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

Office of AIDS Research Advisory Council
Forty-Seventh Meeting

March 27, 2018
5601 Fishers Lane, Room 1D13
Rockville, Maryland

Draft Meeting Minutes

Council Members Present: Dr. Monica Gandhi (Chair), Dr. Elizabeth Church (Executive Secretary), Dr. John J. Chin, Dr. Elizabeth Connick, Dr. Ralph J. DiClemente, Dr. Jennifer Kates Dr. Lynne M. Mofenson, Dr. Scott D. Rhodes, Dr. Charles Wira

***Ad Hoc* Members Present:** Dr. Ingrid V. Bassett, Dr. Margaret L. Brandeau, Dr. Tricia H. Burdo, Dr. Heidi M. Crane, Ms. Lynda M. Dee, Dr. Maureen M. Goodenow (OAR Director), Dr. William G. Powderly, Dr. Jonah B. Sacha, Dr. Kimberly Kay Scarsi, Dr. Bruce R. Schackman, Dr. David M. Smith, Dr. Babafemi Taiwo, Dr. Blanton S. Tolbert

***Ex Officio* Members Present:** 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. Robert Freund, Dr. Franziska B. Grieder, Dr. Rohan Hazra, Dr. Henry Masur, Dr. Alice Pau, Dr. Dianne Rausch, Dr. Norman E. Sharpless

Council Members Absent: Mr. Moisés Agosto-Rosario, Dr. David Celentano, Ms. Dazon Dixon-Diallo, Dr. Daniel Kuritzkes

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Welcome and Meeting Overview
Monica Gandhi, MD, MPH, University of California San Francisco

Dr. Monica Gandhi welcomed participants to the forty-seventh 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-sixth OARAC meeting held on November 16, 2017. Members of the council motioned and voted to accept the minutes from the forty-sixth OARAC meeting. Dr. Gandhi reviewed the forty-seventh meeting agenda, noting the inclusion of time for public comments.

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

Dr. Maureen M. Goodenow welcomed the members of the council, colleagues from the NIH and other government agencies, and guests from professional and lay organizations whose interests and activities align with the mission of the OAR. She thanked retiring members for their service

to the OARAC, welcomed new voting members and new ad hoc members, and noted that four voting members were unable to attend the forty-seventh meeting.

Dr. Goodenow highlighted the upcoming meeting dates for the OARAC in 2018 and 2019. Starting in 2019, the OARAC will have three in person meetings each year. In November 2018, the OAR will hold an annual half day in-person orientation for OARAC members that will include discussion of the roles and responsibilities of the OAR and the OARAC.

Dr. Goodenow updated the council on key appointments in the government relevant to the function of the OAR and the OARAC. She acknowledged the President signed the FY2018 Consolidated Appropriation Act to fund the United States (US) government through September 30th, 2018. Dr. Goodenow updated the council on changes in OAR senior staff and remembered our dear colleague and friend, Dr. Bonnie Mathieson, who passed away shortly after her retirement from the OAR. Dr. Goodenow also remembered The Foundation for AIDS Research (amfAR) Founding Chairman, Dr. Mathilde Krim, and Dr. David Cooper, past president of the International AIDS Society, both of whom recently passed.

Dr. Goodenow updated the council on OAR continued stakeholder engagement. The OAR sponsored and hosted “HIV and Beyond: The Benefits of HIV Research” for World AIDS Day 2017. Dr. Goodenow presented at the International Conference on Emerging Infectious Diseases in the Pacific Rim in January 2018. She also has given opening remarks at multiple NIH workshops, meetings, and symposiums. Dr. Goodenow and OAR senior staff attended the 2018 Conference on Retroviruses and Opportunistic Infections (CROI) in Boston where they engaged with multiple stakeholders. The OAR launched a Twitter account and will soon launch a new website for further dissemination of information.

The OAR is authorized to provide a professional judgment budget for the allocation of HIV research funds across the NIH based solely on the research opportunities and priorities, without regard to the probability that funds will be appropriated. For fiscal year(FY)2018, the OAR requested a fifteen percent increase over the FY2017 enacted budget for HIV and HIV-related projects. The FY2018 professional judgment budget was submitted directly to the President after review by the NIH Director and the Secretary of HHS. The FY2019 professional judgment budget is under review and is expected to be posted in the next couple of months. The FY2020 professional judgment budget is in development and will be informed by the FY2019/2020 Trans-NIH Strategic Plan for HIV and HIV-related research.

Updates to the HHS HIV/AIDS Treatment and Prevention Guidelines from the Working Groups of the OARAC

Alice Pau, PharmD, Executive Secretary for the HHS Panel on Antiretroviral Guidelines for Adults and Adolescents, National Institute of Allergy and Infectious Diseases, NIH

Henry Masur, MD, Leadership for the HHS Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents, NIH Clinical Center

Rohan Hazra, MD, Executive Secretary for the HHS Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV,The Eunice Kennedy Schriver National Institute of Child Health and Human Development, NIH

Dr. Alice Pau presented on behalf of the Panel on Antiretroviral Guidelines for Adults and Adolescents. The first Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents living with HIV were published approximately twenty years ago in the Centers for Disease Control and Prevention (CDC) Morbidity and Mortality Weekly Report (MMWR). In April 2018, the Panel on Antiretroviral Guidelines for Adults and Adolescents will hold an annual retreat

where they will honor Dr. Martin Hirsch who will be resigning from the Panel as a co-chair and welcome seven new members.

