

Report of a consultation:

Preparing for Pre-Exposure Prophylaxis (PrEP) Results: from research to implementation

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Acronyms

3TC	lamivudine
ART	antiretroviral therapy
ARV	antiretroviral drugs
CDC	U.S. Centers for Disease Control
EFV	efavirenz
EMA	the European Medicines Agency
FDA	U.S. Food and Drug Administration
FTC	emtracitabine
HBsAG+	hepatitis B surface antigen positive
HBV	Hepatitis B virus
HIV	human immunodeficiency virus
IDU	injecting drug user
iPrEx	Pre-exposure Prophylaxis Initiative
MSM	men who have sex with men
MTN	Microbicide Trials Network
NIH	U.S. National Institutes of Health
TDF	tenofovir disoproxil fumarate
UNAIDS	Joint United Nations Programme on HIV/AIDS
VOICE	"Vaginal and Oral Interventions to Control the Epidemic"
WHO	World Health Organization

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WORLD HEALTH ORGANIZATION

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Introduction

Safe and effective new approaches to HIV prevention are urgently needed. More than 7,000 people continue to become infected around the world every day (approximately 2.7 million per year). Evidence is mounting to support the observation that antiretroviral agents may be able to play an important role in reducing the risk for HIV transmission.

Pre-exposure prophylaxis (PrEP) is the use of antiretroviral drugs for the prevention of HIV infection. The proof of concept of PrEP rests on experience with the prevention of mother-to-child transmission, on the experience with using post-exposure prophylaxis (PEP) and on evidence of viral load suppression following treatment and specific animal studies. While the potential is great, a string of recent failures in biomedical prevention trials argues for measured optimism until the results of the PrEP trials are available. Coupled with the many possible hurdles for PrEP implementation, careful planning and the development of a clear strategy are called for.

If proven safe and effective, PrEP could provide an important new prevention method to be added to the existing range of prevention options. Key populations which may benefit from PrEP could include those at higher risk of HIV exposure such as men who have sex with men (MSM), people who inject drugs (IDU), and sex workers, or all those at risk of sexual transmission in areas with endemic or hyperendemic HIV transmission such as southern Africa. PrEP could also address the urgent need for a female-initiated prevention method for women worldwide who are unable, because of power imbalances and other possible cultural barriers, to negotiate condom use.

Currently, trials are being conducted on four continents. One Phase II trial of PrEP was completed in west Africa in 2007 (Peterson et al 2007). It demonstrated the safety of the approach but was not powered to detect efficacy. Trial effectiveness, of PrEP is currently being assessed in three ongoing and planned Phase III trials, most in low- and middle-income countries and many of which are multi-

site trials (iPrEx, Partners PrEP and Fem-PrEP) and in five additional Phase II, Phase IIb or Phase II/III studies (CDC 4323, Caprisa 004, MTN 003/VOICE, CDC 4370 and CDC 4940). The majority of these trials are assessing the efficacy of daily oral PrEP using either tenofovir disoproxil fumarate (TDF) or TDF plus emtricitabine (FTC). The two Phase IIb trials are assessing 1% topical TDF gel, either pre- or post-coital dosing compared to placebo (Caprisa 004) or with daily dosing of TDF gel compared to daily oral TDF or daily oral TDF/FTC, compared to two placebo arms. These trials are taking place in a number of countries: the United States, Thailand, Peru, Ecuador, Brazil, Botswana, South Africa, Kenya, Uganda, Malawi, Tanzania, Zambia and Zimbabwe. Taken together, these trials are enrolling more than 20,000 research subjects and are designed to produce results in diverse populations—representing multiple routes of HIV transmission—including:

- people who inject drugs in a trial in Thailand (CDC 4370);
- gay men and other men who have sex with men (MSM) in trials in Brazil, Ecuador, Peru, Thailand, and the United States (iPrEx and CDC 4323);
- heterosexual men and women in a trial in Botswana (CDC 4940);
- sero-discordant heterosexual couples in a trial in Kenya and Uganda (Partners PrEP); and
- women (considered “high risk” or “sexually active” depending on the study) in trials in eastern and southern Africa (Fem-PrEP, VOICE and Caprisa 004).

