusters of infected populations, and prevention of new infections. The plan focuses on 48 counties, seven states, Washington, D.C. and San Juan, Puerto Rico, which have the greatest burden of new HIV diagnoses. Centers for AIDS Research (CFARs) and National Institute of Mental Health (NIMH) AIDS Research Centers (ARCs) are key to this effort. A major focus of the work will be to translate existing research generated by the NIH into practice, including behavioral and social sciences research, research on microbicides, and both vaccine and nonvaccine prevention methods.

Dr. Goodenow updated attendees on the recent meeting of the President's Advisory Council on HIV/AIDS (PACHA), which has been reconstituted and includes new co-chairs. She added that PACHA will be seeking additional members.

### Discussion Highlights

When asked about the low funding amounts for the "Research Toward a Cure" priority, Dr. Goodenow explained that this measurement seems lower than it actually is because coding for such research was implemented more recently than the research itself. She added that differences in funding for the priorities do not reflect the priorities' importance; basic science research requires less funding than animal or human trials, so any comparisons must consider the focus of research across any projects being evaluated. Dr. Goodenow emphasized that resources will be reallocated to meet changing needs based on new scientific discovery.

A council member commented on the need to support early stage investigators in the HIV field. Dr. Goodenow explained that the NIH has a number of efforts in place to track and support early stage investigators; the OAR is examining the HIV portfolio to align these efforts.

Dr. John Brooks responded to a question about the gap between evidence and translation to practice, explaining that the Centers for Disease Control and Prevention (CDC) aims to raise awareness of successful strategies, such as pre-exposure prophylaxis (PrEP), both among people at risk and health care providers, and to increase training. A member commented on a new survey of the U.S. general public, noting that, although only 40 percent of respondents had heard of PrEP, this was a significant increase from the 14 percent who had heard of PrEP in 2014.

Members asked what OARAC members could do to inform Ending the HIV Epidemic implementation and dissemination and encouraged the OAR to consider proven implementation science when trying to reach marginalized communities in a coordinated way. Dr. Wira acknowledged the importance of understanding the unique aspects of each area of the country before implementing any strategies.

In response to a question, Dr. Goodenow confirmed that funding for research into aging with HIV has increased 50 percent over the past 4 years.

# 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., Weill Medical College of Cornell University
Bill G. Kapogiannis, M.D., Eunice Kennedy Shriver National Institute of Child Health and Human
Development (NICHD), NIH
John Brooks, M.D., CDC

Dr. Trip Gulick commented that the guidelines are fulfilling their mission to provide treatment recommendations for U.S. providers, as proven by hundreds of thousands of page views, app downloads, and increasing rates of use. Within the past year, the section on substance use in HIV in the adult antiretroviral therapy (ART) guidelines was updated significantly to expand the information on opioid use. An upcoming revision will address many other substances with the help of three new members of the guidelines panel who are substance use experts. Other updates this year will include the "When to Start" section—particularly the information on early initiation of therapy—and the section on treatment and prevention. Additional planned edits to

the "When to Start" section include information on HIV-2, cost considerations, drug interactions, and neural tube defects related to the Botswana study.

A new section with information on transgender individuals and HIV currently is in development. Dr. Gulick commented that the transgender population is overrepresented in the HIV population, with about 14 percent of transgender individuals diagnosed with HIV. Two new members of the guidelines panel with expertise in this area were recruited for this effort. Transgender issues planned for this section include drug-drug interactions between ART and gender-affirming hormonal therapy, challenges in the care continuum, interpretation of laboratory parameters, and specific comorbidities related to hormonal therapy. Dr. Gulick commented briefly on membership changes to the adult ART guidelines panel.

Dr. Brooks noted that the adult opportunistic infections guidelines continue to thrive. The panel is considering succession planning and has robust leadership communication. The sections are updated as close to real-time as possible by updating each chapter independently. Each chapter now lists the date of last review or update.

One important update to these guidelines is the creation of a new alphabetized table of contents for pathogens. Dr. Brooks noted that, although information on some pathogens changes rarely, information on others—including tuberculosis and hepatitis C—evolves rapidly, so being able to find this information easily is particularly important. Other sections updated since the last meeting include the hepatitis B chapter and expansion of its discussion of the new two-dose hepatitis B vaccine and chapters on progressive multifocal leukoencephalopathy, mycobacterium avium complex, human papillomavirus (HPV), tuberculosis, herpes viruses, and hepatitis C. A new section on immunization overviews has been implemented as well. Planned updates include the sections on bacterial repository, *Pneumocystis* pneumonia, *Cryptosporidium*, histoplasmosis, talaromycosis, and microsporidiosis.

Dr. Bill Kapogiannis presented on updates to the pediatric ART and opportunistic infection guidelines and the perinatal guidelines. Several sections of the pediatric guidelines, shared with the perinatal guidelines, were updated since the last meeting of the OARAC. The next pediatric guidelines publication was scheduled for April 2019.

The major update to these guidelines relates to the safety concerns regarding the use of dolutegravir at the time of conception and during pregnancy. Pediatric and adolescent providers are advised to discuss the potential risk of neural tube defects with patients who are receiving or initiating dolutegravir and with their caregivers before these patients become sexually active. Relevant updates in the pediatric ART guidelines include the sections on regimens for initial therapy of antiretroviral-naive children, specific issues in ART for adolescents living with HIV, modifying ART in children with sustained virologic suppression, recognizing and managing ART failure, and dolutegravir and the Appendix A pediatric antiretroviral drug information. These updates have been harmonized with and linked to the adult and adolescent ART and perinatal guidelines, with specific recommendations on the initiation and use of dolutegravir in women with childbearing potential and pregnant women.