A new integrase-based regimen of bictegravir/tenofovir alafenamide/emtricitabine (BIC/TAF/FTC) for treatment naïve people with HIV (PWH) over eighteen years of age and PWH with durable viral suppression lacking resistance mutations for BIC, TAF, or FTC was approved in January 2018. In March 2018, ibalizumab, a long-acting monoclonal antibody that inhibits post-attachment to CD4, was approved as the first drug of its class for people with multi-drug resistant HIV.

The Panel on Antiretroviral Guidelines for Adults and Adolescents plans to release a one-page guidance for BIC/TAF/FTC given its recent approval. Planned updates to the Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV include recommendations for BIC/TAF/FTC and ibalizumab, an expanded discussion on the clinical use of the proviral DNA genotypic assay, recommendations for switching to a simpler or less toxic regimen, and updated recommendations for substance use treatment as well as tuberculosis (TB). Dr. Pau thanked the volunteers and AIDSinfo staff who contribute to updates for the guidelines.

Dr. Henry Masur provided an overview of the use of the five guidelines prepared by the working groups of the OARAC. He presented data for increased use of all five of the guidelines over time, and gave examples of the search terms and platforms used to access the guidelines which are most frequently accessed via the web or an app.

The Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents (Adult OI Guidelines) that started in 1989 as the PCP Prevention Guidelines now include recommendations for the prevention and treatment of many opportunistic infections. The Adult OI Guidelines are managed by the NIH in partnership with CDC and the Infectious Diseases Society of America. Dr. Masur explained updates to the Adult OI Guidelines rely on observational studies and plausible inferences more frequently than randomized trials given the reduction of incidence of OIs with highly active ART.

Dr. Masur highlighted sections and tables in the Adult OI Guidelines that were viewed to demonstrate what sections the readers refer to most often. He summarized sections of the guidelines which were updated in the past six months. He outlined the process for real-time updates and explained the Adult OI Guidelines are maintained by volunteers who serve three-year terms with an option to renew.

Planned updates to the Adult OI Guidelines include the withdrawal of the recommendation for primary prophylaxis for Mycobacterium avium Complex (MAC), new information about immunization options for zoster and hepatitis b virus (HBV) vaccines, an expanded discussion of the interactions between hepatitis A virus and HBV with hepatitis C virus (HCV), the management of human papilloma virus (HPV), and new prophylactic regimens for TB. New prophylactic regimens for TB include a one-month course of isoniazid, (INH), and rifapentine, as presented at CROI 2018.

Dr. Rohan Hazra presented on behalf of the Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (Pediatric Treatment Guidelines Panel), the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission (Perinatal Guidelines Panel), and the Panel on Opportunistic Infections in HIV-exposed and HIV-infected Children (Pediatric OI Guidelines Panel). He reviewed recent updates that included

joint recommendations from the Pediatric Treatment Guidelines Panel and the Perinatal Guidelines Panel.

The Pediatric Treatment Guidelines Panel plans to publish an updated version of the Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection (Pediatric ARV Guidelines) next month. The updated Pediatric ARV Guidelines will celebrate the 25th anniversary of this NIH-led national guidelines committee for pediatric HIV and the 20th anniversary for the first federal guidelines for the use of anti-retroviral therapy (ART) in pediatric HIV infection.

Planned updates for the Pediatric ARV Guidelines will include an expanded discussion on what to address and whom to involve in discussions when selecting an ART regimen for a child. The Pediatric Treatment Guidelines Panel will recommend viral load measurements every three to four months, as well as ART for all children regardless of symptoms or CD4 count, raltegravir down to birth, and elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya) as an alternative regimen for children six to less than twelve years of age weighing twenty-five kilograms or more.

Planned updates to the Pediatric ARV Guidelines also include recommendations for TAF and TAF/FTC as a preferred nucleoside reverse transcriptase inhibitor (NRTI) combination for children less than or equal to six years of age and adolescents, tenofovir disoproxil fumarate (TDF) plus lamivudine (3TC) or FTC as an alternative NRTI backbone for children two to less than twelve years of age, and zidovudine (ZDV) as an alternative regimen depending on the availability of TAF-containing formulations. Recommendations will also be made for the treatment and management of HIV for foreign-born children who were diagnosed with HIV in the US.

The section on the role of therapeutic drug monitoring will be removed from the updated Pediatric ARV Guidelines. The Pediatric Treatment Guidelines Panel will collaborate with the Perinatal Guidelines Panel to make real-time recommendations for the treatment of a baby born in a high-risk situation. Additional recommendations may include BIC/FTC/TAF as an alternative INSTI regimen for adolescents and a new low dose efavirenz containing fixed dose combination for pediatric use.

Dr. Hazra announced Dr. Nahida Chakhtoura as the new Executive Secretary for the Perinatal Guidelines Panel and shared the most common page views for the Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States (Perinatal Guidelines). The Perinatal Guidelines Panel plans to publish periodic updates for new ARVs for pregnant women prior to the next full update.

The new Executive Secretary for the Pediatric OI Guidelines Panel, Dr. Bill Kapogiannis, was announced. Dr. Hazra briefed the OARAC on groups that collaborate with the NIH to develop the Pediatric OI Guidelines, the most accessed pages in the last year, and summarized updates in the final steps of being cleared for publication.

