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

Office of AIDS Research Advisory Council
46th Meeting

November 16, 2017
5601 Fishers Lane, Room 1D13
Rockville, Maryland

Meeting Minutes

Council Members Present: Dr. Monica Gandhi (Chair), Dr. Elizabeth Church (Executive Secretary), Mr. Moisés Agosto-Rosario, Dr. David Celentano, Dr. John J. Chin, Dr. Ralph J. DiClemente, Dr. Daniel R. Kuritzkes, Dr. Lynne M. Mofenson, Dr. Scott D. Rhodes, Dr. Charles Wira

Ad Hoc **Members Present:** Dr. Ingrid V. Bassett, Dr. Tricia H. Burdo, Dr. Elizabeth Connick, Ms. Lynda M. Dee, Ms. Dázon Dixon Diallo, Dr. Roy M. Gulick, Dr. Kimberly Kay Scarsi, Dr. Bruce R. Schackman, Dr. Babafemi Taiwo

Ex Officio **Members Present:** Dr. Victoria J. Davey, Dr. Carl W. Dieffenbach, Dr. Jonathan Mermin, Dr. Julie Ake (designee of Dr. Nelson Michael)

Advisory Council Representatives Present: Dr. Richard E. Chaisson, Dr. Alan E. Greenberg, Dr. Steffanie A. Strathdee

Invited Speakers and Guests: Dr. Rebecca Fuldner, Dr. Melissa Gerald, Dr. David Goff, Dr. Rohan Hazra, Dr. Jacques Normand, Ms. Manizhe Payton

Council Member Absent: Dr. Jennifer Kates

Welcome and Meeting Overview
Monica Gandhi, M.D., M.P.H., University of California, San Francisco

Dr. Monica Gandhi welcomed the participants to the 46th 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 of the 45th OARAC meeting held on July 18, 2017. Members of the Council motioned and voted to accept the minutes from the 45th OARAC as written. Dr. Gandhi then briefed the Council on the agenda for the day, noting the inclusion of time in the agenda for public comments.

Report of the Office of AIDS Research (OAR) Director
Maureen M. Goodenow, Ph.D., OAR, NIH

Dr. Maureen M. Goodenow welcomed the members of the Council, representatives from the NIH and other government agencies, and guests from professional and lay organizations whose interests and

activities align with the OAR. She particularly welcomed for new voting members; six new *ad hoc* members, and noted 180-day term extensions for four voting members. Dr. Goodenow then covered key appointments in the government relevant to the function of the OAR and gave an update on the OAR staff.

Dr. Goodenow then highlighted activities of the OAR. She explained that the OAR is working to expand opportunities for the younger generation to have a voice in OAR's activities. She introduced the vision of the OAR is to advance research to end the HIV pandemic and improve the health of people living with HIV worldwide. Dr. Goodenow explained the OAR functions to catalyze, coordinate, and convene the trans- NIH HIV/AIDS-related activities and to liaise with other programs in the U.S. Department of Health and Human Services (HHS) and other federal agencies on HIV-related work. Dr. Goodenow highlighted a trans-agency initiative, Undetectable = Untransmissible (U=U), which promotes the finding that people living with HIV who maintain an undetectable viral load are unlikely to transmit the virus to an HIV-negative partner. Promoting this message should reduce stigma in those living with HIV in terms of their sexual health and encourage more people with HIV to seek treatment.

Dr. Goodenow reviewed activities in the OAR's congressional authorization, including the Fiscal Year (FY) 2018 Professional Judgment Budget and the FY 2019 Trans-NIH Plan for HIV-Related Research (Strategic Plan). She commented that the Caribbean Primate Research Center was destroyed in the recent hurricane that affected Puerto Rico and highlighted collaborations the OAR is undertaking to recover the infrastructure. Dr. Goodenow also highlighted the intersection between the opioid and HIV epidemics, which will be discussed in more detail later in the meeting. She noted the upcoming World AIDS Day commemoration at the NIH (open to the public) which focuses on the cross-over benefits of HIV research.

Discussion Highlights—Report of the OAR Director

Dr. Gandhi asked if the NIH endorses the U=U movement. Dr. Carl W. Dieffenbach clarified that the NIH does not endorse movements but is interested in translating science into practice. Dr. Jonathan Mermin of the Centers for Disease Control emphasized that critical questions must be answered about improving access to treatments that allow for virologic suppression and its benefits on prevention to be maintained.

Ms. Dázon Dixon Diallo commented that the U=U campaign is an important step in unifying advocacy and scientific communities, and echoed Dr. Mermin's point about the importance of solving problems of unequal access to treatment. She recommended examining the messaging around U=U to ensure that it does not increase stigma for those who have not yet achieved undetectable viral loads.

