The United States President's Emergency Plan for AIDS Relief (PEPFAR)
PEPFAR Scientific Advisory Board (SAB) Meeting
October 14, 2015
US Department of State, Washington, DC
Meeting Minutes

PEPFAR Scientific Advisory Board Members in Attendance

Please note: Carlos del Rio, MD serves as the PEPFAR Scientific Advisory Board Chair

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

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

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

Judith Currier, MD, MSc—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, MD—Chair, Department of Global Health, Rollins School of Public Health and Professor of Medicine, Division of Infectious Diseases, Emory University School of Medicine

Sofia Gruskin, JD, MIA—Director, Program on Global Health and Human Rights, Institute for Global Health, University of Southern California; Harvard School of Public Health

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

Musimbi Kanyoro, PhD—President and CEO, Global Fund for Women

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

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

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

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

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

Kenneth Mayer, MD—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, JD—Fellow, Altarum Institute; Chair Emeritus, Black AIDS Institute

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

Christine Nabiryo, MBChB, DPH, MMed PH, MBA—Public Health Consultant, Uganda

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

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

Rev. Edwin Sanders—Senior Server, Metropolitan Interdenominational Church; Chair, The Legacy Project, a collaboration with the HIV Vaccine Trials Network

Fredrick Sawe, MBChB, MMed—Director, HIV/AIDS Research, Walter Reed Project, Kenya Medical Research Institute
Albert Siemens, PhD—Chair, FHI Foundation
Carole Treston, MPH—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, PhD—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, University of KwaZulu (South Africa)
Mark Heywood, MA—Executive Director, SECTION27, O'Neill Institute for National & Global Health Law; Chairperson, UNAIDS Reference Group on HIV/AIDS and Human Rights
Nyambura Njoroge, PhD—Ecumenical HIV and AIDS Initiatives and Advocacy; Project Coordinator, World Council of Churches

PrEP Expert Working Group Members

Quarraisha Abdool Karim, PhD—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, University of KwaZulu (South Africa)
Jared Baeten, MD, PhD—Vice Chair, Global Health, University of Washington School of Public Health
Connie Celum, MD, MPH—Director, International Clinical Research Center, Department of Global Health, University of Washington School of Medicine
Robert Grant, MD—University of California, San Francisco; San Francisco AIDS Foundation; Betty Jean and Hiro Ogawa Gladstone Institute of Virology and Immunology
Nina Hasan, PhD—Director, HIV and TB Programs, Population Services International
Colleen Kelley, MD, MPH—Emory School of Medicine
Fabio Mesquita, MD, PhD—Director, STI/AIDS and Viral Hepatitis Department, Ministry of Health, Brazil
Helen Rees, OBE, MBBChir, MA, DRCOG, DCH—Executive Director, Wits Reproductive Health and HIV Institute
Heidi Van Rooyen, PhD—Research Director, Human Sciences Research Council
Mitchell Warren—Executive Director, AVAC: Global Advocacy for HIV Prevention

Test and START Expert Working Group

Linda-Gail Bekker, MBChB, DTMH, DCH, FCP(SA), PhD —Deputy Director of the Desmond Tutu HIV Centre at the Institute of Infectious Disease and Molecular Medicine, University of Cape Town
Judith Currier, MD, MSc—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, MD—Chair, Department of Global Health, Rollins School of Public Health and Professor of Medicine, Division of Infectious Diseases, Emory University School of Medicine
Diane Havlir, MD—Professor of Medicine, University of California, San Francisco; Chief, HIV/AIDS Division, San Francisco General Hospital

Etienne Karita, MD, MSc—Site Leader, Project San Francisco, Rwanda Zambia HIV Research Group
Rev. Edwin Sanders—Senior Server, Metropolitan Interdenominational Church; Chair, The Legacy Project, a collaboration with the HIV Vaccine Trials Network
Fredrick Sawe, MBChB, MMed—Director, HIV/AIDS Research, Walter Reed Project, Kenya Medical Research Institute
Carole Treston, MPH—Chief Nursing Officer, Association of Nurses in AIDS Care

Office of the U.S. Global AIDS Coordinator
Ambassador Deborah L. Birx, MD—United States Global AIDS Coordinator
Julia Mackenzie, PhD, MPH—Senior Technical Advisor, Office of Research; Designated Federal Officer, PEPFAR Scientific Advisory Board, Office of the Global AIDS Coordinator (OGAC)
Douglas Shaffer—Chief Medical Officer, OGAC
Maureen Goodenow, PhD—Acting Director, Office of Research and Science, OGAC
Cornelius Baker—Senior Policy Advisor, OGAC

Opening Remarks
Welcome
Douglas Shaffer
Dr. Shaffer addressed Ambassador Deborah Birx, Dr. del Rio, and colleagues, welcoming everyone to the first face-to-face meeting of the PEPFAR Science Advisory Board (SAB) since its charter renewal and renewed membership in late March, 2015. He noted that 24 of the 27 board members were in attendance, including those who had traveled from Kenya, Rwanda, South Africa, and Zimbabwe. Dr. Shaffer acknowledged the PEPFAR Principals, Deputy Principals, and designees from US government departments and agencies in attendance, as well as members of the SAB expert working groups (EWGs). He noted representation by Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), Department of Defense (DoD), United States Agency for International Development (USAID), and other agencies. Dr. Shaffer expressed gratitude for the interest of and participation by members of the public through more than 100 available domestic and international call-in lines, and he recognized members of the public in attendance including World Vision, the National Alliance of State & Territorial AIDS Directors (NASTAD), Abt Associates Infectious Diseases Society of America, and Social & Scientific Systems.

Dr. Shaffer acknowledged the presence and contributions of many members of the OGAC staff, both in person and by phone.

With PEPFAR introducing new and ambitious preventions and treatments at the United Nations General Assembly meeting (UNGA) just a few weeks ago, followed by new guidelines released by the World Health Organization (WHO) on September 30 and by the International Association of Providers of AIDS Care (IAPAC) on October 1, Dr. Shaffer noted the timeliness for this convening of the SAB, comprising consideration and discussion of critical items related to PEPFAR and the HIV/AIDS response and, ultimately, the opportunity for the board to advise AMB Birx on implementation and policy issues.

Dr. Shaffer explained that he would be supporting SAB Chair Dr. del Rio and that Designated Federal Official Julia Mackenzie would be overseeing the meeting. He expressed his gratitude to AMB Birx for her time and continued commitment to seeing an AIDS-free generation, to Dr. del

Rio for his leadership as SAB chair, to Drs. Celum and Abdool Karim for their co-leadership of the Pre-Exposure Prophylaxis (PrEP) EWG, and to Drs. Currier and del Rio for co-chairing the Test and START EWG.

FACA Overview

Julia Mackenzie

Dr. Mackenzie reminded the members that the SAB is a Federal Advisory Committee Act (FACA)-chartered advisory committee and, therefore, the deliberations of the SAB are open to the public; members of public were in attendance and on the phone, and the minutes of the meeting and presentations made during the meeting will be made available.

EWG Presentations

Julia Mackenzie

Dr. Mackenzie noted that the SAB would hear from two EWGs today: the PrEP EWG and the Test and START EWG. She added that the day's business would include determining whether other EWGs should be initiated under the SAB and, if so, what their focuses would be.

Composition of the SAB

Julia Mackenzie

Dr. Mackenzie pointed out that all members of the SAB serve as representative members, and she made clear the expectation that they would speak on behalf of non-US government institutions and embody a variety of points of view. It was acknowledged that some members may be affiliated with the projects discussed and would be asked to declare those affiliations.

Meeting Overview

Carlos del Rio

Dr. del Rio welcomed everyone and introduced himself, sharing that he is the chair of the Department of Global Health at the Rollins School of Public Health and professor of medicine in the Division of Infectious Diseases at Emory University School of Medicine. He also serves as program director of the Emory AIDS International Training and Research Program and co-director of the Emory Center for AIDS Research (CFAR).

Dr. del Rio thanked AMB Birx for convening the SAB at this interesting moment in the AIDS epidemic. With new evidence and new guidelines, updated strategies are needed. Dr. del Rio acknowledged that better results will not come from continuing to employ the same strategies, and that the goal of the SAB is to consider approaches that PEPFAR can undertake to move the work to the next level. He recognized the volume of work necessary as well as the existence of both challenges and opportunities. Currently, at best, half of those needing HIV/AIDS therapy are being treated.

Dr. del Rio thanked everyone for their time (including related to travel), thoughtfulness, and efforts prior to today's meeting, including the work done by the EWGs. He invited all members in attendance to introduce themselves; their self-introductions are reflected in the member attendee list at the beginning of this summary.

Opening Remarks and Presentation

Ambassador Birx, US Global AIDS Coordinator

AMB Birx noted the impressive collection of leaders at the table and remarked that each member of the SAB has helped to advance and shift her thinking over the past several decades, thereby prompting her to change and evolve. She pointed out that this group is comprised of leaders who were motivated to change the status quo of the AIDS epidemic and who contributed to the efforts in inspirational, transformative ways—by taking risks, standing up for others, and bringing compassion and passion to this work. Each member was selected based on her/his platform, vision, background, fortitude, and willingness to push government—to ask, "Why not?" AMB Birx expressed her appreciation and tremendous respect for SAB members' participation here as well as their efforts in the field, and she explained that she would sit in on the session as a listener and resource after her presentation and would be available to answer questions about the activities of OGAC throughout the day. She thanked the multidisciplinary team supporting PEPFAR, making note of the effective partnerships OGAC enjoys with USAID, CDC, and DoD, as well as assistance in the form of science provided by NIH, the work done by the Health Resources and Services Administration (HRSA), and the geographic mapping by the US Census Bureau. OGAC is continually working to translate data into maps to render them understandable.

AMB Birx called attention to the importance of bringing people from many fields together to advance this work, giving the example of her own background as a cellular epidemiologist who watched at the onset of the AIDS crisis as so many leaders from different areas coalesced, relinquishing the extraordinary work in which they were involved in order to save lives. She specifically named Mark Harrington for his efforts related to tuberculosis (TB) and thanked him for joining this group.

History of the HIV/AIDS Epidemic

AMB Birx briefly reviewed the statistics and history of the AIDS epidemic, with the goal of demonstrating to the SAB the way in which she presents the information. She noted the dramatic reductions in HIV incidence rates from 1990 to 2013—the time span of PEPFAR and the global response to the crisis—as well as the incredible progress made during that time period in treatment, health systems, life expectancy, productivity, and economic development.

AMB Birx mentioned that what has not been successfully impacted during this era are stigma and discrimination, which she depicted as equally adverse and likely growing. She suggested the need to work through every type of media and in every area possible to affect positive change in stigma and discrimination in order to achieve success.

Current Demographic Realities

AMB Birx commented that the trends look to be favorable to controlling the epidemic until one realizes that 30% more adolescents are alive today—with 1.8 billion young people ages 10-24—than were at the beginning of the HIV/AIDS crisis. Adolescents make up 30-40% of the population in Africa, and the youth population is growing most rapidly in the countries with highest HIV burden.

Within this generation are 600 million adolescent girls with specific needs, challenges, and, hopefully, aspirations for the future. AMB Birx used a series of graphs to illustrate the demographic shift in South Africa, with a 30% increase in girls and women at risk since 1985. She purported that the response to this reality will determine whether this epidemic is eliminated as a public health threat or not, noting that maintenance of the current incidence rate will lead to

30 million new infections. Current levels of treatment are barely affordable; a doubling of the need would make effective control impossible, cause the inability to access life-saving treatment, and create social unrest. Fortunately, noted AMB Birx, the tools exist for solving this problem.

Using a bar graph, she demonstrated that changing the rate of infection in the women will subsequently change the rate of secondary infections in men. This translates to the following: If infections in women decrease by 25%, they will decrease in their male partners at the same rate of 25% over the following 3-4 years. AMB Birx next presented a cartogram representing new, updated UNAIDS data; the map clearly displayed the burden of disease, both by prevalence and by size of country.

A Critical Time Window

AMB Birx commented on the fast track strategy document released by UNAIDS Executive Director Michel Sidibé: In it, he explains that business as usual will allow for 2.5 million new infections and will return to fighting over 10,000 new infections daily as occurred before treatment was available. The document asserts that the scientific tools exist to avoid this, and Mr. Sidibé has visited country after country to help expand the political will and awareness about what is possible, including decreasing new infections worldwide to 200,000 annually.

AMB Birx next used a graph to explain a critical five-year window—2015-2020—in which we can use the fiscal resources currently available to create a different future with the fast track strategy's ambitious targets or continue business as usual and contend with 28 million additional new cases between 2015 and 2030 that will go untreated. She noted that 70% of people living with HIV/AIDS are in sub-Saharan Africa, which contains 68% of new infections and 68% of AIDS-related deaths worldwide. Ninety-two percent of PEPFAR funds are directed to that region; this is based on PEPFAR's strategy to focus funding where the epidemic is the worst.

Country-Level Data and A Success Story

Based on UNAIDS 2014 estimates, new HIV infections in sub-Saharan Africa are highest in South Africa, followed by Nigeria. Uganda is again contributing the third highest number of new infections after removing its focus from the epidemic. AMB Birx explained the Uganda had been touted as a winner and remarked that it only takes a couple of years to go from being a winner in this fight to losing the battle against new infections and deaths. Mozambique, Zimbabwe, and Tanzania have the next three highest incidences, with the remaining countries in the region contributing lower rates of infection.

AMB Birx shared country-level disaggregated data from all PEPFAR-funded nations in sub-Saharan Africa that showed percent change in new HIV infections since the initiation of the Millennium Development Goals (MDGs). She noted a 43% increase in infections in Uganda and called specific attention to Malawi and Kenya. She noted, using a graph specific to pediatric new HIV infections, that enormous progress has been made since 2000 in the decrease of mother-to-child transmission; prevention of mother-to-child transmission (PMTCT) has led to a dramatic decline in pediatric new infections in almost all PEPFAR countries except Nigeria. However, adult new infections over the last 15 years have *not* decreased as dramatically, and in Uganda, new adult infections *have increased* dramatically.

AMB Birx pointed out that the only country with strong decreases in both pediatric and adult new infections is Malawi, where they have developed country-specific solutions that have allowed them to effectively roll out HIV and TB treatment (including PMTCT Option B+), and promote family planning in what was one of the weakest health systems in the region at the start of the HIV epidemic. Tasks have been shifted to a new cadre of health worker—workers we would consider similar to health medics in the USA—located primarily at health posts. These medics are able to administer immunizations, perform rapid HIV and malaria testing; and refer complicated cases to health centers, which are primarily staffed by nurses. This Malawian response to the epidemic has served to decongest health centers, improve quality of care at the community level, and lessen the burden of the nurses' work at health centers.

Celebrating Progress and Looking Ahead

As is well known to SAB members, 15 million people are currently on antiretroviral therapy (ART). Approximately 15 million more are still in need, funding of HIV/AIDS work is flat, and retention of patients in care remains a challenge. As well, some high-burden communities around the world and in some US cities were left behind: needed HIV services were simply not available everywhere they were and are needed. Hence, PEPFAR is pivoting to shift focus to the geographic areas and sub-populations most in need of HIV prevention, treatment and care services.

AMB Birx presented PEPFAR and UNAIDS ART retention data. She noted that, because PEPFAR has been a driver of data acquisition and data use from the beginning of the epidemic, the data from the two entities are one and the same. As well, The Global Fund to Fight AIDS, Tuberculosis and Malaria (The Global Fund) and PEPFAR have linked together for maximum impact: In many countries, The Global Fund is buying the commodities, and PEPFAR is providing the services.

President's Vision: An AIDS-free generation

In 2013, President Obama called for an AIDS-free generation. After great success around PMTCT, the children—currently 10-14 years old—who were effectively prevented from infection *in utero* and during infancy are now at great risk of HIV infection in many areas. The President's words were a directive to help those children maintain an HIV-free status; this and the awareness of the many new adult infections has shifted the thinking and focus of our programs.

At the Sustainable Development Goals (SDG) Summit on September 27, the President announced:

> "As more countries take ownership of their HIV/AIDS programs, the United States is setting two new bold goals. Over the next two years, we'll increase the number of people that our funding reaches—so that nearly 13 million people with HIV/AIDS get lifesaving treatment—and we'll invest $300 million to help achieve a 40% reduction in new HIV infections among young women and girls in the hardest-hit areas of sub-Saharan Africa. And I believe we can do that—the first AIDS-free generation."

The President declared, "We are proud of what we have done in the MDGs (N.B. Millennium Development Goals). We are proud of the improvement in the under-5 survival, which has increased by 50%. But now those 50% of children are now also adolescents. We're proud of our PMTCT work. We're proud of what we've done in malaria. We're proud of what we've done in TB. But we have unfinished business." The President reminded people that issues still exist with TB, HIV, and malaria, taking the opportunity to announce the new PEPFAR targets. The fact that

the President gave so much attention to this issue in his SDG speech shows his and his staff's level of commitment to realizing the vision of an AIDS-free generation.

Furthermore, the President advanced the most extraordinarily aggressive impact targets to date. This marks the first instance in which two prevention strategies and one treatment strategy make up the targets; AMB Birx affirmed that this signals the seriousness of the US government's investments in prevention (now increased by $500 million dollars) as well as its impact.

The targets include a 25% reduction in HIV incidence among adolescent girls and young women (ages 15-24) within the highest-burden geographic areas of 10 sub-Saharan African countries over the next 12 months and a 40% reduction over the next two years. The other prevention targets announced by the President involve 11 million voluntary medical male circumcisions (VMMCs) for HIV prevention cumulatively over the next 12 months and 13 million cumulatively over the next two years.

Treatment targets include supporting a total of 11.4 million children, pregnant women receiving B+, and adults on life-saving ART over the next 12 months and 12.9 million over the next two years.

AMB Birx explained that, while the President's proposal sounds daunting, it represents the minimum necessary to maintain the current infection rate as the adolescent population continues to grow.

AMB Birx added that US Secretary of State John Kerry—attending the SDGs' large United Kingdom poverty reduction event on the same day that the President made his comments—highlighted the importance of an AIDS-free generation as part of a poverty reduction plan, noting the effects of HIV prevention on economic development in sub-Saharan Africa. He said:

> "We all have a fundamental responsibility, and we can bring about an AIDS-free—wholly AIDS-free—future for children. We are near that—provided we act in accordance with the pledge that we made today."

US National Security Advisor and Former Ambassador to the United Nations Susan Rice made an official statement that same weekend that included the following:

> "Today, we are setting a bold, new course by announcing ambitious PEPFAR prevention and treatment targets for 2016 and 2017...No greater action is needed right now than empowering adolescent girls and young women to defeat HIV/AIDS."

US Deputy Secretary of State Heather Higginbottom also made remarks on the subject at the September 27 "UNAIDS – Ending AIDS by 2030" heads of state event:

> "...Imagine the creation of an AIDS-free generation that eliminates HIV as a public health threat. This is precisely what UNAIDS has laid out before us. And that is why earlier today President Obama announced new PEPFAR targets. President Obama and Secretary Kerry believe that this is the moment."

AMB Birx asserted that we need to bring back the passion and focus that shows we understand that we have the tools and are going to use them to end this epidemic. She remarked that

actress Charlize Theron was in attendance at the UNAIDS event led by Mr. Sidibé, notable as Ms. Theron is dedicated to young women's issues, including HIV prevention.

Concurrent with the above statements and target declarations was an announcement by PEPFAR critical to the roadmap and achievement of those targets and in line with the organization's goal of sustainable development: a $10 million contribution to the Robert Carr Civil Society Networks Fund (RCNF) and a challenge to additional donors—those who are supporting the regional and international network of activists and advocates that is strengthening the grassroots organizations in numerous countries—to invest. PEPFAR also announced a $4 million two-year PEPFAR/UNAIDS faith initiative and a $3 million contribution to, and partnership with, the Global Partnership for Sustainable Development Data. AMB Birx asserted that participating in the data revolution is key to reaching PEPFAR's goals.

