The United States President's Emergency Plan for AIDS Relief (PEPFAR)
Scientific Advisory Board (SAB) Meeting
October 12, 2018
U.S. Department of State, Washington, DC

PEPFAR Scientific Advisory Board Members in Attendance

Judith Auerbach—Independent Science and Policy Consultant; Professor, Center for AIDS Prevention Studies, University of California San Francisco School of Medicine

Peter Berman—Professor, Global Health Systems and Economics, T.H. Chan School of Public Health, Harvard University

Connie Celum—Director, International Clinical Research Center, Department of Global Health, University of Washington School of Medicine

Carlos del Rio—Chair, Department of Global Health, Rollins School of Public Health, and Professor of Medicine, Division of Infectious Diseases, Emory University School of Medicine

Mark Harrington—Executive Director, Treatment Action Group (TAG)

Mark Heywood—Executive Director, SECTION27, O'Neill Institute for National & Global Health Law; Chairperson, UNAIDS Reference Group on HIV/AIDS and Human Rights

Jennifer Kates—Vice President and Director, Global Health and HIV Policy, Kaiser Family Foundation

Etienne Karita—Site Leader, Project San Francisco, Rwanda Zambia HIV Research Group

Ruth Macklin—Professor Emerita of Bioethics, Einstein School of Medicine

Celia Maxwell—Associate Professor of Medicine and Associate Dean for Research, Howard University College of Medicine; Infectious Disease Specialist, Howard University Hospital

Kenneth Mayer—Co-Chair and Medical Research Director, Fenway Health; Director, HIV Prevention Research and Attending Physician, Beth Israel Deaconess Medical Center; Professor, Harvard Medical School and Harvard School of Public Health

Jesse Milan—President and CEO, AIDS United

Angela Mushavi—Coordinator, Mother-to-Child HIV Transmission Prevention and Pediatric HIV Care and Treatment, Ministry of Health and Child Welfare, Zimbabwe

Christine Nabiryo—Public Health Consultant, Uganda

Nyambura Njoroge—Project Coordinator, Ecumenical HIV and AIDS Initiatives and Advocacy, World Council of Churches

Edwin Sanders—Senior Server, Metropolitan Interdenominational Church of Nashville; Chair, The Legacy Project, a collaboration with the HIV Vaccine Trials Network; Member, Presidential Advisory Council on HIV/AIDS (PACHA)

Fredrick Sawe—Director, HIV/AIDS Research, Walter Reed Project, Kenya Medical Research Institute

Albert Siemens—Chair, FHI Foundation
Carole Treston—Chief Nursing Officer, Association of Nurses in AIDS Care
Mitchell Warren—Executive Director, AVAC: Global Advocacy for HIV Prevention

PEPFAR Scientific Advisory Board Members Not in Attendance

Quarraisha Abdool Karim—University of KwaZulu-Natal; Associate Scientific Director, Centre for the AIDS Programme of Research in South Africa (CAPRISA); Professor of Clinical Epidemiology, Mailman School of Public Health, Columbia University; Professor of Public Health, Nelson R. Mandela School of
Judith Currier—Division Chief, Infectious Diseases and Associate Director, University of California Los Angeles (UCLA) Center for Clinical AIDS Research and Education (CARE); Professor of Medicine, UCLA School of Medicine
Musimbi Kanyoro—President and CEO, Global Fund for Women
Lejeune Lockett—Operations and Program Manager, Global Health, Charles Drew University of Medicine and Science; Angola Military HIV Prevention Program, Drew Cares International
Jean William Pape—Professor, Weill Medical Cornell College; Director, GHESKIO (Haiti)
David Peters—Chair, International Health, Johns Hopkins University School of Public Health
Emilio Emini—Director, HIV Program, Bill and Melinda Gates Foundation
Sofia Gruskin—Director, Program on Global Health and Human Rights, Institute for Global Health, University of Southern California
Robert Redfield—Director, Centers for Disease Control and Prevention, Atlanta, Georgia

PEPFAR Senior Management Team

Ambassador Deborah L. Birx—State Department, Office of the Global AIDS Coordinator (SGAC)
Andrew Forsyth—Director, Office of Research and Science, SGAC

Synopsis

On October 12, 2018, the U.S. President's Emergency Plan for AIDS Relief's (PEPFAR) Scientific Advisory Board (SAB) assembled in Washington, D.C. to offer advice to the U.S. State Department Office of the Global AIDS Coordinator (SGAC) on key considerations for country operational planning and program implementation. As per the agenda, board members discussed priorities for Fiscal Year (FY) 2019; updates for the Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe (DREAMS) initiative; new strategies for monitoring countries' progress as they approach or exceed their 95-95-95 targets; and considerations for PEPFAR investments in Western and Central Africa. In addition to a discussion of lessons from two, large combination prevention clinical trials, SAB members considered the latest research

and policy developments pertaining to the antiretroviral medication, dolutegravir, along with their implications for its scale-up as the preferred first-line regimen for persons living with HIV infection. Finally, the group considered evidence informing the selection of a human papillomavirus (HPV) vaccine vaccination strategy for Africa, and offered recommendations for future SAB meetings.