Specific sections updated include expanded recommendations for what regimens to start and what not to start in antiretroviral-naive children, specific issues in ART for adolescents living with HIV, management of medication toxicity or intolerance, and management of children receiving ART. The drug sections have been updated to include newly approved drugs or those that have been endorsed for use in children and adolescents; older antiretroviral drugs have been archived.

Recent revisions to the pediatric opportunistic infection guidelines include updated recommendations for preventing vaccine-preventable diseases, such as meningococcal vaccines and the 9-valent HPV vaccine. Remaining sections of these guidelines have been updated within the last 3 years or are in earlier stages of revision.

A full revision of the perinatal guidelines is published once a year, and the next publication is expected in late fall or winter. The major change in this area is the significant portion of members rotating off the panel; and new members with relevant expertise have been added from diverse parts of the country.

# Update on the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) and NIH

James Anderson, M.D., Ph.D., DPCPSI, NIH

Dr. James Anderson recounted the history of DPCPSI as a connecting body that helps coordinate and plan research that cuts across the NIH. Four offices already in existence when DPCPSI was created—the OAR, the Office of Research on Women's Health, the Office of Behavioral and Social Sciences Research, and the Office of Disease Prevention—report through DPCPSI and directly to the NIH director. Dr. Anderson noted that DPCPSI oversees the Common Fund, which supports projects that do not fit under the mission of a single ICO. Other offices supported by DPCPSI include the Office of Research Infrastructure Programs, the Sexual and Gender Minority Research Office (SGMRO), the Tribal Health Research Office (THRO), and the Office of Data Science Strategy (ODSS).

Dr. Anderson explained that DPCPSI's work to coordinate across ICOs helps expand research and its effects; DPCPSI aims to identify and address research barriers as well. For example, the SGMRO has worked to develop strategies to measure LGBTQ status and ensure that researchers incorporate those measures into their work. The SGMRO adds to this effort by supporting community-building strategies, such as career development, mentor connection, and regional workshops to build a national network of researchers working in LGBTQ health.

The ODSS works to collect disparate data generated by researchers and make it interoperable. Dr. Anderson noted that the ODSS soon will start a program for undergraduates in computational sciences who are interested in serving the public. Another new program aims to recruit people from Silicon Valley who can bring computational expertise to the NIH for several years, but this program has no participants yet. The ODSS currently is looking for a director, which will be a challenging job for someone who has both computational skills and the ability to work in the NIH space.

Dr. Anderson reminded attendees of the seriousness of the opioid crisis, noting in 2017 more than 70,000 deaths from opioid overdose were reported. NIH's Helping to End Addiction Long-Term (HEAL) Initiative is a set of new coordinated funding opportunities across ICOs to address research questions necessary to solve this issue. Research for the HEAL Initiative focuses on better pain management—including nonaddictive pain medications, sodium channel modifiers, and electrical modification of the autonomic nervous system—in addition to prevention and treatment strategies. Dr. Anderson emphasized that this is a multi-ICO collaboration, an approach that has been an increasing trend in the NIH over the past 10 to 20 years. The HEAL Initiative covers prevention, basic, translational, clinical, and implementation science, including some novel approaches. Dr. Anderson noted that more research is needed in the criminal justice system and health care setting.

In response to the HEAL Initiative, the Common Fund developed a program called Acute to Chronic Pain Signatures to address basic science challenges in this sphere. The goal is to determine biosignatures to predict a tendency toward chronic pain syndrome or opioid dependence. This will measure basic clinical characteristics—including social characteristics, mental health, and co-occurring pain syndromes—and incorporate imaging studies. Once an approach to quantify pain is identified, biospecimen studies, such as whole-genome sequencing, can be conducted to determine how the many variables of chronic pain susceptibility can be organized. Several sites will recruit patients from various contexts, then all data will be sent to common centers for integration and released as quickly as possible.

Another Common Fund program is the Somatic Cell Genome Editing program, which capitalizes on the most recent and powerful gene-editing approaches, including CRISPR-Cas9 and related systems. After holding workshops with companies working in this space, the NIH identified a need for standardized approaches to safety assessment, better methods for delivery, and expansion of the technology. This program takes a target-agnostic approach to improve the safety of the toolkit used for genome editing.

Dr. Anderson requested Council members' input on NIH's response to the Moderate Alcohol and Cardiovascular Health (MACH) Trial, which was intended to be a multicenter randomized trial to assess the potential benefits of one alcoholic drink per day on cardiovascular disease outcomes and new cases of diabetes. The trial was funded partly by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), but other funding came from private donations by alcoholic beverage industry members. The Advisory Committee to the Director (ACD) was asked to review whether the scientific premise was sound and found that several NIAAA staff members, including the investigator eventually awarded the trial, had frequent engagement with industry representatives. Combined with these concerns, the ACD determined that the MACH Trial was not powered appropriately to find the adverse effects and recommended that the trial be stopped. Additionally, the ACD recommended that the NIH examine additional ways to monitor staff and review the mechanisms for public-private partnerships.

To ensure greater transparency, funding opportunities should be cleared by advisory bodies, such as OARAC; Dr. Anderson suggested that such committees would be used for advice more often than in the past. He emphasized that because program officers play many roles, the NIH must ensure that they understand their relationship to extramural parties and their role as advocates for the science. In conjunction with this idea, workshops and funding opportunities should be more open to public attendees and other viewpoints.