The Pediatrics OI Guidelines Panel plans to include newer agent recommendations for candida infections, strengthen the recommendation for nitazoxanide in addition to ART for cryptosporidiosis, update testing prophylaxis and therapy for cytomegalovirus (CMV), and expand the testing and evaluation recommendations for the section on HCV. The Pediatrics OI Guidelines Panel endorses MAC prophylaxis, is evaluating when to use prophylaxis for ART patients treated with disseminated MAC and plans to update the TB and varicella zoster

sections. Dr. Hazra thanked the over 200 volunteers who prepare the five guidelines, the AIDSinfo staff, and the OARAC members.

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

Ms. Lynda Dee asked Dr. Masur about the rationale for changes in the Adult OI Guidelines for Mycobacterium avium. Dr. Masur replied that the change is based on observational data and explained there was an era where MAC prophylaxis made sense given the frequency of disease. Currently PWH start antiretroviral therapy at diagnosis so a small number of people are at risk for or diagnosed with MAC. Of those diagnosed with MAC, it is difficult to determine if the symptoms are due to an active infection or an immune reconstitution inflammatory syndrome (IRIS). The consensus from the Adult OI Guidelines Panel is that the benefit of prophylaxis for MAC is very small for PWH on ART.

Dr. Gandhi questioned whether recommendations in the guidelines would change based on data presented in a meeting abstract that is not yet published in a manuscript. Dr. Masur responded that the panels perform due diligence to make sure that the data is solid prior to making recommendations in the guidelines based on a presentation. There is also an effort to ensure the DHHS HIV/AIDS Treatment and Prevention Guidelines are not markedly different from guidelines published by other federal agencies. Dr. Pau added that each abstract is carefully considered on a case by case basis prior to utilizing data for recommendations.

Dr. Richard Chaisson asked Dr. Pau how the Panel on Antiretroviral Guidelines for Adults and Adolescents plans to handle data presented at CROI for the use of rifamycins with TAF. Dr. Pau explained the data will be carefully examined prior to an updated recommendation.

Dr. John Chin complimented the panels for the remarkable usefulness of the guidelines. He asked Dr. Pau if the HHS treatment and prevention guidelines are considering clinical practice recommendations regarding the effect of ART on prevention of HIV transmission. Dr. Pau replied that this topic will be discussed at the upcoming annual retreat.

Members of the Council motioned and voted to approve the planned updates as presented for all five DHHS HIV/AIDS Treatment and Prevention Guidelines.

Update on the AIDS Study Sections
Robert Freund, PhD, Center for Scientific Review, NIH

This year, there will be a reorganization of the AIDS and AIDS-related research (AARR) study sections at the Center for Scientific Review (CSR) for the first time since 2003. Dr. Robert Freund acknowledged and thanked those involved in the reorganization. He oriented the OARAC to the current CSR AARR Integrated Review Groups that are responsible for the reviews of basic, translational, clinical, and behavioral research applications. He clarified that his presentation is specific to CSR-reviewed applications and noted that all AARR applications are reviewed on an expedited review cycle by a chartered study section or a special emphasis panel (SEP).

In 1987, CSR had one study section for HIV/AIDS applications. One year later, when Congress mandated expedited review for HIV/AIDS applications, the CSR established three study sections and additional study sections were added over time. In 2003, the current nine study sections were chartered.

Five of the current AARR study sections review basic and preclinical/translational research, one study section reviews basic to clinical research, and three study sections almost exclusively review clinical and population studies. Approximately 2,000 applications per year, or about 700 each council round, are referred to CSR. For each council round, approximately 400 to 500 applications are directed to an AARR study section, while as many as 200 applications cover emerging areas of research and special topics which are reviewed by SEPs.

Dr. Freund showed data from the past two years of review consistent with a decline in the number of applications received each council round for the majority of the AARR study sections, while the three more clinical AARR study sections receive approximately seventy applications per council round. The CSR decided to reorganize the AARR study sections to align with the current state of science, incorporate the emerging scientific areas and special topics, and administratively balance applications to average between 60 to 80 applications per study section meeting.

The CSR began the reorganization process with an internal review and assessment of the AARR study sections. In May 2017, a small external working group met for input and refinement of the CSR plan. Next CSR reached out to NIH stakeholders for input and subsequently brought a revised plan to the CSR advisory council. In the last few months, the CSR has developed descriptions and names for the new study sections which were shared with people internal and external to the NIH for comments.

The CSR reorganization was based on science proposed in previously received applications and aligned well with the current OAR priorities. The six AARR study sections will include one basic science study section, which will cover molecular virology, cell biology, and drug development; three study sections for translational and clinical research on immunopathogenesis and vaccine development, co-morbidities and clinical studies, and co-infection and associated cancers; and two study sections for clinical research and population studies for individual level determinants and behavioral interventions and for epidemiologic, population and public health approaches. The six proposed AARR study sections span all areas of HIV and HIV-related research including scientific research areas that are not mentioned in the study section names.

Currently, the new AARR study section names and descriptions are in development. The CSR will soon post the new study sections on the CSR website. The new study sections will review applications submitted to the NIH for the September 2018 deadline. Of note, the CSR performed a mock reassignment of previously submitted applications which resulted in a more even distribution of proposals among the new proposed study sections.

Discussion Highlights—Update on the AIDS Study Sections

Dr. Steffanie Strathdee commended the CSR for undertaking the reorganization of the AARR study sections. She asked if one mock sort of applications was enough to ensure even distribution between the new study sections. Dr. Freund replied that the bullets for the scientific area reviewed in each study section are being finalized in an effort to minimize fluctuation of the number of applications assigned to each new study section for a given council round.