Opening Session

Ambassador Deborah L. Birx provided an update on PEPFAR as it enters the COP 2019 planning cycle. She began by reporting on SGAC participation at the United Nations General Assembly (UNGA) meetings in September on tuberculosis (TB), which has made only modest gains in prevention and treatment in recent years. Drawing on the PEPFAR experience, Birx made an impassioned plea to strive for epidemic control using data-driving program to fine-tune testing and prevention strategies that can stem new infections, protect national budgets from the costs associated with rising infections, and avert associated morbidity and mortality, particularly for persons living with HIV infection (PLHIV). PEPFAR has committed to the integration of TB services into PEPFAR so that all those diagnosed with TB have access to HIV testing and all PLHIV have access to TB testing, prevention, and treatment.

For the Country Operational Plan (COP19) process, Ambassador Birx foreshadowed a new activity-based costing (ABC) initiative intended to better ascertain actual site-level costs associated with a data-driven, targeted, national response to the HIV epidemic. More granular cost data will be instrumental for budgeting at the national level and ministry of finance to ensure sustainability of effective programs. Relatedly, Ambassador Birx described interagency efforts to ensure that 70 percent of the funding for program implementation goes to local, indigenous partners. PEPFAR seeks the realignment and optimization of its considerable yet finite resources through scaling up effective and cost-effective pilot programs, streamlining costs, sharing direct hires, and other strategies that will accelerate progress toward epidemic control in 13 focus countries by 2020.

Another new initiative underway seeks to engage communities of faith more directly in the national response to countries' HIV epidemics by finding men who are living with undiagnosed HIV infection, reducing sexual assault and rape, and enlisting a broader range of community leaders. Key to this effort will be messaging the importance of HIV medical treatment as a means of preserving or restoring health, reducing onward transmission, and reducing HIV-associated mortality. Collaborations with faith-based organizations (FBOs) may also assist stakeholders to respond effectively to other infectious diseases (e.g., tuberculosis).

Ambassador Birx next highlighted several persistent challenges facing PEPFAR, such as addressing the needs of persons 35 years or younger who have lower HIV diagnosis and viral load suppression rates. Programmatic data attest to enduring disparities by sex and age, particularly in HIV diagnosis and achievement of viral load suppression. At the same time, lessons across country contexts provide some reason for optimism. Due to political will and astute leadership, Namibia now reports serostatus awareness at 86 percent of PLHIV and has drastically increased it viral suppression rates 91 percent; by contrast, other countries struggle to achieve such gains, such as Cote d'Ivoire, which reports only 37 percent awareness among PLHIV and 76 percent viral suppression rates. These gaps are pronounced in countries where the HIV epidemic is concentrated in key populations (e.g., men who have sex with men, sex workers, persons who inject drugs), suggesting the need for intensified efforts to eliminate structural or other barriers to services (e.g., stigma, discrimination, in/formal user fees).

Ambassador Birx also noted that, with improvements in countries' capacity to absorb and deploy PEPFAR funding, spending levels have increased significantly to approximately $3.8 billion per year. The corollary is that there is no longer resource available in pipeline for emergencies or unanticipated developments or opportunities. In FY18, all PEPFAR funds reported to SGAC to be obligated except for approximately $4 million. PEPFAR is exploring other means for preserving a margin for unanticipated expenses (e.g., reducing pipeline requirements).

In the open discussion, SAB members asked for clarification about a range of topics, such as garnering lessons from selected countries that are making exceptional progress reaching men (e.g., Lesotho). Further, they encouraged making explicit the connection for Finance and Health ministries between population and fiscal health at the national level, and extending the HIV prevention and treatment model to other disease conditions (e.g., non-communicable diseases). Future considerations included the need to understand better disease progression and transmission risk among those with low level, persistent viremia; integrating gender-based violence prevention broadly into PEPFAR programming; and clarifying whether apparent low viral load suppression rates in select countries (e.g., Zambia) is attributed more to stockouts for test kits and reagents than performance deficits.