Update from the HHS HIV/AIDS Treatment and Prevention Guidelines, Working Groups of the OARAC

Roy M. Gulick, M.D., M.P.H., Weill Cornell Medicine
Rohan Hazra, M.D., Eunice Kennedy Shriver *National Institute of Child Health and Human Development (NICHD), NIH*

Dr. Roy M. Gulick reviewed the adult antiretroviral therapy (ART) guidelines, which were updated in October 2017. Changes include a shift to people-first language classification of antiretroviral regimens to provide one set of recommendations for the majority of people living with HIV and different recommendations for use in certain clinical situations. Additionally, therapy combinations with high rates of virologic failure have been removed completely from the recommended regimens section. Improvements were made to the sections on hepatitis B virus and hepatitis C virus coinfection, and a new section on adherence to the continuum of care was added. Several drug classes have been added or expanded throughout the Drug Interaction section.

Dr. Gulick noted that the guidelines for opportunistic infections (OIs) are managed by a partnership between representatives from the NIH, Centers for Disease Control and Prevention (CDC), and the Infectious Disease Society of America. As field experience with HIV-related OIs has decreased, providers increasingly rely on the guidelines, so use of both the OI and ART guidelines remains high. Dr. Gulick commented that the membership of the guidelines panels has broadened as longstanding members rotate off and new volunteers are recruited; the panels review the guidelines four times a year.

Dr. Rohan Hazra reviewed the proposed changes for the update of the pediatric guidelines for ART and OIs. Like the adult guidelines, the pediatric guidelines are administered by representatives from the NIH, CDC, and other organizations. Updates for the perinatal guidelines were released just prior to this meeting. As in the pediatric and adult guidelines, the perinatal guidelines also now incorporate people-first language and align content with the other guidelines. Dr. Hazra commented that the perinatal guidelines panel has added junior and mid-career investigators to broaden expertise. He emphasized that all five sets of guidelines are intended to be part of an integrated process.

AIDSinfo is working with all five guidelines panels to develop brief versions to be used on handheld devices at the point of care. The five panels hope to release these versions in the spring of 2018. These brief guidelines will offer links to the full versions for additional information. Dr. Gulick added that guidelines have been updated to address issues relevant to people displaced by recent hurricanes. Dr. Hazra thanked the leadership of the panels, volunteer panel members, and AIDSinfo staff.

Discussion Highlights—Update from the HHS HIV/AIDS Treatment and Prevention Guidelines, Working Groups of the OARAC

Ms. Lynda M. Dee asked about the revisions related to linkage, retention, and adherence. Dr. Gulick explained that because the previous adherence section focused on ways to improve adherence, the updates added methods pertaining to other aspects of the care continuum, such as linkage and retention.

Dr. Steffanie A. Strathdee commended the panels for including language addressing the effects of hurricanes on treatment and emphasized the importance of developing language that would address potential future large-scale losses in health care-related infrastructure.

Dr. Bruce R. Schackman asked whether future updates would address costs beyond those of medications, particularly for OIs. Dr. Gulick responded that a section on costs has been added to the adult ART guidelines, but that is not the case for the OI guidelines. Dr. Gulick indicated that Dr. Schackman's suggestion will be made to the panel.

Dr. Monica Gandhi asked if the removal of darunavir/ritonavir-based regimens from the recommended agents for most people living with HIV could be perceived as a demotion of the boosted protease inhibitor (PI). Dr. Gulick responded that the various panels of the new recommended antiretroviral agents are not meant to designate hierarchy and that boosted darunavir-based regimens remain important options for those with certain clinical conditions, such as anticipated issues with adherence.

Dr. Mermin asked if the adult guidelines could include practice recommendations for the use of ART to prevent transmission. Dr. Gulick explained that the panels have had some discussion of successful studies for reducing transmission, but practical questions about the strictness of adherence to treatment must be answered before such recommendations can be included. He also stressed that the treatment guidelines were focused on benefits for the individual living with HIV.

OAR Ad Hoc Cost-Sharing Task Force
Peter Kim, M.D., OAR, NIH

Dr. Kim provided an update on the OAR Cost-Sharing Task Force, which helps OAR fulfill its mission of allocating funds to the highest priorities in HIV/AIDS science. He emphasized the interconnected nature of HIV research and other disease states. Because a significant portion of the HIV research portfolio includes common interests between HIV and other areas or applications that include both HIV and non-HIV priorities, developing a cost-sharing policy is critical to the path forward for HIV research. The Cost-Sharing Task Force will review current practices and policies for allocating HIV/AIDS funds and recommend a trans-NIH cost-sharing policy for topically based groups of applications, rather than a focus on individual applications. Dr. Kim noted that the first iteration would review only extramural plans. He thanked the internal and external members of the Task Force and noted their intent to have a recommendation ready to present at the next OARAC meeting in the spring of 2018.