The time to completion for these event-driven trials has been hard to estimate as incidence in many sites has dropped, a commonly encountered phenomenon when research subjects are exposed to the standard of HIV prevention that is ethically required. Nonetheless, it is imperative to take steps now to prepare for actions that will be needed following the release of first results. The first results, from the US-based TDF safety trial (CDC 4323), are expected in the first half of 2010 with two other trials (iPrEx and CDC 4370) expected to report later in 2010 or early 2011.

Even if these trials show proof of effectiveness, it is not clear that PrEP can be effectively implemented to realize its prevention potential in actual application. While the focus of attention is currently on demonstrating trial effectiveness, steps must be taken now to assure that PrEP has the chance to be the major prevention advance that all are hoping for.

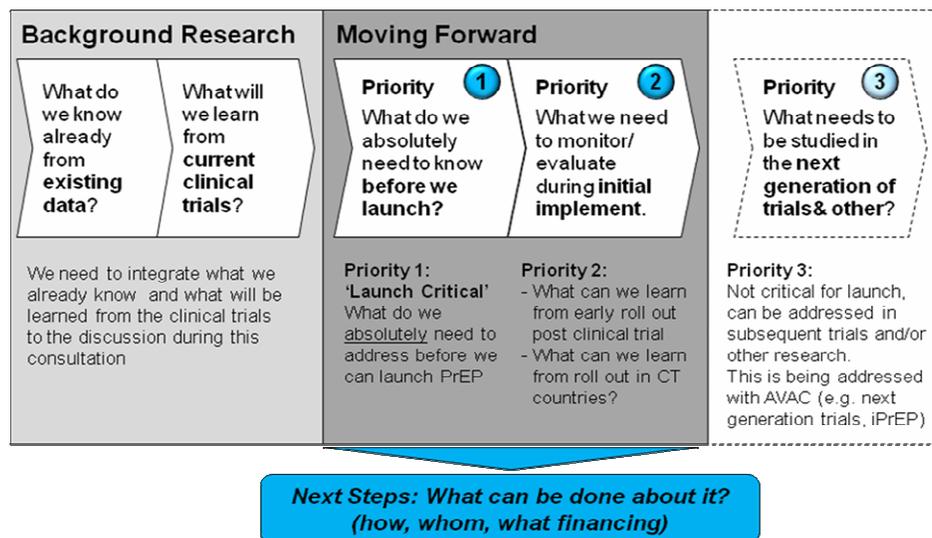
Aim and Process of this Consultation

The aim of this consultation was to focus on the additional research that will be required, should current trials show effectiveness, to assure that PrEP reaches its theoretical effectiveness in actual application. Prioritizing a list of research questions seen as critical for a successful PrEP launch and defining how we can answer those questions remains a pressing need. Other fields such as microbicides and vaccines have done a lot of work in these areas already. By bringing together

trialists, civil society, representatives of national ministries of health, investigators and funders of research trials, this consultation offered an opportunity for cross-fertilisation and cross-linking among the participants. Working in groups focused on health systems and users' issues, the participants were asked to define:

- A. What is known now from existing evidence in PrEP research and other fields?
- B. **What research** will be needed to prepare for implementation?
- C. Which issues have **highest priority** (launch critical) versus lower priority?
- D. How can the **additional information** be collected? (How, who, where, which funding, etc.)

While it is clear that the more is known, the better those who are planning for PrEP implementation and scale up will be to decide and act intelligently, some questions are more pressing than others. Participants were asked to rate each of the 'research questions' they deemed important keeping those temporal needs in mind. Specifically, they were asked to rate the research needs as 'priority 1, 2 or 3' following this schema:



In a background paper prepared for the consultation, participants were guided to consider the following questions:

- *What is already known about PrEP potential from existing data?* The current PrEP trials have benefited from previous research experience in HIV/AIDS and public health in general. Additional information could be drawn from other areas in public health where certain similarities exist. For example, some comparable information on risk compensation may be available from the

experience of providing male circumcision. Other daily prevention regimens like oral contraception may also provide useful parallels for daily adherence to PrEP. What can be projected about scaling up PMTCT that may provide a useful parallel for what to expect in scaling up PrEP. Other examples may exist and participants were expected to share their own suggestions.