During UNGA, the selected "White House Chart of the Week" was a map that showed where in the world the burden of HIV remains greatest. AMB Birx explained that being selected as chart of the week illustrates the level of commitment at all levels of the Obama Administration to disseminate AIDS-related information in a comprehensive way. She then shared a graphic image of the current PEPFAR prevention and treatment targets, also available on the PEPFAR website.

AMB Birx asserted that the confluence of commitment in the White House, the US Department of State, and UNAIDS has produced a historic moment for controlling the epidemic, and she iterated the reasons behind the pivot, making note that it is not based on an escalation of millions of dollars to meet treatment needs. She credited the space and political will being developed by Mr. Sidibé, along with his access to heads of state throughout the world, with the alignment of the resources necessary to combat the epidemic. She added that Mr. Sidibé is laying out the vision that PEPFAR endorses.

Approach: A Tailored Response According to Need and Context

Example 1: Uganda

AMB Birx presented as an example the successful Uganda PEPFAR program pivot that occurred in 2011-12, explaining that the country is moving from having the most new infections among adults to being able to achieve the UNAIDS Fast Track Treatment Targets (90-90-90, or 90% of people with HIV know their status, 90% of them on ART, and 90% of them virally suppressed, all by 2020). A related graph illustrated new infections and death rates in the country, and AMB Birx shared the history of the Uganda program pivot: Ambassador Eric Goosby, her predecessor and current UN Secretary-General's Special Envoy on Tuberculosis (TB), sent out a high alert when the rate of new infections increased; at that point, many of those in today's meeting traveled to Uganda to help bring the situation under control and decrease the number of new infections.

This scenario occurred not based on significantly increased funding but instead by focusing PEPFAR resources to support evidence-based prevention and treatment programs in the most high burden areas. . This focus has created a sustained change that has remained through the last three years and has enabled the rollout of PMTCT Option B+. While other countries claimed they could not afford to follow the B+ recommendations, the Ugandan government made B+ a priority, and the first lady of Uganda met personally with community elders and chiefs throughout the country to gain their support for the initiative. The results, displayed on a

related graph, show the overwhelmingly positive results, with a very high percentage of women receiving lifesaving ART that protects the fetus, the baby during breastfeeding, and the mother.

In order to illuminate the impact of HIV/AIDS on communities, simple quartile maps have been developed. AMB Birx showed a series of these, illustrating numbers of people living with HIV/AIDS, coverage of VMMC, and orphans and vulnerable children (OVC) served, all delineated by district. She noted that PEPFAR and The Global Fund have worked together to support communities, while Uganda provides a relatively minor amount of funding. AMB Birx then showed a graph depicting Uganda's 90-90-90 targets and the numbers today, what is expected to be accomplished over the next year by PEPFAR, and the gaps needed to be filled in order to achieve those goals.

Example 2: Haiti

AMB Birx next highlighted the accomplishments of PEPFAR Haiti during the last program review cycle in identifying historically underserved sites, pointing out that the areas of the island with the highest levels of burden are those that are the most difficult to reach. Quartile maps allow PEPFAR to overlay disease burden and services to show where there are gaps, which reveal communicates that have not received much-needed services.

Example 3: Kenya, Tanzania, and Cote d'Ivoire

Broad approaches to program implementation do not address the unique community-level issues that are only evident with data disaggregation and analysis. AMB Birx explained that PEPFAR requires countries to provide data down to the site level for mapping purposes. These site-level geospatial analyses, used heavily in the last year to inform program planning, can reveal where services are well-aligned or misaligned with burden and how high and low volume health sites are distributed regionally in other high-burden areas. These analyses have revealed that in Dar es Salaam, Tanzania, 50 PMTCT sites exist in a four-kilometer radius. Similarly, in Kenya, there are some areas of high burden with few sites providing services and others with relatively lower burden and duplicative sites. AMB Birx asserted that this level of duplication of sites in one area and a lack of sites is other areas in ineffective and unacceptable. This mapping will force decisions about the makeup of the health system in the country, both for this epidemic and beyond.

Cote d'Ivoire developed its own country map based on its reality; it shows every delivery site and the number of clients served at each site. The map illuminates the challenge of ensuring quality at low-burden sites with numbers too low to be able to deal with stigma and discrimination or to find a support group (with 25 served, only two are coming to the clinic each month, at most). At the other end of the spectrum, the goal is to decongest the extraordinarily high-volume sites.

Summary: PEPFAR Country Operational Play (COP) Pivots

As part of the COP pivots, PEPFAR became more efficient around processing and moving money. This cut down on workload and time used in developing multiple work plans over the course of a year, and approximately 90% of the COP money was directed during this fiscal year to the agencies and on to partners in single lump sums. By bring country teams into a healthy level of pipeline funding and efficiently moving money to countries to support program, PEPFAR was able to utilize $300 million to increase prevention activities; expand testing to an additional 10 million people and specifically in higher burden sites; increase VMMC by 25%, treatment by

30%, and new-on treatment by 113%. All this is made possible by a focusing of resources for maximum impact.

Impact of the WHO Guidelines

PEPFAR views the new WHO guidelines as the last fundamental tool short of a vaccine needed to ensure success in controlling the HIV/AIDS epidemic. Over the last 12 years, HIV-infected men with high CD4 counts have been enrolled in care services but not put on treatment while in the same period we have dramatically scaled up the number of women being treated through PMTCT programs. The men received this message: "You have HIV but don't need to do anything." Meanwhile they were, and are, infecting young women. With the new normative HIV treatment guidance from WHO, the message can now shift. We need to acknowledge the significance of this reversal and work to help men understand that they need treatment for their own health, and the health of their communities. The guidelines recommend the following:

- Treat ALL (at any CD4)—all people living with HIV
- The sickest remain a priority (symptomatic disease and/or CD4<350)
- New age band for adolescents (ages 10-19)
- Option B not taken forward; Option B+ as new standard for PMTCT
- PrEP as an additional prevention choice for all people at substantial risk of HIV infection (>3% incidence)

Test and START

AMB Birx explained the importance of Test and START, the PEPFAR terminology for treating all who are HIV infected. She raised the question of what impact the ongoing PEPFAR-supported Combination Prevention Trials, all of which use early provision of ART as a cornerstone intervention, will have on decision-makers in the future, and she asked the SAB to think about them differently, as they are clinical trials paid for with program dollars to change program as opposed to those paid for with research dollars.

DREAMS Partnership

The DREAMS initiative is an ambitious partnership to reduce HIV infections among adolescent girls and young women in 10 sub-Saharan African countries. The goal of DREAMS is to help girls develop into "**D**etermined, **R**esilient, **E**mpowered, **A**IDS-free, **M**entored, and **S**afe women". Community involvement, school-based interventions, PrEP, and engagement of older men will each play a part in the success of the DREAMS initiative, which centers around the adolescent in the biomedical, community, and structural worlds. The "Effects of cash transfer for the prevention of HIV in young South African women" (HPTN 068) study may not have shown that cash transfers decrease HIV infection rates, but they clearly demonstrated that secondary school attendance does.

PEPFAR Goals

AMB Birx summarized PEPFAR deliverables for the next two years. These include:

- PEPFAR 2016 and 2017 prevention and treatment targets re: adolescent girls and young women, VMMC, and ART, as described above
- $300 million additional prevention investments for DREAMS, Test and START for men in DREAMS districts, and VMMC
- Funding of $10 million to the Robert Carr civil society Networks Fund over the next three years to build the capacity of civil society
- $4 million two-year initiative PEPFAR/UNAIDS faith initiative

- Challenge for new partners to contribute new resources and ideas to spark innovation into the DREAMS partnership
- $3 million contribution to and partnership in the Global Partnership for Sustainable Development Data

In reference to PEPFAR's donation to the RCNF, AMB Birx recognized the importance of engaging civil society organizations to assist with funding. She shared the example of the Treatment Action Campaign (TAC) in South Africa, which PEPFAR rescued last year and is again on the brink of folding. She noted the reality that none of the donor countries are funding advocacy and activism and that, while PEPFAR is expanding its investment, civil society must lead the effort and requires funding to do so.

Priority Areas for SAB Consideration

AMB Birx shared the priority areas for SAB consideration, and she expressed her appreciation for the PrEP and Test and START documents produced for the SAB meeting as well as her anticipation of forthcoming discussion on those topics:

- Test & START
- PrEP
- HIV prevention in young women and adolescent girls
- Strategies to identify and link men with treatment
- Accelerate access to treatment for children
    - Particularly difficult in light of the UNAIDS revised numbers of children at risk
- Continue momentum towards virtual elimination of MTCT
- Strategic scale-up of VMMC
    - Money alone is not enough; PEPFAR has heavily funded circumcision efforts, and countries are still lagging in implementation.
- Meaningful, impactful civil society engagement
- PEPFAR implementation science funding for significant and swift impact

AMB Birx asserted that SAB members have affected positive, transformative, game-changing work in the past, and she solicited their advice on improving the work of PEPFAR. She added that HIV is equally fatal (just slower to cause death) to Ebola—weekly, 20,000 adults (including 7,000 young women) die from HIV/AIDS and 34,000 more are infected—unacceptable numbers, yet people are paying less attention to this epidemic. She reaffirmed that the global tools exist for responding and succeeding.

US Global AIDS Coordinator Presentation Q&A

Dr. del Rio thanked AMB Birx for her presentation and opened the floor to questions.

Question 1: Mark Harrington

What will you do to better integrate TB and HIV programs, such as monitoring the implementation and uptake of isoniazid preventive therapy (IPT)—which showed very important benefits in the TEMPRANO Study—as well as early-initiation of ART? Perhaps the next meeting could include a discussion about HIV-associated TB?

Answer: AMB Birx

In between SAB meetings, we can disseminate information to members on progress related to HIV-associated TB efforts. IPT has been included in technical guidelines, and active disease is not

ruled out with acceptable speed, as ruling out active disease allows for IPT use; we need insight into how to do that more effectively. We are tracking it now, and it is one of our very specific indicators. We need to determine the reason or reasons for the lack of IPT use; is it political will and/or clinicians' and nurses' lack of understanding of when and how to administer it?

We are still failing on TB diagnoses in HIV+ people; one factor is the number of late-stage individuals still coming for testing, most of them men over 35. We are continuing to expose healthcare workers and others in clinics to TB, and probably to multidrug-resistant tuberculosis (MDR-TB), due to a failure on the HIV treatment side. In response to Mr. Harrington's suggestion, we will set up an EWG to explore this issue.

Question 2: Mitchell Warren
Thank you, Ambassador, for your passion, inspirational impatience, and ambition. The treatment targets are very clear and are relatively easy to measure and to deliver. The incidence reduction in women is most exciting, but how are we measuring success? How will you, we, and the global community view incidence reduction in 2016 and 2017, as it will be too late at that point to correct the course of action if the numbers are not realized?

Answer: AMB Birx
There exists a series of wraparound metrics, but we have deep concern about measurement. In many areas in the past, PEPFAR has not had a reliable baseline. In order to ensure a baseline, we prioritized specific countries one-and-a-half years ago for HIV Impact Assessments (HIA) in order to develop an age-disaggregated baseline to determine where women are infected. Cross-sectional incidence determination will occur within the HIAs using the limited antigen assay and viral load measurements. We also track prevalence of HIV at antenatal clinics as a proxy for incidence among women.

We have a lot of money already in the combination prevention studies; I wonder how they could be modified and utilized to track incidence rates in young women ages 20-25. Scientists already in place in DREAMS communities could gather the data. Approximately $280 million has been committed to those studies—how should they be focused? These types of discussions greatly inform our work, and we will need a large community of experts supporting PEPFAR in order to affect change.

Question 3: David Peters
Thank you for your presentation and particularly for your infectious sense of urgency around these issues. I am curious to know why Malawi is exceptional when many countries have community health worker programs, and task shifting to lower-level cadres is common. How can we affect change to have the successes seen in Malawi occur as the norm?

Answer: AMB Birx
Malawi had a game-changing individual in Anthony Harries, senior advisor and director of the Department of Research of the International Union of Tuberculosis and Lung Disease; he served in the Malawi Ministry of Health as national advisor on both TB and HIV, with responsibility for scaling up ART there. His impact cannot be overestimated. The speed to coverage was extraordinary, far exceeding that of other countries. All changes were implemented within and through the existing system of care, and Malawi has thereby leapfrogged other countries.

Botswana and Namibia have made great progress as well, and we need to learn from the other nations.

During the WHO guidelines discussions in 2013, it was very difficult to have participating scientists accept program data. PEPFAR knows it needs to make program data as accessible, valid, and useful as any scientific data that we have. We invest significantly in the quality of research data and should have the same commitment to our program data, as it is affecting people's lives.

Question 4: Judith Auerbach
Does PEPFAR systematically analyze the program data in a case study methodology? In the social sciences, that methodology is deemed scientific, and it rebuts arguments that purport that program data is not scientific evidence usable for making programmatic evaluations.

Answer: AMB Birx
PEPFAR recently held its first meeting, as part of the data analysis team, of the PEPFAR Oversight, Accountability and Response Team (POART); it involves all of the agencies in an interagency data collaborative. POART analyzes programmatic elements and determines the high performers and the low performers. It also compares those similar among them in the case study methodology, using urban vs. rural vs. peri-urban data, as well as age-disaggregated data. It would be helpful to us to discuss the importance of program managers in making data utilized, understandable, and actionable. That analytic framework promotes thinking about data in that way, which is critical to PEPFAR. The ability to define best practices has shifted from who could best get them published to data-driven practices. When someone tells me they have a best practice, I ask them to present me with the data that proves the practice is different in quality or performance. Advice on this subject is greatly appreciated. The development of an EWG on how to use program data more effectively may be warranted.

Question 5: Musimbi Kanyoro
Thank you for your presentation and for including the faith-based initiative. Can you please say more about that initiative?

Answer: AMB Birx
The PEPFAR-UNAIDS Faith-Based Initiative is a combined effort of the two organizations to understand, dissect, and analyze data about performance in faith-based organizations (FBOs), community-based organizations (CBOs), and public sector organizations to learn what services are being provided and to discover unique, effective approaches to that service provision.

Early on in the crisis, I was working in Mozambique, which is geographically challenging. At that time, we were centralizing the data, and staff discovered that text-messaging the diagnostic results through printers would get the information to health centers. Young lab workers who could learn new technology were trained, and they disseminated the information quickly. The assumption was that everyone was using this method, but workers in other countries, namely Namibia, did not know about it. The logistical information was then shared between countries.

Our challenge is to find innovators in a data-driven way so that information can be translated more rapidly. We believe that there are FBOs that have figured out how to reach men in alternative and church settings. We know this happens in the US, with programs such as the one

run by Rev. Sanders that engage men in unique ways so they may receive compassionate care. The FBOs can perform analysis and mapping and then utilize that information to identify best practices.

Question 6: Carlos del Rio
Do you have targets for what costs of care should be?

Answer: AMB Birx
We have been requiring and receiving expenditure analyses from every partner for the past four years, and that data allows for apples-to-apples comparison within and across countries. For example, we can know exactly what it costs to deliver services in rural areas by population size and by distance from a health center.

PEPFAR's Expenditure Analysis data is used for decision making. For example, PEPFAR is strongly supportive of the health systems, but tracking costs and impact can be difficult. We recently reviewed PEPFAR/Tanzania's health systems portfolio, and we discovered significant duplication of efforts. The analysis revealed a need for better communication, prompted the reduction of duplicative efforts, thereby freeing money for other impactful programs in Tanzania.

We believe that, using the expenditure analyses from multiple countries, we will be able to validate the core activities that are necessary in the health systems' support of this program and the health system at large. As well, we will identify duplication, and that money can then be directed to prevention at 50% and toward care and treatment at 50%, thereby expanding the impact.

It is said, "You cannot manage what you do not measure". Our challenge now that we have measured is to manage what we have discovered. Every management element produces a change and a ripple in the system. Changes can cause discomfort, but once we know what is happening, we need to respond and solve the problems.

Question 6: Connie Celum
I add my thanks for your passion, vision, ambition, and most especially your impatience. I offer this suggestion: Now that two prevention targets have been codified, and given the challenges around knowing how to estimate impact, I would encourage a cost-per-infection-averted target. Particularly for DREAMS, some of the interventions being proposed are not evidence based and are costly to implement. We need to learn as we go and to determine whether resources should be diverted from well-intentioned but potentially less impactful programs.

Answer: AMB Birx
I would like to arrange for SAB members to attend upcoming ACT and DREAMS meetings, likely to occur in January, to deal with the issues that you raise here. Presenters shared successes at the DREAMS kick-off meeting, and we expected teams to return to their countries and adapt what they learned to communities in one age group or another to affect a specific impact; however, that level of innovation and adaptation to unique circumstances did not occur. We would like the active engagement of SAB members in any of those specific initiatives in which you have a special interest and expertise.

Question 7: Angela Mushavi

This is very inspiring, and I am so glad that, within the DREAMS initiative, there is some funding for male partner involvement. One of the challenges we have had is that the rollout of Option B+ was leaving the men behind, and I think this addresses the issue of gender equity.

Thinking about Test and START and more broadly about men, we have the experience of pill-sharing if the woman goes on treatment and the man does not.

The other issue I am so glad you have brought up is that of managing program data and using it to improve our programs. I see that the SAB priority areas include support for implementation science, and I hope that more and more of that will come so that we can learn from the lessons that come out of implementation.

Question 8: Jesse Milan
Thank you, Ambassador, for your presentation, and for discussing task sharing at the level that you did. As a backdrop for our discussion of the Test and START EWG report, please provide an update on the status of the workforce serving those who come out on the other side of treatment.

Answer: AMB Birx
As you know, we had a mandate of 140,000 healthcare workers, and we exceeded that. We continue to be heavily involved in the expansion of the workforce. What has not been effective is workforce retention. Therefore, we spend a lot of time in training nurse-midwives who do not remain in place; in Malawi, we likely trained 1,000-2,000 nurse-midwives, many of whom have moved to other countries such as South Africa, Botswana, and Namibia. We need to work on retention concurrent with supporting various health cadres.

Question 9: Judith Auerbach
Congratulations. I appreciate you commenting that discrimination is ongoing and getting worse. I have a question about the way in which operations research and implementation science research is taking place. Is discrimination being integrated into the conceptualization of research, or is it remaining a stand-alone element?

Answer: AMB Birx
I welcome the SAB's advice in this area. PEPFAR's work around this issue involves two elements. The first one is a series of initiatives that Secretary Clinton and Ambassador Goosby launched around key populations and implementation science. These will drive science, but it is not as clear whether they will affect policy change.

The second piece is implementation at the community level. Large policy changes are not being implemented locally, community organizations are not being funded, and activism and advocacy are desperately needed at this time. Unfortunately, Canada, the Canadian International Development Agency (CIDA), and France are not funding advocacy around the globe as in the past, and the US cannot do it alone.

I came out of the U.S. military, where, at the time, stigma and discrimination were extraordinary due to the policies in place. This was long before Don't Ask, Don't Tell. Military physicians were at the front lines of protecting their clients and keeping them in the military healthcare system, the only place they would get the care they needed.

In 2012, Family Health International (FHI) and USAID led a critical study in Jamaica known as the People Living with HIV Stigma Index. This was a significant study that looked at the discrimination experienced by sex workers, people living with HIV, and Men Having Sex with Men (MSM) at health clinic visits. It was uncovered through an anonymous survey of healthcare workers that they were disclosing individuals' statuses in conversations at a rate of 20%. Patients reported being the subjects of gossip and discrimination.

PEPFAR has asked other countries to replicate the study, because this is a problem within both the public health system that must be addressed if HIV-infected individuals are to access patient-centered and compassionate care.