Discussion Highlights—OAR Ad Hoc Cost-Sharing Task Force

Dr. Daniel R. Kuritzkes asked why some relevant ICs did not have representation on the OAR Cost-Sharing Task Force. Dr. Kim explained that the Task Force's initial discussions on extramural plans include representatives from the four ICs that receive the most HIV/AIDS funding before expanding discussions to all ICs. Dr. Schackman elaborated that the OAR Task Force intends to present its review to the OAR-led NIH AIDS Executive Committee prior to the spring OARAC meeting, at which point all ICs can offer comments. Dr. Gandhi emphasized the importance of creating a two-way conversation that includes entities that receive less NIH AIDS-related funding.

Dr. John J. Chin wondered whether proposals would be grouped for consideration. Dr. Dieffenbach responded that ICs often consider applications in relation to their specific questions and then assess their potential to have broad applicability. Dr. Kim emphasized that grouping applications by topic would result in a fairer process for applications eligible for cost-sharing.

Update from the National Institute of Allergy and Infectious Diseases (NIAID) on the Clinical Trials Network
Carl W. Dieffenbach, Ph.D., Division of AIDS, NIAID, NIH
Manizhe Payton, M.P.H., Division of AIDS, NIAID, NIH

Dr. Dieffenbach provided an overview of the HIV/AIDS Clinical Trial Networks agenda, focusing on research priorities through 2027. The major areas of emphasis are HIV prevention, HIV vaccines, HIV therapeutics, and a pediatric and maternal health research agenda; and therefore, there will be 4 Clinical Trials Networks focused on a) Prevention; b) Vaccines; c) Therapeutics in Adults; and d) Pediatrics and Maternal Health. The core leadership groups for each Network will be responsible for moving each area forward.

HIV prevention involves targeting novel biomedical methods of prevention, behavioral and social scientific partnerships, and protection of populations at risk for acquisition of HIV. What was formerly the HIV Prevention Trials Network (HPTN) and the Microbicides Trials Network (MTN) will be grouped into a single entity focused on prevention. The vaccine focus area (currently reflected as the HIV Vaccine Trials Network, HVTN) aims to establish efficacy for novel vaccines. The therapeutic focus area for adults (currently reflected as the AIDS Clinical Trials Groups, ACTG) aims to identify and refine novel, durable therapies; develop ART-free remission or cure strategies; combat tuberculosis as a comorbidity; and, reduce HIV-related complications, comorbidities, and co-infections. For pediatric and maternal health, Dr. Dieffenbach elucidated several overarching priorities that include preventing sexual transmission in adults, evaluating HIV vaccines in pediatric populations, and developing a pediatric/maternal therapeutics network.

Dr. Dieffenbach also reviewed several administrative changes to the Networks in effort to maintain existing and foster new collaborations and partnerships within the NIH, HHS, foundations, and the private sector. Dr. Dieffenbach ended his presentation by emphasizing that these four areas of research focus will involve partnerships and collaborations between the groups, will solicit feedback from participants in the clinical trials and those affected by HIV/AIDS. He announced a timeline of future activities.

Ms. Manizhe Payton described the vision for refinement of the Clinical Trials Units (CTUs), the protocol-implementing arm of the HIV/AIDS Clinical Trial Networks. The NIH competitively renews the Networks every 7 years, and the CTUs have made significant contributions to the Network enterprise, enrolling more than 10,000 participants since inception. Currently, the NIH funds 37 CTUs encompassing approximately 200 clinical research sites globally. The goal of the upcoming recompetition is to maintain, strengthen, and optimize high-functioning CTUs. Each CTU is anchored by a core administrative unit with a financial component; the CTU oversees and provides shared resources to the included clinical research sites. Currently, the Networks are seeking to maintain sites with demonstrated experience working in a regulated environment and conducting randomized investigational new drug clinical trials.

Ms. Payton reviewed areas for strengthening CTUs including the opportunity to streamline administrative activities, increase flexibility to work across a broader portfolio of infectious disease research, and enhance the ability to perform site capacity assessments. In addition, feedback from several focus group sessions and international stakeholders revealed the need to streamline operational processes, enhance funding opportunities, effectively manage capacity and workloads, and provide adequate training and mentorship. Ms. Payton then covered what components will be included in an application for the new CTUs and provided a timeline.