# Discussion Highlights

A member cautioned against commenting in depth on the MACH Trial without all the information but noted that partnerships with outside organizations are critical in the HIV/AIDS arena, as is transparency. The member added that everybody has a conflict, regardless of whether that conflict is a financial interest or a desire for career advancement. Dr. Anderson suggested that partnerships are acceptable with careful study design. Although there are many nuances to the design of public-private partnerships, the intent is to protect such partnerships to ensure that they can continue with sound science. Members added that public-private partnerships supported many of the key advances in HIV/AIDS research.

Members commented on the importance of workshops in facilitating the exchange of ideas between program and extramural scientists. Additionally, they encouraged the NIH to craft a

response to the MACH Trial that addresses the issues without overreaching in the opposite direction.

# NCCIH Strategic Priorities Related to Resilience and Health Restoration Helene Langevin, M.D., NCCIH, NIH

Dr. Helene Langevin noted that, although NCCIH does not fund much research in the HIV/AIDS domain, many themes of its work are relevant to people living with HIV/AIDS at this time. Although many people living with HIV/AIDS have a near-normal life expectancy with treatment, many continue to suffer, particularly from such conditions as chronic activation of the immune system, systemic inflammation as a result of ART toxicity, and accumulated chronic noncommunicable diseases common to the entire population, which can have additional inflammatory effects. NCCIH is interested in preventive strategies against such inflammation, including behavioral intervention, reduction of psychological stress, improved sleep, and musculoskeletal inflammation.

Dr. Langevin emphasized the importance of connective tissues in working with muscle and bone to produce movement. The connective tissue also contains many immune cells, so Dr. Langevin's research questions whether mechanical forces in connective tissue can influence immune responses, such as inflammation. Connective tissue changes shape throughout life in response to posture, injury, and other activities, leading to an imbalance in musculoskeletal force and causing muscle atrophy, which could allow the muscles to be infiltrated by fibrotic connective tissue. Repetitive movement with excessive force and poor alignment can lead to inflammation. The combination of all these factors weakens the structure of the body and puts vulnerable structures at risk.

Nonpharmacological treatments—mind and body approaches—can have beneficial effects in preventing some of the long-term problems associated with these factors. Mindful exercise and assisted movement-based therapy are successful preventive examples; when connective tissues atrophy beyond the point at which the person can self-correct, manual therapy can help stretch the tissues, restore some mobility, and reduce inflammation. Many of the mindful skills that help with chronic musculoskeletal pain can be applied to sleep, stress, or eating. Dr. Langevin proposed that behavioral intervention—specifically applied with the aim of reducing inflammatory burden throughout the lifespan—would be of great importance to patients with chronic conditions, such as HIV/AIDS, and that complementary and integrative health care should play a role in this area.

### Discussion Highlights

When asked how to convey this information to researchers, Dr. Langevin noted that information dissemination and generation of research opportunities are part of NCCIH's mission. She also noted that the NCCIH has several collaborations in place, including with the National Institute on Aging and within the HEAL Initiative.

In response to a question about mindfulness strategies in relation to adherence issues, Dr. Langevin explained that the NCCIH had funded one grant on mindfulness for medication adherence and emphasized that this critically important area is just starting to be researched. She added that the science of behavior change is critical to understand in preventive medicine. Cognitive behavioral therapy—which incorporates some strategies from nonmedical disciplines like yoga—is becoming more prominent as a treatment for chronic pain.

Dr. Langevin elaborated on the natural products studied by NCCIH. Many clinical trials on vitamins, nutritional supplements, and other such products failed, so the NCCIH is reevaluating whether combinations of natural molecules, including whole-plant extracts, at lower doses could be more effective.

# **Updates from NIH Advisory Council Representatives**

### **AIDS Research Advisory Committee (ARAC)**

Richard Chaisson, M.D., Johns Hopkins School of Medicine, Baltimore, MD

Dr. Richard Chaisson updated the attendees on the ARAC meeting held on January 28, noting the 4.8 percent budget increase for NIAID and the extensive discussion around the recompetition of HIV networks. A number of other ICOs are collaborating in the networks, which have specific goals. The prevention goal involves reducing HIV incidence and developing a range of modalities that are safe, acceptable, desired, and effective at meeting the needs of the people who require protection. In addition, the announcement for this goal stresses the importance of retaining the flexibility to address emerging epidemics and the strategies and tools for doing so. The major foci for therapeutics are novel and durable treatments for HIV, particularly long-acting formulations and broadly neutralizing antibodies. Dr. Chaisson explained that broadly neutralizing antibodies also fall under the concept of a cure or ART-free remission; in general, the idea is to achieve drug-free, treatment-free control, regardless of whether that is also virus-free.

The goals for coinfections and comorbidities are to improve treatments for tuberculosis, improve preventive therapy, focus on extra-pulmonary forms of tuberculosis, and review diagnostic modalities and biomarkers to identify the predictors of risk and response to treatment. For the pediatric network, neurological complications are emphasized; in the adult network, cellular dysregulation, inflammation, preventing end-organ disease, and hepatitis B cure are emphasized. As for vaccines, Dr. Chaisson noted the importance of evaluating vaccines to prevent HIV infection and defining correlates of risk to develop a strategy for vaccinating young people before their sexual debut. In addition, vaccine goals should incorporate behavioral and social science research into HIV prevention. The tuberculosis portfolio aims for more work on tuberculosis vaccines, as well as other methods of prevention of tuberculosis infection and disease.

Dr. Chaisson explained activities under the Ending the HIV Epidemic initiative, emphasizing that the initiative is an implementation of information already in existence. NIH's role is to use implementation research to achieve the initiative's goals, in partnership with the other agencies providing substantial contributions to the effort. Dr. Chaisson emphasized that Johns Hopkins' CFAR will work with its hospital in a high-incidence area of Florida to address HIV in adolescents and young adults. He noted that the Division of AIDS at NIAID has issued an RFA for supplements to CFARs to address the four pillars of the Ending the HIV Epidemic by examining and responding to local-level structural barriers. Dr. Chaisson emphasized that locally defined concepts, developed locally in consultation with local parties, are the major players in implementing the therapies and prevention strategies dictated by this initiative.