- *What will be learned from current clinical trials?* Current trials have conducted some research, for example on user acceptability, in preparation for their effectiveness studies. These trials will also provide a large amount of information once they conclude. The participation of trialists was a major asset to help identify some of the key gaps in our knowledge that may persist even after the conclusion of these trials.

Within these general sets of questions, participants were asked to prioritize according to the following schema:

Priority 1: *‘What absolutely must be known before PrEP is launched?’* This is the priority referred to as ‘Launch Critical’. Participants in this consultation were asked to identify which questions best fit this category, connoting information that absolutely be known before PrEP is launched. Because of the time sensitivity of ‘Launch Critical’ questions, participants were encouraged to consider and recommend among other options how research components might be added to *existing* clinical trials or other *ongoing* research to address these launch critical questions. For example, much can be learned in the early stages after unblinding of the efficacy trials but before roll out and implementation of PrEP. This period corresponds to the agreed time that those who participated in the trials will be provided with the active product if effective. This period varies by trial, ranging from 9 to 18 months and provides an opportunity to explore some implementation issues.

Priority 2: *‘What should be monitored / evaluated during initial implementation?’* It is important to keep in mind that some questions are not answerable from the first generation of trials. For example, risk compensation in actual use, risk for development/transmission of resistant virus are all important questions that may not be answerable before launch and will benefit from careful post-launch monitoring. Much can be learned by carefully monitoring implementation during early launch within countries hosting PrEP trials, based on the premise that PrEP will be implemented first, and more easily, in these countries.

Priority 3: *‘What needs to be studied in the next generation of trials?’* This was not given priority for this consultation and participants were not encouraged to spend much time discussing this. AVAC has been leading a consultation process with researchers separately to address this question. The main focus of this WHO consultation was to make the most out of current and soon available information

from current trials on first generation products. Questions in this priority 3 group on second-generation PrEP products or trials were not to be addressed.

Issues for discussion in consultation: health systems

A number of issues were highlighted to assure that groups considered their import for further PrEP development. For health systems, these were:

- I. Drug resistance:** the risk of resistance is a concern as people may become infected while taking PrEP and in continuing to take it, they will have the potential to develop a resistant virus.
- II. Testing, retesting & counselling:** HIV negative status of an individual must be verified before starting PrEP and for PrEP continuation, on an on-going basis. A strategy for testing and re-testing will be essential to ensure that only those uninfected use it.
- III. Renal dysfunction testing:** TDF may be associated with renal toxicity and serious adverse reactions in people on TDF-containing combination regimens. In seronegative people of PrEP, re-testing to monitor renal function may be necessary on a regular basis. Careful consideration must be given to the optimal frequency of renal testing, taking into account user and provider acceptability and general cost and burden to the health system.
- IV. Infrastructure, financial and human capacity:** current infrastructure, human resource capacity and financial resources are likely too limited to meet requirements for PrEP. The minimum necessary package to ensure an effective roll out will need careful consideration.
- V. Adding PrEP to existing prevention, care and treatment priorities** (either integrating PrEP with other existing programs, or implementing PrEP in addition to other programs): PrEP will be only one HIV prevention method among many. It will also compete for needed resources with ARVs for treatment and possibly ART for prevention. Before launching PrEP, the benefits of PrEP vis-à-vis other biomedical and behavioural interventions for HIV prevention need to be addressed.
- VI. Hepatitis B retesting:** PrEP use may be a problem for people with chronic active hepatitis B. TDF is use to treat chronic active hepatitis B infections; an abrupt cessation can sometimes result in flares and liver damage.