Discussion Highlights—Update from NIAID on the Clinical Trials Network

Dr. Lynne M. Mofenson commended the collaboration between NIAID and NICHD, but voiced a few concerns: what about the inclusion of prevention of mother-to-child transmission (PMTCT); where does prevention in pregnant and breastfeeding women reside; where do immunotherapeutic approaches for cure reside; what about HIV vaccines and monoclonal antibodies in neonates? She recommended that the institutes require networks work together to study pediatric and pregnant populations. Dr. Dieffenbach noted that safety testing of new monoclonal antibodies in adults is needed prior to neonatal use. A lot more work and a lot of discussion is needed before an efficacy trial for PMTCT will be ready to launch. He reiterated the importance of partnership and collaboration between the pediatric and adult groups when seeking to develop a cure for HIV. In terms of the use of drugs during pregnancy, the pediatric AIDS Clinical Trials group, which focuses on therapeutics, would be responsible for testing these therapies in partnerships that include NIAID and NICHD.

Dr. Gulick requested a comment on topical prevention agents. Dr. Dieffenbach stated that this is an important discussion and highlighted that we need to think of where we are in the field. He reiterated that what makes sense right now is one unified network for non-vaccine prevention strategies (e.g. combining MTN and HPTN into one unified network). Dr. Dieffenbach reminded the Council of the basic science research that the NIH supports and made the argument that we need to go back to basics. He commented that innovation is critical for the development of a microbicide that protects both women and men.

Dr. Charles Wira expressed the need for clinical trials to include both men and women, along with a range of age groups, because of fundamental differences in response by type of sex and possibly age. He added that the elderly population and the transgender population also need to be included. Dr. Dieffenbach responded that the Networks have been paying increased attention to transgender populations and this group will be included in future trials.

In terms of vaccine trials, Dr. Dieffenbach stressed that responses must be studied in both men and women. He acknowledged the critical importance of adequate representation of both men and women in vaccine trials to delineate sex-specific responses and perform sex-stratified analyses. In terms of the distribution in current trials, the HVTN 702 is enrolling both men and women (approximately 60 percent women and 40 percent men to date), and the HVTN 705 trial is enrolling only women.

Dr. Gandhi summarized that some questions are in the realm of implementation science rather than requiring study in additional clinical trials. She asked if hepatitis C (HCV) will continue in the therapeutics agenda. Dr. Dieffenbach stated that HCV is not included in the therapeutics network because HCV drugs work equally well in HIV mono- and dually infected people. He argued that implementation is needed to eliminate HCV since highly effective oral therapies are now available. NIH is about innovation and he would like to see a shift to developing therapeutics and a cure for hepatitis B virus.

Dr. Taiwo surmised that resources should be focused toward controlling the community reservoir of HIV and prevent new infections by suppression of viremia. Dr. Dieffenbach noted the existence of technological tools that physicians can use to assist with non-adherence. He stressed the importance of focusing on the continuum of care as a partnership across all federal agencies.

Ms. Diallo noted a need for the HIV community to play a role in research design beyond the good participatory practices and behavioral and social sciences research. She suggested that the NIH be emphatic about the role of community-based participatory research (CBPR) and to build CBPR into the structure of the Networks and in the funding opportunity announcements. Dr. Dieffenbach agreed that it is critical to understand how tools developed will fit into the lives of the end-users. He made the case for community to be involved early in basic science research as well to help develop effective products that will be used.

Ms. Dee asked how researchers can present their ideas on microbicides to the HIV Prevention Trials Network and the Microbicide Trials Network until there is one prevention research clinical trials network. Dr. Dieffenbach responded that the Networks are looking for innovation; new concepts will undergo preclinical testing, and possible Phase I trials will be discussed. Considerations to demonstrate the concept's promise include the manufacturing method and capacity, the target product profile, the details of the final product, and how it will be provided at a large scale for communities. Ms. Dee also asked about the integration of specialty sites into CTUs. Ms. Payton stated that the CTUs are enthusiastic about integration of specialty units and that they must come in an integrative package as part of the CTU application.

Dr. David Celentano commented on the aspirational nature of the idea of administering vaccines to adolescents before sexual debut. Dr. Dieffenbach acknowledged the difficulty in reaching adolescents, but said it is important to have a target population for which to develop a vaccine.

Dr. Richard Chaisson asked how the Networks can integrate with the Fogarty Institute to train the next generation. Dr. Dieffenbach replied that this is a trans-NIH issue that is being addressed in house. Dr. Gandhi asked if training will be a component in the funding opportunity announcements (FOAs) for the new clinical trials networks. Dr. Dieffenbach replied that a synergy across platforms for training is desired.

Dr. Alan E. Greenberg asked whether the upcoming FOA for Networks will model the FOA for the Martin Delaney Collaboratory that asked for synergies with the Centers for AIDS Research.
Dr. Dieffenbach responded that decisions regarding what works best for the local universities and centers must be determined by the individual institution.

