



The United States President's Emergency Plan for AIDS Relief (PEPFAR)  
PEPFAR Scientific Advisory Board (SAB) Meeting  
October 16, 2019  
US Department of State, Washington, DC

[PEPFAR Scientific Advisory Board Members 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 Medicine

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

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

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

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

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

Lejeune Lockett—Operations and Program Manager, Global Health, Charles Drew University of Medicine and Science; Angola Military HIV Prevention Program, Drew Cares International

Ruth Macklin—Professor 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—Interim President, 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, Transforming Communities: A Village At A Time, Uganda

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

Jean William Pape—Professor, Weill Medical Cornell College; Director, GHESKIO (Haiti)

David Peters—Chair, International Health, Johns Hopkins University School of Public Health

Rev. 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

Carl Schmid—Deputy Executive Director, The AIDS Institute; Co-Chair, Presidential Advisory Council on HIV/AIDS (PACHA)

Mitchell Warren—Executive Director, AVAC: Global Advocacy for HIV Prevention

John Wiesman—Secretary of Health, Washington State; Co-Chair, Presidential Advisory Council on HIV/AIDS (PACHA)

### PEPFAR Scientific Advisory Board Members on the Phone

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

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

Albert Siemens—Chair, FHI Foundation

### PEPFAR Scientific Advisory Board Members Not in Attendance

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; Harvard School of Public Health

Musimbi Kanyoro—President and CEO, Global Fund for Women

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

Carole Treston—Chief Nursing Officer, Association of Nurses in AIDS Care

### PEPFAR Management Team

Ambassador-at-large Deborah L. Birx—United States Global AIDS Coordinator

Sara Klucking—Designated Federal Officer and Acting Director, Office of Research and Science, Office of the US Global AIDS Coordinator and Health Diplomacy (S/GAC)

### Opening Remarks

#### Welcome and Meeting Overview

*Sara Klucking*

Dr. Klucking welcomed all in attendance and reminded everyone that the PEPFAR Scientific Advisory Board (SAB) is an advisory body under the Federal Advisory Committee Act (FACA); as such, it provides expert input on policy and programmatic decisions. The board's recommendations do not necessarily reflect the opinions of the US Government but are taken under consideration by the US Global AIDS Coordinator and S/GAC staff to inform PEPFAR. This meeting was open to the public for observation and comment, and minutes and reports made in this meeting will be made available at [www.state.gov/pepfar](http://www.state.gov/pepfar).

### Introductory Remarks

*Carlos del Rio*

Dr. del Rio thanked all attendees for participating in the meeting and expressed appreciation for the efforts of the members of the working groups. Dr. del Rio emphasized the critical role of the SAB in

providing advice to accelerate progress toward controlling the epidemic, and he reviewed the meeting agenda.

## PEPFAR 2019-2020 Update: Optimizing Results

*Ambassador-at-Large Deborah Birx, US Global AIDS Coordinator*

Ambassador Birx stressed the importance of the domestic and global programs learning from one another, and she welcomed as new members to the SAB, Presidential Advisory Council on HIV/AIDS (PACHA) Co-Chairs Carl Schmid and John Wiesman. She shared the following update on PEPFAR's activities:

### Strategic Approach

PEPFAR seeks to accelerate progress toward epidemic control by continually improving the prevention and treatment programs' implementation at scale. AMB Birx explained that, six years prior, National Institutes of Allergy and Infectious Diseases (NIAID) Director Anthony Fauci had noted that all tools for controlling the AIDS epidemic were existent and available, and he had challenged PEPFAR to implement them with fidelity. Today, several countries have achieved the UN goals of 90/90/90 and others likely will do so over the next 12 months. The question becomes why some countries are experiencing this level of control and others continue to struggle.

PEPFAR remains focused on three guiding pillars:

1. *Accountability*: Demonstrate cost-effective programming that maximizes the impact of every dollar invested
2. *Transparency*: Demonstrate increased transparency with validation and sharing of all levels of program data
3. *Impact*: Demonstrate sustained control of the epidemic – save lives and avert new infections

PEPFAR's key goals are to sustain the gains in countries that have achieved control and ensure treatment retention (understanding the prevention and treatment packages, and supporting governments to move into universal health access); accelerate control in the few countries not on the brink of control; and address the rising new infections or slow progress in key population epidemics around the globe. PEPFAR continues to provide leadership by making disaggregated program data widely available that is reliable, validated, and impactful for programs and clients; implementing prevention programming, including DREAMS, VMMC, and condoms; ensuring communities are at the forefront of planning and implementation in partnership with the public sector; and defining actual cost (not dollars spent) for sustainability planning. This last piece includes activity-based costing that ministers of health and their parliaments can use for sustainability and transition planning.