Issues for discussion in consultation: users' perspectives

For users' perspectives, the issues highlighted for discussion at the consultation included:

- I. User and community acceptability for a daily prevention method:** motivating high-risk but uninfected individuals to take a daily dose of ARVs could be challenging, just like convincing men and women to use a condom every time they have sex, or convincing injecting drug users to use clean needles and syringes every time they inject drugs.
- II. Adherence:** actual levels of adherence to a daily regimen might present another challenge.
- III. Risk Compensation:** even though PrEP is likely to be only partially effective, PrEP users or their partners might feel completely protected, and therefore increase the number of partners, decrease condom use and other prevention methods or increase their frequency of sexual acts .
- IV. Social Issues:** PrEP use may have social meanings that are unforeseen. HIV negative individuals taking PrEP might be associated with high-risk groups, assumed to be promiscuous individuals, or stigmatised in other similar ways. Individuals taking PrEP may in fact be thought not to be taking a preventive measure but instead getting treatment for AIDS. As a result, the stigma often associated with HIV in persons taking ART might affect people's willingness to take PrEP or could have a serious impact on their adherence to PrEP.
- V. Safety issues:** a number safety issues linked to the use of TDF and TDF plus FTC may be better understood after the current trials.
- VI. Drug sharing:** Individuals on PrEP might be tempted to sell their pills, share their pills with others, for example with an infected member of the family who needs treatment, or use another untested ARV drug, or even a non-ARV drug, for prevention.

General conclusions of the discussions:

Following a brief period of presentations about PrEP to familiarize all with the current state of the research and what will be learned, the participants were divided into four groups. Two addressed the health system issues, two addressed the user perspectives.

In the feedback from the discussions, it was apparent that strong consensus had formed around two key points: (1) PrEP may have enormous potential as a new prevention approach if proven effective in the current trials but (2) implementing and scaling up PrEP to realize its potential will not be easy. On the latter point, the feeling was perhaps best summarized by the phrase used in one working group

summary: This is not a "no brainer". The consultation was notable for the mixture of optimism and realism in its conclusions.

Each working group, no matter what the topic considered, reached the same general conclusion: PrEP implementation and scale up needs to proceed first through a period of demonstration projects. Strong consensus developed around the need for additional, empirical information to guide next steps in PrEP implementation and scale up. Some dissenting voices offered concerns, not about the concept of demonstration projects but about the extensive list of information hoped for from that research. It was felt by these dissenters that the additional data collection demands would deter programme managers from ever trying to implement PrEP. The response to that concern was that PrEP is currently functioning in a "data free zone", a phrase that was heard more than once in the discussions at the consultation. As additional information develops or is produced by the current trials in the field, the list of question is likely to be reduced, perhaps substantially.

The need for additional information was instrumental in leading to the conclusion that PrEP should not be slated for massive roll out after the conclusion of the necessary number of trials. Instead, demonstration projects in controlled settings, using existing structures, targeting particular populations such as sex workers and their clients, IDU, MSM, discordant couples, those at high risk in generalize epidemics, etc., should be conducted first. These could be put in place most expeditiously by building on the existing clinical trials under an amended protocol. In addition to providing more information, these demonstration projects will also be useful for policy makers while they attempt to balance the need for more resources for universal access to treatment and the need for expanded prevention, especially potentially costly prevention such as PrEP may be. These demonstration projects could then be used to provide additional information on:

- (1) optimal frequency of HIV retesting;
- (2) optimal way and frequency of renal function testing;
- (3) safety of PrEP during pregnancy and breastfeeding;
- (4) acceptability to users;
- (5) feasibility of channels of delivery within and outside the health sector;
- (6) adherence counselling for PrEP;
- (7) pregnancy testing frequency; and other key issues such as frequency of drug sharing in communities with PrEP programmes, additional information on toxicity and the opportunity to refine counselling messages.