Dr. Julie Ake stated that in resource-limited settings, having sites with reliable clinical expertise to care for children and pregnant women is nontrivial and important. She asked about expectations regarding the collaboration with DMID. Dr. Dieffenbach said that continued work with DMID is significant. One research area that could benefit from improved collaboration is in sexually transmitted infections.

Dr. Dieffenbach agreed with Dr. Ingrid Valerie Bassett's recommendation to determine how to disseminate the lessons learned and best practices from within the Networks to investigators conducting research with adolescents.

Dr. Mofenson clarified that she does not think that implementation of currently available interventions will get us to an AIDS-free generation. She clarified that she was talking about innovation in giving immunotherapies to children; developing drugs for breastfeeding mothers living with HIV, and ensuring that vaccines and prevention strategies are studied in vulnerable populations. Dr. Dieffenbach emphasized the need for safety studies prior to moving into the pediatric population.

Update from NICHD on HIV/AIDS Research Activities
Rohan Hazra, M.D., NICHD, NIH

Dr. Hazra provided a brief biography of Eunice Kennedy Shriver and the NICHD, emphasizing the Institute's mission and the populations that fall within NICHD's mission. Dr. Hazra explained that NICHD has the ninth largest budget at NIH and the fifth largest budget for HIV/AIDS.

Dr. Hazra outlined the structure of the NICHD extramural program. The branch that focuses on maternal and pediatric infectious diseases receives 90 percent of NICHD's HIV/AIDS budget. Because multiple diverse branches work on projects related to HIV/AIDS, researchers can draw on expertise across the pediatric and obstetrics research spectrum. Dr. Hazra highlighted the range of research that covers all facets of HIV/AIDS across populations that fall in the mission of NICHD.

Dr. Hazra reviewed several of the NICHD's major projects: the NICHD Domestic and International Pediatric and Maternal HIV Clinical Studies Network, the International Pediatric Maternal Adolescent AIDS Clinical Trials (IMPAACT) Group, the Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN), and the Pediatric HIV/AIDS Cohort Study (PHACS). Together these four programs total approximately half of NICHD's overall HIV/AIDS budget.

Dr. Hazra also described the International epidemiology Databases to Evaluate AIDS (IeDEA), a global epidemiological study, which he hoped would help improve the understanding of the scope of the pediatric epidemic and the adolescent mortality rate given its large sample. He noted the importance of determining whether adolescents living with HIV were infected perinatally or behaviorally in any adolescent-focused study. He highlighted NICHD's research agenda on women's health for Zika virus and HIV coinfection and commented on current research on microbicides and multi-purpose prevention technologies.

Dr. Hazra discussed the grant portfolio, noting that most of the studies are submitted under solicitations. NICHD is willing to accept unsolicited proposals, and it also co-funds grants with other ICs and Divisions to facilitate top-level science and encourage new ideas. One of NICHD's overarching themes is the importance of enhancing partnerships without losing focus on the Institute's mission. The Institute encourages broad-scale data sharing. Dr. Hazra encouraged the attendees to visit the Data and Specimen Hub (DASH), a centralized resource for researchers to store and access data that includes studies for HIV/AIDS.

Discussion Highlights—Update from NICHD on HIV/AIDS Research Activities

Ms. Dee asked what research NICHD is supporting for adolescents as far as implementation science. Dr. Hazra clarified that the Prevention and Treatment Through a Comprehensive Care Continuum for HIV-Affected Adolescents in Resource Constrained Settings (PATC3H) initiative is trying to pair the research investigator and the implementation expert upfront to ensure that the evidence generated is useful to the implementer. He mentioned the institutes are doing a lot of work on adolescents and recognized the need to improve integration of adolescent research across NIH Institutes.

Dr. Kimberly Kay Scarsi advocated for junior investigators to have access to an NICHD R21 program. Dr. Hazra confirmed that NICHD does have an R21 program.

Dr. Goodenow asked about a provision in the 21st Century Cures Act regarding testing drugs in pregnant women. Dr. Hazra explained that the Act calls for a non-funded task force led by NICHD to address the pharmacokinetics and safety of medicines used in pregnant and breastfeeding women. He mentioned the hope is that after the series of task force meetings, funding to support these studies might be available.