### Expansion of Prevention and Treatment

Despite a flat budget, PEPFAR has achieved a remarkable expansion of prevention and treatment services, doubling the number of people receiving treatment in the past five years, quadrupling voluntary medical male circumcision (VMMC), and launching DREAMS. In 2018, PEPFAR's efforts led to 14.6 million women, men, and children being on antiretroviral therapy (ART); 2.4 million babies born HIV-free; 18.9 million VMCMs; 6.8 million orphans, vulnerable children, and their caregivers receiving critical care and support; and 85% of DREAMS districts seeing a continued decline in the diagnosis of new HIV infections.

Fourteen countries have completed the Population-based HIV Impact Assessment (PHIA), PEPFAR's household HIV survey, with more than 350,000 participants tested. A second round of PHIA has just launched and is expected to validate increases in country level viral suppression supported by programmatic data. PHIA allows PEPFAR to validate the UNAIDS Spectrum Model and provide critical data to reaching 95/95/95.

Burden of disease is a cost driver for both prevention and treatment. Through the work of PEPFAR and the Global Fund to Fight AIDS, Tuberculosis and Malaria, combined with host country government leadership and deep community engagement, HIV incidence has declined by more than 50 percent in most high-burden countries. A series of countries is achieving control; further decline in incidence will come from finding the men and prevention programs for adolescent girls and young women (AGYW) such as DREAMS. A youth "bulge" in many African countries underscores the critical role for prevention. PEPFAR hopes to discuss with the Global Fund about moving its AGYW program to a comprehensive, structured DREAMS model to ensure saturation within communities.

AMB Birx reviewed UNAIDS Spectrum Model data showing new HIV infections and total deaths in HIV populations. She noted that, due to the high percentage of the treatment population being over 40, the data soon will start to reflect natural causes of mortality; men continue to present with late-stage HIV and tuberculosis (TB).

The age pyramid for HIV is inverted in countries that are controlling their pandemics with successful HIV programming. Where countries are showing a significant decline in the number of new infections in young people, PEPFAR is exploring cost differential by country and moving to a "sustain" model incorporating recency testing for every new diagnosis and a strong public health response. It intends to learn from Zimbabwe and Malawi, two countries where PEPFAR invested comparatively low amounts in contrast to countries such as Kenya and Tanzania. AMB Birx noted that all PEPFAR countries can learn from Zimbabwe and Malawi where lean funding spurred innovative and cost effective solutions that were used to reach communities and transform disease and mortality rates.

#### Persistent Gaps in Key Populations Prevention and Treatment Programming

Political will, policies, and data matter in achieving prevention and treatment success. Political will includes rapidly adopting World Health Organization (WHO) policies and ensuring implementation of the new policies at the site level. Site-level data allows an unbiased analysis that can get us beyond past perceptions and assumptions to see who needs to be reached, to determine whether clients are being reached, and if they are being served adequately. Data creates the space for an equity-based response.

Using granular data, PEPFAR has identified gaps in its program execution and is tailoring its response to the site-level and the client. The three primary issues are: 1) Access to services for well men, young women, and specific key populations; 2) retention after six months (primarily young people under 30); and 3) clients retained but not virally suppressed (approximately 5 percent). Every country, county, community must be analyzed by age, sex, and risk group to find out who is being missed, determine how to reach them, and adapt testing and service delivery through a client-centered approach to close the gap.

#### Discussion

Discussion focused on the broader challenges of tailoring programs to clients. Focus areas included well men ages 20-30 with HIV, service delivery to key populations, comorbidities such as cervical cancer and

TB, and addressing stigma and discrimination overall. The opportunities and challenges of HIV service delivery in the context of including existing “universal” health systems were also discussed including whether there needs to be exclusivity in the health system relevant to a chronic disease such as HIV versus including it in primary care. There was consensus on a need to look at local context – the community-based, organizational approaches – and the need to partner with communities.

