

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

**Office of AIDS Research Advisory Council
Forty-Eighth Meeting**

**July 12, 2018
Webinar/Teleconference
and
5601 Fishers Lane, Room LD/20
Rockville, Maryland**

Draft Meeting Minutes

Council Members in Attendance: Dr. Charles Wira (Chair); Dr. Paul Sato (Executive Secretary); Dr. David Celentano; Dr. John J. Chin; Dr. Elizabeth Connick; Ms. Dázon Dixon Diallo; Dr. Jennifer Kates; Dr. Lynne M. Mofenson.

Ad Hoc Members in Attendance: Dr. Ingrid V. Bassett; Dr. Tricia H. Burdo; Dr. Heidi M. Crane; Lynda M. Dee, Attorney-at-law; Dr. Maureen M. Goodenow (OAR Director); Dr. Roy M. Gulick; Dr. William G. Powderly; Dr. Jonah B. Sacha; Dr. Kimberly Kay Scarsi; Dr. Bruce R. Schackman; Dr. David M. Smith; Dr. Babafemi O. Taiwo.

Ex Officio Members in Attendance: Dr. Julie A. Ake; Dr. Victoria J. Davey; Dr. Carl W. Dieffenbach; Dr. Jonathan Mermin.

Advisory Council Representatives in Attendance: Dr. Richard E. Chaisson; Dr. Alan E. Greenberg; Dr. Nancy J. Raab-Traub; Dr. Steffanie A. Strathdee.

Additional Speakers and Invited Guests: Dr. Rohan Hazra; Dr. Henry Masur.

Council Members Absent: Dr. Scott D. Rhodes

Welcome and Meeting Overview

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

Dr. Charles Wira, newly appointed OARAC Chair by the HHS Secretary, welcomed participants to the forty-eighth 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-seventh OARAC meeting, held on March 27, 2018. Dr. Jennifer Kates moved to accept the draft minutes from the forty-seventh OARAC meeting; the motion was seconded by Dr. Lynne Mofenson. Members of the council voted to approve the minutes, with Dr. David Celentano and Ms. Dázon Dixon Diallo abstaining. Dr. Wira reviewed the forty-eighth meeting agenda, noting the inclusion of time for public comments.

Report of the Office of AIDS Research (OAR) Director

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

Dr. Maureen Goodenow welcomed 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 OAR. Dr. Charles Wira was welcomed as the new OARAC chairperson. She also thanked retiring *ex officio* Department of Defense (DOD) representative Dr. Nelson Michael for his service to the OARAC and welcomed Dr. Julie Ake as the new *ex officio* representative from the DOD. Dr. Goodenow explained that even though the new members for 2017 have recently been approved by the Secretary of the Department of Health and Human Services (HHS), these new OARAC members on the 2017 list had not yet completed all requirements, so these individuals must remain *ad hoc* members for this meeting. Approval of the 2017 members has allowed OAR to submit the list of 2018 nominations up to the HHS level. In the meantime, to help assure future meeting quorum requirements, OAR is planning to seek the extension of the terms of two currently outgoing voting members, Drs. David Celentano and Elizabeth Connick, to beyond their September 2018 term expiration.

The next OARAC meeting scheduled for November 15, 2018, will be preceded by a half-day orientation for Council and Ad Hoc Members. Dr. Goodenow confirmed that beginning in 2019, the OARAC will hold three in-person meetings each year. Future meetings dates of March 28, 2019 and November 7, 2019, are confirmed, but the planned July 2019 meeting will be rescheduled to avoid potential conflicts with the 2019 International AIDS Society (IAS) conference travel and pre-conference meeting schedules. OAR will provide additional information as soon as they become available.

Dr. Goodenow updated the council on changes to OAR's staff since the previous meeting, including the departure of staff members Drs. Elizabeth Church, Jean Patterson, and Gina Brown. She introduced new staff members Drs. Jay Radke and Yvette Edghill Spano, and noted that OAR continues to recruit for a number of positions, including the deputy director.