Question 10: Christine Nabiryo
I feel I am being mentored today, and I am reflecting back on how the issues discussed here play out on the country level. At last month's annual joint AIDS meeting in Uganda, political will was missing; this was a far cry from the will that existed at the SDG rollout. I am wondering, how do we get scientists to the politics? If we are to make an impact, it is critical that we address this issue for sustainability. That was a large focus of the Ugandan meeting. I hope that sustaining the funding, as you have talked about today, will be an SAB priority.

En route here from Uganda, I was reviewing OVC implementation science and wondering, "How do we help a country with all that is going on, as it relates to the guidelines?"

Answer: AMB Birx
I asked all US ambassadors in PEPFAR countries to return to Washington, DC for two days. About 80% of ambassadors or chargés came, which illustrated a reawakening of the US government's, and specifically Secretary Kerry's, commitment to this issue. Political will was one of five topic areas for the meeting, which included 10 hours of open discussion. The ambassadors were incredibly insightful as to how to deal with this issue. They and the diplomatic corps here are essential to encouraging that political will and serving as a daily booster of it. They are very willing to share talking points with their countries' ministries of health and of finance, explaining how funding this work will save them money and build economic development.

We have the political will at the federal level, and we need it at the community level. Activists and activism, not clinicians, drove access to services. The experience of Ryan White drove funding in a new way for access to services and led to a discussion around human rights. How do we speed up the process so that we can leapfrog elements? Africa has a history of leapfrogging around telecom, when countries did not wait for wiring but went directly to cell phones. They did not wait for ATM machines but moved instead directly to a phone ATM system. Clearly, Africa can leapfrog; we need to be part of that solution as it relates to HIV/AIDS.

Report and Recommendations to the PEPFAR SAB on the use of Pre-Exposure Prophylaxis (PrEP)
PrEP Expert Working Group (EWG) Brief
Connie Celum presented the PEPFAR PrEP EWG's recommendations on the use of PrEP. She began with an explanation of the EWG's charge, which centered on formulating recommendations for the PEPFAR Scientific Advisory Board about implementing PEPFAR-funded PrEP, focusing on prioritization, support, and logistics.

Process Utilized by the PrEP EWG

Members of the PrEP EWG participated in the development of the following recommendations. The group held four teleconferences and engaged in a considerable succession of email correspondence, reviewing existing peer-reviewed documents—including many created by the members of the group—and as-yet-unpublished data, including the recent systematic review commissioned by WHO for its "Guidance on oral pre-exposure prophylaxis (PrEP) for serodiscordant couples, men, and transgender women who have sex with men at high risk of HIV".

Dr. Celum acknowledged Rachel Baggaley and Meg Doherty of WHO; Robert Grant; and Jared Baeten for sharing data and providing access to documents that were not yet in the public domain. She also thanked the PEPFAR Secretariat for granting entry to documents relating to drug access and DREAMS, as well as for excellent and responsive support to the EWG.

Rationale and Evidence about PrEP Efficacy and Effectiveness

Dr. Celum highlighted the key aspects of the rationale for and evidence supporting PrEP. She explained that PrEP is a prevention option for people who are at high risk of contracting HIV. It is meant to be used consistently, as a pill taken every day, and to be used with other prevention options such as condoms.

Dr. Celum applauded Ambassador Birx, OGAC, and PEPFAR for developing ambitious targets that include two prevention targets for young women through the DREAMS initiative as well as those for voluntary medical male circumcision (VMMC). These targets provide a tool against which to measure progress, and reaching them will require hard thinking and effort. Dr. Celum distilled the targets into the following distinct tasks:

- *HIV Testing:* None of these treatment or prevention targets will be attained without appreciable innovation and commitment to scaling up and simplifying HIV testing (e.g., self-testing), reach (community-based strategies), and connecting with marginalized populations. Greater success in reaching men is paramount.
- *Secondary prevention:* Achieving efficiencies in ART delivery, monitoring, and scaling up coverage are of significant importance.
- *Primary prevention:* Ten years have passed since clear data for VMMC were presented as primary prevention, and goals have still not been attained. Dr. Celum hopes that the current, unequivocal PrEP evidence informs implementation far more quickly.
- *Behavioral aspects:* No biomedical intervention—be it testing, treatment, VMMC, or PrEP—will be achieved unless we recognize the key challenges of behaviors.
- *Data:* Data is critical to guiding and evaluating implementation efforts.

Overall Evidence for Antiretroviral (ARV)-Based Prevention

Millions of dollars have been spent to attempt to answer the simple question, "Would ARV-based primary prevention work?" Dr. Celum presented a chart of the relevant studies entitled "Overall evidence for ARV-based prevention for HIV prevention: February 2015"; the graph demonstrated that seven of the twelve studies showed efficacy, with the top two being true effectiveness studies. Dr. Celum noted that two trials involving young women did not show efficacy.

Lessons learned from the research are:

- Efficacy in four of the six randomized, placebo-controlled oral PrEP trials ranged from 44% to 75%.
- Adherence was a major factor in efficacy results.
- Factors associated with low uptake and adherence in oral PrEP trials in young African women were identified:
    - Non-health care users were asked to take a daily pill or use gel daily or pericoitally in an essentially entirely new intervention.
    - Motivation to participate in the trial was low.
    - A young, newly sexually active person whose risk is derived from his or her partner's risk in a generalized epidemic has low accuracy of risk perception.
    - It is difficult to believe in a trial's benefit when you are randomized to either a placebo or a product of uncertain efficacy.
    - Concerns include:
        - Stigma exists around taking a drug known in the community as a treatment; the same holds true for taking preventative medications.
        - Side effects: The consent agreement made the preventatives sound like toxic drugs.
        - Partner reaction
- Adherence equals efficacy: Oral PrEP is effective when taken.
    - The degree of HIV protection in PrEP trials was directly related to the proportion of subjects who were adherent to PrEP.
- PrEP works for high-risk persons, including:
    - Heterosexuals
        - *Reporting having had sex without condoms*
        - *With an STI*
        - *With an HIV+ partner who has a high plasma HIV viral load*
        - *Women less than 30 years of age*
        - *Women using Depo-Provera (DMPA) for contraception*
    - MSM/Transgender Women (TGW)
        - *Use cocaine*
        - *Have syphilis*
        - *Engage in anal sex with an HIV+ partner*
    - HIV protection estimates for these subgroups were often as high or higher than for the trial population as a whole, because adherence was often greater for higher-risk persons.
- Serodiscordant couples were highly motivated to participate in trials due to recognition of risk, desire for pregnancy, and support from the other partner. Those who adhered to the protocol early in the trial continued to do so at 12 months.
- Women also self-sorted into adherers and non-adherers:
    - Although a low proportion of women overall in the VOICE trials used the product, a minority were consistent users.
    - Adherence was impacted by concern about partners' reactions, stigma, uncertainty about antiretrovirals (ARVs) for prevention, and discussions with other women in the trial.
    - Women in FEM-PrEP voiced concern about losing benefits if they disclosed non-adherence.

- Participants in the iPrEx open label extension study, who knew they were getting a medication that worked and not a placebo, experienced 100% protection with as few as four pills a week.
- Results of implementation effectiveness were far better than effectiveness in clinical trials.
    - 44% vs. 86% effectiveness in one comparison, and 75% vs. 96% in a second comparison
    - Time-limited PrEP used in the last of the studies listed achieved almost total elimination of transmission.
    - Real-world studies can have big impacts; people recognize and are motivated to reduce their risk, and they are able to use PrEP sufficiently well to achieve high prevention benefits.
    - N.B. In phase 3 randomized clinical trials, evidence of 90% effectiveness was seen.
- Small trials provided importance lessons as well:
    - In one example, NIH funded a trial that was run by Dr. Grant; it compared daily and non-daily oral PrEP dosing in 179 women ages 18-29.
        - At 30 weeks, there was 79% adherence, based on drug levels among women randomized to the daily oral PrEP group in a township outside Cape Town, South Africa.
        - Women on daily dosing, with tenofovir (TDF) or Truvada, experienced higher adherence and higher coverage of sex acts as compared to those on less-than-daily dosing.
- According to PrEP takers, the treatment offers protection and the following additional positive aspects:
    - Decreased anxiety
    - Increased communication, disclosure, and trust
    - Increased self-efficacy
    - Increased sexual pleasure and intimacy

In summary, implementation experience shows that one-pill-a-day PrEP:

- Can be used discreetly and can be independent of one's partner (and his or her behavior).
- Has the potential to significantly reduce HIV acquisition at an individual and population level.

Also, open label studies and demonstration projects indicate that if persons at substantial risk, including young women, know that PrEP works:

- They are more likely to use it and be adherent.
- Uptake is higher in those who self-identify as at HIV risk.
- Feasibility and deliverability are existent.

PrEP EWG Recommendations to the PEPFAR SAB

Dr. Celum began with an overview of PrEP's intervention applications:

TDF-based PrEP is a proven intervention for:

- Use during periods of HIV risk
- Having sex with a partner of unknown HIV status

- Engaging in unprotected sex when trying to conceive (important for serodiscordant couples)
- Casual partners or those in the early stages of a relationship
- Those unable or unwilling to negotiate or utilize condoms

PrEP is an additional option for HIV prevention in high-HIV-incidence settings for:

- Young women in Africa
    - This first focus was chosen based on the DREAMS initiative.
- Serodiscordant couples
    - PrEP can act as a short-term bridge until the HIV+ partner initiates ART and is virally suppressed.
- MSM, intravenous drug user, and sex worker populations

PrEP has moved from medical trials to early implementation studies and now to guidance, policies, and programs. It is an element of the combination prevention package in DREAMS. Finally, the WHO guidelines that were released approximately two weeks ago, which were heavily analyzed and are evidence driven, include this statement:

> "Oral PrEP with TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches."

<u>Recommendation Areas</u>

Realizing that using the 3% incidence rate threshold is difficult to translate into policy and practice, the question is how to reach at-risk populations. The PrEP EWG made recommendations to the PEPFAR SAB in nine topic areas, based on the fact that PrEP is an evidence-based, proven intervention that can be used successfully in a time-limited manner.

1. Involvement of and Partnerships with Local Governments and Civil Society Structures including Non-Governmental Organizations (NGOs) and Community-Based Organizations (CBOs)
2. PrEP Drug Selection
3. Licensure Status of TDF-based PrEP in Countries Outside the US
4. PrEP Delivery
5. Safety Monitoring of PrEP in PEPFAR
6. PrEP Adherence Monitoring
7. PrEP Use in Pregnancy
8. Sentinel Surveillance for Monitoring PrEP Use
9. Implementation Science and Operations Research Priorities for PrEP Delivery

Dr. Celum expanded on each topic area:

1. Involvement of and Partnerships with Local Governments and Civil Society, including NGOs and CBOs

- It will be necessary to **cultivate strong partnerships with local governments and civil society** to address stigma and cultural barriers to PrEP implementation and to build support for PrEP implementation.
    - NGOs and CBOs will be key to getting buy-in, sustainability by messaging, demand-creation strategies, and marketing and positioning of PrEP.

    - Partnerships with local governments, NGOs and CBOs, and users will facilitate PrEP programmatic scale-up and synchronization within existing programs and prevention efforts.
- Specific useful activities to support PrEP activities in PEPFAR include:
    - Meeting with local PEPFAR leadership, particularly in the 10 DREAMS countries, for updates and advocacy with government, FBOs, policy-makers, provider groups, and other key decision-makers.

2. Drug Selection

- The data is comparably strong for both oral TDF and/or TDF/FTC; therefore, **daily dosing of either drug combination can be offered,** and this allows for flexibility in drug selection in implementation at a country level.
- The **choice of using TDF or TDF/FTC** for PrEP should be guided by the drugs approved for HIV treatment in each country.
- Both **generic and patented drugs** should be offered.
    - Generic medication can lower costs and can be provided in settings where patented drugs are unavailable or inaccessible.
    - As part of DREAMS, there is a memorandum of understanding (MOU) in process with Gilead for donations over the next two years. The goal is to develop long-term policies that go well beyond the Gilead donation period.
- **Supply chain systems should be ensured** to enable continuity of drug access.

3a. Licensure status of TDF-based PrEP

- Truvada is registered for HIV treatment in many countries; it is not yet registered for PrEP indication outside of the US.
- Lack of registration may create a regulatory obstacle:
    - The drug may be considered an experimental treatment, requiring provision under research protocols and regulatory approval, both which lead to delays in PrEP access.
- For countries that decide to introduce PrEP, guidelines that support off-label use could expedite access. This has been done with other drugs.
- **Fast-track registration for TDF and/or TDF/FTC for PrEP** should be recommended by the sponsor. Where registration is ongoing, PEPFAR should support timely completion.
- Recommend **local Ministry of Health (MoH) memoranda** enabling TDF or TDF/FTC off-label use for PrEP.
- OGAC could **facilitate PrEP drug availability and distribution** on an individual country basis.

3b. Social Marketing and Private Sector Access

- As demand grows for PrEP, the private sector may be an important delivery partner.
    - Consider **service delivery models** for users who can afford to buy PrEP from health facilities, qualified pharmacies, and other points.
    - The private sector could **support a market for PrEP,** expand access to those who don't want to use the public sector, protect donor funds, and relieve financial burden and overcrowding in the public sector.
- Consider **providing subsidies directly to patients** to offset the price of drugs where prices are prohibitive, and titrate this subsidy based upon both need and willingness to pay.

- **Identify generic formulations** for TDF and TDF/FTC PrEP, and support market-based interventions to make these formulations available.
- Use landscape analyses to **identify and try to overcome other barriers** to bringing TDF & TDF/FTC PrEP to market.

4. PrEP Delivery

- **Identify HIV testing strategies** to increase coverage and reach (e.g., self-testing and community-based testing).
- Need sufficient horizon to **ensure adequate time for PrEP implementation and lessons learned to inform scale-up** (i.e., >2 years of DREAMS).
- **Offer PrEP in a variety of contexts,** including:
    - Private clinics, family planning clinics (these are not generally welcoming to young, unmarried women), HIV care clinics with partner testing to identify HIV+ partners, programs for key populations.
- **Evaluate "how" and "where" to deliver PrEP** for key populations in different settings.
    - We need to get out of a facility-based testing mode.
    - Consider community-based testing, local testing, and use of self testing.
    - Partner testing rates need to improve/opportunity to incentivize programs.
- Better information is needed on **patterns of PrEP use** (duration, stopping, and starting).
    - PrEP is meant to be used during "seasons of risk", and stopping needs to be encouraged.
- **Encourage use of electronic patient databases** in HIV clinics to know who is receiving PrEP to:
    - Facilitate ART delivery and monitoring
    - Identify HIV+ persons with a partner of unknown status, promote partner testing, and offer PrEP as a bridge to ART initiation in the HIV+ person.
- **Mobile phone apps and social media** could reach key populations not receiving care.
    - "There's something new, there's something for you."

5. Safety monitoring of PrEP in PEPFAR

- The general principle of safety monitoring is to **keep it simple and focused** to facilitate safe and effective delivery and thereby have a significant public health impact. This is not a toxic drug combination, and there is much experience with it in treatment.
- *Baseline HIV testing:* **Use available in-country HIV testing algorithms** so as not to create a barrier to testing. Testing is important so as not to use PrEP with people who are acutely infected.
- *Renal monitoring*: **Make PrEP renal monitoring parallel to ART monitoring** (no greater than for ART monitoring for TDF regimens).
    - Where possible, follow WHO guidelines, which will be revised as new information is available.
    - Conservatively, begin with Creatine testing q3 months for 12 months, then q12 months (if such testing is available).
    - Offer Hep B vaccine to those who test negative.
    - Revise as more information is available from PrEP provision in demonstration projects.
- *Bone demineralization:* Small reductions that did not progress and were not associated with excess bone fractures were discovered.

    - Baseline and ongoing monitoring of bone demineralization is not recommended.
- *Hepatitis B testing:*
    - HBsAg testing: helpful but not required to start PrEP. Identifies HBsAg+ people who could benefit from Hepatitis B treatment.
    - Countries should not have to develop lab testing for Hep B in order for PrEP.
    - When Hep B testing is conducted, **Hep B-negative patients should be offered Hepatitis B vaccine** (but not required before initiating PrEP).

6. PrEP Adherence Support

- Adherence monitoring may not be necessary for a public health PrEP strategy.
- **Clear messaging:** Should you take it? Is it for you?
- Do not compromise programmatic scale-up of PrEP by making adherence monitoring too complex or too costly to implement.
- **Provide information about how well PrEP works** when taken, and **recommend daily use.**
- **Provide adherence support** using client centeredness, peer support, and non-judgmental provider approaches.
- **Make simple suggestions,** such as linking PrEP-taking to a daily habit.
- Counsel about potential mild and time-limited **GI side effects.**
    - Occurs in approximately 10% of patients.
    - Symptoms usually abate within one month.
- **Weekly SMS reminders** can be helpful but are not essential.
- Persons who recognize their risk of HIV will be more motivated to take PrEP well.
- Given that risk is dynamic, **risk and motivation should be periodically reassessed.**

7. PrEP Use in Pregnancy

- With increased risk of HIV seroconversion in pregnant women and increased risk of PMTCT during acute HIV, **PrEP in pregnant women at risk for HIV should be considered.**
    - Data from Partners PrEP indicate safety in women who became pregnant, with no increase in adverse pregnancy or infant outcomes.
    - CDC and FDA acknowledge that PrEP can be used in pregnancy.
- Women who are pregnant or intending to become pregnant who are at substantial risk of HIV should receive **counseling about PrEP safety overall and in pregnancy,** as well as PrEP efficacy.
    - It should be a woman's choice whether to start or continue PrEP when pregnant.
    - Information allows women to make an informed choice.
- TDF-based ART regimens in HIV-infected mothers may be associated with a small reduction in low birth weight and bone mineralization in infants.
    - It is important to **collect data on the safety and effectiveness of PrEP use in pregnancy** including both maternal and infant outcomes.
- Given high rates of unwanted and/or unplanned pregnancies and higher maternal mortality rates in young people, **prevention of pregnancy through family planning services**—and TOP referral where legal—is critically important.

8. Sentinel Surveillance for Monitoring PrEP

- Use **routine data collection** to monitor PrEP uptake and patterns of use.
- Avoid setting up new systems to collect data. Instead, **identify what systems exist, who uses them, and how they use them.**
    - **Assess feasibility of expanding the database** to include a few key PrEP use variables (e.g., demographic characteristics, PrEP uptake, sexual practices, patterns, and duration of use).
    - A key metric of impact is whether PrEP is preferentially taken up by people with the highest exposure to HIV.
- **Conduct sentinel evaluation** of persons who become HIV infected within three months of receiving PrEP medications.
    - **Ideally evaluate drug resistance and TDF drug concentrations** at the time of the first laboratory evidence of HIV infection.
    - **Surveillance for drug resistance monitoring needs to be included** and could be built into existing ARV resistance surveillance introduced for ARV treatment monitoring.
    - Dried blood spots are the most convenient and best validated biomarker of PrEP use.
- Pharmacovigilance systems should:
    - Be aligned with existing national ARV treatment surveillance strategies.
    - Assess PrEP use in pregnancy with monitoring of maternal and infant outcomes in sentinel sites.

9. Implementation Science and Operations Research

- Where feasible, **evaluate HIV incidence as well as process outcomes.**
- Rigorously **evaluate social marketing strategies and social media** to increase awareness and motivate persons at substantial risk to initiate PrEP.
    - Use other messaging than the negatively framed prevention messages currently employed.
- **Assess if ongoing creatine monitoring is required for safe PrEP use.**
    - Can we back off from existing recommendations and still provide PrEP safely?
- **Identify provider training needs** for risk assessment in HIV+ persons.
- **Evaluate strategies to reduce visits** (e.g., HIV self-testing).
- **Assess use of pharmacies** for PrEP supply and resupply to reduce provider burden, clinic visits, and opportunity costs for PrEP users.
- **Evaluate brief and scalable adherence support strategies.**
- **Conduct costing and time-motion studies** of PrEP delivery in different settings, and estimate incremental cost-effectiveness.

