

**PrEP Implementation Policy Forum**  
**Developing Country-Level Preparation and**  
**Capacity for PrEP Implementation**

22 July 2007  
Sydney, Australia



**International  
AIDS Society**

Stronger Together

## Participants

**Co-Chairs** Craig McClure, International AIDS Society (IAS)

Renee Ridzon, Bill & Melinda Gates Foundation

**Organisers** Rodney Kort and Yasmin Halima, IAS

<b>Aaron Brinkworth</b>	Gilead Sciences, USA
<b>Ward Cates</b>	Family Health International (FHI), USA
<b>Katchit Choopanya</b>	Bangkok Tenofovir Study Group, Thailand
<b>Kevin De Cock</b>	World Health Organisation (WHO), Switzerland
<b>Florindo de la Hoz Gomez</b>	Ministry of Health, Botswana
<b>Carl Dieffenbach</b>	US National Institutes of Health (NIH), USA
<b>Mary Fanning</b>	NIH, USA
<b>Telmo Fernandez</b>	PrEP Trial Site, Ecuador
<b>Amy Flood</b>	Gilead Sciences, USA
<b>Pedro Goicochea</b>	Impacta, Peru
<b>Robert Grant</b>	University of California San Francisco (UCSF), USA
<b>Catherine Hankins</b>	UNAIDS, Switzerland
<b>Nick Hellman</b>	Bill & Melinda Gates Foundation, USA
<b>Mina Hosseinipour</b>	Investigator, Malawi
<b>Mathias Joshua</b>	Ministry of Health, Malawi
<b>Somyot Kittimunkong</b>	Ministry of Public Health, Thailand
<b>Javier Lama</b>	Impacta, Peru
<b>Michael Martin</b>	US Centers for Disease Control and Prevention (CDC), Thailand
<b>Veronica Miller</b>	Collaborative Forum for HIV Research, USA
<b>Bizwick Mwale</b>	National AIDS Commission, Malawi
<b>Jeffrey Nadler</b>	NIH, USA
<b>Lynn Paxton</b>	US CDC, USA
<b>Jim Rooney</b>	Gilead Sciences, USA
<b>Zeda Rosenberg</b>	International Partnership for Microbicides (IPM), USA
<b>Dawn Smith</b>	CDC, USA
<b>Shaleena Theophilus</b>	Global Campaign for Microbicides (GCM), Canada
<b>Suphak Vanichseni</b>	Bangkok Tenofovir Study Group, Thailand
<b>Mitchell Warren</b>	AIDS Vaccine Advocacy Coalition (AVAC), USA

## Introduction and Background

With the support of the Bill & Melinda Gates Foundation, the International AIDS Society (IAS) convened a meeting engaging researchers, policy makers, community members, and representatives of normative agencies and the pharmaceutical industry to discuss implementation of pre-exposure prophylaxis (PrEP) in light of anticipated clinical trial results from several major PrEP trials over the next few years. In welcoming participants, IAS Executive Director Craig McClure outlined the meeting's two primary objectives:

1. Provide guidance on anticipating and translating results from PrEP trials to different country situations, epidemiology, and local circumstances
2. Discuss possible strategies for implementing PrEP in different country settings including:
  - Potential need for bridging studies to ensure findings are relevant to country epidemics
  - Assess feasibility of implementing a PrEP programme using tenofovir disoproxil fumarate (TDF) and/or Truvada (co-formulated TDF and emtricitabine)

Through its Industry Liaison Forum (ILF), IAS has been convening dialogue among major stakeholders regarding scientific issues related to PrEP. IAS has also been involved with organising multi-stakeholder consultations in conjunction with the Bill & Melinda Gates Foundation to resolve ethical and operational challenges as they relate to clinical trials of PrEP. This meeting represents the first attempt to convene

stakeholders specifically to address delivery of this particular intervention.

The meeting began with presentations by Lynn Paxton and Dawn Smith of the US Centers for Disease Control and Prevention and Cate Hankins of UNIADS.