DREAMS Update

Acting Principal Deputy Coordinator Dr. Angeli Achrekar updated SAB members about the Determined, Resilient, Empowered, AIDS-free, Mentored, and Supported (DREAMS) initiative, which was announced on World AIDS Day in 2014 and launched as a $385 million public-private-partnership (PPP) with the intention of altering the epidemic for adolescent girls and young women (AGYW) in ten sub-Saharan African countries. In subsequent years, the initiative

has expanded to 15 countries, been incorporated into country operational plans, and led to the investment of over $760 million in four years. DREAMS now supports services to more than 2.5 million AGYW and provides pre-exposure prophylaxis (PrEP) to over 12,000 AGYW in 11 countries. Most communities that have received broad coverage of DREAMS-supported programming have reported declines of HIV incidence.

More specifically, analyses of DREAMS implementation and outcomes using survey, administrative, and new qualitative data have offered important insights about the initiative. For example, the program continues to face challenges reaching those AGYW most vulnerable to infection. Similarly, districts continue to struggle to document the layering of interventions in a systematic manner. Despite these limitations, there is evidence of significant declines in new diagnoses in more than 60 percent of intervention districts, particularly in rural areas and districts with full geographic coverage. Ongoing efforts are underway to standardize ways to reach those most at risk, track intervention layering to unique program recipients, and improve interagency coordination at the local and national levels. Additional univariate and multivariate analyses will help to clarify how to optimize programming in urban settings, understand outcome differences by district, and illuminate factors accounting for most of the observed effects.

In the open discussion, SAB members discussed the limited evidence in the initial, 6-month assessment of service disruptions or other adverse impacts of the Protecting Life in Global Health Assistance policy. The State Department will release in January 2019 a follow-up 12-month assessment. Other members urged SGAC to find options for assisting AGYW to remain on PrEP over time and ensuring that those most in need are the ones who receive the intervention. Still other SAB members recommended that DREAMS serve as a platform for effectiveness trials of new prevention technologies, such as the Dapivirine vaginal ring, which has the potential to both avert HIV infection and serve as a contraception delivery device. SAB members urged the integration of sexually transmitted infection (STI) testing into DREAMS.

Monitoring Progress toward Epidemiological Control

Deputy Coordinator Irum Zaidi initiated a discussion of new approaches to monitoring the achievement of epidemiological control by reminding SAB members of SGAC's use of process, outcome, and impact indicators at every level of program planning. She highlighted examples of country programs that have made major progress toward epidemic control, as evidenced by rates of new infections falling below rates of all-cause mortality among PLHIV. SGAC anticipates that achieving and sustaining epidemic control will require patient-centered, integrated services; monitoring new diagnoses, infections, and deaths; index partner testing; same-day, universal antiretroviral treatment for all persons newly diagnosed with HIV infection; population viral suppression rates of 86 percent across sex and age groups; and case-based surveillance.

In 2019, PEPFAR plans to expand the use of recency testing in order to strengthen HIV surveillance systems that can detect, characterize, monitor, and intervene in outbreaks associated with newly diagnosed persons. Toward this end, SGAC requested that the SAB host a 1- or 2-day consultation with select ministries of health, PEPFAR implementing agencies, and community stakeholders to document how countries have utilized recency testing and identify best practices for case surveillance, partner notification, and messaging to providers and other stakeholders. Outcomes may include a compilation of operating procedures and a determination of levels of effort needed for human resources for health.

During the open discussion, members proposed additional indicators for monitoring epidemic control and monitoring the efficiency of health systems for responding to new infections. Suggestions included indicators for latency between HIV diagnosis and viral suppression, incident STIs, human resources for health, and activity-based costs for services. Members recommended collaborating with US-based institutions (e.g., NY State AIDS Commission) on the development or selection of new indicators that help, for example, to identify where in the treatment continuum persons are most likely to be lost to follow-up or perish due to HIV-associated disease.

New Directions for Western and Central Africa

Deputy Coordinator Irum Zaidi also highlighted recent findings from the UNAIDS's "Miles to Go" report[1], which shows that the HIV response in Western and Central Africa lags behind that in Sub-Saharan Africa despite a catch-up plan initiated in 2016. According to the report, this may be attributable, in part, to a lack of urgency in addressing the needs of key populations and

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[1] UNAIDS (2018). Miles to go—closing gaps, breaking barriers, righting injustices. http://www.unaids.org/en/resources/documents/2018/global-aids-update

AGYW. Although armed conflict, terrorism, and other factors contribute to these shortcomings, the lack of political will for eliminating barriers to prevention and treatment services uptake figures prominently. According to the report, the region is characterized by slow expansion of essential services despite available funding, slow policy adoption, formal and informal user fees that limit services uptake, and unrelenting stigma and discrimination. In past COP cycles, country teams were alerted that lackluster progress toward eliminating structural and other barriers to services uptake adversely affect funding envelopes in the region for COP19 and beyond.