Update from the National Heart, Lung, and Blood Institute (NHLBI) on the Multicenter AIDS Cohort Study (MACS) and the Women's Interagency HIV Study (WIHS)

David Goff, M.D., Ph.D., NHLBI, NIH

Dr. David Goff remarked that HIV is evolving to be a chronic condition in which survival is improving but the comorbidities are increasing, especially those associated with the NHLBI's purview. The increasing importance of comorbidities spurred the shift of the MACS and WIHS stewardship from the NIAID to the NHLBI. Dr. Goff covered the history and the current active participants and clinical sites of the MACS and WIHS. He emphasized that the MACS and WIHS are in partnership with the OAR and 11 other ICs, the research investigators, and the participants. He highlighted the participating Institutes and discussed the need to balance the interests of all ICs, investigators, and participants to determine how to provide the greatest return on investment.

Dr. Goff covered a short list of the main topic areas of interest. He stressed that the multiple research interests for these cohorts could increase participant burden and stressed the need to minimize burden on participants and be judicious. He covered NHLBIs interests in the MACS and WIHS. The NHLBI has discussed adding echocardiograms or cardiac magnetic resonance images (MRIs) to address the importance of heart failure research in this population, and electrocardiography could be used to assess the increased risk of dysrhythmia. Measures to study venous thromboembolism, pulmonary health, and sleep in this population also have been discussed. NHLBI is also interested in understanding how comorbidities are being managed from the perspective of implementation science.

The next phase of funding will emphasize retaining the current cohorts and recruiting new participants in a targeted manner to ensure that underrepresented populations of PLWH, including black and Hispanic men, more men and women from the southern part of the country, more recently infected individuals, and younger individuals are all represented. New FOAs for a data analysis and coordinating center and for the clinical sites are planned. Dr. Goff covered the timeline for the core funding opportunities. The NHLBI is also discussing other ways to leverage the cohorts to support ancillary studies. Dr. Goff asked the Council for thoughts on how to support ancillary studies and thanked the MACS/WIHS team.

Discussion Highlights—Update from NHLBI on MACS and WIHS

Dr. Tricia H. Burdo asked what percent of patients have coronary angiograms, PET CTs or other cardiovascular measures. Dr. Goff said that inclusion of such measures has not yet been part of the

protocol. Dr. Goff confirmed that going forward there is a hope to have an emphasis on cardiovascular measures now that cohort studies are being housed in NHLBI; there is also interest in cognitive assessments and brain MRIs. Dr. Chaisson commented that, for the Johns Hopkins University MACS, the CFAR is supporting several sub-studies focused on cardiovascular measures. Dr. Goff theorized that such ancillary studies may have a period of exclusivity before their data can be shared with other investigators. Moreover, one way to reduce burden on MACS and WIHS participants of multiple sub-studies is to have site-specific studies.

Dr. Taiwo suggested that MACS and WIHS are resources for junior investigators and asked if the FOA will include this focus. Dr. Goff theorized that the requests for applications might include skills development components and gave the other possibility of applying for ancillary studies.

Ms. Dee emphasized the importance of including long term PLWH and suggested recruiting new persons involved to provide new ideas and new approaches to approach key questions. Dr. Goff replied that he will take this information back to the MACS and WIHS team and encourage them to consider ways to include new perspectives. The other opportunity is to encourage the participating Institutions to identify new investigators in areas of interest for the cohorts.

Ms. Diallo questioned messaging around the inclusion of women as a priority population. Dr. Goff agreed on the importance of women's participation in the studies and planned to review the messaging to ensure that it reflects the value of women participants clearly.

When asked if the FOAs include specific community engagement language, Dr. Goff suggested that the value of collaborating with community-based organizations currently delivering care to these populations could be emphasized in meetings with the investigators; he theorized that many already are working with such organizations.
Drs. Gandhi and Gulick asked for clarification if the new FOA plans to recruit new participants at existing sites. Dr. Gulick suggested that recruitment could be diversified either by telling existing sites to improve or finding new sites that serve the populations of interest. Dr. Goff responded that the studies plan to recruit new participants through existing sites and stated there is no plan to find additional sites. Dr. Moisés Agosto-Rosario asked how new participants will be recruited from underrepresented communities at existing sites. Dr. Goff explained that some existing sites are positioned to recruit from the communities of interest, and the FOA would focus on encouraging sites to propose new approaches tailored to their populations. Dr. Schackman suggested that awards could be tied to recruitment goals for specific populations. Dr. Goff noted that the NHLBI prefers to encourage sites to innovate for recruitment. Dr. Schackman asked whether award amounts are tied to achieving recruitment goals. Dr. Carolyn Williams, NIAID, NIH, explained that grants held in cooperative agreements may have restrictions, so recruitment progress will be closely monitored by the NIH. Dr. Chaisson reassured the attendees that the studies are firmly embedded in their communities and recruitment historically has been successful.