## Translating research into policy

**Lynn Paxton** and **Dawn Smith** addressed issues related to translating research into policy. One safety trial of TDF PrEP in African women was completed last year. Ongoing efficacy trials are evaluating TDF in injecting drug users (IDUs) in Thailand, Truvada in young heterosexual male and female adults (18-29 years of age) in Botswana, and Truvada in men who have sex with men (MSM) in Peru and Ecuador. A separate safety trial of TDF in US MSM is also under way. Preliminary results of the Thai trial will be available in 2008. Results of all three efficacy trials should be presented in 2009. Other trials are planned in serodiscordant couples and heterosexual women.

Lynn Paxton noted that results of these trials will shed light on four issues:

- Efficacy of PrEP in IDUs, heterosexuals and MSM
- Safety and required frequency of clinical monitoring
- Emergence of viral resistance among seroconverters
- Communication strategies that help researchers promote understanding to trial participants of PrEP, e.g. how it should be taken (in the context of a trial), possible side effects, risk of drug resistance as well as determining community acceptability.

However trial results will not demonstrate (1) how PrEP with TDF or Truvada will work in "real-life" conditions where risk compensation and rare side effects become apparent, (2) safety of PrEP in important unstudied populations such as adolescents and pregnant women, (3) efficacy of alternative dosing strategies. Perhaps most importantly, results from a trial in a specific sub-population may not be directly relevant to the epidemic characteristics of affecting another country.

Dr Paxton stressed that each country will need to address the appropriate use of PrEP given the characteristics of its epidemic and its prevention and treatment infrastructure. Still, any PrEP program should include certain core elements:

- Usage guidelines
- Drug procurement and distribution strategies
- Plans for initial and ongoing voluntary counselling and testing
- Communications strategies
- Clinical monitoring and adverse event follow-up
- Behavioral monitoring
- For seroconverters, viral resistance testing and access to second-line therapy, if needed

Dr Smith proposed reasons why stakeholders should begin thinking about implementing PrEP now instead of waiting until trial results are analyzed:

- There is reason to be optimistic that PrEP will succeed
- It will take time to plan effectively because:
  - new prevention technologies are urgently needed in order to respond to the needs of countries with high-incidence of HIV
  - many factors must be accounted for in planning to maximize safety and efficacy
  - multiple viewpoints and needs must be considered

Dr Smith suggested it is reasonable to prepare for the possible efficacy of TDF and Truvada because of:

- Biological plausibility
- Concentrations achieved by these drugs in the genital tract
- Effectiveness in animal studies
- Safety data reported in the Family Health International trial in Ghana

Finally, despite imperfect adherence, antimicrobial PrEP has proved effective for prevention of mother-to-child transmission (PMTCT) of HIV, malaria, opportunistic infections, and other conditions.

In the event that trials do not demonstrate the efficacy of TDF and Truvada for PrEP, planning now will yield strategies that will help with implementation of other biomedical interventions, such as microbicides or an HIV vaccine.

Dr Smith argued that implementation of PrEP with TDF or Truvada may have certain advantages compared to vaccine or microbicide implementation because, unlike those other two strategies, TDF and Truvada:

- Are already approved for treatment of HIV infection
- Require no new regulatory procedures
- Require no new manufacturing processes

- Are available at reduced cost for the public sector in the US
- Are being licensed to generic manufacturers

However, Dr Smith stressed that PrEP will bring its own challenges such as the need for periodic follow-up for incident HIV and adverse effects.

Because pharmaceuticals can be prescribed for off-label indications in the United States, Dr Smith observed that guidance on use of TDF and Truvada for PrEP will have to be in place if ongoing trials demonstrate efficacy.

If PrEP proves successful, funding will clearly be a paramount issue. Countries that implement PrEP will need to tap new funding sources or will have to divert some funds from other programs, perhaps including antiretroviral efforts. Countries that do decide to back PrEP will have to plan for rapid introduction of this strategy to achieve sufficient coverage, intensity and duration to have an optimal effect. Dr Smith proposed that rollout programs should be built to take advantage of several advantages of PrEP vis-à-vis other preventive strategies:

- More gender neutral
- Covert use feasible
- Coitally independent
- May work for more than one type of exposure (for example, for an injecting drug user who has unprotected sex)
- Can discontinue PrEP during periods where individuals are not engaging in activities that place them at risk for HIV infection
- Periodic risk reduction counseling and HIV testing
- Opportunity to link men as well as women to preventive care

Planning a successful PrEP program will depend on systematic evaluation of numerous data sources, including:

- Trial data
- Existing data on behaviors in high-incidence populations
- Population-targeted implementation planning data collection (Even in countries with a generalized HIV epidemic, the target population cannot simply be all HIV-negative people.)
- Demonstration and pilot projects

Before implementation of PrEP, countries will also have to establish evaluation criteria and mechanisms for inputs, processes, intermediate outcomes, and HIV incidence.