# National Advisory Council on Drug Abuse (National Institute on Drug Abuse [NIDA] Council)

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

Dr. Carlos del Rio reminded attendees that the role of NIDA is to address research around substance use; he noted the importance of understanding the intersection between substance use and HIV. NIDA's research priorities include basic research, prevention research, therapeutics, comorbidity research, and addressing the HIV care continuum.

One recent approval relates to leveraging big data to elucidate the neurobiologic basis of substance use disorder. Another is to explore the precision of pharmacology and assess how the opioid epidemic affects HIV. The role of inflammasomes in substance use and HIV comorbidities will be studied; another RFA will support more research into PrEP use among substance use populations.

Dr. del Rio mentioned the HIV Prevention Trials Network (HPTN) 074 study, a NIDA co-funded randomized trial to assess scalable integrated interventions to engage people who inject drugs in HIV treatment and medication-assisted treatment through systems navigation. The study showed that the interventions improved biologic control of those who have HIV, increased use of medication-assisted therapy, and decreased needle sharing and other risky behaviors. Dr. del Rio emphasized the importance of implementation in ending the HIV epidemic, noting that designing new implementation strategies and implementing existing strategies are equally important.

Dr. del Rio commented on the Director's Pioneer Awards, which offer investigators the ability to conduct innovative research but have not received enough applicants. He encouraged council members to urge researchers at their institutions to apply.

Several new RFAs have been released relevant to this area. In addition, NIDA is considering integrating several HIV and substance use cohorts. NIDA also continues to collaborate with many ICOs around the issue of HIV. Dr. del Rio noted the importance of ensuring that researchers understand the right questions around how substance use disorder relates to HIV and integrate them more effectively into clinical trials. He recommended increasing the number of substance use investigators conducting HIV studies.

#### **National Cancer Advisory Board (NCAB)**

Robert Yarchoan, M.D., HIV and AIDS Malignancy Branch, National Cancer Institute, NIH

Dr. Robert Yarchoan presented an overview of recent activities within the NCI. The AIDS Malignancy Consortium (AMC) RFA was reissued recently. The AMC develops and evaluates clinical interventions for the treatment and prevention of malignancies, conducts trials, investigates the biology of malignancies in the context of these trials, and collects specimens that can be distributed to other investigators. NCI's focus in AIDS is largely on malignancies in the context of AIDS; an intramural program focuses on HIV research directly. AIDS cancer has been an increasing cause of death in people with HIV, particularly focused on non-AIDS-defining tumors in some geographic areas and AIDS-defining cancers and associated malignancies in others. The AMC has had successful accrual at a number of domestic sites and some sites in Africa; the establishment of sites in South America and Central America is in progress.

Accomplishments in the recent grant cycle include evaluating immunotherapy approaches to determine the success in people with AIDS and low CD4 counts, new frontline treatment for AIDS lymphoma, treatment with novel mechanists of action for Kaposi sarcoma, and assessing HIV-associated aggressive lymphoma. Dr. Yarchoan noted that transplantation has been efficacious and safe for such patients.

He explained the Anal Cancer High-Grade Squamous Intraepithelial Lesion (HSIL) Outcomes Research (ANCHOR) study. Anal cancer is caused by HPV, is preceded by HSILs, and is one of the most common cancers in people with HIV. The ANCHOR study is a randomized controlled trial to establish whether treatment of anal HSILs is effective to prevent anal cancer, as well as to measure the effects of screening on quality of life and elucidate molecular pathogenesis. Although ANCHOR is a treatment trial, the ultimate goal is to determine whether HSIL screening is warranted.

Other activities include studies of the transmission of Kaposi's sarcoma herpesvirus, the virus that causes Kaposi sarcoma, Castleman's disease, and one type of lymphoma; studies of the tumor niche; a U.S./Latin American clinical trials network to prevent HPV and HPV-associated diseases in Latin America; and the Provocative Questions initiative, in which investigators identify areas that are understudied but are ready for study. Dr. Yarchoan concluded by inviting attendees to a meeting on AIDS malignancies in the fall.

# **National Advisory Mental Health Council (NAMHC)**

Alan Greenberg, M.D., M.P.H., Milken Institute School of Public Health, The George Washington University

Dr. Alan Greenberg noted that he was asked to provide an overview of the Enhanced Comprehensive HIV Prevention Planning Project (ECHPP), which was released by the CDC in 2010 and prescribed 14 required interventions, many of which are the same as the interventions used in the Ending the HIV Epidemic initiative. He explained that a supplement was released days after the announcement of the Ending the HIV Epidemic initiative to allow CFARs and AIDS Research Centers to compete for planning grants, which will be used specifically for work in collaboration with health departments and community-based organizations. Responses have arrived quickly, suggesting that it will be a highly competitive and productive initiative. Proposals must address the four key pillars and work synergistically, as they did in the CFAR ARC ECHPP initiative.

The CFAR ECHPP workgroup was formed to promote collaborations between CFARs and the Department of Health on implementing ECHPP, which was instrumental in reducing barriers between academic and public health spheres. The NAMHC's partnership with the D.C. Health Department succeeded in reducing newly diagnosed HIV cases in D.C. by more than 70 percent.