Dr. Goodenow informed attendees that she and Drs. Radke and Paul Gaist will attend the 2018 IAS conference in Amsterdam, the Netherlands. She will give presentations on aging with HIV, the NIH HIV research agenda and will participate in a number of other sessions and roundtables. Dr. Radke will speak about NIH grantsmanship strategies and peer review; Dr. Gaist will serve on a session panel, present a poster, and speak about the conceptualization and application of behavioral and social sciences research within HIV/AIDS research. Dr. Goodenow invited any council members attending the IAS conference to email her about scheduling sidebar meetings.

She updated the council on the project to reconstruct the Caribbean Primate Research Center., a key supplier of rhesus macaques for NIH-sponsored biomedical research for more than 80 years. Both physical sites of the Caribbean Primate Research Center were very badly damaged by Hurricane Maria in the fall of 2017. OAR partnered with NIH Office of Research Infrastructure Programs (ORIP) to develop a request for applications (RFA) to reconstruct the Caribbean Primate Research Center's facilities. Applications have been received and reviewed; funding decisions are expected before the end of fiscal year (FY) 2018. Dr. Goodenow commended the speed with which the collaboration between OAR and ORIP has advanced plans for reconstruction.

Dr. Goodenow presented an overview of the overall NIH budget for FY 2018, in which most increases were designated for the 21st Century Cures Act and the *All of Us*SM Research

Program initiatives; NIH initiatives contributing to the national response to the current opioid abuse crisis; and research on Alzheimer's disease and related dementias. In the proposed FY 2019 budget, which is undergoing congressional action, the HIV/AIDS research budget looks to remain flat at around \$2.9 billion. The FY 2019 HIV/AIDS research Professional Judgement Budget—created annually to define the amount of funds needed to optimally fulfill the trans-NIH HIV/AIDS research agenda—requested a \$450 million (15%) increase over the FY 2018 enacted budget and recommended allocating funds in different proportions. Dr. Goodenow thanked OAR staff members for their work on this document, likely to be available for public release by the end of July.

The congressionally mandated Trans-NIH Strategic Plan for HIV and HIV-Related Research [the trans-NIH Plan] guides and informs the HIV research scientific community regarding NIH HIV/AIDS research directions. Previously, the trans-NIH Plan was developed annually, but this year, the trans-NIH Plan will cover FY 2019 and 2020. Beginning in FY 2021, the plan will delineate a multi-year strategy spanning 3–5 years. These changes will allow the strategic plan process to align more closely with funding cycles at NIH Institutes, Centers, and Offices (ICOs), as well as with OAR's budget development process. The NIH AIDS Executive Committee (NAEC) provided suggestions that were incorporated into the FY 2019–2020 trans-NIH Plan. OAR now is finalizing the trans-NIH Plan. Dr. Goodenow commended OAR staff for their expert guidance on this project. OAR is analyzing responses to a recently closed request for information (RFI) on future multi-year strategic plans. Dr. Goodenow anticipates further discussion of this topic during the November OARAC meeting.

Dr. Goodenow referred to the *Ad Hoc* Cost Sharing Task Force overview presented at the March OARAC meeting and noted that discussions with the NAEC, ICO directors, and other stakeholders are ongoing. She emphasized the complexity of HIV/AIDS research, illustrated by the need for cost sharing. At the same time, cost sharing has the potential to foster collaboration between HIV/AIDS and non-HIV/AIDS research and enhance prospective approaches to planning the NIH HIV/AIDS research budget. Annually, OAR and interested ICOs will consider cost sharing for selected and specific research areas in which HIV and non-HIV science intersect. After OAR and the ICOs identify appropriate scientific areas, the total investment and level of cost sharing will be determined. Cost sharing might involve funding opportunity announcements (FOAs), and/or groupings of related investigator-initiated applications.