With a view toward facilitating potential PrEP implementation, Dr Smith noted that the CDC has (1) initiated conversations with a wide range of stakeholders, (2) assembled a multidisciplinary study group to work on implementation planning and evaluation questions, (3) surveys of national stakeholders, program managers, and potential participants to consult on implementing PrEP, and (4) planned focus groups with potential users.

Dr Smith listed the following country-specific factors in planning for PrEP implementation:

- Priority groups to maximize reduction of HIV incidence
- Provider types and sites
- Barriers and implementation designs to overcome them
- Lessons learned from scale-up of PMTCT and antiretroviral therapy
- Reproductive health and pregnancy issues
- Funding and implementation partners

## Lessons learned from implementation planning for male circumcision

**Cate Hankins** described ongoing planning for country-wide implementation of male circumcision to prevent HIV infection and highlighted issues that may apply to a PrEP rollout.

Dr Hankins outlined six red-flag issues in implementing circumcision and messages that may be derived from analysis of those issues:

### 1. Racial overtones, religious and cultural sensitivities, stigma

Whether circumcision is widely used in a country depends on cultural issues. Among the estimated 30% of adult males in the world who are circumcised, two thirds are Muslim, 13% are American, and less than 1% are Jewish. In several countries, prevalence of nonreligious circumcision has undergone rapid increases and decreases as a result of cultural mixing. Thirteen studies suggest that the biggest barriers to male circumcision are cost, concerns about safety, and pain. The first two will certainly apply to PrEP, Dr Hankins observed.

*Message:* Successful implementation depends on amongst other factors, sensitivity to cultural issues, which can be approached through exploratory

conversations and open dialogue to see if the strategy will be acceptable. Stigma will have to be discussed in these dialogues.

## 2. Human rights: consent, coercion, nondiscrimination

Mechanisms for ensuring voluntary and informed consent will differ for male infants and children, male adolescents and male adults. Will stigma about not being circumcised emerge if women express preference for circumcised men? In those countries in which circumcision is considered a rite of passage into adulthood, can one refuse without disapproval or without becoming a man? Group male circumcision, common in some African cultures, raises questions of freedom of expression and religion versus individual informed consent.

*Message:* Implementing nations must develop legal and regulatory frameworks that ensure respect for human rights while guaranteeing safety

## 3. Costs, health system constraints, incentives

*Message:* Although initially there may be a need for vertical programmes to satisfy emerging demand safely and to train more providers, the eventual goal is for integrated services. The price should be kept low to reduce the risk that people will resort to unsafe providers. Dialogue should be opened with traditional practitioners. Settings, equipment, and provider expertise must be assessed.

## 4. Safety concerns, postoperative follow-up

Adequately trained and equipped providers have low complication rates. Training, supervision and quality assurance are important. Patients need to be counseled and commit to post-surgical abstinence for prevention for 6 weeks or until complete wound healing has occurred.

*Message:* Pre-procedure counseling should be done to assess understanding and capacity to provide postoperative self-care; involve female partners in post procedure reinforcement.

## 5. Gender and sexuality, conflation with female genital mutilation (FGM)

Potential harmful outcomes of promoting male circumcision for HIV prevention include: risk compensation (misperception that male circumcision provides complete protection which may lead to increased unsafe sexual behaviour), sexual violence

and conflation of male circumcision with FGM, sometimes inappropriately referred to as female circumcision.

*Message:* The dangers of FGM must be clearly addressed. Services should address the sexual health needs of men, actively counseling and promoting safe and responsible behavior, including zero tolerance for gender violence.