ECHPP expanded in three supplements from supporting nine CFARs in cities with the highest prevalence to including ARCs and additional CFARs. Dr. Greenberg noted that national meetings likely will be a component of the Ending the HIV Epidemic initiative; the two national meetings during ECHPP's lifespan aimed to present project results and propose methods. He added that many of the representatives of health departments who attended had not previously met CFAR representatives in person.

Dr. Greenberg commented on several interesting studies over the course of ECHPP and noted some lessons learned. The CFAR-ECHPP working group successfully linked public health-

oriented investigators from across the United States. The national meetings built teamwork and publications demonstrated productivity. The successful links between CFARs and local health departments operated on a foundation of implementation science. ECHPP addressed the National HIV/AIDS Strategy (NHAS) by linking with other agencies; the NIMH played a major role in helping to oversee the CFAR-ECHPP initiative. Some challenging lessons were learned, such as how to resolve the occasional discrepancy between priorities at departments of health and those of academic research. Ensuring clear communication and coordinating among many groups with scientific foci determined by local concerns were additional challenges. Dr. Greenberg stressed the importance of staffing coordinating working groups with employees who are able to manage the complex coordination of the projects.

He reiterated that the infrastructure and collaborations built by the CFAR-ECHPP working group can serve as a foundation for the NIH implementation science component of the Ending the HIV Epidemic initiative, adding that the lessons learned position the NIH and CFARs to initiate effective programs quickly.

# Discussion Highlights

In response to a question about how to reach areas that do not have CFARs, Dr. Chaisson stressed that the use of the CFARs is a strategy for nimbleness—a first step to start the initiative quickly and efficiently. CFARs' overlap with high-burden areas is imperfect, but many within the CFARs are experts in implementation science and contribute to an inter-CFAR implementation science working group. Broader implementation is planned for the future. Dr. del Rio added that end-of-year supplements to CFARs helped jump-start the initiative and reminded council members that the bulk of the Ending the HIV Epidemic funding will be implemented in FY 2020.

When asked about studies of medication adherence, Dr. Greenberg noted that applications relevant to PrEP have been received. Dr. del Rio added that in some countries, PrEP is available at a very low cost, which affects uptake and adherence.

Members emphasized the importance of defining specific standards for engagement with community-based organizations to ensure that involvement with the community is supportive and robust.

Dr. Greenberg compared the pioneering nature of ECHPP and its use of much smaller projects to the Ending the HIV Epidemic initiative, which aims to develop scalable interventions. He reiterated that community engagement will be strong within this initiative. Dr. del Rio added that the Ending the HIV Epidemic initiative was mentioned specifically by the president and stressed that it is not a research initiative and that the bulk of the effort will be conducted by other organizations, whereas the NIH's focus will be on implementation.

When asked about NCI's success in ensuring that individuals with HIV are included in clinical trials for non-HIV-related cancers, Dr. Yarchoan commented that the guidelines for this inclusion are very exciting and have been much discussed, but actual inclusion has been less successful. Inclusion and exclusion criteria for each protocol are being reviewed and updated.

# Update from the National Heart, Lung, and Blood Institute (NHLBI) on HIV/AIDS Activities—HIV-Focused Research at the NHLBI

David Goff, M.D., Ph.D., Division of Cardiovascular Sciences, NHLBI, NIH

Dr. David Goff described some of the HIV-related initiatives at the NHLBI, which began to address HIV-related comorbidities slightly more than 10 years ago. The NHLBI's strategic goals are to understand human biology, reduce human disease, advance translational research, and develop the workforce and resources. Dr. Goff noted that these broad goals are refined by each division to apply to their area of interest. In terms of HIV, the foci are on mitigating comorbidities related to heart, lung, blood, and sleep; and accelerating the search for a cure.

To mitigate comorbidities, the NHLBI is working to understand lung diseases in patients with HIV. Specific topics include emphysema, tissue-destructive phenotypes, and other ways that HIV infection changes the lung microbiome. In cardiovascular disease, topics of interest include whether protease inhibitors lead to cardiac dysfunction that may contribute to the heart failure experienced by patients with HIV. Dr. Goff noted that the NHLBI is particularly interested in heart failure with preserved ejection fraction, a common comorbidity for patients with HIV.

Dr. Goff expressed NHLBI's humility in its role as the lead steward Institute for the Multicenter AIDS Cohort Study (MACS) and Women's Interagency HIV Study (WIHS) combined cohort. NHLBI staff are working closely with staff from 15 other ICOs to chart the next phase, which will shift the focus toward comorbid conditions. Protocols are in development for the initial examination; some award notices have been released, and others will be released later this spring. The NHLBI is interested in supporting echocardiograms and cardiac magnetic resonance imaging to assess cardiac structure related to heart failure, studying dysrhythmias that occur in people with HIV, and collecting data around biomarkers that may be related to cardiovascular and pulmonary conditions.

The Division of Lung Diseases is interested in supporting pulmonary function testing, computerized tomography scans to assess lung fibrosis, and sleep studies. The NHLBI's Center for Translational Research and Implementation Science will help inform successful delivery of PrEP and other kinds of guideline-based care for prevention of comorbidities. Dr. Goff commented that improved integration could be an appropriate challenge for the NHLBI to tackle.

A sleep study in the MACS trial revealed that 90 percent of the cohort has sleep apnea, and 17 percent of the cohort has pathogenic periodic leg movements. In the WIHS component, sleep pilots are entering the recruitment phase, so the results can reveal more about sleep disorders in men and women.

The ImPlementation REsearCh to DEvelop interventions for People Living with HIV (PRECluDE) initiative supports multidisciplinary collaborative teams conducting late-stage translational research and implementation science around comorbid conditions in heart, lung, blood, and sleep. This initiative looks at vulnerable populations, including the medically underserved, rural patients, low-income patients, and patients from racial and ethnic minorities. Five awards have been given in this space for very different projects.