<u>Summary of Recommendations</u>

The PrEP EWG feels that PrEP is an important part of prevention, coupled with HIV testing, ART, and VMMC. It has the potential to have a major impact on public health. It is the first tool in addition to VMMC in decades that gives someone control over preventing infection with HIV. We will need strong partnerships to advance PrEP as prevention.

We must meet challenges around eliminating HIV/AIDS. The implementation pipeline includes learning if a vaginal ring works within one year; later will conceivably come an injectible drug. Hopefully within our lifetimes, a vaccine will have been developed. There exists a real opportunity to learn how to deliver primary prevention to hard-to-reach populations.

We will understand by running demonstration projects, with incremental introduction with countries that know how to scale up appropriately, and with monitoring and evaluation.

The PrEP EWG believes that PrEP is an opportunity we cannot miss.

Please see (LINK) for the final SAB PrEP recommendations

PrEP Q&A Session

Dr. del Rio thanked Dr. Celum and acknowledged the significant effort put forth by the PrEP EWG in producing the report and recommendations.

Question 1: Kenneth Mayer

Congratulations to Dr. Celum and the committee for its thoughtful report. I want to call attention to the issue of provider training focused around cultural competency and helping patients to feel comfortable in healthcare settings, and delivering appropriate disclosures regarding testing and treatment. The "purview paradox" means that barriers to PrEP uptake, at least in the US, include HIV providers who do not consider themselves as being in the role of treating the uninfected, as well as providers who treat people who might benefit from PrEP but are themselves intimidated by the medications. As well, training will involve educating a cadre of healthcare workers who haven't been involved in HIV treatment efforts to date. Such workforce issues as these will likely exist in PEPFAR countries.

Separately, one model for providing PrEP at cost is an existing Red Cross program in Bangkok, Thailand in which packets of medications are available for one dollar a day; this could be an interesting model to consider scaling up in countries with more resources.

Answer: Connie Celum

Provider training is clearly necessary; however, we need to acknowledge a reality in which we will likely never truly train providers to ask questions in an entirely neutral way. Perhaps some risk assessment tools can be removed from the critical initial intake, thereby allowing a patient to determine if PrEP makes sense for them without dealing with a provider s/he feels is not supportive.

Question 2: Ruth Macklin

I would like to gain clarification on the use and implications of the term "implementation science" in this case. The term could mean research, which would involve a set of questions that would relate to the ethical requirements of conducting such research; alternatively, it could mean program evaluation. The answer affects whether consent forms are needed and begs the question of what such forms would need to include.

If used for research, a product does not require licensure. WHO describes implementation research as the testing of something that works elsewhere. Using the research conception of implementation science, one could use an unregistered product. Historically, WHO has required program research to be presented to its research ethics committees; it is unlikely that program evaluation would be held to the same requirement.

Answer: Connie Celum

One key element in this discussion is that Truvada is coformulated, and therefore many countries do not have it available in isolated form. I believe we should be moving as efficiently as we are able from the important early demonstration projects that would probably not meet the definition of implementation science to larger-scale implementation in which consent forms are not required. Use of data collection instruments that capture core basic material could improve the process.

Question 2: David Peters
In response to Dr. Macklin's question regarding implementation science and research, there is not much consistency in WHO around definitions and application, particularly with respect to institutional review boards (IRBs). Increasingly, there appears to be a move toward defining implementation science as research that employs scientific methods. Whether consent forms and IRB sessions are required seems to be inconsistent and appears to depend more on the type of intervention and whether one is trying to produce generalizable knowledge—that is, quality assurance versus the research continuum.

Congratulations on great work done by the PrEP EWG. I see this report as a mandate to move science to address the questions presented, from community engagement in overcoming stigma to social marketing and PrEP delivery and surveillance. Questions around implementation research crosscut the recommendations, and issues may arise as to whether it is implementer-led research vs. implementers or external researchers utilizing the data. I see no end to test-of-concept types of implementation research that can be done in terms of strategies, and I wonder if it is possible to link some of the implementation questions that need data to drive decision-making to those discussed in the previous session. How do we encourage locally driven solutions using data vs. formulating specific best questions and implementation solutions? Both are important, and we may end up with a set of standard regimes as a result of that exploration. How do we engage communities to surmount stigma, which is a standard implementation science problem? Instead of looking at cost-effectiveness of a particular strategy, what may prove more useful would be to explore how we use program data to influence where and how to implement it and then compare costs and effectiveness within and across countries.

Another question centers around what the best platforms are for reaching various types of populations, not only around PrEP but with other services as well. I wonder whether we can link many specific questions to some of the broader themes we address in this group.

Regarding social marketing, I am uncomfortable with using patient willingness to pay as a mechanism for determining price or subsidy. Firstly, I am not sure that it falls under the category of scientific recommendation. Secondly, as we attempt to create demand and encourage adherence, I am more concerned with understanding financial barriers to care than using willingness to pay—it is a strong profit-maximizing strategy, but I believe we should consider a more holistic principle regarding subsidies.

Thank you to the EWG for its great work on this topic.

Question 3: Mark Harrington
In New York, we are wrestling with the same issues. Governor Cuomo has detailed a three-point plan to reduce the number of new HIV infections to just 750 (from an estimated 3,000) by 2020. One of the key issues relates to integrating a monitoring plan that establishes specific evaluation

markers and ensures outreach to correctly identified populations. We now have many population-based early HIV treatment studies, mostly in southern Africa, where the HIV-negative population is being told it needs no intervention; some of these people are imminently at risk for HIV acquisition and therefore would greatly benefit from oral PrEP. I recommend modifying some of the ongoing studies to take into account these questions. We are still very much at the beginning of mapping where the new infections are occurring and identifying populations to target. It will be a significant task to modify our data system to ensure that we capture the correct indicators.

How will we create our prevention cascades and integrate them into our ongoing work? This is an opportunity to link our treatment and prevention cascades. Congratulations to the EWG.

Question 4: Sofia Gruskin
This is a wonderful report. I appreciate the focus of the report on key populations and would like to concentrate on adolescent young women in general and the attention to young women. One element of concern as we move this work forward is the larger legal environment and the difficulties we face in general around young women's ability to access testing without parental consent. The implications of that issue in this case provide a larger opportunity to engage with it in a concrete manner. If we do not do so, we may miss dismantling an enormous barrier to young women's ability to take advantage of the prevention.

Answer: Connie Celum
This subject came up often in South Africa last week.

Question 5: Rev. Sanders
You have my appreciation for your presentation. We are clearly significantly committed to documenting our research. If we are effective in our messaging to address the spread of the disease, and if we identify initiatives structured around social marketing, I am curious to observe the effects in the larger community when people see PrEP as a path to being free from fear of infection and possibly not be required to go through a formal self-identification process in order to receive treatment. Marketing efforts may include messaging that PrEP works even without perfect adherence. Accessibility to prevention—especially with the potential for a generic option becoming continually greater—and reasonable cost are also factors. What might be the downside to these types of messages, particularly in communities that have the highest need? PrEP does have the potential of becoming a street drug.

I noticed that the last two weekly episodes of the TV show "How to Get Away with Murder" included very large ads for PrEP. Such messaging lends credibility to the prevention strategy.

Answer: Connie Celum
Impact issues in the US are very different than those in South Africa. In South Africa, we are not reaching young women, and they do not have access to care. I think there will be relaxation of condom use based on lower motivation to protect self and others. We need to keep the focus on the fact that people already do not use condoms 100% of the time regardless of flooding the market in Africa with them; young women are not always able to negotiate their use and have difficulty accessing them safely. The short-term view of this prevention is one of a harm-reduction strategy.

In regard to the gay male population, the Kaiser Foundation last month released a paper showing no new HIV infections; however, cases of gonorrhea and chlamydia are increasing. PrEp is not a perfect tool, and we will do ourselves a big disservice if we sell it as the be-all-end-all. We must sell it as a short-term solution until a couple is in a regular, stable partnership in which they can negotiate condom use, all while we continue to work toward a vaccine and/or other longer-term strategies.

Question 5: Jennifer Kates
I appreciate the last response, which serves as a reminder that we are just at the beginning of this great work. It is exciting to think of looking back in a few years and noting that PEPFAR, the world's largest funder of HIV prevention and treatment, implemented the WHO guidelines in a substantial way.

Please clarify what it is exactly that we are voting on with regard to the recommendations. I sense that the crux of that which the EWG seeks endorsement, with specifics in each of the areas mentioned, is expressed on page 5:

> "PEPFAR should utilize the partnerships in place with governments, advocacy groups, and civil society structures, and use its strategic advantage for the introduction of, access to, and provision and promotion of PrEP in the context of country responses to the HIV/AIDS epidemic."

Answer: Carlos del Rio
That is exactly the point about the vote; we will need to distill exactly that which we will endorse.

Question 6: Carole Treston
Thank you for this thorough review and report. In the vein of distilling the board's response to the recommendations, my focus is on the information presented in Recommendation #9: "Identify provider training needs for risk assessment in HIV- persons." I encourage a stronger callout about provider training. The Association of Nurses in AIDS Care (ANAC) came out strongly two years ago in support of PrEP, and I cannot overstate the surprisingly considerable amount of time and investment—likely to be mirrored in the global setting—that is required to shift the paradigm in the provider community around HIV prevention.

Also, alternative provider settings for PrEP are critical. Concern exists around task-shifting, as doctors' tasks are shifted to nurses while nurses' tasks continue to remain their responsibility. Nurses can do a lot but cannot do everything. Questions remain as to how we expand the workforce and—seemingly more importantly—the types of people who (and in what settings) can more appropriately or more openly discuss issues around sexuality and sexual risk in a way that is not viewed as threatening or judgmental. This clearly identifies the need to involve nontraditional providers in this process. I request that this be elaborated upon in the written recommendations, as your comments today have reflected agreement with mine.

Question 7: Mitchell Warren
I served on the EWG and congratulate Dr. Celum in representing the group so well. I believe we cannot view the PrEP recommendations in a silo. As we approve them and as we consider Test and START, we need an advisory board to acknowledge that neither prevention (PrEP) nor treatment (Test and START) is a stand-alone effort. It is very important that we articulate that

one of our greatest strengths is in accelerating the first "90" in the 90-90-90 cascade by providing a new treatment option as well as prevention options.

I suggest adding a small footnote to the recommendations based on the idea that PEPFAR does not need to go down the PrEP path alone, as a number of other groups including the Gates Foundation are engaged in this work at the funding level. The importance of coordination with these groups is essential.

The language surrounding this work has become unclear over the last few years. People have different pictures of demonstration research, implementation science, and operations research. My sense is that the EWG's deliberations involved very specific implementation science questions to be asked and answered; however, there is implementation to be done that does not have to be followed by science or research. My question is, if we do need to perform implementation research (as we believe we do), where does it fit in the larger effort? We want to encourage host governments, civil society, and providers to get on the task of scaling this up where appropriate and supported. Fundamentally, approval of the EWG's recommendations is a license to act, especially now that WHO has presented the guidelines. I do not want us to get bogged down in the science and lose our ability to impact this epidemic, as there is implementation to be done. The working group gravitated strongly to the issue of bridging to scale.

Answer: Carlos del Rio
A key component here is that we should not allow scientific questions to interfere with implementation. A big piece of the answer to this question may be in ensuring that robust program evaluation exists. When we get to the vote, we clearly need to consider endorsement of the entire idea; however, there are some specific areas on which we will need to focus.

Answer: Connie Celum
I want to clarify that the EWG strongly endorses PrEP as part of the DREAMS initiative and feels that it needs to move forward on a larger scale than has been proposed in many countries. We hope that the board will endorse that as well. We are asking for endorsement of the overall package of recommendations, with adjustments and clarifications based on today's discussion.

Question 8: Christine Nabiryo
Thank you to Dr. Celum and to the EWG for pushing this work forward. I agree that I would not want to be sitting around this table in 10 years discussing that we should have done this. In looking at the politics of the science, this needs to be higher than local governments, as central governments need to be involved in the decision-making process. In one example, years of research were done in Uganda's capital city of Kampala; however, that research was never used because the Ugandan government did not support the research nor implement the findings. For scale-up, the politics need to be larger; this will also affect programmatic integration. Providers are still the same people, and implementation needs to be very clear.

Question 9: Celia Maxwell
I wish to underscore many of the comments made here—it was an excellent presentation. Washington, DC is ostensibly one of the wealthiest cities in the country. Yet, it includes one ward that could be located on another planet, given its level of citizen need and lack of service delivery. I have a concern about cost; even a dollar a day is too much for many people; in some

countries, $1 represents meals for a family of four for an entire week. Integration with other services is key; as an example, a poor woman with small children and no means of getting to testing or treatment will not come unless she is provided with a babysitter, food, and transportation. What is proposed is an excellent program that needs to be integrated with the provision for other needs. If that does not happen, it certainly will not work for the population which I serve.

Question 9: Peter Berman
I wish to echo Rev. Sanders's comments regarding access to PrEP in the public domain, particularly in countries with very weak regulatory systems. Both India and Nigeria have high numbers of new infections and weak regulatory structures. After listening to discussion about self-testing and alternative providers, I envision PrEP taking the route of daily intake of low-dose aspirin.

Providing a "license to act" is a great concept, as this clearly is an important innovation and tool in the epidemic. AMB Birx discussed at length PEPFAR strategies to increase efficiency, focus, and targeting as the organization's response to the resource constraints it has been facing. I think it is necessary to separate the global, national, and local license to act—and advocating for national authorities, civil society, and others to act—from the challenges PEPFAR faces in the efficient use of its constrained resources. The efficiency or cost-effectiveness of this strategy will depend a great deal on how it is used in conjunction with other things and in relation to the level of risks that people face.

I suggest that PEPFAR look even more carefully at that question and how it relates to various populations and settings and in conjunction with other interventions.

Question 10: Jesse Milan
Talking about sensitivity, I have been HIV+ for 33 years, and I just went on an ARV regimen that includes Truvada. I had the prescription filled at the pharmacy the other day along with one for a painkiller, and the pharmacist announced for all to hear that I could not take the painkiller because I was on Truvada. It was a very upsetting moment.

I endorse Dr. Kates's recommendation that we focus on the middle paragraph on page 5, because we are dealing with a wider cultural shift that is addressing both providers and the community at large.

I am concerned about the wellness and safety of young women and girls around the world. The domestic violence by fathers, uncles, and brothers perceiving that their daughter/niece/sister is sexually active makes me appreciative of the focus on the importance of DREAMS initiative.

I believe we should make the recommendation as stated on page 5 and endorse the entire report.

Question 11: Fredrick Sawe
I want to ensure that young women and girls have access to these prevention technologies, from family planning to reproductive health. We need to break down the barriers and get these services into the healthcare system. In epidemic areas, we may have to present them as part of a package.

The trials were all done using TDF and FTC, but in real-world applications, the combination is TDF and 3TC. Please explain the reasoning behind the change.

Answer: Connie Celum
The EWG did not spend much time focusing on this and may need to revisit it in future discussions. Speaking for myself, the data on FTC and 3TC are so close that we should not be afraid to substitute 3TC. I invite Dr. Grant of the San Francisco AIDS Foundation, University of California San Francisco, and WHO to share his thoughts on the subject.

Answer: Robert Grant
The recently completed meta-analysis commissioned by WHO indicated that tenofovir and FTC tenofovir had equivalent impact on HIV incidence. The studies that generated those data were focused on heterosexual populations. We can have confidence, based on both the Partners PrEP study and the meta-analysis, that 3TC/TDF has the equivalent activity to FTC/TDF for heterosexual populations. The question about 3TC vs. FTC bears on PrEP's use in MSM populations, where we do not have fully powered efficacy studies; we have only one small study. The US Safety Study had six seroconversions, all of which occurred while patients were off TDF PrEP, and zero seroconversions after PrEP with TDF was instituted. This is a signal toward efficacy but not enough evidence to use for WHO decision making.

In treatment settings, FTC/TDF and 3TC/TDF have equivalent activity. We feel that treatment is a more stringent test for the drug protocol, as HIV exposure is 24/7. Had there been a problem with 3TC/TDF, we would have seen it in the treatment setting, and we did not. I believe that the next round of WHO implementation guidance will highlight the recommendation that TDF-containing regimens are effective and that 3TC/TDF is a TDF-containing regimen.

Question 12: Albert Siemens
Congratulations to the working group for its outstanding job. Many of us have concerns around issues of cost and practicality, now and going forward. I would caution that, as we act on recommendations, we think about what these recommendations mean for the future. We know that PEPFAR will not continue to be able to support program grants as it is able to do today. Therefore, we need to take into account how things may change. We need to influence policy that will ensure this will continue and be incorporated into health systems going forward. I caution not to overemphasize particular intervention technologies, such as vaginal rings and injectables that do not significantly change data in terms of acceptability and preference, unless you have definitive data that large populations will prefer and utilize a specific technology. I suggest that we do not spend a lot of money on products that may not provide a long-term benefit.

Question 13: Angela Mushavi
Thank you very much to the EWG for a job well done. With the early release of the WHO guidelines, I believe a lot of countries are looking with keen interest at some of the recommendations that have been made vis á vis Test and START and PrEP (including implementation). In my country of Zimbabwe, we are grappling with cost of ARVs for treatment as we look at Test and START. Even looking at people with CD4 counts above 500 cells/mm^3 (CD4>500), we are looking at financial gaps for ARV treatment. This contextualizes the situation in which implementation is driven by competing priorities among treatment generally,

treatment of those in dire need of intervention, and prevention—or "closing the tap" and reducing new infections in adolescents, women, and men. That tension always exists. Regarding implementation, when we look at who will use PrEP, we are going to filter whatever recommendations are presented through an understanding of the populations that will be served.

In the recommendations, is there some way to provide some guidance around focusing on an order in which to focus on specific populations? Perhaps we need a scaled-up approach, in which we can determine the size of a particular population and evaluate what resources are needed to serve it, and so on as we reach more and more populations.

Another area of concern is risk compensation. We face this even with VMMC, with people assuming there is no risk once a male is circumcised. With people believing that risk is nonexistent, STIs are increasing. This is a red flag to make sure we continue to look at PrEP as part of a combination strategy, not as a magic bullet. Finally, the concern around HIV drug resistance exists.

Question 14: Lejeune Lockett
Thank you for a very informative study. As we think about consistency of use, I am hearing a lot of discussion about PrEP being used in the clinical setting. I think about my own experiences working in the field in various countries where health care occurs in the clinical setting; however, a whole other realm of healthcare provision exists in what people refer to as the alternative or traditional healthcare scenario. I wonder to what extent other healthcare models and beliefs can impact people's access to and consistent use of PrEP. If other healthcare models or beliefs are in play that may negatively affect the consistent use, how does this affect outcomes? Thinking about that will help us to determine who else should be at the table as we talk about integrated teams of providers as they relate to a rollout of this type of intervention.

I really appreciate the discussion of the variety of contexts for application. As we think outside the box, are there other settings in which this should be considered?

Recommendations and Vote
Dr. del Rio suggested that the SAB approve by consensus the PrEP document and that it specifically endorse that PrEP be considered a priority as part of the DREAMS initiative. The EWG and other Board members would then have an opportunity to provide written amendments that reflect today's discussion.

Dr. Berman commented that he would like to add a statement of recognition of funding issues to the recommendations, in view of discussion around working within constrained budgets.
Dr. del Rio urged board members to consider the PrEP recommendations, and later the Test and START recommendations, within the larger picture of aligning testing, treatment, and prevention. Dr. Berman agreed. Dr. del Rio questioned what specific metrics—of people, program, and/or process—around PrEP can be used to determine progress and ensure accountability.

Mr. Warren added that obvious mapping of Test and START relates directly to the target advanced by the President; the PrEP recommendation does not have as clear guidance. Perhaps the SAB needs to work with that leadership to develop similar mapping for PrEP.