Dr. Tricia Burdo asked how many people will serve as reviewers for each of the new study sections. Dr. Freund responded that each study section will have approximately 20 members. Additional ad hoc members will be recruited as needed for additional expertise.

Dr. Chin noticed that the names of the new study sections did not include the word prevention and asked how the prevention applications distribute in the new study sections. Dr. Freund explained that most prevention applications will be reviewed in the following proposed study sections: HIV Immunopathogenesis and Vaccine Development, HIV/AIDS Individual Level Determinants and Behavioral Interventions (HIBI), or Epidemiologic, Population and Public Health Approaches to HIV/AIDS (EPPH).

Dr. Charles Wira expressed concern for one basic science study section that covers multiple major areas of scientific research. He advocated for the inclusion of women and girls and the aging population as bullet items in the descriptions of the new study sections. Dr. Freund responded that mucosal immunity and the microbiome, as well as women and girls and comorbidities for the aging population will certainly be included areas of scientific research reviewed. He explained that this should become clearer when the description of each study section is fleshed out further.

Dr. Strathdee echoed Dr. Chin who astutely pointed out the word prevention is missing from the names of the new AARR study sections and commented that the social sciences also do not neatly fit into the new study sections. She asked for the preliminary descriptions of the new study sections. Dr. Freund agreed to share the preliminary descriptions with the OARAC.

OAR Ad Hoc Cost Sharing Task Force
Jean Patterson, PhD, OAR, NIH

Dr. Jean Patterson explained that the OAR identified the need for cost sharing of AIDS-designated dollars in 2015. At the end of 2017, the OAR formed an ad hoc cost sharing task force as one part of the OAR information gathering process for cost sharing. The OAR ad hoc cost sharing task force delivered recommendations to the OAR in February 2018.

Dr. Patterson reviewed background pertinent to the need for a cost sharing policy. She presented the names and professional titles/associations for the members of the OAR ad hoc cost sharing task force that were both external and internal to the NIH. The task force met four times between November 2017 and February 2018. Dr. Patterson commended the OAR ad hoc cost sharing task force for providing expert, thoughtful recommendations in a very short timeframe.

Dr. Patterson briefed the council on guiding principles for the OAR ad hoc cost sharing task force. In addition to the guiding principles, the OAR ad hoc cost sharing task force was charged to recommend 1) how to ascertain proportionate or percent levels of support using HIV/AIDS-designated dollars when an area of science is not explicitly or solely focused on HIV and 2) a way to apply cost sharing prospectively to topical areas of science.

To determine proportionate levels of cost sharing for topical areas of science, the OAR ad hoc cost sharing task force recommended the OAR and the NIH Institutes, Centers, and Offices (ICOs) consider the incidence and prevalence of a condition among PWH and the translational potential of the proposed basic research. Cost sharing levels should be determined in accordance with proposed criteria for HIV-relatedness and the scientific priorities identified in the Trans-NIH Strategic Plan for HIV and HIV-Related Research. The task force recommended periodic review of cost sharing levels for each topical grouping to ensure cost sharing levels remain appropriate for the science and burden of disease.

Dr. Patterson reviewed examples for suggested areas of science for cost sharing proposed by the OAR ad hoc cost sharing task force. The task force defined HIV-related and relevant science as activities where HIV or AIDS is a meaningful component of the science proposed; science where knowledge about HIV will be enhanced; and/or HIV is one of multiple components or where a comparative cohort of PWH is being proposed for a population where HIV is not the primary focus. The OAR ad hoc cost sharing task force recommended transparency across the NIH ICOs on the levels of cost sharing for each topical area of science.

The OAR was encouraged to plan prospectively to maximize flexibility, facilitate a meaningful agreement, and implement a trans-NIH process. The OAR ad hoc cost sharing task force also encouraged the OAR to consider applying the cost sharing recommendations to intramural activities. Moving forward, the OAR will gain input from all stakeholders, and with NIH leadership, to finalize a policy on cost sharing the OAR will implement.

Discussion Highlights — OAR Ad Hoc Cost Sharing Task Force

Dr. Ingrid Bassett asked Dr. Patterson to speak more about cost sharing for topical groups as opposed to an individual grant and what that would mean in practice. Dr. Patterson explained that an HIV-relevant area of science would be identified for a cost-sharing discussion between the OAR and the ICOs at a stage during the budgetary process before a new initiative is announced and prior to receiving individual applications.

Dr. Bruce Schackman, Chair of the OAR ad hoc cost sharing task force and ad hoc member of the OARAC, added that the guidance from the OAR to the OAR ad hoc cost sharing task force was to think about a prospective structure that would not require the evaluation of cost-sharing potential for each individual project. The task force provided recommendations regarding a process that could accommodate changes to research priorities and be flexible for the ICOs and the OAR to support projects that have HIV and non-HIV components. The OAR ad hoc cost sharing task force recommended transparency in future reporting for cost sharing by the OAR and the ICOs.

Dr. Carl Dieffenbach spoke from the perspective of an NIH ICO with support for prospective cost sharing on topical areas of science. He gave examples of types and areas of science research that are critical for PWH that could benefit from a trans-NIH cost sharing policy. Dr. Patterson added that there is variability on how ICOs cost share presently and the OAR would like to apply cost sharing in a very consistent way across the NIH.