New initiatives have been approved for FY 2020. Heart, Lung, and Blood Comorbidities Implementation Models in People Living with HIV (HLB SIMPLe) is an international, low-income country version of PRECluDE that assesses ways to stimulate implementation science to prevent HLB comorbidities in low-income international settings. This study could lead to generalizable knowledge for other countries or settings. Another new initiative, a Notice of Topic

of Special Interest (NOTSI), invites grant applications for novel research on heart, lung, blood, and sleep comorbid conditions in existing cohorts. These R01 applications will be reviewed through standard study sections. Dr. Goff commented that NOTSIs are particularly helpful when existing study sections are available that could evaluate the applications; the NHLBI believes that this field has developed to a point where it can support productive research in this area. The Stimulating Exploratory Research on HIV/AIDS Contributions to Heart, Lung, Blood, and Sleep Comorbidities (SEARCH) NOTSI is intended to support smaller basic research grants to bring early career and basic HIV scientists into the heart, lung, blood, and sleep field to apply their expertise.

The NHLBI is accelerating research toward a cure, particularly hematopoietic stem-cell transplantation. Much progress has been made to reduce the risk in this procedure after its initial contributions to the cure reported for the Berlin patient. In the Beyond Heart program, major achievements include enhanced T-cell progenitor seeding of the thymus, T-cell neogenesis, diversification of the T-cell receptor repertoire, increased peripheral T-cell reconstitution, and donor CD4 regulatory T-cell generation and improved survival after hematopoietic stem-cell transplantation. Dr. Goff commented that these significant breakthroughs promise greater applicability of this approach; several other patients recently have been announced as HIV-free. Dr. Goff noted that the cure area is advancing quickly and may soon be ready for wide-scale implementation.

The Division of Blood Diseases and Resources also focuses on the safety of the blood supply, which relates to the successes of surviving patients. The current risk to the blood supply is very low but could still result in a couple cases of transmitted HIV per year. Some concern is related to ART and PrEP, which suppress antibody conversion and the ability to detect the virus in the blood. Although individuals taking ART or PrEP are not supposed to donate blood, some studies show people donating anyway. The need to determine a way to detect HIV infection without the usual HIV antibody is of active interest in the NHLBI, particularly in relation to low- and middle-income countries.

NHLBI's implementation science group leads its efforts in crosscutting areas, such as translation and implementation science research. Additionally, the NHLBI is interested in training the next generation of scientists who will be working in this space for comorbidities and a cure. Dr. Goff noted an upcoming NIH-wide workshop, led by the NHLBI with participation from other groups, to tackle HIV comorbidities more broadly. The workshop will have components for epidemiology and population research, pathogenesis, clinical research, and implementation science and will explore the syndemic concept as it applies to HIV and HIV comorbidities. Dr. Goff explained that the syndemic concept is when multiple social situations and social influences contribute to co-occurrences of multiple epidemics in a single community or population, such as the propensity of people affected by opiate addiction, depression, and anxiety to also be affected by posttraumatic stress disorder, cardiovascular conditions, pulmonary conditions, cancer, and HIV, among other problems. Dr. Goff stressed the importance of thinking about these complex questions horizontally across focus areas.

# Discussion Highlights

One member commented on studies indicating significant cardiac and respiratory morbidity in children with HIV, both youth who are infected perinatally and children who are exposed to HIV but are not infected. Dr. Goff explained the intent to determine a collaboration between Pediatric HIV/AIDS Cohort Study (PHACS) and MACS-WIHS, particularly if participants age out of the

PHACS cohort and can then join the MACS-WIHS. He added that this does not address the issue raised, which he will make a note of to ask his colleagues.

In response to a question about the costs of stem cell transplant research, Dr. Goff commented that this approach to a cure is in its earliest stages—determining ways to make it safer is the first step. Bone marrow transplantation is very expensive, but to date, such procedures have been conducted only in patients who are already requiring a transplant; Dr. Goff hoped that technological advances would reduce the costs within a few years.

# Updates from the NHLBI on HIV/AIDS Activities—Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE): Study Status

Patrice Desvigne-Nickens, M.D., NHLBI, NIH

Dr. Patrice Desvigne-Nickens introduced REPRIEVE, a collaboration among ICOs, industry investigators, and the HIV community. Because ART has reduced AIDS-related deaths, the population with HIV is living longer, leading to an increase in cardiovascular disease and cardiovascular disease—related deaths in this community. REPRIEVE is the first outcomes trial for adverse cardiovascular events in patients living with HIV, a prospective double-blind, randomized, placebo-controlled multicenter study. The primary hypothesis is that statin therapy will reduce major adverse cardiovascular events (MACE) in participants with moderate or low atherosclerotic cardiovascular disease (ASCVD) risks. A mechanistic substudy evaluates the plaque burden, morphology, and changes over the course of treatment.

The main study currently is in the follow-up stage; primary outcomes are expected to be available in 2023. Dr. Desvigne-Nickens noted that this population has both traditional risk factors for cardiovascular disease and HIV-specific risk factors, such as chronic inflammation, activated monocytes, endothelial dysfunction, and side effects from ART. HIV infection is known to both cause immune dysfunction and activate a subset of T cells. As the viral load increases, immune activation also increases, which increases the risk of cardiovascular disease and the speed at which cardiovascular disease progresses in patients with HIV.