Specific recommendations on health systems questions

The two groups that discussed issues in PrEP implementation and scale up from the perspective of health systems offered the following conclusions and recommendations:

- 1. Drug resistance:** these issues were not considered to be "launch critical" and were given a priority 2 rating. Analysing what evidence of resistance is discovered in the current PrEP trials will be important for obtaining national approval for PrEP implementation. After initial launch, it will be possible and important to monitor resistance in demonstration projects, including evaluating mutations at seroconversion and over time to assess persistence. As resistance is considered such an important issue, any demonstration projects should be adequately powered to detect levels of resistance and to assess transmitted versus acquired resistance. CDC and others are currently planning for demonstration projects to follow their clinical trials and should be encouraged and facilitated to develop protocols that address the key needs for PrEP implementation and scale up.
- 2. HIV testing, retesting & counselling:** it was agreed that WHO should be responsible for developing a standard for the frequency of retesting before the implementation of PrEP begins. This makes this a critical priority for the near future. Striking the right balance will be challenging, but an approximation of the best interval could be informed by examining resistance data from the current trials and through modelling. Additional data on resistance, the consistency of the drug supply, risk compensation and user acceptability, all potentially important for establishing the best retesting interval, could be drawn from ART programmes, the FemPrEP roll out study, exit interviews that could be conducted in the existing trials and through specific demonstration projects. Any guidance on retesting frequency needs to balance concerns over resistance with additional burden on the health system and the tolerance of PrEP users. It was also observed that any general recommendation on retesting frequency will need to be adjusted based on observed incidence in specific sites and that demonstration projects can also help with this. Guidance on how best to address risk reduction and adherence counselling could also be informed by the experience of the current trials and the observed risk compensation in those; specific exit interviews may be helpful (being careful to ascertain treatment assignment in any such interviews).
- 3. Renal dysfunction / bone testing:** Renal dysfunction testing was generally seen as a "launch critical" area. General safety monitoring should be informed by the experience of the current trials. For comparative purposes, data are needed from less healthy populations than those typically enrolled in the current trials. A point-of-care test for renal dysfunction does not exist yet but is badly needed. In the absence of such a test, or even if such a test becomes available, it may still be useful to devise an algorithm for use in low resource settings. Bone testing was discussed but limited data on what

constitutes normal bone density in many of the populations where PrEP may be used complicates its measurement in actual use. It was given a lower priority.

- 4. Infrastructure, financial and human capacity:** These issues were considered to be top priority and badly in need of additional data. Some of the ongoing studies will provide some information; the roll out study included in FemPrEP was specifically mentioned. In addition, it may be productive to look at the reproductive health literature on systems and deliverability for more insights. Furthermore, additional thinking and modelling will be helpful in comparatively assessing the costs of alternative delivery strategies. The discussion groups also pointed out that the segment of the health sector that will be responsible for PrEP implementation and scale up will vary by context but will certainly include ministries of health, nongovernmental organizations and the private sector. The needs of each in addressing the challenges presented by PrEP implementation and scale up will vary as well. It will be important to be prepared to meet as many of those needs as possible.

One group also focused on the need to start the regulatory process early, involving national regulatory authorities. It recommended that WHO stimulate or facilitate a regional approach to regulatory approval that could expedite the process in countries.

Costs, and the complexity of costs, were addressed by one group. In addition to the obvious cost of the necessary drugs for PrEP, this group also highlighted the costs of testing (both for HIV and for safety/monitoring), additional staff burden, training for staff to provide PrEP, additional infrastructure, communications, among others. The question of how much these costs will be and what effect they have on the cost effectiveness of PrEP will need to be addressed. Who will pay these costs is also a key question to address. The potential contribution from health insurance needs to be addressed. In the process, it will be important to position PrEP not as competing with other prevention methods but as an element of a combination package for prevention. It should be a key goal of the clinical trials and the proposed demonstration projects to establish what this minimum combination package should be.

The Bill and Melinda Gates Foundation is supporting two grants that will feature prominently in this area. One is with the Georgetown University and Imperial College and the other is with the World Health Organization (WHO) and UNAIDS. Taken together, this work addresses the question of deliverability of PrEP and is the start of planning for eventual implementation and scale up, should PrEP trials show sufficient efficacy. National and regional consultations are being planned, to see what the anticipated barriers to implementation look like from the perspective of those who will ultimately be responsible for delivering PrEP. The responsibility for following through on this area of work, then, rests primarily with WHO/UNAIDS and Georgetown/Imperial College.