Dr. Pape pointed out that implementation requires national governments. This takes time, and the work needs to be included on countries' national agendas. Dr. del Rio agreed strongly and added that, with the WHO guidelines including PrEP, countries now can compare themselves to the recommendations. And, PEPFAR has a license to act with the guidelines as a basis. The SAB needs to recommend that PrEP is a mainstream part of PEPFAR's work as directed by the President.

Dr. Mayer made the point that prevention is an important element of the strategy to arrest the epidemic. Because need for prevention is not as clear as that for treatment begs the necessity for iteration and for local evolution and development. He expressed hope that the SAB would provide positive guidance today and then again with the specific recommendations once they are clarified. Perhaps the EWG will need to monitor implementation to gather the lessons learned in disparate settings. Dr. Kates added that, if PrEP is implemented well, it will identify people who are in need of treatment as well as those at risk of infection.

Ms. Gruskin asked that the recommendation explicitly address young women in the final version's sub-recommendations.

Dr. del Rio invited and encouraged anyone on the SAB to participate in the work of the EWG. Hopefully, the document will be a working one, continually being updated as new information comes to light.

Dr. Shaffer proposed a way forward by asking for consensus agreement on the following points:

1. Endorsement of the PrEP EWG document
2. PrEP moves forward as a priority within DREAMS.
3. Using the two-week period before the document is public to revise it with specific recommendations related to training, adherence, and the paragraph on page 5

The SAB gave its unanimous approval to all points.

AMB Birx recounted the concerns expressed today about the larger issue of young women and, more specifically, the impact of the current DREAMS proposals. She asked that SAB members inform her as to their willingness to work on that subject in general and as it relates to PrEP.

Dr. Shaffer clarified that the PrEP EWG will use the upcoming two-week working period to update its proposal based on the comments it has received today. Therefore, the final version of the document may look different than what we see here. Dr. del Rio added that the SAB is seeking explicit recommendations for the Board to review and approve to advise PEPFAR.

Dr. MacKenzie will recirculate the SAB's charter and membership balance plan to all members in order to provide clarity about the board's role. In the interim, she provided a review of FACA, reminding the members that this group uniquely creates consensus advice from a variety of views for this office in an actionable way. Transparency and openness to the public and the independence of members are also elements of the FACA-chartered board. All members are representative and come with known biases; these biases and points of view are balanced and speak to the care with which OGAC selected the membership in order to ensure that balance.

Report and Recommendations to the PEPFAR SAB on the use of Test and START

Test and START Expert Working Group (EWG) Brief

Dr. Currier presented the PEPFAR Test and START EWG's report and recommendations, explaining that the EWG had worked together in multiple conference calls over the span of one month. The group utilized a series of guiding questions in examining issues surrounding early treatment. These questions were as follows:

- What are key logistic and operational considerations in Test and START initiatives (e.g. capacity, host MoH, ethics)?
- What lessons learned from test and treat among pregnant women in B+ settings should be applied to Test and START?
- What are recommendations regarding establishment of priority populations and countries for Test and START initiatives?
- How may PEPFAR best proceed in Test and START initiatives that address critical implementation issues along the clinical cascade (testing, linking to care, ART initiation, viral suppression, and retention), particularly in males 30-50 years of age and in key populations?
- What are other priority questions the EWG and PEPFAR should consider in Test and START initiatives?

Treatment is already a mainstay, and early ART has shown clear benefits; the challenge now is to determine the most efficient and effective way to implement early intervention.

Scientific Evidence and WHO Guidelines

It has been known for a long time that early treatment can delay progression of disease, but no definitive, randomized trials of people with CD4>500 starting ART had been performed. However, we did have early evidence suggesting that early treatment would improve survival over time.

The HIV Prevention Trials Network (HPTN) 052 trial and companion Hepatitis & HIV Clinical Trial Group (HCTG) component taught us that immediate ART provides benefits. In that trial, HIV+ individuals were randomized to immediate ART or ART delayed until CD4<250. The analysis showed clear benefits of early treatment for HIV+ individuals in terms of a reduction of clinical events, most commonly TB. The START study, a randomized trial of 4,685 HIV+ adults CD4>500, has now provided definitive evidence that early treatment for CD4>500 is beneficial to health outcomes and life expectancy, with no additional harm. This allows us to move forward with early treatment.

The revised WHO Guidelines recommend ART for all individuals diagnosed with HIV: "Antiretroviral therapy (ART) should be initiated in everyone living with HIV at any CD4 cell count." This encouraging statement bolstered the EWG's recommendations.

Principles Behind the Recommendations

Dr. Currier shared the general principles discussed by the EWG in its development of the group's recommendations to the SAB. She added that this proposal is not simply a plan to continue to treat and to provide treatment to more people, but is a new approach of "treatment for your own health". This is a shift away from treating pregnant women only for the sake of their children and from sending people away because they did not need treatment for their health.

Treatment for health includes prevention of infection or staying healthy once infected. Therefore, the EWG asserts the importance of:

- **Expediting Test and START implementation**
    - Critical implementation science research in the field, such as the combination prevention studies, should be used to define best practices.
- **Concentrating initially on high-burden sites** and using that experience to **optimize program delivery** in rural and peri-urban lower-incidence settings
- **Prioritizing the sickest people** during the Test and START rollout, as this is an ethical imperative
- **Improving access for children and adolescents** with HIV/AIDS
- **Improving and enhancing the education of all healthcare team members** in the benefits of prevention and treatment of Test and START
    - Message: We are using treatment to keep people healthy, not simply to prevent death.
- **Strengthening viral load testing**
    - This informs adherence and allows this modality to be used most effectively.

<u>Recommendations</u>

Testing

Support from national programs is critical to Test and START. Being able to provide treatment to those who test positive and offer evaluation of the benefit of PrEP to those who test negative creates an intersection for prevention and treatment.

Barriers for treatment need to be removed at testing centers, and all providers need to be educated about Test and START. Wherever possible, integration of treatment into testing centers should occur, along with risk reduction counseling and clear instruction on accessing services. All counseling messages should be reviewed to ensure their clarity, and mental health services should be included in the testing milieu.

Linkage

For social acceptance and normalizing HIV treatment as a medical intervention, it is imperative to develop non-technical public messages promoting Test and START. All health providers should be trained in the change in paradigm, with nurses and peer-educator instruction emphasized. The workforce should be expanded to include others so that nurses do not bear the load of task-shifting.

The EWB also recommends that CD4 testing be removed as a barrier to providing treatment; the lack of availability of CD4 testing should not preclude one's ability to offer treatment. Deliberation about how to work around that lack of testing availability is necessary.

Service delivery needs to be increased and strengthened, with the addition of clinic locations, staff, and hours of operation. Health centers need to deliver multiple services—testing, prevention services, and treatment. Finally, mobile and community-based resources should be employed to link people to care more efficiently.

Treatment

It is crucial that we redefine and emphasize comprehensive HIV care to include TB screening, IPT, evaluation of vaccine status, sexually transmitted infection (STI) testing, and contraception.

We need to expand point-of-care diagnostics and to integrate PMTCT programs into ART. Countries that have rolled out B+ have experienced successful integration and could serve as models to other sites.

Expansion of viral load testing and monitoring of adherence are important to our efforts. As well, we need to develop differentiated care means to avoid requiring people return to clinics every three months; possible mechanisms include adherence clubs, ART dispensation at testing sites, and motorbike ART delivery. Efficiency and savings will be realized once care is expanded in a way that allows people with undetectable viral loads to receive medicine in a community-based setting or to return to clinics only every six months or even annually. University of Cape Town's Institute of Infectious Disease and Molecular Medicine's Desmond Tutu HIV Centre Deputy Director Linda-Gail Bekker, PhD shared interesting data from South Africa about adherence clubs, with one representative collecting the medications for all club members as long as no member is experiencing acute issues.

ART needs to be compatible with hormonal implants and other long-acting reversible contraceptives, such as IUDs and vaginal rings, so that family planning is integrated into ART delivery. And, second-line ART for HIV-infected patients failing first-line therapy needs to be improved to utilize best option, low-side effect versions. New, improved options must be integrated as they become available.

Finally, as treatment has become, and will continue to become, more effective and successful, we need to shift the paradigm for community support teams from AIDS-related mortalities to age-related morbidities.

Treatment services present a definitive need for adjustment and innovation.

<u>Summary of Recommendations</u>
Test and START is a paradigm shift from stopping death from AIDS to stopping AIDS itself. It will require massive, long-term, consistent investment in training, communication, staff, facilities, and infrastructure. The investment is worthwhile, as people we treat now and those we get on prevention will not need future treatment, and that will help us get on the blue line so that we do not add more people who will need treatment later.

We need to continue to innovate wherever possible to make treatment effective. There has been massive investment in combination prevention studies that are evaluating some of these issues, such as whether to start people on treatment the day they visit the clinic vs. waiting until later to begin treatment. The information that informs best practices will come from current studies in the field, and that knowledge will be critically important to the success of our future efforts.

<u>Test and START Q&A Session</u>
Dr. del Rio thanked Dr. Currier and echoed her explanation of the workings of the EWG, of which he is a member. He noted that her presentation distilled much of the discussion that occurred among the group.

Question 1: Jean William Pape

Thank you for your presentation. We have an ongoing NIH study that we call "Same-Day ART". I believe this will be easier to implement and to scale up than PrEP. The biggest issue for rapid implementation will be TB diagnosis. If we do not emphasize this early on, people will die from acute TB. That will create a huge problem for implementation.

Answer: Carlos del Rio
Excellent point.

Question 2: Mark Harrington
A few weeks ago, I attended the IAPAC Treatment as Prevention (TasP) PrEP Evidence Summit in Paris. I asked the following of some of the people who are doing community-based population research studies on test and treat: Had they notified their catchment areas, population, or even their clinical trial staff about the results of starting Temprano? I was disappointed that the majority of them had not done so. This raises the issue that has been mentioned more than once today regarding study modification. Did this EWG discuss opportunities to modify existing studies to attempt to answer some more integrated questions around how to optimize outcomes within programs without having to bust the budget?

Answer: Judith Currier
I suggest tabling that question until later today. One area we discussed was the fact that not everyone is aware of what is occurring, including the different trials. We talked generally about how information reaches and informs PEPFAR from ongoing research studies. What is the channel, and what is the mechanism by which this news is shared? How do we ensure the delivery of what is being learned? We did not discuss anything specific to any studies.

Answer: Carlos del Rio
There is an afternoon session dedicated to this topic. That is clearly a subject in which the SAB needs to be involved.

Question 3: Ruth Macklin
I want to ask about priority-setting, one of the most difficult issues with which anyone deals—how to set priorities and what those priorities are. The subject comes up in two places within the presentation, under guiding questions and again under general issues. The second mention—"Prioritize the sickest people during Test and START rollout: This is an ethical imperative"—can be based on the underlying principle of "Serve those in urgent need". Regarding the first mention—"What are recommendations regarding establishment of priority populations and countries for Test and START initiatives?"—what parameters or criteria would be used? After addressing the sickest, who is next, and how would one decide? On the basis of a country? A population within a country? A range of possibilities beyond "the sickest" exists, such as "those who are hard to reach", who are likely to get worse because of their inaccessible locations. I believe that the criteria for selecting the priorities need to be spelled out, at least in rough categories.

Answer: Judith Currier
We did not grapple with that issue as much as we should have or could have, as we ran out of time. I do think it needs to start at the country level. As for within countries, I am brainstorming one approach: If the goal of Test & START is to reduce morbidity and decrease incidence, we want to prioritize high incidence areas.

Answer: Carlos del Rio
This is a huge issue, and the conversation reminds me of something that happened here in the US when CDC tried to prioritize certain states as high-impact states. My experience while in college in South Carolina involved state legislators deciding they did not need to invest any more funding into HIV because CDC listed the state as a non-priority. The challenge is that local efforts are withdrawn when the state (or country) is not named a priority. More than just a scientific issue, it is a political issue. How do you message this in a way that tells people that they are not a priority but are still important and that they need to focus on the issue?

When I was involved with research in Mexico, we were given the news that we did not have an incidence rate high enough to be part of the studies. It was seen as "good news but bad news", as the researchers and others very much wanted to be included in the study. This all presents a challenge, because delineates with whom you are not going to work.

Question 4: Mitchell Warren
Regarding prioritization, I want to call attention to the sense that exists in many governments and implementing agencies that treatment needs to come before PrEP. I want to clarify that PrEP and treatment share HIV testing as a gateway. They also share drugs or drug combinations. PrEP is as much a part, or more a part, of the prevention landscape, and I would hate to see us not act on it because of a priority on treatment. We need to view PrEP not only as part of treatment but also as part of prevention. We would need to be very explicit about not making big recommendations that create unintended consequences.

Answer: Carlos del Rio
This is a big issue. For example, we do not want to be unable to treat the sickest because we have used all of our Truvada in prevention. We need to be careful about how we address that.

Question 5: Connie Celum
Thank you, Dr. Currier. I would like to point out a place in which we could be even more specific. If we assume that we need to double the number of people in treatment and that resources are relatively flat, the only solution is to use the metric of cost-of-person-treated as a target. We would need to decentralize care, spread out visits (this could paradoxically improve retention), replace CD4 testing, and be smarter about lab testing use.

Answer: Judith Currier
I agree with that approach. Using local data and targets, we could start with how much money there is to spend and develop goals within that.

Question 6: Rev.Edwin Sanders
I appreciate the comments that were just made. Over and over, we see these overlapping and parallel dynamics that continue to point to priority populations. Perhaps we do not often enough utilize various mapping initiatives that have already been done, around food shortage and other determinants that always seem to be in parallel regarding incidence; that could assist with prioritizing communities.

Regarding prevention vs. treatment, prevention has consistency while treatment is a shifting landscape. Social determinants of health (SDoH) can inform decision-making in that arena as

well. I am adding to the references made already in conversation, as we so easily get in our silos of research and forget to appreciate what is happening in other areas that can inform our work and allow us to project with some effectiveness where the priorities lie.

Question 7: Jennifer Kates
The new WHO guidelines clarify to those who work on HIV that this is the standard of care; that is a really powerful statement. The EWG recommendations are great; I would like to propose the following friendly amendment: New money does exist to fund what we are discussing, so this approach, which makes so much sense scientifically, needs to be something PEPFAR does in concert with The Global Fund and others. We need to identify the places in which Test and START can be fully implemented, but the US government cannot do it all alone. A recommendation should include collaborating with partners to determine the best way to pool resources to create the scale-up.

Question 7: Christine Nabiryo
Thank you to the EWG. None of this can happen without the strengthening of community health systems. A discourse is being led by The Global Fund around this issue; there is need for PEPFAR to link into that and see how that can be integrated or cross-referenced in our suggestions.

Question 8: Angela Mushavi
Thank you very much to the EWG. From a country perspective, this recommendation is something countries would not have much difficulty implementing; they have, over time, experienced positive results from treatment for the health of the people, returning them to the labor force, and more. There are clear social, economic, and health benefits to treatment. In terms of embracing Test and START, I participated in the WHO guideline development group, and I can report that conversation is already ongoing at the country level; that makes this recommendation manageable for countries to consider. Based on the HPTN 052 trial, we have a clear HIV prevention benefit as well. We have demonstrated 93% reduction in HIV transmission with early ART, very efficacious in terms of prevention.

To situate the benefit of PrEP in that context and to get the political buy-in for that prevention, I believe that we need to message this carefully. It is clear to me that, with a resource envelope that is not expanding and difficult decisions to make, most countries would likely choose Test and START over PrEP. Please explain the benefit of scaling up PrEP to the same degree as the Test and START scale-up. If you had limited resources, where would you put your dollars first?

Answer: Carlos del Rio
That is the really complicated question that every political leader in every country is likely asking. I defer to Connie Celum.

Answer: Connie Celum
Your very well-asked question partially illustrates why the PrEP EWG brought its thinking beyond young women. The demonstration project conducted after the efficacy trials showed that PrEP can be delivered in a time-limited, cost-effective way in serodiscordant couples. To take a holistic approach, scaled-up testing could identify these couples (noted at 67% in one study) and then offer the HIV- partner limited (six-month) PrEP while the HIV+ partner receives immediate adoption treatment and moves to become virally suppressed.

I hope we can avoid pitting these two strategies against one another, because we have also found that this a shared burden for couples. If you were to do something now, I would suggest partner testing and scaled-up treatment regardless of CD4 count. I would divert some approaches out of CD4 testing around viral load into community-based approaches. In parallel, we must conduct testing for young women, because we are not going to quickly solve issues around testing men and getting them on treatment.

Answer: Judith Currier
The two working groups were developed because we needed to engage in significant discussion around both areas. What country directors really need is to learn how to integrate the two in a national program. Bringing these two things together will be a critical challenge through which a lot of good assistance could be provided.

Answer: Carlos del Rio
This is a good place to begin working to strengthen health systems and impel them to work together.

Question 9: Celia Maxwell
This is an excellent presentation and a great start. I have a question regarding long-term retention and care. We deal with treatment fatigue, and I wonder if incentives could be attached to the support and the motivators. When we maintain individuals in treatment, we make a significant impact.

Answer: Judith Currier
The EWG discussed retention, particularly what lessons have been learned from rolling out B+ in countries where they have had that experience. The sobering findings show women not staying in care after a time. I think that messaging around Test and START needs to clearly promote the benefit to individual health so that it becomes the motivator for long-term adherence. Not understanding the need to remain on treatment, distance to clinics, and other factors could be involved. Work ongoing in the field can inform the best ways to promote adherence.

Answer: Carlos del Rio
I think we are spending a lot of time and effort globally testing people and linking them to care, and we are not focusing enough on retention. This is not about retaining people over a year, and I wonder how we retain people over a lifetime in an effective way. These implementation issues will affect not only HIV but chronic conditions such as hypertension, diabetes, and many others. Designing the healthcare system for long-term retention and optimal outcomes could benefit health systems overall.

Question 10: Etienne Karita
Thank you for your presentation. I think that the example of the implementation of the Peer InterCity programs. This example should guide us should inform implementation of Test and START. How can we increase the opportunities for people to get tested? For the Peer InterCity programs, we have integrated HIV testing and antenatal care. In the context of the healthcare facility, can we consider an opt-out HIV testing approach to everyone who visits?

Answer: Judith Currier

I think that is a very good idea. The Sustainable East Africa Research on Community Health (SEARCH) study has presented some very exciting data about its massive cross-disease testing campaigns in communities in which HIV testing has been integrated into screenings for hypertension and diabetes. That successful approach needs to be replicated in other settings, as you suggest.

Answer: Carlos del Rio
I agree wholeheartedly. We cannot back ourselves into a corner by siloing HIV. We need to normalize HIV testing as part of integrated care. I am on the Data and Safety Monitoring Board (DSMB) of SEARCH, and SEARCH has been great at finding people with HIV but has been even better at finding people with hypertension and other problems! The question is, how do we use HIV delivery to test and treat across the board and to improve overall health?

Question 11: David Peters
I love the work of the EWG. This appears to be another "license to act" with more local implementation research in terms of how to do the work and balance it with budget constraints and other barriers. I like the idea of efficiency metrics around cost per treatment; I just want us to become and remain aware of unintended consequences if they are unbalanced. Particularly, if one of the priorities is to reach critical populations, costs may be higher. We need to balance money issues with individual treatment ethics and strategic goals.

Answer: Carlos del Rio
I was thinking the same thing; some patients I treat in my clinic are very expensive because the only way to get them into care is to provide them with many other things that normal individuals do not need. Not taking care of those individuals brings the cost of care down; however, I believe the ethical imperative is providing those people with therapy irrespective of the expense. Factors beyond cost need to be considered. Transportation, food security, and other factors need to be addressed.