Statins have been proven to reduce cardiovascular risks across numerous patient groups and may be particularly beneficial for patients living with HIV. Compared with placebo, statin therapy reduces the noncalcified plaque volume and high-risk plaque features in patients with HIV and subclinical coronary atherosclerosis. Dr. Desvigne-Nickens noted that the most important question, which REPRIEVE addresses, is whether these mechanistic findings correlate to actual reduction of coronary events.

Statin therapy has not been used widely in treating patients with HIV because of safety concerns, but Pitavastatin is potent, has no adverse effects, does not interfere with ART, and has a very low safety profile. In addition, it is a single-dose, once-a-day medication, which is an advantage for patients with HIV who already have very complicated medical regimens. REPRIEVE is using an ASCVD risk calculator developed without patients with HIV, although it is unclear how it will correlate with risk in patients with HIV.

Dr. Desvigne-Nickens explained that REPRIEVE was able to respond to initial worries that the study would be underpowered by nimbly increasing the sample size and the allowed ASCVD risk, as well as extending the follow-up by 2 years. These changes resulted in additional costs, notably more than doubling the person-year follow-up costs. With assistance from collaborating ICOs and the OAR, \$18 million of the estimated \$21 million additional funds have been identified.

REPRIEVE has now exceeded its enrollment. Retention to date is much better than expected; adherence is more than 80 percent. The mechanistic substudy has exceeded its target enrollment as well; at baseline, the study is more than 98 percent complete. Dr. Desvigne-Nickens highlighted some of the baseline demographics, including 32 percent women, a median age of 50 years, more than 94 percent of patients who are statin-naive, a 10-year ASCVD risk score of 4.3, and a well-dispersed race and ethnicity. The baseline cardiovascular disease history and risk factors confirm that the trial has enrolled successfully a low- to moderate-risk HIV cohort. Dr. Desvigne-Nickens emphasized that these are patients who would not normally have been treated with statin medications. Cohorts have been recruited in other countries as well.

Testimony from three patients indicates altruistic reasons for participating in the trial, even participants at a site in Puerto Rico affected by Hurricane Maria, suggesting a high likelihood of success. Four ancillary studies are included as well, which increase the impact of REPRIEVE. Dr. Desvigne-Nickens reiterated that the use of statins as a primary prevention strategy in a large group of patients with HIV with normal or near-normal atherosclerotic risk is novel, important, and needed.

### Discussion Highlights

When asked to comment on the anticipated lost-to-follow-up rate, Dr. Desvigne-Nickens suggested that the patients currently lost to follow-up might reappear at later visits, but the study's power anticipates a 5 percent per year loss over the 8 years of the follow-up. She noted that patient testimonials suggest that the will is strong but that the study team will need to monitor this carefully.

Dr. Desvigne-Nickens responded to a question about ancillary studies on the brain, noting that although several such studies have been through peer review, none have been funded yet. When asked about objective measures of adherence, Dr. Desvigne-Nickens explained that adherence is monitored by prescriptions and patient reports. She also noted that this study does not specify ART, but participants' medication histories are collected and reviewed. Members suggested that differing ART regimens could compound regional comparisons; for example, populations in sub-Saharan Africa likely will be taking standard first-line regimens.

Dr. Desvigne-Nickens clarified that the cohort's demographics reflect the demographics of HIV prevalence. Although the percentage of women enrolled is 32 percent overall, researchers think that this will be sufficient to answer the question for the subgroup. One potential ancillary study would be to look for specific findings related to sex-specific differences in cardiovascular disease in nonaffected women. She added that the country-specific percentages of women enrolled vary depending on the context of the epidemic; for example, in Thailand, where the epidemic is related to sex work, 56 percent of enrollees are women, whereas in the United States, the HIV epidemic largely is in gay men, so the percentage of women enrolled is much lower. A member commented that many clinical trials include 20 percent women or less, so a 32 percent sample is a remarkable feat.

#### **PACHA Update**

Carl Schmid, M.B.A., The AIDS Institute

Carl Schmid provided an update on PACHA, specifically in reference to the Ending the HIV Epidemic initiative, emphasizing that now is the time when the confluence of data, tools, and leadership can make progress on this issue. He noted that tackling new infections requires

finding both people living with HIV and those who do not yet know they are infected, particularly in the areas of highest prevalence. He added that HIV in the South is becoming concentrated increasingly in specific populations, including black gay men, Latino gay men, and people who inject drugs, particularly in relation to the opioid epidemic for the latter group.

Currently successful strategies include getting people on treatment—particularly because undetectable viral loads have been found to be untransmittable—and getting PrEP to everyone who needs it. Another successful initiative is the Ryan White HIV/AIDS Program, which ensures that people have the medical care and support services to receive and adhere to care. Mr. Schmid emphasized that this is a "whole-of-society" initiative that will involve collaboration with patient groups, nonprofit organizations, academic institutions, people living with HIV, state and county health departments, and federal partners.

Mr. Schmid reported on the recent PACHA meeting, noting that the Council has 11 members, and anticipates adding more before the next meeting. PACHA passed a resolution in support of the Ending the HIV Epidemic initiative, and the goal is to provide advice to the HHS Secretary as the plan is being developed and the national strategy is being updated. PACHA will form three subcommittees to meet in between the full Council meetings. Mr. Schmid noted that this initiative has started much discussion within the community and put AIDS back on the front page of papers. He emphasized the importance of additional funding and collaborative, community-driven efforts in making this initiative more successful than previous efforts.

### Discussion Highlights

When asked whether support services are included in the retention strategies, Mr. Schmid explained that the intent to provide additional funds in the budget to the Ryan White program confirms the inclusion of the support services. He reiterated that the released budget covers only the first year, so funds are likely to increase further, as are the number of agencies collaborating in this effort. He added that much of the effort likely will be in supporting community health centers to increase prevention strategies.