5. Adding PrEP to existing prevention, care and treatment priorities: This was also seen as a "launch critical" topic and given the highest priority. Before key decisions can be made, donors will need cost-effectiveness analyses, comparing PrEP to other interventions. These analyses will have to be reviewed with country policy makers. In addition, pharmacovigilance programmes will need to be developed, largely a WHO responsibility. The responsibility for the rest of this work rests primarily with the PrEP Delivery Working Group, convened and co-chaired by Georgetown/Imperial and WHO/UNAIDS.

6. Hepatitis B retesting: this area was seen as not launch critical and was given the lowest priority. It was felt that screening for Hepatitis B virus (HBV) prior to initiating PrEP was not supported by the current evidence. Demonstration projects should specifically include participants who are hepatitis B surface antigen positive (HBsAG+) , however. Further analysis of the cost benefit of HBV vaccination for those susceptible to Hepatitis B could be useful. The Bill and Melinda Gates Foundation are supporting an effort on data pooling across the PrEP trials currently in the field. This pooling can be used to inform recommendations about screening for Hepatitis B in the future.

The health systems group also discussed additional questions. Significant by their absence are any data on PrEP use in pregnant women; they are specifically excluded from the current trials, either at recruitment or dropped from the trials if pregnancy takes place. Clinical data on pregnant women will likely be sought by regulatory agencies like the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA). To meet this need, the group suggested the possibility of short-term safety study in HIV negative pregnant women. In addition, other opportunities for using existing or upcoming data on the safety of use during pregnancy of the same drugs being assessed for PrEP were identified. These included:

- i. the PROMISE study has an RCT comparison of TDF plus FTC versus AZT plus 3TC in the third trimester of pregnancy in HIV/HBV co-infected women. This study is also looking at Truvada (tenofovir) levels in breast milk;
- ii. an ANRS study comparing TDF/FTC/EFV versus AZT plus 3TC in the third trimester of pregnancy; and
- iii. the possibility of including breast feeding women in future demonstration projects.

The FEM-PrEP roll out study was also identified as a potential source of data. This qualitative study will conduct 120 exit interviews with participants to gather information on user perspectives. It will also interview key stakeholders and community leaders to gather qualitative information on the perspectives of those inside the systems that will be key players in PrEP implementation and scale up.

Finally, the health systems group strongly recommended that PrEP implementation and scale up profit from existing work and perspectives to the greatest extent possible. In that regard, specific mention was made of the Strategic Approach, a systems framework originally developed for the introduction and scaling up of new contraceptive technologies. Its applicability more generally has now been well established and its use for the implementation and scale up of PrEP could be very beneficial.

Specific recommendations on users' perspectives questions

Two groups discussed the important questions in PrEP implementation and scale up from the perspective of potential users of PrEP. These groups felt that there should be agreement on what level of evidence is needed to justify moving on to the implementation of PrEP. It was also strongly felt that large scale roll out and implementation prior to carefully designed demonstration projects was not justified, given the substantial amount of information that will still be needed to make PrEP implementation and scale up feasible and successful. At a national level, a considerable amount of information will be needed to facilitate the decision making process about whether PrEP is a good investment and addition to existing prevention strategies. Knowing the epidemic, the potential target audiences, the environment into which PrEP will be introduced, as well as those at continued risk of HIV to whom PrEP may be specifically targeted were all seen as essential information that must be at hand before planning for PrEP implementation and scale up. Key stakeholders to consult in this preparation for possible PrEP implementation and scale up include researchers, clinicians, community groups (and especially potential users of PrEP), local authorities, programme planners and implementers (such as ministries of health and others) and social marketers.

An extensive matrix of possibly beneficial information was presented (appendix 1) and subsequently challenged in discussion for being too all encompassing. In defending the extensive nature of the matrix, it was remarked that the current "data free" state in which planning for PrEP implementation and scale up exists argues for this degree of additional information. Nonetheless, the matrix presented should be regarded as a road map for consideration in the design of demonstration projects and not to be proscriptive. Furthermore, as the current trials produce results over time, some of these information needs may be adequately addressed and the extent of the data sought in the matrix may possibly be reduced.