Dr. Gandhi asked if only HIV dollars are moving towards other related topics. It was clarified that the OAR cost sharing policy will include a collaborative bi-directional approach.

Ms. Dee wondered how many ICOs support prospective cost sharing. Dr. Patterson replied that the six NIH institutes with the largest HIV budget allocations were represented on the OAR ad hoc cost sharing task force and the task force recommendations were presented to the NIH AIDS Executive Committee (NAEC) which includes members from ICOs who fund HIV research. The ICOs are cautiously optimistic that cost sharing could reveal new opportunities.

FY2019/2020 Trans-NIH Strategic Plan for HIV and HIV-Related Research
Gina Brown, MD, OAR, NIH

Dr. Gina Brown presented the process for development of the FY2019/2020 Trans-NIH Strategic Plan for HIV and HIV-related research, a process that involves internal and external

stakeholders with the goal of prioritizing research to bring an end to the HIV pandemic and improve the health of PWH. The OAR is legislatively authorized to develop a trans-NIH strategic plan that coordinates HIV research across the NIH. The Trans-NIH Strategic Plan for HIV and HIV-Related Research provides the blueprint by which the budget for HIV research is set across the NIH and ultimately, how funding decisions are made to ensure the highest priority research is supported.

The FY2019/2020 Trans-NIH Strategic Plan for HIV and HIV-Related Research will provide research priorities prior to the scientific and budget planning process for most of the ICOs that support HIV research such that research priorities outlined in the plan will prospectively guide funding decisions for future research. In FY2021, the OAR will provide a three-year Trans-NIH Strategic Plan for HIV and HIV-Related Research that will be reviewed annually to ensure support for priority research.

During development, there are opportunities for stakeholders internal and external to the NIH to recommend research gaps and opportunities that may be incorporated into the Trans-NIH Strategic Plan for HIV and HIV-Related Research. In addition, the OAR data analytics team will utilize data from different funded areas of research to shed light on what research has already been well supported. These data together with stakeholder input will inform which research areas should be prioritized in the plan and how to best coordinate research across the NIH to end the pandemic and improve lives of PWH.

Dr. Brown shared the timeline for the FY2019/2020 Trans-NIH Strategic Plan for HIV and HIV-Related Research beginning with the request for information (RFI) from stakeholders in 2017. She summarized highlights of research areas recommended for support from the 318 RFI responses as well as noting that the NAEC provided input in February 2018. A smaller working group of the NAEC comprised of representatives from the top six NIH Institutes by HIV allocation will provide input to focus the research priorities for the final presented plan.

The OAR is currently incorporating comprehensive language that covers the depth and breadth of research to be accomplished, as well as specific language for targeted areas within the overarching priorities.

Discussion Highlights — FY2019/2020 Trans-NIH Strategic Plan for HIV and HIV-Related Research

Ms. Dee commented community participation might be skewed for the RFI since one response came from thirty organizations. Dr. Brown explained the OAR accounted for all known participant organizations for each response.

Ms. Dee expressed that the community is concerned about the insufficient inclusion of behavioral research, implementation science, crosscutting research, the cascade, and cure research. Dr. Brown assured Ms. Dee that in addition to the RFI, the NAEC was asked about the areas of research mentioned, and that the OAR plans to incorporate the areas mentioned into the FY2019/2020 Trans-NIH Strategic Plan for HIV and HIV-Related Research.

Dr. Gandhi commended the NIH on messaging the importance of early-career investigators. She stressed how important it is to continue supportive messages as early-career investigators learn about the NIH budget and consider their academic careers.

Ms. Dee wondered how the OAR coordinates collaboration between the ICOs. Dr. Brown gave examples of specific programs where collaboration was driven from in-person discussions between the OAR and ICOs. Dr. Goodenow explained the OAR convenes monthly meetings with the NAEC to facilitate collaboration between the ICOs that fund HIV research.

Update from the National Cancer Institute (NCI) on HIV/AIDS Research
Norman Sharpless, MD, NCI, NIH

Dr. Norman Sharpless informed the council that NCI has a large portfolio focused on AIDS-related cancer. Dr. Sharpless highlighted NCI-supported seminal contributions to the understanding of HIV. He gave a breakdown of the vibrant NCI research portfolio for HIV and HIV-related research.

The burden of HIV-associated cancers for PWH in the US differs from low- and middle-income countries with a high burden of HIV. For PWH in the US, cancer diagnoses include virally associated malignancies, as well as non-virally associated cancers with lung cancer being an important cause of mortality. Dr. Sharpless made the argument for inflammation as an area of research that would benefit both lung cancer and PWH.

The NCI portfolio includes studies throughout the world. Dr. Sharpless noted that Kaposi sarcoma and cervical cancer are the most common tumors overall in parts of sub-Saharan Africa, which is quite different from the epidemiology in the U.S. In the U.S., the number of cases of Kaposi sarcoma has decreased with the widespread use of anti-retroviral therapy. Dr. Sharpless explained that treatment for HIV and HIV-associated cancers has improved the health of PWH in the US.

NCI supports research to develop HIV maturation inhibitors, understand clonal proliferation, and stimulate the immune response to HIV via vaccines or immune checkpoint inhibitors. NCI supports the Anal Cancer HSIL Outcomes Study (ANCHOR) study that aims to screen participants for moderate or high grade squamous interepithelial lesions (HSIL) to randomize them to a strategy of intervention versus watchful waiting with the ultimate goal of decreasing progression to HPV-associated anal cancer.