In the open discussion, SAB members were mixed about the most appropriate response to persistent underperformance in Western and Central Africa, with some members cautioning against changing funding envelopes while others offered to draft letters of support for this option. Members also explored how best to respond if user fees and other barriers are not eliminated, including the development of alternative health systems, working more directly with providers, and engaging faith-based organizations to deliver services not provided by government clinics.

Additionally, members suggested engaging third party countries with close diplomatic ties to Western and Central African countries and advocated for closer coordination in the elimination of structural barriers to services with Global Fund, World Bank, International Monetary Fund, and UNAIDS. Although the UNAIDS report describes the key structural interventions in detail, some members suggested that additional analysis were needed of the barriers and impediments prior to reducing funding support.

Combination Prevention Trials: Implications for Program

Dr. Maya Petersen presented findings for the Sustainable East Africa Research in Community Health (SEARCH) project, which is a cluster-randomized trial of 32 communities testing an evidenced-based, combination prevention intervention to avert new HIV infections in rural communities in East Africa using a multi-disease approach.

The study observed a 32 percent reduction in annual HIV incidence in both the control and intervention arms with nearly equivalent viral load suppression rates, 23 percent reduction in HIV mortality, 59 percent reduction in HIV/TB by year 3, and 26 percent increase in non-communicable disease control. There was no difference in cumulative HIV incidence between the arms, likely due to an active control condition: Communities were rapidly expanding access to universal ART over the course of the trial. Given the salience of a 48 percent reduction in annualized HIV infection in men, Petersen highlighted the male-specific services that the team

believes contributed to these observed outcomes, including the use of community mobilization, male-centered health services, and peer-led activities.

On behalf of the Botswana Combination Prevention Project (BCPP), Dr. Jan Moore presented primary results for a cluster-randomized trial testing in 30 communities an enhanced prevention package that included ART initiation for all participants living with HIV infection, regardless of CD4 count or HIV disease severity. The study tested community-delivered, prevention and treatment services hypothesized to reduce population-level, cumulative HIV incidence in a defined geographic area over 3 years. The study observed a 30 – 38 percent reduction in incidence between control and intervention conditions. The study also recruited and enrolled large numbers of men 25 – 44 years old living with HIV infection using home-based testing.

In sum, BCPP demonstrated the value of: a) a multi-modal testing strategy which worked differently for women and men, b) tracking and tracing using electronic systems to reduce loss-to-follow-up significantly, c) same-day treatment can reduce days to viral suppression by 50 percent, and d) that it is possible to achieve 95-95-95 targets in high prevalence countries. Future costing and phylogenetic analyses are expected to offer additional insight into the value of community-wide interventions.

In the open discussion, SAB members noted that the speed and coverage of treatment initiation remained a relative weakness for these combination prevention studies due to initial political barriers to immediate ART initiation. Members noted the value of both continuing the trial through its completion despite early objections and the importance of sharing preliminary, non-endpoint driven results with PEPFAR for the purpose of informing broader program implementation. All concurred that this exchange of data in near-real time offers tremendous programmatic benefit and encouraged PEPFAR to establish interim data sharing agreements whenever feasible. Members asked how immediate ART might be optimized to ensure timely access to treatment and reduce attrition; others highlighted the need to ensure access to prevention programming for persons tested and found not to be living with HIV infection. Of note was the use of the Botswana's OMANGA electronic medical system, which offered a case example of the integration of data systems to improve both clinical and population level outcomes through contact tracing for those who have ostensibly fallen out of the clinical care continuum.

Dolutegravir Update

Acting Deputy Coordinator for Program Quality, Dr. Heather Watts offered attendees an update on an early safety signal from the Botswana Tsepamo trial suggesting an association of

dolutegravir (DTG) use in women during the time of conception and the occurrence of neural tube defects (NTD) in their offspring. Recent birth defect surveillance data suggest that the observed NTD estimate of 0.94 per 1000 births has fallen to 0.67 per 1000 births. However, many health ministries' interpretation of the May 2018 World Health Organization (WHO) alert[2], which warned of a potential safety issue affecting women using DTG at periconception, has led to significant declines in orders for DTG-containing regimens compared to transition plans approved for COP18. In some countries, only men are permitted access to DTG-based ART. Separate modeling studies continue to a clear benefit of the DTG-based regimen relative to efavirenz-based regimens.[3] Further, consultations with African women living with HIV infection indicate clearly that they seek a voice in decision-making that has a bearing on their treatment interests.