User and community acceptability for a daily prevention method: Targeting young women for PrEP use was seen as advisable. The possibility to package daily PrEP with daily oral contraceptive pills was also seen as a possibly advisable step. Coupled with appropriate messaging, this may help increase uptake and adherence to PrEP among one group that would be likely to benefit.

Adherence: Though there was concern about the black market in the provision of PrEP, as the drugs are available in countries and can be sold through unofficial channels without the necessary

precautions, concern was also voiced about the "white" market. If the logistics and supply system in a country are not up to the task of providing a steady and adequate supply of drugs for PrEP, then problems with adherence outside the control of the user will arise and prevention opportunities will be lost. Assuring the adequacy of the logistics and supply system before implementing PrEP may be an important step.

Risk compensation: It was taken as a given that some level of risk compensation is likely to take place. Assessing how much that might be a priori was not seen as an important question. No strong endorsement of research to measure risk compensation everywhere, to characterize it better or to assess its impact on potential effectiveness of PrEP was voiced. Accepting it as likely and preparing to minimize it with a comprehensive PrEP delivery programme was recommended. Delivering PrEP as a component of a comprehensive prevention package should be planned from the outset.

Social issues: it was felt that HIV-associated stigma, common against those who take treatment, could occur for PrEP as well, as the popular perception might fail to distinguish between the two. Careful messaging in the provision of PrEP should take this possibility into account, to counter it from the outset, and not wait until it is recognized as a problem.

Safety issues: these issues were generally felt to be less important, given that the drugs under investigation for use as PrEP are well studied and for the most part have well-established safety profiles. The question of safety for adolescent girls and pregnant women, as mentioned above, may still require further study, as these two groups are specifically excluded from the current trials.

Drug sharing: This topic was not addressed in the discussion groups.

Conclusions: The meeting was successful in reducing the amount of pressing or urgent questions, referred to as the "launch critical", to a more manageable number: (1) HIV testing and retesting; (2) testing for renal dysfunction; (3) developing the necessary infrastructure for safe and continual delivery of PrEP; (4) adding PrEP to existing prevention efforts; and (5) addressing the stigma which may affect PrEP use. It was also successful in achieving consensus on the critical need for demonstration projects to explore the best implementation and delivery options for PrEP should the existing trials demonstrate sufficient efficacy. Strong consensus was also formed around the importance of knowing the context into which PrEP would be delivered and the need to develop, or tailor, implementation approaches to accommodate these. Helpful guidance for future implementation was also expected from other efforts being undertaken including mathematical models now under development and a review of the history and experience of other efforts to implement public health interventions at scale. Future discussions of roles and responsibilities among the international agencies and donors were also encouraged, to assure that this important agenda can be moved ahead and coordinated.



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Factor	IDU	DU	FSW	MSW	Hetero men	Hetero women	MSM	Other groups
Group								
POST-REGISTRATION								
Demonstration projects								
Provider behavior studies								
INPUT - EPIDEMIOLOGY								
HIV incidence								
STI incidence								
Risk factors								
- demographic								
- behavioral								
Existing levels of protection								
- condom use								
- clean needles								
- needle access								
FOR TARGETING								
- those at continued high risk								

Factor	Group	IDU	DU	FSW	MSW	Hetero men	Hetero women	MSM	Other groups
<i>MONITORING</i>									
HIV incidence									
STI incidence									
Demand									
Adherence/Uptake - regimen adjustment									
Side effects									
Risk compensation - condom use - partners - non-condom use risk reduction - sero-sorting - PrEP positioning - drug use behavior									

Factor \ Group	IDU	DU	FSW	MSW	Hetero men	Hetero women	MSM	Other groups
HIV testing frequency								
Acceptability								
- Individual								
- Community								
- Authorities								
Access to services								
- barriers								
- sensitivity								
PrEP drug sharing								
Black market supply								
White market supply								
Social marketing activities								
Stigma								
Legal issues								
Discrimination								
Domestic violence								

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