A number of the approximately seventy NCI Cancer Centers support research in low- and middle-income countries (LMIC). NCI is working to organize global oncology efforts in LMIC. They have established collaborative consortia to study HIV-associated cancers in LMIC and the AIDS Malignancy Consortium is conducting clinical trials in sub-Saharan Africa.

Dr. Sharpless confirmed that funding from the OAR is important for the NCI mission. He gave examples of types of research the NCI can support following release of the NIH HIV/AIDS Research Priorities and Guidelines for Determining AIDS Funding notice (NOT-OD-15-137) that outlines priority topics for HIV dollars. He noted limitations for the use of HIV funds for Epstein-Barr virus (EBV) and HPV research.

In the US approximately six times as many individuals develop EBV-associated malignancies, as opposed to Kaposi sarcoma virus (KSHV)-associated malignancies. A high percentage of the EBV-associated cancers develop in PWH. Dr. Sharpless expressed concern that the current policy is forcing support of research outside of the best interest of PWH. Dr. Sharpless argued for cost sharing for key topics of scientific interest that benefit both HIV and cancer.

Discussion Highlights — Update from the National Cancer Institute (NCI) on HIV/AIDS Research

Dr. Elizabeth Connick commented that it is difficult to understand why HPV is not a high priority. Dr. Sharpless clarified that HPV research is a very high priority for the NCI and is an area where the NCI has a longstanding tradition of high-impact research. He explained that HPV research as it relates to HIV-associated malignancies is an area to consider for cost sharing. Dr. Sharpless then gave examples of other areas of cancer research relevant to cost sharing.

Dr. David Smith asked if there was a difference in the number of applications and the millions of dollars spent between KSHV and EBV for the Six Provocative Questions Addressing Cancer with Underlying HIV Infection funding opportunity announcements. Dr. Sharpless referred to Dr. Robert 'Bob' Yarchoan from NCI who responded that KSHV and EBV were examples for the basic research the NCI could and could not fund with the current priorities, respectively. Dr. Sharpless added that a prospective cost-sharing policy would allow flexibility for funding research relevant to HIV.

Ms. Dee commended the NCI on the ANCHOR study. She asked Dr. Sharpless if NCI is committed to more research if OAR develops a trans-NIH cost sharing policy. Dr. Sharpless confirmed that NCI is committed to research on cancer that affects PWH and on HIV-relevant basic immunology, including aging of T cells; checkpoint inhibitors for HIV and for cancer therapy; immunotherapy development; and, HPV. Dr. Sharpless confirmed that NCI is committed to cost sharing. For cost sharing, NCI dollars and OAR dollars would both be used to support research that is in the best interest of PWH.

Dr. Babafemi Taiwo asked how the NCI will fund HIV related, high priority research for the institute that does not already fall under the high priorities for HIV. Dr. Sharpless answered with different scenarios for moving forward. He shared that he thought the best system is one that adds flexibility to the current policy and is considerate of the health of PWH.

Dr. Jonathan Mermin gave examples of strategies academics might use to support research and asked what strategies the NCI uses to support the research portfolio. Dr. Sharpless replied that NCI takes multiple approaches. He clarified that NCI intends to support programs that require large amounts of funding and expects to apply cost sharing approaches to the investigator-initiated science, cooperative agreements, or bio bank projects.

Dr. Jennifer Kates commented that the OAR ad hoc cost sharing task force discussed the exact issues presented. The OAR ad hoc cost sharing task force recommended that levels of cost sharing for broad scientific areas be based on incidence and prevalence for PWH in different settings. The OAR ad hoc cost sharing task force recommendations provided an updated framework for the OAR and the ICOs to negotiate prospective levels of funding for each scientific topic. She reminded the OARAC that tough decisions will have to be made to divide the available funds.

Dr. William Powderly complimented NCI for the recent emphasis on implementation science related to disadvantaged populations, rural populations, et cetera and asked how this fits with the NCI HIV/AIDS portfolio. Dr. Sharpless replied that NCI has a large growing portfolio for cancer health disparities. Overall the disparity in mortality rates as well as the overall mortality rate is decreasing between African-Americans and Caucasians related to cancer. The disparity between urban and rural areas for cancer mortality and non-cancer mortality is increasing with rural areas having a greater cancer and non-cancer mortality rate.

Update from the Office of Research Infrastructure Programs (ORIP) on HIV/AIDS Research Activities
Franziska Grieder, DVM, PhD, ORIP, NIH

Dr. Franziska Grieder explained the Office of Research Infrastructure Programs (ORIP) was founded in December 2011 on the same date as the establishment of the National Center for Advancing Translational Sciences (NCATS) and the dissolution of the National Center for Research Resources. The shortened ORIP mission is “Infrastructure for Innovation”. ORIP includes the Division of Construction Instruments and the Division of Comparative Medicine. The ORIP strategic plan focuses on Trans-NIH activities and precision and reproducibility, a topic of high importance to the NIH and to shared resources.

ORIP partners with the OAR to support the National Primate Research Centers (NPRCs). The seven NPRCs are located at Emory University, the University of Wisconsin-Madison, Tulane University, Texas Biomedical Research Institute, the University of California Davis, Oregon Health & Science University, and Washington University. The NPRCs collectively house over 20,000 animals that span eight non-human (NHP) species. The centers provide NHPs to over 1,000 NIH research projects and to over 2,000 research scientists.