Dr. Goodenow outlined two recently initiated pilot projects. In partnership with the National Institute on Aging, an RFA seeking applications proposing basic and clinical research on the molecular and cellular mechanisms of age-related HIV neurodegeneration was issued. After standard NIH review processes are followed, the plan is to select between six and eight meritorious applications for award before the end of FY 2018; research effort will be shared equally and/or collaboratively between HIV/AIDS researchers and Alzheimer's and related dementias researchers. OAR also has a pilot project encouraging ICOs to submit initiatives with proposed cost-sharing as part of the preliminary FY 2020 budget development process that will begin before the end of FY2018. OARAC will be provided further updates at future meetings. When asked about the implementation timeline, Dr. Goodenow explained that the progress of the current pilot projects and ICOs' responses will guide future implementation.

Dr. Goodenow emphasized the many benefits of cost sharing, reiterating that it enhances prospective planning and aligns with current NIH budget processes. Cost-sharing plans are based on topical scientific areas and allow flexibility. Cost sharing also catalyzes transdisciplinary collaboration and facilitates strategic steering of the research agenda. Cost-

sharing implementation is a priority activity for OAR in 2019. The November OARAC meeting will include further discussion of cost-sharing initiatives and related data analytics.

Updates from the U.S. Department of Health and Human Services (HHS) HIV/AIDS Treatment and Prevention Guidelines Working Groups of the OARAC

Rohan Hazra, M.D., Eunice Kennedy Shriver National Institute of Child Health and Human Development, NIH

Roy (Trip) Gulick, M.D., M.P.H., Weill Cornell Medicine

Henry Masur, M.D., NIH Clinical Center

Dr. Rohan Hazra explained that the most recent revised edition of the HHS HIV/AIDS Treatment and Prevention pediatric guidelines were published shortly after the previous OARAC meeting; in addition, the perinatal guidelines are officially scheduled to be updated later in 2018. Recently all HHS HIV/AIDS treatment guidelines panels focused on addressing an issue related to dolutegravir (DTG) use in antiretroviral therapy (ART) that was identified in a preliminary analysis of data as part of a birth outcome surveillance study in Botswana. Within the first 2 years of the study, Botswana began using DTG as part of first-line ART for all adults with HIV. Initial data on the safety of DTG exposure of pregnant women beginning ART with DTG during pregnancy were reassuring. In preparation for the World Health Organization (WHO) HIV/AIDS treatment guidelines meeting in the spring of 2018, WHO requested an unscheduled review of safety data from the Botswana study on DTG exposure from the time of conception. This review captured data on women in the Botswana birth surveillance study who began DTG-based ART regimens as early as when they became available in the country and who subsequently became pregnant. The study team identified neural tube defects in approximately 1 percent of infants born to women on DTG-based regimens; by comparison, the rate of such defects in women on ART regimens not including DTG at conception was 0.1 percent.

WHO had been preparing to endorse ART regimens including DTG for all adults with HIV, but these results caused significant concern. All three HHS HIV/AIDS treatment guidelines panels worked closely with one another and with the FDA, as well as with other U.S. and international agencies to develop a coordinated message about the continued use of dolutegravir. On May 18, 2018, a consensus message from all HHS HIV/AIDS treatment guidelines panels that was timed to coordinate with an FDA drug safety communication on DTG based on the same Botswana data, was released emphasizing the need for women to be counseled about the potential risks of dolutegravir use. The HHS HIV/AIDS treatment guidelines panels subsequently released a more comprehensive set of recommendations on May 30 to answer questions and acknowledge the need for additional data. Dr. Hazra noted that if this safety signal is confirmed, one important question that will need to be answered is whether this effect is specific to dolutegravir or is a class effect relevant to other integrase inhibitors. He emphasized that all guidelines panels are continuing to review the data carefully to determine their impact across all their current documents and to ensure coordination of recommendations across panels.