Update from the National Institute on Aging (NIA) on HIV/AIDS Research Activities
Melissa Gerald, Ph.D., NIA, NIH
Rebecca Fuldner, Ph.D., NIA, NIH

Dr. Rebecca Fuldner remarked on the NIA's mission to broadly support and conduct research on aging, foster the development of research and clinical scientists specializing in aging, and provide resources and disseminate information on aging to the public. The prevalence of older people living with HIV in the United States has been increasing, and the immune changes experienced during normal aging may occur earlier in chronically HIV-infected individuals. Natural aging processes and HIV may be synergistic to drive further decline of the immune system. Although ART has been successful in preventing AIDS and

improving health, the risk for developing comorbidities—including cancer, cardiovascular disease, cognitive impairment, osteoporosis, and overall frailty—remain high. The NIA supports, through the R01 and R21 funding mechanisms, multidisciplinary HIV/AIDS and aging studies.

Dr. Melissa Gerald reported on key NIA HIV/AIDS programs. These include a collaboration between the CFARs and the Claude D. Pepper Older Americans Independence Centers (Pepper Centers) that measure geriatric performance in PLWH. Another is the "Losartan to Reduce Inflammation and Fibrosis Endpoints in HIV (LIFE-HIV)" trial, a first-of-its-kind multisite study that aims to test the immunomodulatory and anti-fibrotic properties of a well-known antihypertensive agent, losartan, in ART-treated PLWH. The study is expected to be completed in December 2018, and the NIA is optimistic about the therapeutic promise and potential to increase understanding of immunosenescence in HIV infection.

Dr. Gerald elaborated on two large-scale international projects being supported by NIA's Division of Behavioral and Social Research: (1) "Health and Aging in Africa: A Longitudinal Study of an International Network for the Demographic Evaluation of Populations and Their Health (INDEPTH) Community in South Africa (HAALSI)" and (2) "Study on Global AGEing and Adult Health (SAGE)–Well-Being of Older People Study (WOPS)." Dr. Gerald concluded by calling attention to NIA's newest program, "Grants for Early Medical/Surgical Specialists' Transition to Aging Research (GEMSSTAR)."

Discussion Highlights—Update from NIA on HIV/AIDS Research Activities

Ms. Diallo asked about efforts to include hormonal indications into the inflammation studies for transgender persons and postmenopausal women. She also wondered whether other centers had observed increased incidences of lupus in women from minority populations for women of color living with HIV that are postmenopausal. Dr. Fuldner stated that the NIA's Division of Aging Biology and Division of Geriatrics and Clinical Gerontology supports research on the postmenopausal effects in women living with HIV. Many of these changes also will be studied in the MACS and WIHS cohorts. She was not aware of increased lupus incidences. Dr. Gerald added that the NIH recently issued an FOA addressing the health of transgender populations.

Dr. Wira asked whether any studies are planned to understand the underlying biology or behavioral changes that lead to HIV acquisition in the aging population. Dr. Gerald replied that the CDC has reported an increase in the incidence of HIV among older persons and that the NIA is interested in supporting such work.

Update on HIV and the Opioid Epidemic

Jacques Normand, National Institute of Drug Abuse (NIDA), NIH

Dr. Jacques Normand explained that 27% of the population in the U.S. misuses/abuses drugs with marijuana as the top drug of abuse. The second drug of abuse is psychotherapeutics that includes pain relievers including opioids. Dr. Normand covered the demographics of injection drug users in the US, and explained the change in opioid prescriptions since 1999. The main adverse health outcome of opioids is overdose, which has increased substantially since 2000. The opiate that has exacerbated the epidemic is fentanyl, which was traditionally used as a painkiller for chronic pain in cancer patients.

A major barrier to a public health response is minimal interest on the part of pharmaceutical companies to develop non-opiate painkillers or new modalities for treating substance use. Other barriers include a lack of infrastructure for securing access to opioid use disorder treatment and lack of reimbursement for medication. Dr. Normand recognized that no single strategy will be sufficient to overcome all barriers. He advocated that the US needs to improve access to treatment for HIV, HCV, and substance use disorder; implement prevention interventions; and, monitor the continuum of care for each adverse health issue.

NIDA is investigating how to identify key biomarkers that could predict the risk for overdose. It also has been the key contributor to the NIH Pain Consortium and provides curriculum for medical schools to better train physicians on pain management and substance use treatment. A series of meetings at the NIH have taken place to engage the pharmaceutical industry and develop special collaborations to address opioid substance abuse and development of nonaddictive pain medication. In addition, in December 2015, a meeting involving NIDA, CDC, the Substance Abuse and Mental Health Services Administration (SAMHSA), the Health Resources and Services Administration, and the Appalachian Regional Commission was convened to determine interest in collaborating and addressing the opioid issue in the Appalachian region. As a result, NIDA, CDC, SAMHSA, and the Appalachian Regional Commission issued two different FOAs to investigate the epidemiological information, policy, and best efforts for addressing gaps and improving stakeholder engagement in the first phase. The second phase will implement combined interventions to address the problem. Grants were issued earlier this year.