Question 12: Kenneth Mayer
Both EWGs have done great work. Dr. Mushavi raised a question about balancing choices that are on this and every table. We need to take the PrEP recommendation out of the treatment landscape and bring it into the prevention landscape. The common theme is about how to do more with flat line budgets. It is not necessarily about doing all the treatment and then looking at PrEP but about doing treatment and rethinking what prevention looks like and how to deliver it. Perhaps the next EWG that needs to be developed is one that looks at giving meaning to combination prevention for PEPFAR, for countries, and for UNAIDS in this new era of normative guidance.

I think we should be providing treatment for all now, and I think we should be utilizing PrEP when possible and for people at substantial risk as part of combination prevention—not to be treating with PrEP.

Answer: Carlos del Rio
I disclose that I am part of the group that authored a paper for the IAS, USA on this subject. We discussed behavioral prevention and biomedical prevention, and it was a difficult discussion, as many research results are not scalable and cannot be implemented. However, we must acknowledge that many of these things, such as getting tested and taking one's medications, are

driven by prevention. What we have developed as a science around prevention must be scalable to the levels we want to create.

Answer: Kenneth Mayer
In very well-resourced countries where permissive guidelines have existed for many years, rates of biologic suppression are still not optimal. We need to be realistic about the kinetics of getting everyone who needs treatment on it and stably biologically suppressed. It is very important to have the PrEP conversation now, because we need to bring more people the benefits of treatment.

Answer: Carlos del Rio
The question is, how do we do it? How do we make prevention and treatment work together to decrease the number of new infections? This is still the question on everyone's mind.

Question 13: Frederick Sawe
With test and treat, patients are missing from care. I think using prevention improves overall retention.

Dr. del Rio thanked Dr. Currier for the discussion.

Recommendations and Vote
Dr. del Rio recommended that the SAB approve the following:

1. We are in consensus agreement with the Test and START EWG document and its initial recommendations.
2. We are in consensus agreement that PEPFAR expedite the implementation of Test and START.
3. Opportunity for comments on the document will last for the upcoming two weeks.
4. The Test and START EWG will bring back to the group specific recommendations on prioritizing treatment, thereby finalizing a document for presentation to AMB Birx.

There was unanimous agreement on all points.

PEPFAR Updates
Dr. del Rio commented that we have affected a lot of the reachable populations. Reaching the next group of populations, such as the asymptomatic population and those in very remote areas, will be more difficult. A lot of implementation questions need to be addressed.

Dr. Shaffer, on behalf on the OGAC staff, again expressed appreciation for the highly insightful discussion around the core specific questions laying the foundation for some of the next steps and activities of the SAB.

As Dr. del Rio mentioned, WHO guidelines recommending treatment for all regardless of CD4 count and recommending PrEP were released on September 30, and IAPAC released its guidelines across the continuum of care the very next day. OGAC staff had forwarded the guidelines to all SAB members, and the IAPAC guidelines can be found on the organization's website. PEPFAR's activation of two EWGs—focused on two cornerstones of the new WHO guidelines: PrEP and Test & START—was a way to catalyze rapid advice about how to move forward implementing the new guidance.

WHO Guidelines-Inspired Discussions

Time was reserved to receive SAB members' thoughts, discussion, and advice around the WHO guidelines in two additional areas:

1. Are there remaining topics and questions that should be discussed around PEPFAR-supported programs and around Test and START or PrEP?
    a. We are hearing a very solid message that several EWGs are needed—around combination prevention, data use, and financing and sustainability. These questions will likely develop into work activities for the SAB.
    b. Dr. del Rio will facilitate the discussion.
2. Are there other PEPFAR program implementation issues that need to be considered?
    a. The SAB is asked to consider issues related to PEPFAR-funded combination prevention trials—not to redesign the studies or go into the details, but to look at necessary prioritizations based on a rapidly changing global standard of care.
    b. As Dr. del Rio serves on the SEARCH DSMB, Dr. Currier will facilitate this discussion.

<u>Facilitated PEPFAR Program Discussion</u>

Dr. del Rio raised two issues for discussion around implementation:

1. Integration of HIV care, PrEP, and more into healthcare systems
    a. Different models will work in different scenarios. It is important to document and understand a host of designs.
2. Integration of HIV treatment with treatment of TB specifically, as well as with other diseases
    a. This is necessary in order for implementation to be scaled up on a significant level.
    b. We need to learn from disseminated studies and need to apply best practices.

Dr. Berman asked if PEPFAR has quantified evidence of who is delivering which types of services to which people in populations in countries where it works—that is, is it happening through an integrated primary care facility, an HIV-specific clinic, a hospital infectious disease department, or another site? Are we mapping where certain services are being provided according to a typology of health care delivery structure? With the awareness that poor data exists in this area, Dr. Berman recommended quantifying service in a programmatically meaningful way using existing delivery survey instruments. A deep richness of understanding delivery systems would serve as an important analysis for addressing structuring of the delivery system for integrating services or expanding their scope.

Dr. Celum described, based on discussions with her contacts, the reporting in PEPFAR-funded countries as "numerators", which she called understandable. She asserted that the new guidelines should force, at the national level and ideally at a more granular one, delineation of the denominator; COPs should focus on who is being missed and how service is to be provided in a cost-effective manner.

Secondly, Dr. Celum expressed the need for a critical review of what has been funded under the rubric of treatment in order to speak to the new prevention targets.

Mr. Harrington reflected on two important elements related to TB and HIV:

1. The TEMPRANO Study indicated the additive value of early combined ART/IPT.

2. Karoline Aebi-Popp, MD stressed the importance of TB screening as part of the ART/START process.
    a. This is highly pertinent, as ¼ of people with AIDS die of diagnosed TB, and another ¼ likely die from TB that is never diagnosed.

Mr. Harrington explained that IPT serves as both PrEP as well as disease prevention for those with latent illness. WHO has developed its "Three I's" strategy for TB/HIV scale-up: intensified case-finding (ICF), IPT, and infection control (IC) at all clinical encounters in HIV care settings. He suggested that the burden of providing that care falls on the AIDS program, as HIV+ individuals are dying of TB. He noted the generally holistic approach of the HIV community and promoted investigating the TB crosslink, it being another opportunity for health systems integration and saving of resources.

Mr. Harrington reported that someone who is co-diagnosed with HIV and TB and is started on TB treatment but not on ART faces a much higher chance of mortality. He explained that many such people get sent to a TB program and have no re-linkage back into HIV care when they are ready. Mr. Harrington asserted that PEPFAR and The Global Fund could have a major impact and could affect huge efficiencies downstream if they get countries to perform such work and to document it.

Dr. Siemens affirmed that integration of services is vitally important to handling the workloads and the costs. He noted that HIV care has not been integrated, with diagnostic and treatment facilities invariably off campus or, at a minimum, in a back room. Biases must be superseded, and ways of integrating and of scaling using existent infrastructures need to be developed. If care is delivered in silos, it will be cost-prohibitive.

Regarding priorities, Dr. Siemens added that all of the work being discussed is prevention; the reality is that treatment equals prevention of morbidity and mortality, while PrEP is about preventing new infections. He asserted that we need to think about and promote both PrEP and treatment as prevention strategies that are imperative for our future.

Dr. del Rio added that labs are separate facilities, and that a major focus needs to be placed on integrating them around prevention.

Mr. Warren asked that explicit mention be made in both sets of recommendations focusing on the word "offering" as these documents appear in the public domain. There exists a fear that PrEP and treatment are being coercively forced on individuals, and Mr. Warren suggested that PEPFAR be exceedingly clear with messaging around the offering of services, be it ART or PrEP.

Dr. del Rio followed Mr. Warren's comment with a report that this subject was discussed at length in the Test and START EWG. He pointed out the acute difficulty in reversing the messaging after many years of assuring people they did not need to be in therapy. Regarding the offering of prevention and treatment, the question lies in how these are presented; if the community health worker or physician is not convinced that the service is helpful, s/he is not going to offer it as it needs to be offered. Dr. del Rio affirmed the need to change how people think, particularly through initial community-level health care provider training. The challenge here is not to be underestimated.

Dr. Currier acknowledged the strong emphasis on initial treatment, when people are actually going on regimens for the rest of their lives. She stressed the importance of investing in ascertaining how to maximize the benefit of the treatments that exist over the longest possible duration. We need to integrate new tools such as testing, or we will cycle through drugs far too quickly. A lot of knowledge around doing that most effectively needs to be assembled.

Dr. del Rio added a comment made by one of his patients: "HIV is no longer a death sentence, but it is a life sentence." While HIV doesn't kill the infected person who is being treated, treatment lasts a lifetime. He expressed concern that, with the push to get more people on therapy, the risk of utilizing suboptimal therapy due to its lower cost—for example, drugs no longer being used in this country—is real.

Dr. Auerbach asked the reasoning behind the short duration of funding for the DREAMS partnership given the need to collect significant data around adolescents and young women. She then noted the lack of, and need for, political scientists involved in analyzing successes and failures. She recommended seeking opportunities to embed systematic social science assessments in PEPFAR's programmatic activities to collect real data on such topics as the role of stigma and discrimination in affecting implementation. Also, the messaging shift around the need for treatment will likely cause a range of reactions—including one that pharmaceutical companies are trying to sell more drugs—and that should be systematically documented and analyzed. Assessment as part of PrEP, DREAMS, and Test and START would provide some burden of evidence and data that could be used to explain what is and is not working.

AMB Birx outlined the parameters around funding initiatives based on the federal funding cycle of approvals. Because of the funding cycle, there are restrictions of the bounds of the initiatives funding right now, but the only way that critical initiatives such as ACT and DREAMS would not continue would be if they fail. That is the reason the targets for those programs are so important.

AMB Birx then weighed in on the issue of cost. She explained that, when PEPFAR began, the cost driver was the medication; now, the cost of service delivery is 3-4 times the cost of the drugs because the cost of drugs has decreased dramatically. In the discussion of modifying ways patients are followed or of altering the service delivery model, it becomes clear that that twice as many people could be on treatment if service delivery costs were decreased by 50%. Integration needs to be viewed in a novel way. The focus needs to be on how other (non-HIV) programs integrate HIV elements into care while we continue to integrate family planning and other services into HIV services.

Stand-alone clinics have essentially vanished due to direct referrals to health centers. This poses a new set of challenges, as men do not access the healthcare system in the same way. Maternal-child health clinics abound, but no men's clinics exist (although male wards are in fact part of the women's clinics).

AMB Birx again expressed her appreciation for the consistent thought process of the SAB.

Dr. Nabiryo asked how sustainable financing fits into PEPFAR and what the SAB's role would be in that area. She added that someone needs to be focused on the money and determining from where investments and support will come. She mentioned that UNAIDS is doing some of this

work and suggested that perhaps PEPFAR's documenting of expenditure analysis could add to the discourse. She debated whether this is a cross-cutting area that could be integrated across discussions or whether, as such an important issue, it needs its own working group and focus.

Around sustainable financing, Dr. del Rio discussed the ending of the MBGs, which comprised limited goals including HIV and which were incredibly helpful to getting this work to where it is today. He explained that the SDGs are many, one of them being the broad "good health" with nothing specific to HIV. Dr. del Rio shared his worry about diffusion of resources with so many goals and stated that this issue has huge global health implications. What, he asked, will happen to global financing on HIV once the SDGs take place? He deferred to Dr. Kates, who supported creating an EWG around the issue of financing and sustainability.

Dr. Peters noted that the discussions in this meeting have focused around integrating for the sakes of affordability and sustainability as well as around person-centeredness. He pointed out the importance of recognizing that integration does not always translate to better efficiency or effectiveness, depending on the specific outcome markers. For example, decentralization of care can lead to an intervention having the same label across locations while looking entirely different in every place it is conducted.

According to Dr. Peters, integration is partly about managing stakeholders in different contexts and about identifying common principles. It will also bring us back to questions around data; if the question is which platforms can take on more HIV services and what other services HIV can take on, there is a need to have a much broader way of incorporating the discussion. Stakeholders may not be used to dealing with their issues in that larger context.

Dr. Peters added that this programming will not be one size fits all, and the need is great for stimulating more "Malawis"—countries that are developing programs themselves based on their particular populations, needs, and outcome goals.

<u>PEPFAR Programmatic Activity Wrap-Up</u>

Financing and Sustainability

Dr. Shaffer shared that financing and sustainability is a key component of *PEPFAR 3.0: Controlling the Epidemic: Delivering on the Promise of an AIDS-Free Generation.* OGAC has been very fortunate to have Mike Rutherford from the US Department of the Treasury involved in this area, and there appears to be great interest in developing such a group. Dr. Shaffer noted the incredible expertise at the table and the wonderful resources available through OGAC to support a Financing and Sustainability EWG.

TB/HIV

PEPFAR acknowledges its commitment and passion around TB/HIV as well as the significant amount of work that remains to be done in this area. Dr. Shaffer noted that relevant guidelines have not positively affected care on an acceptable level and that the development of a TB/HIV EWG looks to be necessary.

Combination Prevention and Prioritization

Dr. Shaffer conveyed that OGAC looks to the SAB to make considerations and subsequent recommendations. Today has illuminated tensions around funding and prioritizing PrEP and around Test and START. Also, combination prevention as it relates to implementation science

and research will soon be discussed. Dr. Shaffer highlighted a need for a cross-cutting Combination Prevention EWG, which he suggested Mr. Warren may be willing to lead. He acknowledged the difficulty of these decisions and added that recommendations across the issue areas are appreciated.

Data

Data-related issues include determining the level of granularity of the data in hand. PEPFAR has unique data down to the facility level from the most recent set of COPs, and it is important to have a group look at the substantial data and at the expenditure analyses. POART is working with partners in each country to collect and analyze quarterly site monitoring data, indicators, targets, and achievement of goals; this provides a unique opportunity to triangulate data. OGAC would welcome an EWG to explore what data exists, disseminate the information, and develop programmatic recommendations.

Facilitated Discussion of Combination Prevention Trials

Dr. Shaffer noted the natural progression in the agenda to a discussion of prioritizations, sustainability, and funding decisions in light of the new WHO normative guidance. PEPFAR welcomes the SAB's recommendations.

Dr. Shaffer called members' attention to a document in their meeting folders presenting contextual information around the PEPFAR-supported Combination Prevention Trials (CPTs) as well as a list of discussion questions. He then offered an overarching background and picture of the CPTs in order to create a context for today's discussion:

In fall 2011, PEPFAR announced three CPT research awards to examine the effectiveness of combination approaches to HIV prevention (combination prevention, or CP). These CPTs were implementation science studies, designed both to inform how best to provide interventions and to understand the impact of the CP approach by directly measuring HIV incidence. Early ART was a cornerstone of the intervention package in all studies, which includes enhanced HIV testing and linking to care, VMMC, PMTCT, and condoms. In most, but not all, of the CPT study countries, national treatment guidelines moved from CD4<350 to CD4<500 before study implementation occurred, or shortly thereafter. The studies in those countries have been amended to reflect the updated guidelines.

The three CPT studies take place in Botswana, Kenya/Uganda, and Zambia/South Africa. The overall budget is roughly $240 million; of that amount, about $175 million has been transferred to study sponsors and the remaining approximately $65 million is yet to be transferred. All studies are overseen by DSMBs, two—BCPP and PopART—by a single DSMB and SEARCH by its own DSMB.

Two of the studies are roughly one year into implementation and cohort follow-up, and the third is more than 1.5 years into implementation and cohort follow-up. All studies are projected to report out in late 2017 or early 2018. Following the release of the START Trial results—which served as both the definitive trial demonstrating benefit for treatment of all adults regardless of CD4 count and as a major foundation for the new WHO guidelines—the study principal investigators (PIs) and their teams have held discussions with local partners and have been preparing amendments to their studies to adapt to the evolving standard of care. All of the CPT PIs met with AMB Birx, and the sponsors met after the START Trial results were released in May;

this topic was a large part of the discussion. The new guidelines have since shifted the standard of care.

Dr. Shaffer added that the goal of this overview is to inform the SAB's discussion around its consideration of questions. He reminded members that they are representatives and asked that they disclose any involvement with one or more of the studies being discussed here. He recalled that Dr. del Rio is a member of the DSMB for the SEARCH study.

Discussion Question 1:
Dr. Currier pointed out that each study has a DSMB and that all are designed to compare the intervention with the local standard of care, with the understanding that the standard may evolve. She then presented the first of the discussion questions to the group:

What is the impact of the new WHO guidelines recommending treatment for all regardless of CD4 count and PEPFAR's aggressive Test and START strategy from a programmatic perspective upon clinical equipoise as it relates to the CPTs and their continued funding?

Dr. del Rio requested an update on the French large HIV CPT study—Neurobehavioral Rating Scale: an interrater reliability study in the HIV seropositive population—expressing curiosity about the direction of discussion around it. Dr. Shaffer reported that the study was presented at the International AIDS Society (IAS) Conference in July, and AMB Birx added that the study is expected to be completed within the next 12-18 months, with data to be provided in 2016.

AMB Birx explained that the PEPFAR-funded CPT studies opened in the 2010-2011 time frame, with plans for complete enrollment by the 2012-2013 time frame and report-out in the 2015 time frame. However, a slip of three years occurred for a couple the trials due to significant granting delays, enrollment and intervention roll-out. She added that, when AMB Goosby launched the trials, the commitment was that they would be completed with data in four years; the current projection is 6-7 years, and possibly even longer.

AMB Birx also clarified that while the study money has been transferred, just half has been spent. A significant amount of money went to partners for implementing the services noted in the PEPFAR intervention arm, such as Test and START.

Dr. Mayer called attention to the fact that these studies are CPTs and that other factors being studied include various methods of providing counseling and testing; scaling up VMMC; and coordinating around other health conditions, such as SEARCH does.

Dr. Mayer expressed hope that the sovereign nations in which the studies are being conducted can be encouraged through PEPFAR to consider their timelines for scaling up WHO-guided implementation, being aware that it will not happen instantly. These are complex conversations between the implementers, biostatisticians and bioethicists who will play key roles as appropriate due diligence is performed for people who need treatment and could have access to it. Dr. Mayer suggested that a biostatistician could calculate what it would look like if everyone was on treatment tomorrow, and then that could be scaled back to what will happen to the rate of implementation at the various sites. It is a challenge that is real but not insurmountable or problematic in terms of lessons learned.

Mr. Harrington reflected on something done after the Surrogate Markers for Assessing Response to Treatment (SMART) trial was released: A multi-stakeholder meeting including every research group, with representatives of all of the communities involved in the studies, was convened; at the session, all research groups presented their studies and discussion followed. A consensus emerged that studies using treatment interruptions should be continued with modifications while other studies were likely superfluous and needed to be closed. With that experience in mind, Mr. Harrington proposed that a larger group be convened to engage in these very important discussions. Dr. Currier agreed strongly with that suggestion.

Mr. Warren posed what he identified as the missing question: When the SAB meets at the end of 2017 or in early 2018, what results would we expect and actions would we want to have taken? We have already recommended moving ahead with Test and START and want to move PrEP. However, none of the three trials have included PrEP, and that is an enormous challenge in this moment. "With the WHO guidelines released, how does a 2015 CPT not provide PrEP?", he wondered. These trials could become a pivotal setting to transition toward answering this question, which needs to take the form of a conversation between investigators, countries, and current funders.

Mr. Warren purported that the advisory board can determine what more information PEPFAR needs and the best ways to collect that information. One option may be to retool studies with input from trial investigators and the community at large. Regardless, it is necessary to determine the critical questions and to ask and answer them in the most appropriate and cost-effective manner possible. Course correction can be made if current trials don't fit with the community vision.

Dr. Auerbach endorsed Mr. Harrington's and Mr. Warren's comments and suggested that too many questions are presenting themselves than can be answered without more voices and more information. The DSMBs will evaluate science and ethics, but underlying questions exist around financing and prioritization, among other considerations. She recommended that PEPFAR bring together stakeholders in the way Mr. Harrington suggested.

SAB members agreed that trial leaders should meet in light of new information and evidence that has become available.