In addition to developing treatment considerations for country teams, SGAC planned to attend a November 5 – 7, 2018 DTG Consultation in Johannesburg, ZA that seeks African women's input on their preferences for DTG treatment access and share lessons for advocating for increased DTG access. In the meantime, SGAC will prepare for three contingencies as additional NTD surveillance data come in – viz., a) null effect, b) undetermined, and c) verified association with DTG use at conception. SGAC remains committed to broad implementation of DTG-based regimens as first- and second-line treatment and it is working with country teams to advocate for its broad availability to women. Further, SGAC supports the integration of reproductive health services into HIV care and it is working with countries to increase their mix of contraceptive options. Finally, SGAC will continue to support ongoing birth defect surveillance in Uganda and Malawi. Like others, it eagerly awaits additional pregnancy outcome data from Botswana and other sources.

In the open discussion, SAB members endorsed SGAC's support for integrating family planning services in HIV clinics and its plan to improve coordination with Global Fund for contraceptive options other than condoms. Attendees considered that countries' responses to the WHO alert may result in a delay of a DTG rollout of approximately 12 – 24 months, which might have been mitigated with earlier input from women patients themselves.

Cervical Cancer: Which is best for Africa

Acting Deputy Coordinator for Program Quality, Dr. Heather Watts also presented SAB members the latest data on the efficacy of the Gardasil-9 vaccine, which has a demonstrated 98 percent efficacy in 9 – 14 year old females for prevention of common human papilloma virus (HPV) subtypes and 97 percent efficacy against other subtypes in HIV-uninfected women. She

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[2] http://www.who.int/medicines/publications/drugalerts/Statement_on_DTG_18May_2018final.pdf

[3] http://www.aidsmap.com/Dolutegravir-update-on-infant-neural-tube-defects-from-Botswana/page/3312898/;

noted that that women with HIV infection are 4 – 5 times more likely to develop persistent precancerous lesions that may progress to aggressive types of cervical cancer, resulting in higher associated mortality rates among women living with HIV infection in Africa than women living in other parts of the world. Moreover, a review of the literature shows that common HPV subtypes targeted by the nonavalent vaccine, but not targeted by the quadrivalent vaccine, contribute to at least 30 percent of cervical cancers and to a higher proportion of high-grade cervical lesions in Africa than in other parts of the world. Watts concluded that the nonavalent vaccine appears to be superior to the quadrivalent vaccine for prevention of cervical cancer in African women.

In the open discussion, SAB members concurred that the costs of vaccine administration in the PEPFAR program would be modest, even with expanded eligibility beyond 9 – 14 year old, adolescent girls and young women living with HIV infection. Moreover, the current three-dose regimen recommended by WHO for women living with HIV infection is expected to be cost-saving within 5 years. Members encouraged consideration of the clinical and population health benefits of also vaccinating young males 9 – 26 years living with HIV infection.

No public comments or questions were raised at the end of the meeting. However, SAB members offered a number of suggestions for consideration at future SAB Meetings, including:

- Update on progress toward achieving tuberculosis targets and a follow-up from the working group's recommendations from 2016.
- Identify SAB members willing to participate in the planning and implementation of the recency assay consultation with ministries, implementing partners, and others.
- Explore opportunities to engage with recompeting NIH clinical trials networks to ensure alignment of research priorities and encourage the timely sharing of interim data that may inform program implementation.
- Summarize the influence of SAB input and recommendations on PEPFAR implementation.
- Examine how communities and stakeholders can best be engaged in research, from study design, data collection, analysis, interpretation, to findings dissemination.[4]
- Discuss how SAB may assist in bolstering provider-education, particularly for those supported by faith-based organizations.

Final Comments

[4] See Journal of the International AIDS Society (2018) Special edition: Science, theory, and practice of engaged research: Good Participatory Practice and beyond. http://www.iasociety.org/Web/WebContent/File/JIAS_Vol21-S7_complete_file.pdf

In her final comments, Ambassador Birx thanked SAB members for their commitment and for sharing their expertise, noting the many examples where doing so has helped to inform key decisions for program implementation. Included among these were its advocacy for improving TB prevention and treatment, supporting the continuation of large combination prevention trials, more precise tracking of mortality outcomes, and development of prevention cascades and related indicators. She also raised the possibility of hosting the next SAB meeting concurrently with the COP19 approval meetings in Johannesburg, South Africa in 2019. SAB members were thanked for their thoughtful contributions, astute observations, and dedication to ensuring that PEPFAR continues to achieve its core mission. The meeting adjourned at approximately 4:00 PM.