## Expert Working Group Recommendations on Communicating Recency Testing Results to the Individual

*Quarraisha Abdool Karim*

Dr. Abdool Karim, chair of the expert working group (EWG), reported on behalf of the EWG. The EWG consulted with a broad stakeholder group and developed recommendations based on the current generation recency tests, human rights and public health perspectives, and current testing practices including voluntary assisted partner notification. Dr. Abdool Karim shared the following key outcomes of the EWG’s review:

- No blanket recommendation on the return of recency test results to individuals can be made at this time due to the diversity in epidemic typology, magnitude, and populations at risk; preparedness of users and providers; and legal, human rights, and ethical considerations.
- In the context of widely available access to HIV testing, care and prevention services, there is little perceived added value in returning recency test results to the individual whether they are undertaken as part of point of care service provision or field or laboratory surveillance.
- Current recency assays could be an important public health surveillance tool and adjunct to field and laboratory surveys to identify clusters of new infections. Recency information could be especially helpful in the context prioritizing HIV testing and case-finding efforts toward achieving the first 90.
- Important knowledge gaps remain on the risks and benefits of providing an individual with their recency test results. This EWG recommendation should be revisited as new generation assays are developed that enable detection of acute infection, as these may have substantial individual and public health implications.

EWG member Ruth Macklin added that, in the group’s analysis, the harm-benefit calculus of communicating individual results from recency testing was clearly on the side of harm. Dr. del Rio concurred that, at this moment, the risks far outweigh the benefits.

## Discussion

A rich discussion followed focused on whether being told one’s HIV-positive status and how recently they were infected (greater or less than one year) should be presented to clients. Points included the pros and cons related to client agency, partner notification, and health information ownership and privacy. The variation and diversity of factors at the country level in client communications, counseling, complexities of couples counseling, the risk of social harm, the potential for intimate partner violence (IPV), and complex legal considerations were also discussed. Finally, the ethical considerations of test result ownership including the balance of individual and public rights were discussed. Thirteen countries currently are implementing recency testing, and 15 more will add it in 2020. The implementation models vary widely with some ministers of health choosing to provide results to individuals and other using the data only for community surveillance and public health decision-making.

At the conclusion of the discussion, the members of the full PEPFAR SAB accepted the recommendations of the EWG without edits.

## The Next Generation of Biomedical HIV Prevention

SAB member Mitchell Warren presented new biomedical approaches for HIV prevention, including the Dapivirine vaginal ring, Tenofovir-based oral PrEP, a bi-monthly long-acting injectable, bi-monthly antibody infusions, and HIV vaccines. All products but oral PrEP are at various stages in the research/clinical trial pipeline. He noted that tools on the horizon are not lacking, but the science and art of delivery remain to be refined and options are likely to be important. Questions that need to be grappled with by the SAB, advocates, funders, and researchers include where the greatest unmet need is, what products people want and will use, what study designs can best answer the questions quickly and ethically, how best to “balance the portfolio”, and how to keep research and development (R&D) part of the “ending AIDS” narrative. HIV prevention implementation is currently lacking, with a 1.3 million-person gap between the current prevention rate and the 2020 target (current: 500,000; target: 1.8 million) and actual implementation of prevention tools that has been far lower than models predicted.

## HIV Prevention R&D Spectrum

Approved prevention options include Oral PrEP with TDF/FTC, VMMC, male and female condoms, syringe exchange programs and treatment as prevention. The Dapivirine ring and a new oral PrEP with F/TAF are in regulatory review, and the following remain under development:

- *In efficacy trials:* Long-acting injectables, preventive vaccines, and broadly neutralizing antibodies
- *In pre-clinical and clinical trials:* Long-acting oral PrEP and implants, preventive vaccines, broadly neutralizing antibodies, inserts, patches, an enema, and combination oral PrEP/oral contraception (OC).

Progress in the next three years is expected on the vaginal ring, oral PrEP, long-acting ARVs, antibodies, and a preventive vaccine. A combination PrEP/OC oral tablet could be available on the market in 2021, and vaccine licensure of a global vaccine is possible by 2023. It will be important to consider each product across a broader domain of issues and to balance clinical, policy and program, and personal considerations for each. Recently, there has been a slight increase in total global HIV R&D investment to \$1.14 billion. The US public sector comprises 73 percent of HIV prevention research funding, and NIH accounts for 87 percent of that US public sector funding.