## 6. Risk compensation, misperceptions

Circumcision may create a false sense of security among circumcised men and their sex partners. Women may start to consider male circumcision an "invisible condom" and be less concerned about unprotected sex.

*Message:* Provide correct and clear communication for men and women about risk reduction (not protection) with circumcision.

She noted that circumcision and PrEP share at least two broad features: both are products that are currently available, and, if demand is not met with safe services, both may cause serious problems. More specifically, Dr Hankins noted the following as lessons that can be inferred from the response to male circumcision trials relevant to informing PrEP implementation:

- a) The provision of PrEP may create inequities in a health care system. For example, if governments provide PrEP for free, will this compound existing inequalities in the provision of other preventative technologies or health services?
- b) Conversely, it may be that a PrEP programme may in fact strengthen existing services by creating opportunities for counseling and support.
- c) If proven effective, PrEP can increase choices for prevention, allowing individuals to make decisions based on lifestyles, levels of risk or exposure and ease of use.
- d) PrEP, like circumcision, has the potential to create a false sense of security. Those who use PrEP, or engage with someone who does may consider it safe to have unprotected sex. Providing clear and accurate messaging for both men and women will be critical to the success of PrEP.

- e) As with male circumcision, PrEP must be provided within the context of other prevention methods, i.e. developing a combination or synergistic approach to prevention.
- f) Successful intervention of PrEP will rely on an understanding and sensitivity to the cultural context in which sexual behaviour and values manifest, and the debilitating impact of stigma on prevention choices and access.
- g) Countries will need to develop legal and regulatory frameworks that enable the implementation, accessibility and acceptability of PrEP.

**Kevin De Cock** of **WHO** added that the sequence of events in the study and early adoption discussion of male circumcision — scientific, organizational, political — was logical and should be followed in the study and potential implementation of PrEP. Although plentiful circumstantial evidence indicated that male circumcision would reduce HIV transmission risk, the science had to be convincing before countries would proceed. The experience with contraception — involving regular intervention to prevent an outcome — may also apply to PrEP.

Dr De Cock added that he is not sure whether PrEP should be considered gender neutral. He can envision social disapproval weighing more on women than on men.

### Country-level preparedness: perspectives from Ministry of Health representatives

Craig McClure asked representatives from Thailand, Malawi, Botswana, and Ecuador to address two questions:

1. Assume that the first PrEP trial shows a 70% reduction in HIV infection using single daily TDF. How might you use PrEP in your country, for example, would you target PrEP at high-risk populations or instead promote accessibility to the general population?
2. What principal obstacles will you have to overcome in implementing PrEP if it proves effective?

**Biziwick Mwale** of **Malawi** stressed that questions of PrEP implementation will differ in countries with

a generalized HIV epidemic, like Malawi, and those in countries with population-specific epidemics, where much PrEP research is being done. “First we want to see results” from ongoing trials in Thailand, Botswana, Peru, and Ecuador, he said. Only then will Malawi be able to discuss how best to implement PrEP “across the board” for a generalized epidemic. In addition, Mwale added, “We must learn from what we’ve already seen” with other preventive interventions.

Cost will perhaps be the greatest hurdle to implementing a strategy like PrEP in Malawi or any country with a generalized epidemic. Malawi is already spending resources in scaling up antiretroviral therapy and considering circumcision programs. A second challenge, Mwale added, is ensuring that people have the confidence and freedom to make their own choice about circumcision or PrEP. He stressed that both interventions must be built in the context of other health programs, not in isolation.

**Somyot Kittimunkong** noted that **Thailand** has already learned valuable prevention lessons from PMTCT trials and programmes and from HIV vaccine trials. Results of the first randomized PrEP trial, in IDUs, will come from his country in 2008. Thailand and countries with similar experience should look for ways to apply those lessons to PrEP.

A key obstacle to PrEP implementation in Thailand will be determining which populations should be targeted. At this point it remains unclear if all sexually active people—or only specific risk populations—should be target groups. Dr Somyot believes a decision on targeting must be made before trial results are analyzed.

A second concern is deciding whether PrEP should be covered under the national public health program. If PrEP proves effective, Somyot noted, implementation should be synergistic with voluntary counselling and testing (VCT) and risk reduction programs including condom use. He suggested that Thailand would first assess PrEP implementation in a pilot project and then determine how scale-up should proceed.