Members recommended that additional PACHA members include more women, transgender individuals, people living with HIV, and other such underrepresented populations. When asked about pharmaceutical industry representation on PACHA, Mr. Schmid explained that industry representation is not new, and he emphasized the importance of partnership with industry, as well as governments and nonprofit organizations, to solve the issue.

Mr. Schmid discussed drug pricing for PrEP, noting that although the price is high, there are ways to decrease it; he added that other barriers to accessing PrEP likely have more effect, such as the difficulty of getting patients who need PrEP to places where PrEP can be acquired. Members emphasized the importance of including insurers and immigrant advocacy groups in the conversations.

An attendee clarified that the correlation between undetectable viral load and untransmittable status (U=U) does not apply in the context of blood transfusions, noting the Transfusion-Transmissible Infection Monitoring System developed to monitor changes in risk.

#### **Update from the NIAAA**

Kendall Bryant, Ph.D., NIAAA, NIH

Dr. Kendall Bryant noted that alcohol as a driver of the HIV epidemic has been underappreciated. Alcohol is the most prevalent substance of abuse among patients with HIV, along with tobacco, and is used in critical populations of young gay men at very high rates. Such chronic alcohol use affects the care cascade at every step, particularly in adherence to HIV medications. It affects both prevention and crosscutting behavioral and biological issues. Alcohol as a syndemic aspect of the HIV epidemic is important in terms of clusters of shared coinfections, comorbidities, and complications. Alcohol amplifies many common mental health problems, such as depression; intermittent bingeing patterns are common to those at greatest risk for infection in many contexts. Such patterns can interfere with the uptake of preventive interventions, especially PrEP.

Dr. Bryant suggested that the most important question is to determine whether alcohol is additive to the HIV epidemic or synergistic. He pointed out that in some areas of the world—including eastern Europe, Russia, and South Africa—rates of HIV infection are increasing and noted that these areas are the same on maps of high levels of alcohol use. Alcohol-related and HIV-related deaths share common causality around liver injury.

Studies have shown that there is no level of alcohol consumption that improves health; it has a high level of harm and strong ramifications for public health. Alcohol has been shown to be harmful in populations with HIV, even those who are virally suppressed. Even moderate levels of drinking may be linked to higher risks for death and alcohol-related health issues. Dr. Bryant suggested that there is no safe level of alcohol consumption for people with HIV; however, many do consume alcohol, the effects of which are amplified by comorbid conditions. Alcohol is considered a structural driver of HIV risk. Comprehensive HIV prevention programs are needed—research shows that interventions to reduce gender inequality, partner violence, harmful alcohol use, and other structural factors are as significant as biomedical interventions.

Alcohol imparts a range of effects, affecting immunological functioning, HIV progression, viral replication, metabolic issues, treatment sustainability, presence and severity of comorbidities, sexual transmission, depression, neurological problems, and behavioral problems related to adherence. Abstaining from or reducing alcohol use has been shown to positively affect the viral load. More complex models look at basic biology questions, such as assessing microbial translocation and its effect on immune activation and coronary outcomes.

Heavy drinkers have been shown to struggle with achieving and maintaining viral suppression. Despite its substantial burden in HIV and related illness, alcohol often is overlooked as a barrier to care for people living with HIV. Both people living with HIV and HIV care providers often incorrectly perceive alcohol use as a low priority for HIV care. Additionally, care providers are subject to burnout, depression, and misuse of alcohol. Primary care, which often is the entry point into HIV care, is inadequate at diagnosing and treating alcohol use, even for patients who do not have HIV and more so for patients with HIV.

Biomarkers and other measurement strategies for alcohol use are in development. One promising new approach is phosphatidylethanol and transdermal monitoring, allowing a 3-week measure of exposure to alcohol.

The NIAAA has supported multiple research consortia, which provide the basis for multidimensional research. Additionally, the NIAAA engages other ICOs to improve alcohol

measurement and sensitivity to the frailty and HIV outcomes. Aging is the comorbidity of greatest interest in these cohort studies because of its importance in treating the chronicity of alcohol use in HIV; components that can be studied include behavioral and biological factors, basic exposures, including oxidative stress, and incremental depletion of organ and system reserve, leading to functional decline and premature death.

Dr. Bryant emphasized that alcohol use, smoking, and depression are isolated behaviors over time, seen in both infected and uninfected populations, and that this aspect should be a focus of some of the research. Many successful behavioral interventions are available now. The NIAAA has used simulation models to assess which interventions to support and is reviewing the results with the help of OAR.

#### **Public Comments**

Charles Wira, Ph.D., Geisel School of Medicine at Dartmouth

Dr. Wira invited members of the public to comment. Bruce Richman, the Executive Director of the Prevention Access Campaign, encouraged attendees to be more proactive in informing patients and the public about U=U, emphasizing the particular need for more information in marginalized communities. Mr. Richman also reminded the council that the task section of the Treatment Guidelines should be updated to include U=U.

# **Closing Comments**

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

Dr. Goodenow thanked the Council members, guidelines working groups, and speakers. Potential agenda items for the June OARAC meeting include information on implementation science and presentations by the directors of Tribal Health Research Office (THRO) and the Sexual and Gender Minority Research Office (SGMRO).

### Adjournment

Charles Wira, Ph.D., Geisel School of Medicine at Dartmouth

Dr. Wira thanked the council members and adjourned the meeting at 4:50 p.m. EDT

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

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Charles Wira, Ph.D.	Date		
Chair, Office of AIDS Research Advisory Council			
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Jay Radke, Ph.D.	Date		
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Executive Secretary, Office of AIDS Research Advisory Council			