Discussion Highlights—Update on HIV and the Opioid Epidemic

Dr. Ake asked about the extent of NIDA's collaboration with the U.S. Department of Veterans Affairs (VA). Dr. Normand responded that the VA was not identified as one of the five key agencies. Dr. Victoria J. Davey, an ex officio member of the OARAC from the VA, noted that the Department has a very active program in opioid use treatment and should contribute to these discussions. She will raise this issue at the VA.

Ms. Dee commented on the change in demographics of the opioid epidemic and that new drugs used to combat such situations can be worse than heroin. Dr. Normand acknowledged that the issue did not receive much attention until it affected the Caucasian population. He agreed that the dropout rates in the continuum of care are high and that those who attend a rehabilitation program relapse relatively quickly. Ms. Dee commented that it is important that the HIV community be educated about the drug-drug interactions between fentanyl and antiretroviral therapy.

Ms. Diallo reminded the participants of the history of racism in pain management and the shift in heroin to fentanyl is due to who gets the prescription and asked if we know about the biology and management based on demographics. Dr. Normand commented that the, although the opioid epidemic blossomed in rural areas, and because of fentanyl, it is moving to urban areas which means the older minority males who are injection drug users will be affected. Dr. Schackman echoed that the urban communities of color are being affected because of fentanyl and the mortality rates in these communities are being heavily affected.

Public Comments

Dr. Mary Marovich, NIAID, NIH, asked Dr. Normand to comment on a recent study on the Medicaid population that had overdosed with heroin or opioids. She asked if it is true that heroin users get treatment more than an opioid user. Dr. Normand replied that he is not aware of the specific study, but he did acknowledge that patients get discharged from the emergency room without any referral to drug treatment and they are at higher risk of experiencing a subsequent overdose.

Ms. Jessica Salzwedel, AIDS Vaccine Advocacy Coalition, expressed disappointment about the lack of inclusion of topical products in prevention projects moving forward and wondered whether women, in particular African women, were involved in this decision. Dr. Dieffenbach responded in a letter to Ms. Salzwedel that NIAID plans to continue to support the development of topical HIV prevention products. Microbicides remain a promising, possible component of an HIV prevention toolkit and are thought to offer advantages for women should a modality reach regulatory approval. While microbicide research is not ending, only one successful microbicide product—the vaginal dapivirine ring—is under regulatory review and may become available to women in the near future. The remaining candidate microbicides

currently in the research pipeline have limited proven efficacy, and it has not been demonstrated that the most vulnerable users would choose or adhere to these products. He added that a focused discussion is needed on what it means to fully protect women from HIV. Developing safe, effective, and desirable prevention tools for women has been a longstanding goal for the NIH and remains a top priority.

Ms. Salzwedel echoed Ms. Diallo's comment regarding the inclusion of good participatory practice (GPP) as part of the standard criteria to evaluate CTUs and including this in the FOA. She stated that we know that stakeholder engagement is a critical part of ethical research and the conduct of successful trials and advocated for it to be included in the stable funding for the CTUs. Ms. Salzwedel asked if going back to basics in microbicides means a mandate for dual compartment products only. Dr. Dieffenbach replied in a letter that NIAID agrees that GPP and frequent consultation with community members are essential to the conduct of ethical scientific trials. He highlighted that next generation solutions for topical prevention will require creativity and innovation beyond what is already in clinical study to move to next generation solutions.

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

Dr. Goodenow thanked the participants and Council members for their active engagement and commented that the OAR is looking forward to engaging with the Council as our expert advisors. She remarked on the robust, complex, and broad-reaching HIV/AIDS portfolio within the NIH and across the government agencies and departments. She noted the value of partnerships in program development which provides scientific partnership opportunities and financial opportunities. Dr. Goodenow highlighted the OAR Cost-Sharing Task Force that was presented in the morning and indicated that partnerships are going to be important going forward to leverage resources.

Adjournment
Monica Gandhi, M.D., M.P.H., University of California, San Francisco

Dr. Gandhi adjourned the meeting at 4:16 p.m. on November 16, 2017.

Certification

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

– S – 03/26/2018

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Monica Gandhi, M.D., M.P.H. Date
Chair, NIH Office of AIDS Research Advisory Council
Professor, University of California, San Francisco

– S – 03/26/2018

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Elizabeth Church, Ph.D. Date
Executive Secretary, NIH Office of AIDS Research Advisory Council
OAR, Division of Program Coordination, Planning, and Strategic Initiatives, Office of the Director, NIH