**Florindo de la Hoz Gomez**, from the Ministry of Health in **Botswana**, noted that his country has demonstrated strong political will in rolling out antiretroviral therapy, which now reaches 90,000 people, and PMTCT, which covers 85% of eligible

women. At the same time, Botswana is now considering implementing circumcision. PrEP would have to be integrated with these programs. As a result Botswana, which hosts an ongoing PrEP trial, must be convinced that this strategy contributes to HIV prevention before implementing it as part of the country's treatment and prevention package. Overcoming stigma remains a problem in encouraging condom use in some populations.

As in Malawi, Dr Gomez noted, Botswana would face a challenge in determining which populations to target since the country has a generalized HIV epidemic.

Finally, if PrEP proves promising, Gomez stressed that false expectations of its effectiveness must not be created so people do not abandon the principles of HIV prevention.

**Pedro Goicochea** an investigator from the PrEP trial, representing Impacta in **Peru** noted that his country and others in Latin America face the challenge of translating PrEP trial results from heterosexual and IDU communities to their largely MSM HIV population. PrEP trials in Ecuador and Peru will address this; results from other countries will be available first.

At the same time, Dr Goicochea added, Peru is working with civil society groups to characterize other high-risk groups that remain hidden behind a "curtain of stigma." The unique needs of each target population must be identified, he proposed, before implementation begins.

## Priorities in designing global and national PrEP guidelines

**Renee Ridzon** of the **Bill & Gates Foundation** asked country representatives to consider several questions related to formulating PrEP guidelines:

- If PrEP looks promising, will you want guidelines from a normative agency?
- Do you anticipate formulating your own guidelines?
- Will you wait for global guidelines from a normative agency before formulating your own?

**Biziwick Mwale** of **Malawi's** National AIDS Commission said his country will probably develop its own guidelines as soon as trial results are sufficient

to indicate that PrEP should be implemented. Still, he noted that global guidelines would be helpful as a model for guidelines specific to Malawi.

Cate Hankins observed that most donor groups or national agencies, such as PEPFAR and ANRS, want to see guidelines from normative agencies before they start supporting national programs. All six countries with circumcision guidelines, she said, had their own stakeholder meetings to consider the relevance of the scientific data for their settings before the WHO/UNAIDS global guidelines discussion.

After presentation of the South African circumcision results in July 2005, the UN partners (UNAIDS, WHO, UNICEF, UNFPA and the World Bank) decided that the best policy was to wait for results of the two other African randomized trials before developing guidelines and to focus their efforts on supporting countries' decision-making through a broad preparatory workplan financed by NIH, ANRS, the Gates Foundation and UNAIDS. These six countries, with assistance through the first UN Workplan on Male Circumcision and HIV, convened stakeholder meetings in 2006 before the Montreux consensus consultation. As a result, those nations had a clearer understanding of their own attitudes about acceptability and their technical needs when the global guidelines were issued. Thus, she argued, even before guidelines move ahead on a global level, countries can and should move forward on their own to discuss possible implications and conduct situational analyses.

Countries that do decide to move ahead, Dr Hankins continued, and garner support from international partners are "early adopter countries" which can serve as models for other nations. They may become study tour sites where other nations get guidance on planning and launching their own programs.

Kevin De Cock added that international guidelines should be seen as advisory and not prescriptive. Each country should develop its own guidelines adapted to their national profile.

But global guidelines from normative agencies provide at least a minimum standard that countries can use as a template. At the same time, global guidelines are important not only for what they say, but also because they bring together representatives from diverse culture and constituencies.

## How much data justify steps toward preparedness?

Consideration of hurdles to implementation and needs in formulating guidelines led to a discussion of how much trial data normative agencies and individual nations need to conclude that they should begin considering an intervention such as PrEP.

**Ward Cates** of **Family Health International** noted that ongoing PrEP trials involve three different cultural and HIV risk populations. As a result, it may be difficult to apply results from one of these trials to another country or another risk population. Participants in the Thai PrEP trial, for example, are IDUs, and results of that trial will be available first. If those findings support PrEP as a preventive intervention, would Thailand also want a trial in MSM before considering PrEP for that population? Or would Thailand wait for results from the MSM trial in Peru and Ecuador and consider those results applicable to their MSM population?