## Deployment and Scale-Up Considerations

The experience around implementation of oral PrEP is illustrative, with many small-scale studies that were not well coordinated and that were not designed to address the WHO’s questions or timed to inform decision-making at the global or country level. Large-scale demonstration projects were not planned in parallel to clinical trials, leading to delays in scale-up. The global community will need to be better aligned strategically in order to move more quickly on new products. The best advance planning possible will be critical to a successful and timely rollout effort.

Planning for success includes mapping decision-maker questions against studies, planning in parallel with clinical trials, and a shared strategy developed by diverse stakeholders. In our global community, the stakeholders who develop a product may not be those who deliver product and a more seamless strategy is needed. We need to collaboratively plan for success, and organizations will need to connect to the shared strategy. Programs need to be clear about what a product can actually do, what providers and health systems can do, and what users want; then, an appropriate research agenda need to be

developed. Planning needs to start today. Plans can be adapted to a range of next generation of products, including oral PrEP, the vaginal ring, and injectables.

### Discussion

Member discussion focused on the need to learn the lessons from past prevention product development and roll out efforts. Topics included marketing and demand creation; the tentative introduction of oral PrEP; “failure” messaging and inaccurate messaging from medical personnel; and the overmedicalization of PrEP. Suggestions for improvement focused on framing prevention in the context of sexual health; tailoring regulatory approvals and messaging to those at risk including young women, adolescent girls; using modern technology tools (i.e. smartphone apps) for users and decision-support tools for clinicians; circulating best practices, including training family planning providers around PrEP; using data to show how programs would target PrEP; being honest about realities of teen sex; and partnering with professionals who address young people’s sexual and reproductive health.

### Update on Dolutegravir containing ART formulations

*Heather Watts, S/GAC, and John Koethe, Vanderbilt University Division of Infectious Diseases*

#### Dolutegravir and Risk of Neural Tube Defects

Dr. Watts presented an update on neural tube defect (NTD) prevalence rates due to exposure to dolutegravir (DTG) containing ART formulations, summarizing recent publications and scientific conference reports.

Pregnancy outcomes for women and infants was summarized from observational studies in multiple countries across as well as modeling studies. The data confirm that, when taken at conception, DTG is likely associated with the slightly (<1%) increased risk for neural tube defects. Nonetheless, this integrase inhibitor remains the preferred first- and second-line antiretroviral because of its high efficacy, ease of administration, infrequent side effects, and high barrier to resistance. Compared with other regimens, DTG leads to better outcomes for women and infants because of improved maternal health and fewer perinatal HIV transmissions

Consistent with updated WHO guidance, PEPFAR maintains that the community of women living with HIV must be included in treatment decision-making at every level and should be allowed to make an informed health decision about their ART regimen, and contraception should be available to women who desire it but should not be a condition for receiving a DTG containing regimen.

PEPFAR remains committed to broad implementation of DTG-based regimens as first- and second-line treatment as required in Country Operational Plan (COP) 2019 guidance. S/GAC staff continues to work closely with country teams to advocate for broader availability of DTG for women and to provide resources for implementation. PEPFAR is continuing to support multiple efforts to obtain additional data on birth defect risk and to support ongoing birth defect surveillance.

#### Weight Gain on Integrase Inhibitor-Based ART

Dr. Koethe shared data on weight gain in PLHIV who are on an integrase inhibitor (INSTI)-based regimen. In a large North American observational cohort study and several clinical trials, PLHIV starting INSTI-based regimens, particularly DTG, experienced greater weight gain which, in turn, may increase the hazard of developing diabetes or other metabolic disorders. Women and non-Whites seem to be at highest risk of weight gain with INSTIs, and preliminary data from the North American study showed a

higher risk of diabetes incidence in non-White women. Clinical trials also show an independent effect of tenofovir alafenamide (TAF) on weight, which was greatest for women in ADVANCE (South Africa). Longer follow-up and more data are needed to inform possible public health decision making and any linkage between weight gain, DTG, and diabetes remains an active area of investigation.

## Discussion

Discussion focused on how PEPFAR can learn from this information for risk communication and implementation. Topics included the association between folate deficiency and NTDs; “clinical inertia” despite changes in guidelines; weight gain intervention for PLHIV with higher body mass index (BMI); complications with BMI collection and ease of BMI measurement.

The Board considered adapting a recent *Annals of Internal Medicine* editorial titled *Decision Making in a Time of Uncertainty: Dolutegravir for Reproductive-Age Women* into a one-pager for health ministers and other policy makers. The discussion focused on developing this as a case-study that could inform improving health policy decision-making in the future in areas such as stakeholder engagement; uncertainty and the use of modelling data; providing clear messaging; and helping people understand that every intervention has risks and benefits that must be considered in the context of and by a client.