The rhesus macaque, pigtail macaque, sooty mangabey, and the Mauritian cynomolgus macaque are most relevant for HIV/AIDS research. The NPRCs provide research investigators with tools and techniques, expertise, and animal care. In many cases, investigators outside of the NPRCs rely on the centers for NHP research studies.

The seven NPRCs function as a cohesive consortium. The NPRC consortium website houses information on areas of expertise and investigation as well as tools and technologies available at each center.

The ORIP in collaboration with the OAR funds eleven specific pathogen free (SPF) NHP colonies located at six of the NPRCs, at the Johns Hopkins University, and at the Caribbean Primate Research Center (CPRC). Most of the SPF NHPs are free of four viruses while the enhanced SPF colonies are free from greater than four pathogens. Approximately 7,500 animals are maintained by the eleven SPF colonies and approximately 7,000 are available to researchers. Currently there is a larger demand than supply for SPF NHPs.

The CPRC at the University of Puerto Rico houses a large SPF colony including a free-ranging colony on the island of Cayo Santiago that sources SPF NHPs to HIV and other investigators. Dr. Grieder showed the geography of the field station with the corrals, where many of the animals, specifically SPF colonies, are housed. She pointed out the research labs, the main indoor facility, and the isthmus that connects little Cayo to the main island.

In September 2017, the eye of hurricane Maria moved across Cayo Santiago. Dr. Grieder showed the devastation of the hurricane which included destruction of the isthmus between little Cayo and the main island. The isthmus was the bridge used by caretakers to deliver supplies to the animals. During the hurricane, the animals survived with very few animals lost.

ORIP and the OAR partnered to release a Construction Funding Opportunity for limited competition to rebuild facilities, renovate and update destroyed infrastructure at the CPRC. The funding announcement was entitled: HIV/AIDS-related Non-Human Primate Animal Research Facilities Restoration Program in the Aftermath of Hurricane Maria.

Further, ORIP and OAR partnered to administer and support the HIV/AIDS Vaccine Scholars Program which started in FY2016. The K01 mentored research program, which ensures the pipeline of highly trained early stage investigators that conduct pre-clinical research with potential to translate to the clinic, supported HIV vaccine research in FY2016 and FY2017. For FY2018, the program included topics in each of the OAR priority areas.

Discussion Highlights — Update from the Office of Research Infrastructure Programs (ORIP) on HIV/AIDS Research

Dr. Gandhi asked which scientists qualify for the K01 scholars program. Dr. Grieder clarified that early stage investigators with a variety of degrees can apply.

Dr. Connick wondered if Zika research increased the demand for NHPs and asked if there has been an increase in funding for the centers to compensate. Dr. Grieder confirmed that requests for NHPs increased due to Zika. She explained that future funding announcements or future directions for the NPRCs are reviewed by the advisory council for ORIP.

Dr. Dieffenbach asked if TB facilities will expand. Dr. Grieder acknowledged the majority of NHPs at the centers are dedicated to HIV/AIDS but many research questions are being asked in the NHP model including neuroscience, reproductive questions, and infectious diseases. TB is challenging to study due to containment. Some of the centers support TB research.

Dr. Gandhi commended the shared instrument program and asked about the limitations of the program. Dr. Grieder responded that the shared instrument program has one annual receipt date. She clarified that there are two S10 programs differentiated by the cost of the instrument requested. Considerations are given to applications that propose to share the instrument between a number of NIH funded research projects and program staff considers applications from all states including those with historically low level of NIH funded research.

Dr. Burdo asked if ORIP has considered accepting applications for the S10 grants more frequently than once a year since a resubmission in response to reviews can result in funding two years or more after the initial application. Dr. Grieder responded that ORIP changed the high end S10 applications to an annual receipt date rather than a biannual receipt date. She reasoned for an annual receipt date and acknowledged ORIP is open to reconsider receipt date frequency for the program in the future.

Ms. Dee wondered if the center in Puerto Rico is up and running after hurricane Maria. Dr. Grieder responded that even though the water treatment system and power supply was damaged the CPRC was operational relatively soon after the hurricane. The animal workers and staff of the CPRC were amazing and walked to the site to care for and maintain the colony. Additionally, external support for the CPRC was provided by the NPRC consortium program.

Update from the National Institute of Mental Health (NIMH) on HIV/AIDS Research Activities
Dianne Rausch, PhD, NIMH, NIH

Dr. Dianne Rausch spoke on behalf of Dr. Joshua Gordon, Director of NIMH. NIMH is the lead federal agency for research on mental health supporting more than 3,000 extramural research grants and contracts and approximately 600 intramural scientists. Dr. Rausch shared the vision and mission of NIMH and reviewed the four objectives in the NIMH Strategic Plan for Research.

NIMH has four divisions that cross basic, translational, and interventional research. NIMH collaborates with other federal agencies, local organizations, and healthcare systems to provide a variety of ways to ensure evidence-based practice research reaches the public domain. The NIMH Division of AIDS Research (DAR) is one of the cross-cutting divisions that supports research across basic, translational, and implantation science. All of NIMH's HIV/AIDS portfolio resides in DAR and is 100 percent relevant to HIV/AIDS.