Dr De Cock suggested that how many trials you need is partly a scientific question and partly a political one. One reason the trial-to-guideline process with circumcision took a long time is that the intervention is so unique. Yet other interventions, like post-exposure prophylaxis (PEP) became widely used with fewer data. He forecast that PrEP will probably fall somewhere between these two timelines.

It was noted that if PrEP is proven efficacious, further PrEP trials should focus on safety in different population groups such as pregnant women and adolescents rather than additional studies for efficacy, since there is no a priori reason to believe that efficacy would be different.

**Carl Dieffenbach** of the **NIH** noted that the Drug Safety and Monitoring Boards (DSMBs) for the two NIH-sponsored circumcision trials in Africa played an important role in determining whether those trials should proceed after results of the South African trial were presented. As those trials continued, the NIH team actively considered what recommendations might be made if results of the three trials were 3-to-0 in support of circumcision's efficacy, or 2-to-1, or 1-to-2.

In the same way, added Lynn Paxton, those involved in the Andean and Botswana PrEP trials should be considering right now how they might proceed based on early results reported from the Thai trial.

Dawn Smith concurred on that point, adding that contingency planning based on early results of ongoing PrEP trials is even more pressing than it was when circumcision trials were under way because TDF and Truvada are readily available, while wide implementation of circumcision is not. Stakeholders must also consider scale-up contingencies in the event that PrEP proves 80% or 90% effective versus, say, 50% effective.

Dr Dieffenbach of the NIH suggested that contingency planning for PrEP scale-up might consider different approaches depending on whether trials show success at 50%, 70%, or 90%.

Dr De Cock cautioned that ongoing clinical trials may demonstrate the *efficacy* of PrEP, but that does not necessarily mean the strategy will be *effective* in practice. Prevention experts had a good sense that circumcision *would be* effective in practice—even before trial results became available—because of plentiful epidemiologic evidence.

De Cock suggested that implementation of PrEP would benefit from research in three other areas:

- Epidemiologic research should be done to indicate the best populations to target. Even in a generalized epidemic, not everyone transmits HIV at the same rate.
- Cost-effectiveness data are needed to estimate how many people must be treated to prevent a single infection with different population-targeting scenarios.
- Specific work on PrEP in young women is needed because PrEP is one intervention that may work particularly well for them.

**Bob Grant** of **UCSF**, an investigator in the Andean PrEP trials, maintained that stakeholders should argue for a high standard of evidence for PrEP. TDF or Truvada is a costly pill, and implementing it will require further resources that could be spent on for example, malaria or TB. As a result countries that consider implementing PrEP deserve abundant evidence of its efficacy, including data on drug resistance. In fact, Dr Grant argued that data on an agent's efficacy as PrEP should reach the same level needed to license a drug: two phase 3 studies or one overwhelmingly positive study. Researchers should also make sure that studies last long enough to determine whether PrEP works in different populations.

**Zeda Rosenberg** of the **International Partnership for Microbicides** noted that PrEP is often considered a potentially valuable strategy for sex workers, yet sex workers are not included in the current trials. Ward Cates however observed that sex workers will be the target population for an upcoming PrEP trial in South Africa.

Dawn Smith argued that a balance must be struck between gathering too few data to begin planning and waiting until complete data from all ongoing trials are available. If PrEP does prove effective and countries wait for a complete data set, they will end up delaying implementation.

Planning must begin, Dr Smith argued, before trials yield data on every single risk group and every population. Trials may not be the only way to gather additional data, she proposed. For example, it may be possible to start planning PrEP implementation in sex workers without waiting for data from a sex-worker trial. Although implementation cannot begin until data confirm a degree of efficacy, there is also a cost in waiting too long.

Craig McClure observed that there have been two decades of vaccine preparedness work in the US and wondered how much that work has actually achieved in terms of readiness to deliver a preventive vaccine if and when one becomes available in the future.