Dr. Trip Gulick acknowledged the important contributions of Dr. Martin S. Hirsch during his many years of service to the HHS HIV/AIDS treatment guidelines for adults and adolescents panel. Dr. Gulick then commented on the outcomes of the panel's face-to-face retreat on April 19, 2018. He reiterated the importance of the data from the Botswana study discussed by Dr. Hazra, explaining that the DTG findings necessitated updates and context across all HHS HIV/AIDS treatment guidelines. These updates were required in sections of the adult and adolescent guidelines related to laboratory monitoring, ART regimen selection, regimen switching, virologic failure, HIV and women, HIV and adolescents, and acute and early HIV infection. Other revisions reflect progress in the field. They include including inclusion of

bictegravir, a recently approved integrase inhibitor, in the “What Regimen to Start” section and tables associated with drug interaction characteristics, hepatitis C, and adverse effects. The drug resistance testing and co-receptor tropism testing sections were revised to expand discussion of proviral DNA genotypic assay, a newer test. The virologic failure section also was updated to include a newly approved drug, ibalizumab, specifically indicated for patients with multidrug-resistant HIV. The regimen-switching section also is being revised to include new data.

Dr. Henry Masur noted that the HHS HIV/AIDS opportunistic infection treatment guidelines panel is in the process of its annual membership rotation, and in doing so striving to better address the importance of including younger members and those from a more diverse set of backgrounds. Because it covers multiple pathogens, the opportunistic infection guidelines are reviewed on a quarterly basis by the different pathogen/subject groups and revised as needed. Dr. Masur emphasized the importance of ensuring that readers can be confident in the accuracy and currency of the documents by providing clear information on the most up-to-date revisions. Current areas under revision include the natural history and diagnostics of herpes viruses; new data about the treatment of retinitis and retinal necrosis; and new data on issues with HPV activation during hepatitis B treatment. Dr. Masur noted the recent debate at the 2018 Conference on Retroviruses and Opportunistic Infections (CROI) on whether to include mention of a new, alternative, short-duration (1-month) preventive treatment regimen for tuberculosis. The panel decided to acknowledge the data but reserve formal recommendation until after scrutiny of a more comprehensive peer-reviewed publication of trial results, rather than basing panel recommendations on the preliminary and abbreviated data presented at CROI.

Dr. Masur pointed out that the only current significant change to the HHS guidelines for the prevention and treatment of HIV/AIDS opportunistic infections is related to immunizations. After ongoing discussions with the Centers for Disease Control and Prevention (CDC) and its Advisory Committee on Immunization Practices (ACIP), all parties agreed that, in some situations available data might not be specific enough for ACIP to make a recommendation, but it would be appropriate for the HHS HIV/AIDS opportunistic infection guidelines to acknowledge the availability of new immunizations or new schedules and make recommendations that help practicing clinicians deal with the newly available data or product(s).. This situation, for example, applies to a new vaccine for zoster, Shingrix™, and is relevant to the new hepatitis B vaccine with a novel immunostimulatory adjuvant, HepB-CpG. Dr. Masur anticipated that an expert recommendation for these vaccines would acknowledge data on safety and immunogenicity in HIV-negative individuals, and to a limited extent in HIV-positive persons. The data would suggest that both products are likely reasonable to use - while recognizing that the HepB-CpG vaccine raises some safety concerns – all of which will need to be reviewed and discussed before any revisions to the HIV/AIDS opportunistic infections guidelines are made. He added that a new section of the opportunistic infections guidelines will specifically collate information on immunizations from all the sections and provide slightly more nuance than ACIP and CDC guidelines.

No discussion points were raised. The motion to approve the HHS HIV/AIDS treatment guidelines updates as presented was advanced by Dr. Mofenson and seconded by Dr. Celentano. The motion passed with no abstentions.

Public Comments

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

Dr. Wira noted that no request to present public comments had been received.

Closing Comments

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

Dr. Goodenow thanked the council members and guidelines working groups, as well as OAR staff, for their hard work and support.

Adjournment

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

Dr. Wira thanked the attendees and adjourned the meeting at 12:16 p.m.

Certification

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



8/22/18

Charles Wira, Ph.D.
Chair, Office of AIDS Research Advisory Council

Date

08/23/2018

Paul A. Sato, M.D., M.P.H., CDR, USPHS
Executive Secretary, Office of AIDS Research Advisory Council

Date