## Universal Test and Treat (UTT) Trials and HIV Epidemic Control in 2019

Dr. del Rio explained that first generation UTT trials are completed and provided an update. These randomized, population-based combination intervention studies integrated HIV testing, prevention, and treatment. They were conducted in both Southern and Eastern African countries during the global transition to “treat all”, “differentiated care”, and “fast track”. The trials pre-dated PrEP roll-out, involved a short follow-up of about three years, and used measurement approaches that also impacted outcomes (HIV diagnosis, viral suppression, and possibly behavior) across both the intervention and control arms.

## Results

In summary, the UTT trials (BCPP, PopART, TasP, and SEARCH) were associated with an overall reduction in HIV incidence. All studies contributed substantially to both the first 90 (PLHIV knowing their HIV status) and the second 90 (those diagnosed with HIV receiving sustained ART). For the third 90 (those on ART achieving viral suppression), suppression was exceedingly high, with all trials attaining over 73 percent. Gains in viral suppression were greater among men however success men continued to lag behind youth. All studies were able to make substantial gains across treatment cascade and were able to bring clients lost to follow-up back into care. Because the standard of care in general was improving in the UTT study sites, it is difficult to tease out exactly which interventions had greater impact.

## The Investment Case for UTT

There are arguments for and against UTT implementation at the country level.

### **The “Yes” Argument**

Solid evidence exists that UTT strategies can rapidly achieve high levels of viral suppression and reduce HIV incidence faster than the standard of care. UTT may be the most effective way to rapidly reduce mortality and is a gateway for prevention (i.e. PrEP). UTT costs could be shared using a multi-disease approach and thereby improve health outcomes broadly.

### **The “No” Argument**

UTT cannot and will never lead to HIV elimination. It is too costly, and the need for universal testing in the current landscape has not been directly quantified. Targeted testing of high-risk persons, including partner notification and use of PrEP is sufficient.

### Discussion

Discussion focused on the interventions having demonstrated a reduced mortality in PLHIV and decreased TB and the need to collaborate to disseminate lessons learned. Specific interventions discussed included incentivizing the participation of youth; identifying data insights on circumcision in 15-30-year-old men; prevention in adolescent girls and young women; integration of HIV screening into other health screenings (e.g., hypertension); measuring migration; more adaptive study design; and how to reach networks to increase visibility and turn study results into a force multiplier.

There was particular interest in ensuring that study insights feed into COP planning. Study leads could try to develop, in collaboration with PEPFAR teams, a list of the most critical programmatic questions that could be addressed through the UTT data sets. This more programmatic research agenda could highlight where countries are struggling and leverage scientist grantees' global connections for innovative solutions. The board also discussed the urgent need to decrease the time between research study publication and communication of results to inform policy and program implementation.

Dr. del Rio suggested that the next SAB meeting include 10-15 recent abstracts or study findings with potential for impact in the field. Preliminary findings from the Conference on Retroviruses and Opportunistic Infections (CROI), the Centers for AIDS Research (CFAR) development projects, and other research findings could provide the basis for convening academic and PEPFAR panels around core shared areas of interest. Brainstorming on these topics at the PEPFAR Annual Meeting prior to the International AIDS Society (IAS) meeting might foster innovations in key areas where PEPFAR is working to improve.

### Public Comments and Questions

No comments from the general public were received. USAID, a key PEPFAR Implementing Federal Agency invited feedback from the SAB and other stakeholders on their current prevention research portfolio.

A presentation on PEPFAR's implementation of PrEP was suggested for the next SAB meeting to include if possible an overlay of PrEP and recency assay data.

### Next Steps and Summary Comments

AMB Birx expressed her gratitude to the SAB for its commitment, for its reflection and action between meetings, and for sharing its insights with PEPFAR, adding that the SAB's wisdom is translated into positive impact in people's lives. She thanked Dr. Klucking, Ms. Solomon, and the entire PEPFAR team for their support. AMB Birx noted that PEPFAR would appreciate the SAB's comments on COP guidance; William Paul is leading that project.

Dr. del Rio commented that PEPFAR is a flagship global public health program and asserted that the SAB and S/GAC should be very proud.

Dr. del Rio adjourned the meeting at 4:00 pm EDT.