**Mitchell Warren** of the **AIDS Vaccine Advocacy Coalition** believes there are lessons to be learned from vaccine planning efforts, beginning with the point that “we love talking about things that don’t exist.” Planning for vaccine implementation began so early, he noted, that the preventive vaccines considered in the original discussions have been almost entirely superseded by the disease-modulating vaccines that research now targets. It was noted that health planners spent much more time considering vaccine implementation than PMTCT, which has now been a reality for several years.

Mr Warren urged that discussions of PrEP implementation remain focused on realistic issues, such as how many people will remain adherent to once-daily dosing and other points outlined in Dawn Smith’s presentation. He added that PrEP rollout planners must also bear in mind that other preventive strategies will compete for attention and perhaps implementation. Thailand, for example, has ongoing vaccine and PrEP

trials. South Africa has two microbicide trials and will soon have a PrEP trial. And implementation of male circumcision is already under way.

Craig McClure summarized this part of the discussion by voicing the emerging consensus that stakeholders must plan to implement a comprehensive combination of interventions that may include PrEP, PMTCT, male circumcision, microbicides, HSV-2 suppression, and perhaps eventually vaccines.

### Will PrEP drugs be ready and affordable?

**Jim Rooney** of **Gilead Sciences** addressed PrEP implementation from the pharmaceutical industry perspective, stressing that the company’s role is neither to interpret trial results nor to anticipate policy. Rather Gilead aims to focus on making sure adequate drug supplies are available if needed. Toward this end, he reported three steps Gilead is taking: (1) expanding manufacturing capacity, (2) finalizing regulatory and distribution plans throughout the world, and (3) forging agreements for production of generic TDF and Truvada. Gilead is also looking ahead to what role Atripla (TDF, emtricitabine, and efavirenz) may play in countries that may use PrEP.

Pedro Goicochea noted that his country and others will face another important question if TDF or Truvada proves effective as PrEP: How much money should a country spend purchasing drugs for a PrEP program when funds are short for purchasing those very drugs for treatment for people living with HIV/AIDS?

# Key take home

## Key take home messages

### 1. The need to study different populations based on individual country epidemics

Trials reflect efficacy rather than effectiveness, i.e. how interventions such as PrEP may work in “real-life” conditions where behavioral disinhibition and rare side effects may occur. For this reason it will be important to study the safety and efficacy of PrEP in unstudied populations such as adolescents and pregnant women. Results in one country or population may not apply to others therefore, each country will need to address the appropriate use of PrEP given the characteristics of its epidemic and its prevention and treatment infrastructure, in particular:

- Priority groups to maximize reduction of epidemic
- Provider types and sites
- Barriers and implementation designs to overcome them
- Lessons learned from scale-up of PMTCT and antiretroviral therapy
- Reproductive health and pregnancy issues
- Funding and implementation partners

Other areas for research including alternative dosing strategies and modeling for epidemiological efficiency and cost-effectiveness.

### 2. The need to define core elements of a PrEP programme

Any PrEP programme regardless of location should include certain core elements for effective implementation. These include:

- Guidelines for usage
- Drug procurement and distribution strategies for those countries that do not already have TDF or Truvada available for treatment
- Exploring the impact of integrating PrEP on the national public health treatment programme
- Plans for initial and ongoing voluntary counseling and testing
- Communication strategies
- Clinical monitoring and adverse event follow-up
- Behavioral monitoring
- For seroconverters, viral resistance testing and access to second-line therapy, if needed

### 3. Implementing prep will be simpler compared to vaccine or microbicide implementation and has certain inherent advantages.

Unlike vaccines or microbicides, PrEP may have advantages in delivery given that:

- TDF and Truvada are already approved for treatment of HIV infection
- Require no new regulatory procedures
- Require no new manufacturing process
- Are available at reduced cost for the public sector in the US
- Are being licensed to generic manufacturers

PrEP has certain inherent advantages over other biomedical prevention technologies, namely:

- It may be used by both men and women
- Covert use is feasible
- Does not have to be used at time of exposure, for example microbicides that require application shortly before sexual intercourse
- May work for more than one type of exposure (for example, for an IDU who has sex)
- Can be stopped during low-risk periods
- Risks for HIV and STDS can be reduced through periodic counseling and testing
- Provides opportunities to link men as well as women to preventive care

### 4. Need to explore funding sources and establish partnerships for delivery

If PrEP proves successful, countries that implement PrEP will need to establish new funding sources or consider diverting funds from other treatment and prevention programs. A roll-out programme will need to allow for rapid introduction to achieve sufficient coverage, intensity and duration in order to have an optimal effect on local epidemics. Policy makers will also need to explore implementation of PrEP in the context of competing national health priorities.