Discussion Question 2:
Dr. Currier posed the second discussion question:

> **How does PEPFAR ensure that the insights from these rigorous research trials remain relevant in the current HIV treatment era and that they are translated at the program level?**

Dr. Celum shared, based on conversations with investigators, that trials differ in terms of how much they are truly CPTs. She suggested that at least two of the three trials could add PrEP at this stage. In order to make information translatable, treatment initiation needs to be done in the most efficient way possible. The question to be asking now is, how fast can you initiate treatment when all barriers to testing and treatment are removed? We need to be providing best practices in testing, simplifying ART initiation, and engaging men for both treatment and VMMC. Finally, Dr. Celum asserted that value would be added if trials could add PrEP in the next 3-6 months.

Rev. Sanders posed the question of whether bringing "unlikely suspects" to the table adds value to the discussion around the kinds of questions that have been raised. He also asked how PEPFAR can impact an outcome that looks like the ends discussed earlier today using the remaining resources, now that roughly $175 million has been transferred. What is the value of today's discussion in the context of that larger conversation?

Dr. Shaffer explained that PEPFAR has already received very helpful feedback around a role for PrEP as well as to have stakeholders beyond this group meet to consider questions around implementation. Regarding funding, there is an evolving standard of care in a budget-constrained environment, and the CPTs are large, important studies funded at a significant amount. The current level of funding activity would be continued, and the question of how PEPFAR will prioritize between PrEP and Test and START will be a continuation of today's discussions.

AMB Birx agreed with Mr. Warren's framing of the question—what answers will we have from these studies that PEPFAR needs? Can the studies be modified to deliver on what PEPFAR deems necessary or be terminated if not? She asked for specific direction from Mr. Harrington regarding convening stakeholders and investigators in the near future.

AMB Birx went on to say that feedback from the SAB is very important on this issue. The CPTs are currently mostly around treatment—testing and treating immediately or based on viral load. Some of the questions have been answered today; the need remains to determine the value added.

AMB Birx clarified that more than half of CPT funds are still available; they have been transferred but are sitting at the agencies and not with the partners. So, decisions can be made regarding directing $130 million based on determining the programmatic value of the trials. The feedback given around questions to address to the investigators is most helpful.

AMB Birx asserted that the focus is to push and aid the adoption of WHO guidelines, so waiting until countries change their guidelines is unacceptable. Every minute of inaction should be viewed as the loss of finite funding that could be going directly toward service delivery.

Dr. Currier contended that investigators have put a tremendous amount of time, effort, and thought into these CPT studies. They are conducting research on the ground and are learning what does and does not work, and they need to have the opportunity to articulate the studies' value and the way in which the research will inform program.

Dr. Mayer clarified the intent of his initial comments around countries potentially delaying incorporation of the new guidelines. He suggested that very skilled biostatisticians can utilize the data collected to this point to inform programmers as to what is likely to happen in each of the PEPFAR countries with the existing resources, with scale-up at the pace that each country is planning. He acknowledged that layering PrEP research adds complexities around beginning a whole new study. PEPFAR needs to proceed in an orderly fashion to learn as much as possible, and some of the necessary infrastructure may not exist in countries to support scale-up as rapidly as one might like. Dr. Mayer endorsed Mr. Harrington's and Mr. Warren's stakeholder-convening ideas.

Dr. del Rio added that ministries of health and communities need to be allowed to weigh in on decisions of how to move forward, as local people need to be informed and to be actively involved. He explained that, although the SEARCH study is considered a CPT, it truly is an implementation trial; people with high CD4 counts are being enrolled, in fact. He suggested that the true value of the CPTs may turn out to be even more about systemic functionality and integrated care than about specific treatments. We need to learn how to ensure people in very rural areas in Uganda and Kenya, for example, are identified, engaged, and offered testing for HIV and myriad other diseases, such as diabetes, hypertension, overweight, and malaria, and then immediately linked to care. Dr. del Rio characterized this as program evaluation or implementation science and expressed interest in having the SAB look at the studies from a place of implementation of early START; evidence demonstrates that early START works, but how do we execute scale-up?

Dr. Macklin questioned the potential of in-process modification of the trial design. She described adaptive trials, which are designed up front to include time points at which changes will occur. If feasible, and based on existing interim-point results, the CPTs could be adapted based on what has already been learned as well as on the WHO guidelines.

Dr. del Rio characterized implementation in a rapidly moving field as all about adaptive design and expressed his belief that the trials can be modified.

Dr. Kates offered the following question to pose to members of the larger stakeholder group when it is convened: If they were designing a CPT study today with the knowledge we now have, what would they do? Answers could then guide adaptation to bridge the current scenario with the ideal, incorporating the existing funding limitations.

Dr. Siemens disclosed his arms-length point of interest with an operations center for the HPTN program (FHI 360). He affirmed that the SAB is not in a position to make specific recommendations on trial modifications. However, he contended that it is important and justifiable to challenge the investigators to provide a sound rationale for proceeding on the current path in the context of the new findings, with the goal of moving forward one way or another. Dr. Siemens also asserted that stakeholders in those trials, be they countries or PIs, should weigh in heavily in the context of the new guidelines, and that the last thing that should happen is any delaying of those guidelines.

Dr. Celum expressed her wish to have at least one trial's investigators answer the following question: After almost two years of implementation after which there will be some effect, how much more effect (if any) do you get by including PrEP for young women and for serodiscordant couples, and does it motivate people to get tested and treated?

Mr. Warren added his emphasis to the role of in-country policymakers and civil society. PEPFAR has made huge strides in engaging civil society in the most recent COPs process, and there is still room for improvement. He purported that this is a wonderful opportunity to return to the existing mechanisms, which involve policymakers and civil society in those countries, to engage in the guidelines conversation. He suggested that using the countries' nascent infrastructures and soliciting input will communicate the importance of the issue and will engage stakeholders.

Dr. Currier summarized the discussion as producing an agreement to develop a convening of the CPT stakeholders. A process to consider the new information and how it affects the trials that involves input from the countries and the investigators is needed. Some very tangible questions and issues that have been suggested here can be addressed, while ensuring translatable findings.

Discussion Question 3:

Dr. Currier read aloud the final question:

Should an EWG under the SAB be convened promptly to further consider relevant implementation science questions and funding priorities?

Dr. Shaffer thanked the SAB for the discussion and the very helpful feedback around the CPTs. He reflected back to following to the group:

- The SAB endorses that the DSMB should meet promptly to address particular questions.
    - Dr. Shaffer expressed the lack of a need for specific EWG around this issue.
- PEPFAR will aim to quickly convene a stakeholders' meeting to include PIs, researchers, PIs, local stakeholders, and civil society.
    - PEPFAR can help inform that meeting with specific questions based on today's discussion, including:
        - If studies were designed today, knowing what we know from the level of evidence around PrEP and around Test and START, what would they look like? Can the current studies be adapted?
        - Questions around the consideration of PrEP in the context of DREAMS can be added.

Dr. Shaffer pointed out PEPFAR's limited budget envelope and expressed appreciation of the SAB's recommendation and counsel regarding priorities, with knowledge that funding challenges exist. That advice provides AMB Birx and OGAC staff with guidance on how to create the strongest impact with the resources available.

AMB Birx added her gratitude for the session. She recognized the deep commitment investigators have to their research and the potential difficulty in stepping back. The SAB's clear recommendations on how to proceed will be coupled with information to be provided by Mr. Harrington in order to develop a successful convening and a thoughtful and meaningful outcome.

Presentation: Affected Populations and Civil Society

A. Cornelius Baker, Acting Deputy Coordinator, Office of Affected Populations and Civil Society Leadership (OAPCSL), OGAC

Mr. Baker introduced the work of OAPCSL, explaining that this new office was created as a focal point for the human rights agenda. It is an element of AMB Birx's vision of implementation across the spectrum of sustainability, partnership, transparency, and human rights as they relate to HIV/AIDS. It includes gender, key populations, and civil society leadership.

OAPCSL is in the process of expanding its staff through a combination of details and fellowships (including Presidential management fellows). Two staff members are dedicated to work on the human rights agenda, and one is set to coordinate a cross-agency process around stigma. Two staff members are focusing on gender, and the key populations team is in the process of being

reconstituted. All staff members work on engaging civil society in specific projects as well as around the COP/ROP planning process, other central initiatives, and the work of the teams on the ground.

Mr. Baker noted that the stigma-focused staff member joined OAPCSL from the US Department of State's Bureau of Educational and Cultural Affairs Office of Sports Diplomacy. He highlighted the ways in which that background can help OAPCSL think about stigma in a new way—for example, adolescents are being excluded from activities, including sports, because of sexual identity or gender. Identifying ways to break down those gender and identity barriers very early on in the cycle as we are trying to influence adolescents' acceptability is key.

Gender Group

The Gender Group has been working on the implementation of the OAPCSL gender strategy. The gender assessments for all countries implementing DREAMS were disaggregated from COP/ROP 16. The office is requesting that countries submit gender strategy drafts in February for OAPCSL review prior to submitting their COPs and ROPs, which will include finalized gender strategies.

OAPCSL recently concluded gender and sexual identity and orientation diversity trainings for all PEPFAR staff and implementing countries, teams, and partners. The trainings, held at OGAC headquarters as well as in every partner country excepting of Burundi and Indonesia, were run by the Health Policy Project (now the Palladium Group). The goal of the training was to develop fundamental understanding of these issues by PEPFAR staff and implementation partners; this certainly will contribute to ensuring success in delivering and implementing prevention programs.

Mr. Baker shared an example from one of the trainings, which mix technical knowhow with personal beliefs: During COP reviews last summer, a PEPFAR coordinator reported that an advocate who spoke to a group was the cousin of a lead staff member; the advocate spoke about her work and her life as a lesbian. The staff member had not spoken to the advocate for 10 years after her family had disowned the cousin. The training created a reconciliation opportunity as well as an educational one for the staff member. Mr. Baker highlighted the fact that those who are making fundamental decisions about this work are, at the same time, living out the realities of stigma. Is it imperative that we help staff get to a place of reconciliation for themselves, so that they can work in this area more effectively?

Key Populations Group

In 2012, Secretary Clinton announced several key population and civil society initiatives; of those, two significant ones were:

- $15 million Key Populations Implementation Science (KPIS) initiative to identify the specific interventions that are most effective for key populations
- $20 million Key Populations Challenge Fund (KPCF) to support country-led plans to expand services for key populations

Mr. Baker explained that none of the protocols had moved along when OAPCSL undertook those initiatives this past summer, three years after they were launched.

KPIS

The office focused on making KPIS programs operational; currently, of the nine countries that were funded to conduct the research, eight have had protocols reviewed or have projects ongoing. The current focus is on accelerating the research and determining the meaning of discovering positive findings as well as how those findings translate to PEPFAR's ongoing work. The staff is looking at what will have been learned in time for the International AIDS Conference (IAC) in Durban, South Africa in July 2016 in order to inform planning going forward.

KPCF
The KPCF initiative focuses on the expansion of services for key populations, and it has generated highly positive results. For example, Thailand has seen a huge magnitude increase in HIV testing among gay male and transgender populations. Questions include how such programs will become sustainable and how lessons learned will play into future program planning and budgeting.

Both of these initiatives are managed separately outside of the PEPFAR planning process and sometimes outside of the supervision and day-to-day work of the staff; therefore, they are not learning from these projects in real time in their countries. Changing that reality is another question around the implementation science framework.

Mr. Baker made note of two other initiatives:

Health4Men
Health4Men is a partnership of PEPFAR and the Elton John AIDS Foundation that began as a pilot program in South Africa. With the positive results seen to date, OAPCSL is debating how best to expand the program.

COP/ROP 16
COP/ROP 16 planning and guidance will include streamlining technical considerations and strengthening the focus on prevention, particularly with key populations.

<u>Civil Society Leadership and Engagement</u>
RCNF
Mr. Baker explained that AMB Birx is co-chairing one of the lead initiatives around civil society: RCNF. This program was created to provide a strong core funding source for the global civil society network, including such organizations as the Global Network for People with AIDS, International Community of Women Living with HIV, and the MSM Global Forum, all of which were struggling over the last five years and play an important leadership role for PEPFAR.
A replenishment meeting was recently held as the program is coming to the end of its first three years; the following results were reported:

- The US has increased its contribution from $6 million to $10 million over three years.
- All original donors have committed to renewed funding:
    - Norwegian Agency for Development Cooperation (NORAD)
    - United Kingdom government's Department for International Development (DFID)
    - Bill & Melinda Gates Foundation
    - PEPFAR
- The Ministry of the Netherlands has recently joined as a funder, making an announcement last week of its $3 million commitment.

- The fund will increase from $18 million to $30 million by the end of 2015.

Local Capacity Initiative (LCI)
Also introduced by Secretary Clinton in 2012, LCI provides technical assistance (TA) and advocacy and community mobilization funding in 14 countries and regions; this is designed to help build capacity of civil society in order to develop strong organizations that can leverage resources and mobilize communities around the HIV response. A meeting of all Africa grantees and ministries of health will be held this month in Mozambique to build a strong TA networking partnership.

Mr. Baker gave an example of the TA provided to a PEPFAR-funded Mozambique group: With PEPFAR's technical support, the group created a community scorecard of the health systems in that country; the scorecard reported that people complained most about wait time and poor service, medications were being stolen and diverted, and no real system of accountability existed. As a result of the scorecard, substandard health agency workers were fired, a better system of management was developed that reduced wait times, and people gained trust in the community. Thought is being put into how this program will be developed, how it will be built into the ongoing work, and who will fund it—the country or other funders—so that its results do not expire at end of 2016.

COP/ROP Process
Representatives from local and global civil society organizations (CSOs) participated in all five COP reviews in 2015. Mr. Baker looks forward to more participation and integration into the POART process and into 2016 planning process and reviews. He reported on a conversation with a woman who works for the Nigerian Association of Young People Living with HIV in which she explained the extreme value of the COP/ROP guidance in helping to inform advocacy in her country.

Human Rights and Enabling Environment
PEPFAR is already involved in some activities that address human rights and discrimination, such as contributing to the State Department's Global Equality Fund. It is also assessing in four African countries how stigma and discrimination impede efforts to address HIV among LGBT people and undermine human rights. PEPFAR has partnered with The Global Fund around this issue, and posters are now hung in all Global Fund/PEPFAR sites; the posters include information on people's right not to be discriminated against around HIV care as well as a Global Fund phone number for reporting incidences of discrimination. A goal is to expand that coverage to other sites.

The next step is to establish ways to affect an impact on the legal environment and on stigma. Through the COP/ROP process, countries were asked to provide assessments of legal environments as well as to administer the People Living with HIV Stigma Index. A key question involves benchmarks to use in addressing stigma and discrimination. Mr. Baker noted that HIV-infected people are included in the 25-year-old Americans with Disabilities Act (ADA) civil rights legislation, and that such a legal framework—which has been critical to efforts in the US—does not exist in most countries.

Stigma is elusive, and different degrees and forms exist. A focus is on making the indices meaningful so as to determine where to focus the efforts that most significantly impact people's

lives. Mr. Baker contended that there is a need to develop a framework to delineate specific actions of discrimination done to people when they are seeking access to HIV prevention, care, or treatment.

In summary, Mr. Baker suggested that the SAB's help is needed to identify ways in which the environment can be changed regarding stigma and discrimination so that people feel safer in seeking HIV services. The goal is to make this an essential component of the OAPCSL's work.

Affected Populations and Civil Society Q&A

Dr. del Rio thanked Mr. Baker for his presentation and AMB Birx for creating the OAPCSL. He noted AMB Birx's comment in her presentation regarding the need to fight stigma and discrimination, and he pointed to the creation of this office as a positive step in that direction.

Question 1: Carlos del Rio

We need to include young people on the staff in order to reach populations of young women and adolescents, and we need to be sure to focus on the MSM population, as it has very high incidence of and risk for HIV/AIDs. This is an obvious need for working with countries in which homosexuality is illegal. Please explain OAPCSL's broader emphasis in addressing countries' legal frameworks that prevent many care and prevention activities from impacting hard-to-reach populations.

Answer: A. Cornelius Baker

To reach young girls and key populations, I see this office as operating on a dual track: The first track is focusing deeply on reducing the epidemic where the burden is greatest by magnifying resources in those places as AMB Birx has laid out and as we are applying in DREAMS. The second track involves developing a plan for success, with success translating to smaller epidemics; these epidemics are more likely to be much more concentrated and to affect key populations. They will be more challenging, as they require affecting the human rights framework and a legal operating environment for making significant change. Looking within US borders, we see a dramatic reduction in the epidemic when legal, cultural, and social environments promote healthy well-being of people and their active inclusion in society. One example of this is San Francisco. It is important that we document the successes we are seeing.

Extreme cultural barriers to inclusion, representation, and full respect of rights of individuals exist in many places in the American South, where the epidemic continues unbridled. We need to realize that, even once we have reached adolescent girls, tremendous challenges will continue to exist around legal rights as they affect drug users, sex workers, and gay men. Ending the epidemic in those environments will be very difficult. The goal is to end this epidemic for all people, not just for some people; this requires forethought.

We do have resources to aid in this effort, including KPIS, KPCF, and LCI, the last being something that could specifically work around the issues of key populations; because we have possessed these resources, we have had a mechanism to move things along and have not needed to challenge governments to acknowledge epidemics in their countries. Now, as those key initiatives come to an end, we must face that challenge and establish them in ongoing future planning. We will need to work directly with governments to propel them to recognize the value of all of their constituents.

Over the last six months, we have seen some progress; one example is the US partnership with Jamaica. AMB Birx spoke about discrimination and access to health care around AIDS on her spring visit to the island nation, and the President's visit included—in a forum on civil society in the Caribbean—publicly acknowledging the work of lesbian activist Angeline Jackson, who runs J-FLAG, the island's LGBT organization. Finally, US Department of State Special Envoy for the Human Rights of LGBTI Persons—the first ever in that position—Randy W. Berry held meetings around LGBT rights. All of this set the stage for Jamaica to be able to hold its first public gay pride event, "Pride JA".

PEPFAR can work across agencies such as the Bureau of Democracy, Human Rights, and Labor (DRL); CDC; the US Agency for International Development (USAID); and others, as well as with assets, to help create incremental change. While we have urgency about achieving and implementing this shift, we have to do it intelligently.

Question 2: Jennifer Kates
Regarding the question you pose in your handout, "What and how do we establish global benchmarks for addressing stigma?", I think broad measures exist, including the existence of anti-LGBT, anti-NGO, and/or anti-assembly laws in countries. OAPCSL likely learned a lot from the in-country staff-level trainings about people's biases and concerns which required your help to adjust and around which you needed to educate. You could use that information to inform benchmarks of change. One example could be certain types of providers or implementers who do not want to provide service access to LGBT clients. PEPFAR could look at specific measures around health and could develop more explicit language and evaluation with contractors and implementers about the meaning of access to health in their facilities. There are likely more specific benchmarks than the ones I am suggesting here.

Answer: A. Cornelius *Baker*
USAID Office of HIV/AIDS Director David Stanton and his team recently assembled to focus on agency-wide efforts on stigma. When they have completed their internal review, they will help pull together other agencies with the new OAPCSL staff member focusing in this area. Also, on November 11-12, UNAIDS will convene a meeting on stigma and discrimination; I believe the results of that meeting will be greatly informative to PEPFAR's work.

Question 3: Carole Treston
This is great, certainly complicated, and very important work. Achieving success with PrEP and with Test and START requires addressing stigma and discrimination. On the macro level, I propose looking at the People Living with HIV Stigma Index, LGBT laws, and other markers by country. On the micro level, nurses, as the largest component of the healthcare workforce, surely play a role in promoting and continuing stigma; therefore, ongoing trainings are important to help change attitudes and behaviors that promote that stigma.

A major challenge with staff training and workforce development is around measuring its outcomes and impact. How do you measure the impact of that investment?