The mission of DAR is to reduce the global incidence of HIV/AIDS, decrease HIV/AIDS related morbidity and mortality, and advance HIV/AIDS cure research. Dr. Rausch explained that NIMH DAR supports research across the life span. She highlighted research interests in the infant, children, adolescent, and aging populations of PWH, as well as health disparities for men, women, under-represented minorities, and hard to reach populations.

Basic behavioral and social sciences research is critical for understanding vulnerable populations, defined risk settings, and approaches to address risks, which may improve the behavioral and social factors that impact risk and risk reduction efforts. Behavioral and social sciences research strengthens biomedical HIV product development and implementation of interventions in clinical trials. And finally, integrative behavioral and social science contributes to implementation of effective strategies in multi-level settings. Dr. Rausch gave examples of how behavioral and social sciences research improves the HIV care continuum.

The clinical picture of neuro HIV has changed in the ART era. HIV enters the central nervous system as early as eight days after infection where the virus resides in glial cells, macrophages and astrocytes. For PWH who are suppressed on ART, there are subtle vascular changes, synaptic degeneration, mild cognitive changes, and some evidence of accelerated aging. To ascertain the clinical picture of neuro HIV, additional clinical manifestations need to be attended to, which is especially important for PWH who face multiple comorbidities and loss of social support that affects adherence to ART.

Dr. Rausch noted that NIMH has a very strong and active program for HIV eradication to understand the viral reservoir. NIMH DAR is also very interested in targeting therapeutics to improve health outcomes and motor cognitive function. NIMH is cognizant of the potential polypharmacy effects and toxicity associated with current ART that may affect the CNS.

NIMH DAR functions collaboratively to support research within and outside of the US. Mental health is a specific priority for NIMH. Depression, the most common mental health disorder among PWH, has a negative impact on the HIV care continuum and is often untreated among PWH. NIMH developed a global mental health and beyond program to expand the strategies to reduce mental health disparities across the world, to support research capacity building, to develop new strategies for depression and HIV, and support research mentoring to build up an interdisciplinary workforce. Mental health disorders and disparity research are potential areas of cost sharing for NIMH.

NIHM has interest in developing useful biomedical mechanisms or markers for depression that can be used to develop a more structured intervention. With available improved technology, researchers can investigate neural immune mechanisms of depression to inform interventions.

Stigma is another scientific area for potential cost sharing. Stigma is a barrier to prevention and treatment for PWH. Dr. Rausch presented a model of the different components and predictors of stigma that can be used to develop targeted interventions that may effectively reduce stigma.

HIV can be a model to understand how monocyte trafficking to the brain with stress and inflammation can influence some mood and behavior outcomes. Dr. Rausch gave an example of trans-NIH research supported by the NIMH in the NIAID Martin Delaney Collaboratories consistent with social structure stress correlating with expression of HIV RNA from the latent reservoir.

The Human Connectome Project is making great progress in understanding connectivity in the brain. NIMH hopes research supported by a recently published funding opportunity informs the neural community about some of these altered neural circuits in response to immune mechanisms, as opposed to other factors. NIMH is also supporting imaging studies to look for signals of neural damage in PWH.

Discussion Highlights — Update from the National Institute of Mental Health (NIMH) on HIV/AIDS Research

Dr. Gandhi asked why NIMH does not post specific pay lines for different grant mechanisms (e.g. K-level grants, R01s, R03s, etc.). Dr. Rausch explained that NIMH shares information about funding but does not post specific pay lines due to their complicated budget. Dr. Mermin asked what proportion of the NIMH DAR budget is focused on basic science versus behavioral science. Dr. Rausch explained that traditionally sixty percent of the NIMH budget supported behavioral and forty percent supported basic neuroscience.

Dr. Mermin commented that Dr. Rausch made a powerful argument for why mental health is important for PWH. He wondered how NIMH's portfolio has adjusted to the recent understanding that the most effective interventions are biomedical and behavioral aspects towards prevention will be through behavioral change related to pill taking, clinician behavior, et cetera. Dr. Rausch indicated that NIMH adjusted by strongly buying into the integrated biomedical behavioral approach.

Public Comments

Dr Gandhi noted there were no written requests for public comment and opened the discussion to anyone present with a comment.

Dr. Leia Novak asked if cost sharing would affect an ICO's budget allocation from the OAR. Dr. Patterson replied cost sharing is a bi-directional process that depends on prospective agreements between the OAR and the ICO.

Dr Rausch commented that in the early days of HIV, the NIH ICOs were siloed by individual missions and agendas. Given the flat budget and the state of the science, the silos are breaking down and the ICOs are working together a lot better.

Closing Comments
Maureen M. Goodenow, PhD, OAR, NIH

Dr. Goodenow commented the presentations today highlighted progress for the HIV research enterprise and collaboration at the NIH. Science is driving the need for collaboration, which is critical for the interactive, trans-disciplinary, multi-faceted approach to overcome the next generation of challenges to end the HIV pandemic and improve the health of PWH. She thanked the OARAC for their input and noted that the next OARAC meeting is July 12, 2018.

Adjournment
Monica Gandhi, MD, MPH, University of California San Francisco

Dr. Gandhi adjourned the meeting at 4:06 pm.

Certification

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

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_____
Monica Gandhi, MD, MPH
Chair, Office of AIDS Research Advisory Council

5/31/18
_____
Date

– S –
_____
Elizabeth Church, PhD
Executive Secretary, Office of AIDS Research Advisory Council

05/31/2018
Date