### 5. How much evidence will be needed for countries to decide on implementing PrEP?

Countries will need to assess the implications of results from current trials including the level of efficacy it considers sufficiently protective as well as how best to apply findings from trials to their specific sub-group or generalised epidemics. DSMBs will play an important role in determining whether safety and

# Key messages

efficacy results mandate a change to protocol and the impact on future PrEP trials.

## 6. Prep will need to be integrated into other prevention strategies and delivered in the context of VCT

If PrEP proves effective, implementation should be synergistic with voluntary counselling and testing (VCT) and risk reduction programs including condom use. A number of clinical trials are currently underway testing a range of biomedical preventative technologies such as microbicides. There are also existing prevention methods such as condoms, treatment of sexually transmitted infections, PEP and circumcision. The key to an effective PrEP programme will be to determine how best to coordinate these new and current modalities to maximise protection against HIV. This may require targeting outreach and messaging to specific groups at risk, customising approaches relevant to a country or community setting. Importantly, this combination, integrated approach to HIV prevention must be reflected in national and international guidelines.

## 7. The need for normative agency and national guidelines

If PrEP proves efficacious in clinical trials, it is evident that guidelines from both normative agencies and those developed by countries themselves will be critical. The latter will reflect concerns specific to the country and its population, whilst the former can provide useful guidance and may serve as an essential pre-requisite for donor agencies funding PrEP. Normative agencies could assist a number of countries that are keen to roll-out PrEP with targeted guidance and support to develop them as exemplary or 'lead-in' countries serving as models for other countries considering PrEP implementation. Policy-planners must bear in mind when making decisions that TDF and Truvada are readily available. Stakeholders must also consider scale-up contingencies in the event that PrEP proves 80% or 90% effective versus, 50% effective.

## 8. Research needed to make prep implementation effective.

Implementation of PrEP would benefit from research in two other areas:

- Epidemiologic research should be done to

indicate the best populations to target. Even in a generalized epidemic, not everyone transmits HIV at same rate.

- Cost-effectiveness data are needed to estimate how many people must be treated to prevent one infection with different population-targeting scenarios.

A balance must be struck between gathering too few data to begin planning and waiting until complete data from all ongoing trials are available. If PrEP does prove effective and countries wait for a complete data set, they will end up delaying implementation.

## 9. What is industry doing to prepare for prep?

Gilead is taking a number of steps in anticipation of results from the PrEP trials:

- (1) expanding manufacturing capacity, (2) finalizing regulatory and distribution plans throughout the world, and (3) forging agreements for production of generic TDF and Truvada. Gilead is also looking ahead to what role Atripla (TDF, emtricitabine, and efavirenz) may play in countries that may use PrEP.

## 10. Coordinating PrEP implementation efforts

There is an urgent need to coordinate implementation efforts across the many different stakeholders who need to be at the table including:

- identifying research strategies for sub-populations, alternative dosing regimens and operational research strategies including cost-effectiveness, addressing allocation criteria, ethics and equity, developing modeling techniques to test epidemiological efficiency and delivery mechanisms
- the development of national and normative guidelines
- coordination of stakeholders across trial sites to prepare for imminent results
- identify early on, and provide guidance to those countries prepared to develop a PrEP programme
- planning for PrEP in the context of available resources and infrastructure
- promoting constructive networks and relationships with funder and donor agencies

**International AIDS Society**

33, Chemin de l'Avanchet

1216 Cointrin

Geneva, Switzerland

Tel : +41 (0)22 7100 800

Fax: +41 (0)22 7100 899

[info@iasociety.org](mailto:info@iasociety.org)

[www.iasociety.org](http://www.iasociety.org)



**International  
AIDS Society**

**Stronger Together**