Separately, I suggest that you address the stigma felt by the hidden population of HIV+ nurses (if 20% of the population is HIV+, there is no reason to think that the same does not hold true for the primarily female nurse population within it), as each suffers a double stigma as both an HIV+ community member and HIV+ healthcare worker. ANAC has partnered with Strengthening Our

AIDS Response (Nurses SOAR!), funded by PEPFAR and based at Georgetown University School of Nursing and Health Studies; the program sends HIV+ positive nurses from the US to serve as peer role models in settings in Africa. I also mention, but do not promote, an International Council of Nurses program that provides separate, stand-alone wellness centers for healthcare workers in sub-Saharan Africa.

Answer: A. Cornelius *Baker*
One of our big challenges is around ongoing training. Coordinating 35 countries and their numerous partners for four-day-long trainings took a tremendous effort that we simply cannot repeat annually. One of the most powerful elements of the training was inclusion of community advocates and creating safe space and dialogue. The reality of implementer turnover creates the need for additional trainings. We are exploring our ability to develop a one-day standardized training including an electronic component that creates the same level of impact as the in-country trainings we have done to date.

In terms of measuring impact, we have a report of the trainings, and we have conducted pre- and post-training surveys. We are planning to add a three-month follow-up survey as well. We will be happy to share all of the results with the SAB.

Question 3: Mitchell Warren
Thank you, as ever, for this amazing amount of work. PEPFAR's relationship with UNAIDS is so strong and robust, and PEPFAR has defined numerous targets that align nicely with aspects of treatment and prevention. I know that UNAIDS has been slow to release publicly both prevention and non-discrimination targets. I would like to suggest that there may be utility in developing one or two targets to establish along with the reduction of incidence among young women and VMMC—a metric around the key population/non-discrimination/human rights base that is both feasible and audacious.

Answer: A. Cornelius *Baker*
From a human rights framework, we have a vision that is reflected in the National HIV/AIDS Strategy and in our global vision on people living in a non-discriminatory environment in the absence of laws that restrict their freedom. The question is, how, within this framework, to begin to establish and adopt achievable targets.

Answer: Carlos del Rio
I think a group should be formed to think about this issue. As Dr. Kates stated earlier, even simply creating a scorecard including countries' laws is really helpful to show the state of affairs and what progress has been made. That would publicize the reality on the ground and would show evidence of program impact.

Question 4: Ruth Gruskin
Firstly, I believe that effective, measured training is an incredibly important component of this work, and your office is uniquely qualified to handle it. In addition to its inherent value, such education sends a strong message to PEPFAR staff and in-country partners.

Secondly, we need to make sure to avoid duplication and to recognize the work many partners are doing in this area. For example, the United National Development Programme (UNDP) has developed an operational guide to conducting national legal, regulatory, and policy assessments

for HIV and has supported countries in undertaking Legal Environment Assessments (LEAs). It also created the National Dialogues on HIV and the Law in the 17 countries of sub-Saharan Africa, many with which PEPFAR collaborates. I disclose that I have been serving as an evaluator on this project.

The LEAs have identified key issues as defined by national stakeholders in the legal environment as well as what needs to be done to affect change. However, an issue exists: Because of the terms of the grant, the key populations focus has centered around women and girls, lesbians, MSMs, and transgender people only; this framing has left sex workers and drug users out of the conversation. Many markers exist, beyond changes in law, that can document shifts in the environment occurring as a result of these projects, and it would be wonderful to create a connection around these efforts instead of duplicating them.

Answer: A. Cornelius *Baker*
Your point is well taken. We have had conversations with UNDP around creating a process for working together, and UNDP has submitted a concept for PEPFAR funding of legal clinics. The larger goal, which I have discussed with The Global Fund and UNAIDS, is to develop an ongoing coordinated strategic process around legal and human rights issues.

PEPFAR wants to be inclusive of all key populations and to focus on them from a country perspective. Therefore, drug users cannot be removed from the conversation. Also, it is important to appreciate that segmentation is not pure; one example might be a gay man in Rio who is using crystal meth and is working as a sex worker with both men and women. Gender and drug use categorizations are fluid— this is a major point of our gender and diversity training. Drug use could range from cigarettes to heroin, and we need to be more equipped to talk about the overarching dynamics with people.

Question 5: Kenneth Mayer
This is incredibly important work. I am curious as to the level of integration in clinical training of providers—who have a vested interest in delivering competent care—around clinical core competencies. As you are promoting human rights and sensitizing staff, are those staff being trained around certain screenings, such as for rectal STDs, and around harm reduction approaches for working with people who use substances?

Answer: A. Cornelius *Baker*
We have been thinking about the technical considerations and about integrating an overall vision towards prevention or care. We have also discussed integrating quality and a human rights approach while being sensitive around the ways of delivering care to various populations. Lisa Nelson, MD and I have been discussing bringing our two groups together very soon around these issues. I defer to her.

Answer: Lisa Nelson
Over the last year's COP-planning process, there has been much greater recognition of key populations and how to include them, within both concentrated and generalized epidemics. In Cameroon, for example, we focused on geography as well as specifically on key populations.

Regarding health worker training, I would recommend looking at the program as a whole and how PEPFAR invests at this time; PEPFAR held myriad trainings early on, and The Global Fund

and other donors have invested millions of dollars in training as well. We now need to look critically at what will offer significant impact, as well as where there are key populations with specific issues. The larger sensitization of healthcare workers in general is really important, but I think it also needs to be contextualized.

Question 6: Musimbi Kanyoro
I very much appreciate that PEPFAR had added to the Robert Carr Foundation's ability to fund FBOs. I am curious to know if you include faith communities in the concept of civil society. It is my experience that you will not make any progress around stigma in Africa without involving churches and FBOs. They have done a lot of work around this issue but have not documented it. Africa has come a long way and has given the world a gift: Religious leaders who are living with HIV have formed an association so they can influence faith communities. I am wondering if you plan to work with The International Network of Religious Leaders Living with or Personally Affected by HIV and AIDS (INERELA+). The organization is doing a lot of work around stigma, discrimination, and key populations, including pioneering LGBTI work on the continent.

Regarding working with adolescents, PEPFAR needs to understand that churches own and manage many primary and high schools. If we can involve them, we can reach that population. Additionally, churches control comprehensive sexual education.

Answer: A. Cornelius *Baker*
We hope that PEPFAR's expanded funding to the RCNF will serve to make current organizations more stable and will create networks that have not been developed to date; these faith and legal networks would create a broader base. The faith component is important to us. In LCI, our Cameroon project is run by the Cameroon Baptist Convention. We recognize that the organization is essential to breaking down existing communications about stigma and about gay male and other populations. It is also essential to developing networks and alliances to support that work, and we will continue to work to build support around those initiatives. To ensure that faith communities are involved and engaged with OAPCSL work, we will coordinate our efforts with the faith initiative run by OGAC Chief Strategy Officer Sandra Thurman.

Just today, we are extending invites to civil society organizations to participate in an upcoming workshop organized around the Accelerating Children's HIV/AIDS Treatment (ACT) Initiative. Within the frameworks of both ACT and DREAMS, we want to mobilize and increase faith-based communities and to develop and define their role. We are currently considering how to develop and formalize FBO networks; already, some interesting models of engaging FBOs have been recommended to us. Faith communities change the culture and will be essential to the family and community mobilization components within both ACT and DREAMS. We will keep you up to date on these efforts, and the SAB's input and suggestions are very welcome.

Question 6: Christine Nabiryo
I congratulate AMB Birx and the team on this good work. I would like to emphasize, from a country-level perspective, that The Global Fund has done a lot of work with numerous groups and that it will be very important to build on the existing infrastructure. Another important element is cross-agency affirmation; I want to underscore the point that coordinated messaging will go a long way to help national programs to focus and to know that all of the agencies are speaking the same language.

On other points, it is imperative to understand, recognize, learn from, document, and build on past efforts to reduce stigma and discrimination. There is hope for countries to identify best practices. Also, I am thrilled to know that alcohol and substance abuse is being included here, as it quietly but greatly affects the epidemic.

We have a population that is not being reached: The middle class, including doctors, in Uganda will die of HIV/AIDS due to self-stigma and an accompanying unwillingness to seek treatment.

Answer: A. Cornelius *Baker*
The Global Fund convened a meeting in Bangkok this past August; the focus was on its Community, Rights, and Gender Technical Assistance Program. The PEPFAR LCI and The Global Fund's initiative—both special and central initiatives of our agencies—are set to end in late 2016/early 2017. If we do not coordinate and create a plan, and if we do not push funding into those country-level programs, we will experience a highly destabilizing exodus of $150-$200 million from communities. Coordination is essential, and planning needs to happen now. Through LCI, we discovered that it is difficult to apply for US government funding, and various application routes exist. Therefore, with monies from a special branch fund, we will offer specialized TA through FHI 360 and our AVP **(acronym unclear)** group to work with organizations over the upcoming six months to ensure they are ready to respond to requests for proposal (RFPs).

AMB Birx has often reminded us that, in many parts of the world, HIV/AIDS is not a disease of poverty but affects the middle and upper classes. We must address this issue, which is strongly affected by cultural code. In the US, big moments that transformed our thinking about the HIV epidemic have included acting star Rock Hudson's diagnosis; wealthy, powerful athlete Magic Johnson disclosing his HIV status on TV; and the story of ordinary, middle class teen Ryan White. These broke phenomenal levels of silence, which is always the result of shame and stigma. Engaging in that conversation around the middle class, around faith, and around leadership is essential to reducing stigma.

Question 7: Jesse Milan
As an attorney, I want to share some observations and some history. The Americans with Disabilities Act (ADA) took a lot of political will to pass, and much litigation followed. The AIDS community has a need for a human rights effort, and the time for this is more ripe than ever. Litigation can only follow legislation and policy; as these have not yet been created, we have a problem ensuring rights. This work is an opportunity to use our moral compass in the role of parliamentarians to create the political will to promote the human rights agenda. We also may be able to pull from past models of policies around discrimination. We need to go beyond large corporations to locally owned businesses in order to discover their models of non-discrimination around people with HIV/AIDS.

Question 8: Celia Maxwell
I see stigma and discrimination as a large entity that must be chipped away at. I also believe that things can be done for healthcare providers regardless of their position. Because they have undergone training, they are likely to accommodate changes. Howard University College of Medicine has instituted a professionalism code that involves consequences, and some students have been dismissed for behavior unbecoming. I suggest that codes of conduct be included as part of PEPFAR-supported programs. Healthcare providers of all kinds are already bound to

abide by the Hippocratic Oath, the Florence Nightingale Pledge, or other principles and can be appealed to on this level. Also, many countries have something similar to HIPAA Privacy Rule in the US, which protects the privacy of individually identifiable health information. Codes of conduct can be stipulated metrics for initial and continued funding.

Answer: Carlos del Rio
You remind me that, when applying for PEPFAR funding many years ago, my team learned that US policy requires all organizations that receive HIV/AIDS funding to explicitly oppose prostitution. We did not have a stated policy and had to create one for inclusion with the application in order for it to be considered and accepted.

Question 8: Lejeune Lockett
The military is another population we have as yet not addressed in this conversation. Drew Cares works with militaries in Rwanda and Angola (I work with the latter program), and the military can be an influential social agent. In many African countries, the military has a significant presence and a strong impact on civil society. I am curious to know if OAPCSL has identified approaches specific to reaching the military, which is a unique culture with particular rules and regulations for operations and engagement. Have you developed training approaches for, or resources directed to, militaries in Africa around stigma and discrimination? If so, what expectations or targets have you set?

Answer: A. Cornelius *Baker*
Thank you for food for thought on these COP-related questions, Dr.Lockett. While OAPCSL is not developing a specific focus on the military, I want us to think about the connections around political leadership and will; in many countries, the military is the social-political leadership. In the US, much of the shift that has accelerated around gay rights likely would not have done so without the repeal of the military's "Don't Ask, Don't Tell" policy. Similarly, Secretary of Defense Ash Carter, before the Supreme Court ever ruled on marriage equality, issued a directive to the DoD to "create a working group to study over the next six months the policy and readiness implications of welcoming transgender persons to serve openly." In the US as well as in other countries, cultures often respect their militaries. Therefore, engaging those leaders is highly important for thinking about how we transform societies. How can militaries help us end AIDS? In Namibia, I saw enormous billboards outside of its department of defense with messages about the military's role in ending HIV and TB.

Answer: Carlos del Rio
The military is great way to reach men.

<u>Concluding Statement</u>
A lot of stigma and discrimination work has been done, and we need to recognize and learn from it. We are far enough into the epidemic to look at how to sequentially build our work. We should learn from both the science and from the community experience, and we should connect those who are in their 50s and 60s into programs focusing on younger populations, such as teens, 20-somethings, and others—sharing the history but not dictating the process, and allowing innovation to emerge and new ways of communities to develop. The goal is to bridge that work so that past efforts inform the process for going forward. At this point, we need to package our work much as we do our technical considerations around family planning and sexual and reproductive health in order to assist countries and advocates.

Regarding culture, I watched the recent Season 2 premiere episode of the US TV series "Empire" while in Jamaica; I observed that all of the scenes involving the gay son had been edited out. As that character has developed into a leading character, the show's ratings have fallen by 3 million viewers. On top of this, a famous rapper posted a negative comment about the gay character being prominent on the show. While he likely was reflecting a sentiment that exists, he subsequently deleted the post after many young people responded to it negatively. There is a shift occurring in African American culture; stigma is still incredibly high, but a new culture is emerging—including in Africa—that is pushing back.

We need to analyze how to bring this all together and how to identify opportunities to make fundamental changes in law—because, at the end of the day and regardless of positive feelings, human rights can only be operated and protected through a system of law. In this window of time until 2030, the laws need to rapidly change along with the science.

Public Comments and Questions

Question 1: Benny Kottiri, USAID

My question is directed to the PrEP EWG: Please clarify the working group's guidance on PrEP; beyond DREAMS, what are the specific recommendations? Are they geared more to demonstration-type projects, of which we already have quite a few? Is the goal to start small and grow slowly, or to develop broader programming?

Answer: Connie Celum

Thank you for your excellent question. Today's discussions have made it clear that the PrEP EWG recommendations require additional specificity. We have numerous demonstration projects queued up, some for as long as three years, due to length of time from conceptualization to implementation. I feel that we need to move more quickly outside of those projects in a targeted way. One exciting example is Kenya, which has done the work at the population and country levels and has a prevention roadmap. In my opinion, that country is ready to initiate significant program with close monitoring and directed evaluation.

Answer: Mitchell Warren

I assert that we should be leading each of those activities when appropriate. When we truly need to demonstrate something that is not already known, we should conduct demonstration projects. Studies should be used to ask and answer implementation science questions, and those studies should be well defined, funded, and conducted. We need to create space for multiple types of the work. PEPFAR and many partner agencies—including USAID, DoD, and CDC—need to ensure coordination on demonstration projects, so as to avoid replication and to ensure intelligent investment.

Question 2: Nina Hasen Population Services International

Thank you to OGAC for this great SAB meeting which I feel privileged to attend. I would like to provide information to the very rich discussion around stigma by sharing what I have recently observed in the field.

HIV testing and counseling has not radically changed in last eight years. Therefore, the messages being given to people in the counseling process may be from a time when treatment was not readily available, and I think we are inadvertently reinforcing stigma. We all have the ability to

review the programs we are supporting and to identify ways to ensure our testing programs reflect current knowledge. PEPFAR has enormous leverage in helping governments rethink guidelines to significantly shift what is happening around testing in order to help make that process notably simpler, much less alarming, and far more practical. PSI is focusing a lot of effort in this area, and we would like to partner with PEPFAR to do more.

Regarding task-shifting, we build entire health cadres in many countries who do only rapid testing and counseling, and who currently deliver alarming messages. I suggest that we retrain some of those workers to perform risk assessment as was discussed in the PrEP conversation so as not to increase the burden on nurses.

These changes and the knowledge that we are gaining through the SEARCH study about patient-centered care will, in practical ways, address the stigma that we are unintentionally creating.

Answer: Carlos del Rio
I completely agree with you. One of the clear messages coming though is that, in order to make Test and START a reality, we need to reframe the messaging. The way we are performing HIV counseling has not progressed to the degree that the science has evolved around knowing your status and getting care. We need to enter a new era, and it does not happen overnight.

Question 2: Robert Grant
I am Bob Grant of San Francisco and Geneva, and I am very grateful to have heard this wonderful conversation. Stigma is a driver at all levels. As Dr.del Rio mentioned, it is the reason people do not get themselves tested or go into treatment. It is also the explanation of why HIV funding is flat, as well as why we cannot secure resources to leverage the enormous opportunities that have been presented over the last two years. If HIV was truly a valued problem owned by humanity, the funding would occur; the money exists.

I want to suggest that PrEP is a concrete intervention and to explain how it works to reduce stigma. This intervention distributes responsibility for ending HIV transmission in couples and in communities; thereby, both PrEP users and their HIV+ partners feel empowered and less stigmatized. Also, sexual connection, which is transformative, feels safer for couples. Finally, PrEP gives HIV- people a reason for using the health care system, challenging as that may be.

Separately, focusing on young women, while warranted, can be stigmatizing and disempowering; it can send the message that women are either victims or worth fearing. I do not think we benefit young women if we exclude their boyfriends or their gay friends; they are in their social networks and are looking for their support.

Answer: Carlos del Rio
You have highlighted the challenge we face. Stigma around delivery access reaches across issues, such as Ebola and HIV. Creating a culture against stigma in healthcare facilities is critical to providing care.

Other Business
Dr. del Rio noted today's discussion about EWGs focusing on HIV/TB, data, finance and sustainability, combination prevention, and implementation science. He solicited other areas for further review and attention from SAB members.

Dr. Kates and AMB Birx pointed out that a DREAMS/ACT group, to convene before the January meeting, has been suggested. Dr. Mushavi mentioned that children have been missing from the discussion and that she is pleased to hear the issue of ACT and DREAMS being raised.

Dr. del Rio advised that OGAC will reach out to members to ask for participation, and he noted the short timeline for getting work in motion. The upcoming July IAS meeting in Durban is a major landmark point; Dr. del Rio proposed that the SAB convene for a one- or two-day meeting prior to that event in order to develop a framework as well as clear recommendations.

Closing Comments

AMB Birx remarked that she learned a lot in this meeting around data use and about issues around Test and START and PrEP. She expressed appreciation that the SAB is changing PEPFAR's thinking about combination prevention, in particular. The SAB is an amalgamation of internationally and domestically focused individuals. Similar issues, including accessibility to the healthcare system, exist for young men of color in the US and young women in Africa.

AMB Birx acknowledged Dr. Shaffer, Dr. Mackenzie, and Dr. Goodenow for their efforts in coordinating and supporting the SAB and this meeting, as well as for developing thoughtful discussion questions.

Dr. Shaffer expressed his appreciation for AMB Birx's passion and for the leadership, efforts, and what AMB Birx calls "infectious impatience" of Drs. Celum, Abdool Karim, Currier, and del Rio and of their EWGs. He noted the SAB's flexibility and pointed out that, by holding today's meeting at the State Department as opposed to in the Marriott Hotel, PEPFAR will be able to fund treatment of approximately 500 children on first-line ART for an entire year. He thanked Drs. del Rio and Currier for governing the meeting.

Dr. Shaffer explained that PEPFAR will quickly be in touch about the new EWGs and will look for feedback in about six months. He thanked everyone for their dedication to fighting HIV/AIDS.

Dr. del Rio shared his gratitude to SAB members for traveling to Washington, DC for the one-day meeting and for focusing so clearly on the issues and topics discussed. He shared his belief that AIDS can be ended, and he again noted that this community is at a critical point to "bend the curve" in the epidemic, with the available tools as well as with the opportunity existing through PEPFAR. With the obvious challenges around the young population, we need to do this work differently so as not to derail past efforts. All of this group's input will be highly valuable in creating that shift and achieving our goal for future generations.