MOSAIC is made possible by the generous support of the American people through the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR) and the U.S. Agency for International Development (USAID) through Cooperative Agreement 7200AA21CA00011. The contents of this presentation are the responsibility of MOSAIC and do not necessarily reflect the views of PEPFAR, USAID, or the U.S. Government.

**An Assessment of HIV Drug Resistance among Seroconversions in Users of Pre-exposure Prophylaxis in [Insert country name]**

**Protocol Chair:**

[Insert Name]



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Abbreviations

|  |  |
| --- | --- |
| 3TC | Lamivudine |
| ART | Antiretroviral treatment |
| ARV | Antiretroviral |
| CAB | Cabotegravir |
| CI | Confidence interval |
| CRF | Case report form |
| EC | Ethics committee |
| FDA | Food and Drug Administration |
| FTC | Emtricitabine |
| HCW | Health care worker |
| HQ | Headquarters |
| GCP | Good Clinical Practices |
| GEMS | Global Evaluation for Microbicide Sensitivity |
| HIV | Human immunodeficiency virus |
| INSTI | Integrase strand transfer inhibitor |
| IRB | Institutional review board |
| MOP | Manual of operations |
| MOSAIC | Maximizing Options to Advance Informed Choice for HIV Prevention |
| NNRTI | Non-nucleoside reverse transcriptase inhibitor |
| PK | Pharmacokinetics |
| PrEP | Pre-exposure prophylaxis |
| TDF | Tenofovir disoproxil fumarate |
| TFV–DP | Tenofovir–diphosphate |
| WHO | World Health Organization |

Protocol investigators

Primary Investigator

[Name]

[Organization]

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Co-Investigators

[Name]

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[Phone]

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Statistician

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[Organization]

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[Phone]

[Email]

# Key roles

**Funding Agencies:** USAID

**Laboratories:**

[Laboratory Name]

[Address]

**Back-up Laboratories:**

[Laboratory Name]

[Address]

Protocol summary

**Short Title:** An Assessment of HIV Drug Resistance Seroconversions among Users of Pre-exposure Prophylaxis in ***[Insert Country Name]***

**Funder:** United States President's Emergency Plan for AIDS Relief (PEPFAR) and United States Agency for International Development (USAID) through Cooperative Agreement 7200AA21CA00011, Maximizing Options to Advance Informed Choice for HIV Prevention (MOSAIC)

**Protocol Chair: *[Insert Name]***

**Sample Size: *[TBD]***

**Study Population:** Individuals who acquire HIV-1 while using an HIV pre-exposure prophylaxis (PrEP) method available in ***[Insert Country]***

**Study Design:** Cross-sectional

**Study Duration:** One-time visit per participant, with accrual continuing until approximately ***[Insert Date]*** or ***[Insert #]*** participants are enrolled

**Study Methods:** Individuals using an HIV PrEP method who have a reactive HIV test will have blood drawn to assess HIV drug resistance. The blood sample will be collected only once for each participant, at the time of the first reactive HIV test result.

**Primary Objective:** To assess the frequency of HIV-1 drug resistance mutations among PrEP clients who test HIV positive after initiating PrEP

**Primary Endpoint:** Mutations in HIV-1 reverse transcriptase and/or integrase known to be associated with drug resistance

**Exploratory Objectives:** To explore the relationship between HIV drug resistance and PrEP adherence in individuals who seroconvert on PrEP

**Exploratory Endpoints:** Proportion of individuals with drug resistance mutations, by PrEP exposure status

Introduction and background  
Primary HIV prevention is an important component of efforts toward the United Nations Programme on HIV/AIDS (UNAIDS) goal of elimination of HIV by 2030.(1) The World Health Organization (WHO) recommends the use of oral pre-exposure prophylaxis (PrEP) with daily emtricitabine plus tenofovir disoproxil fumarate (FTC/TDF) or lamivudine (3TC) plus TDF or emtricitabine and tenofovir alafenamide as a prevention strategy for individuals at substantial risk of HIV.(2) WHO also recommends the use of the dapivirine vaginal ring (“PrEP ring”) for HIV prevention for women at substantial risk of HIV.(3) Injectable cabotegravir for PrEP (“CAB PrEP”) demonstrated high levels of HIV prevention in two large-scale efficacy trials among people at higher likelihood of exposure to HIV(4, 5), resulting in the approval of Apretude (CAB PrEP) by the U.S. Food and Drug Administration (FDA).

Oral PrEP, the PrEP ring, and CAB PrEP have been shown to reduce the risk of HIV acquisition, especially when used in combination with other behavioral preventive methods.(4–8) Although some PrEP users may still acquire HIV, effectiveness in preventing HIV increased as adherence increased in trials, in particular for oral PrEP and PrEP ring.(8-12)

The potential for overlapping resistance and cross-resistance between antiretrovirals (ARVs) used for prevention and for treatment is an important concern for the large-scale rollout of PrEP. The major factors influencing the selection or acquisition of resistance during PrEP use include the level and duration of ARV exposure during unrecognized acute infection, the occurrence of breakthrough infection due to suboptimal drug levels, and the prevalence of transmitted drug resistance in the regions where PrEP rollout is implemented.(13)

Oral PrEP efficacy trials demonstrated that HIV drug resistance (HIVDR) is infrequently selected if PrEP is successfully started before HIV-1 acquisition has occurred and is more likely to occur when PrEP is inadvertently started during undiagnosed acute infection. Among the 348 seroconversions reported among individuals while prescribed oral PrEP, 35 occurred when PrEP was initiated during undiagnosed acute infection; of these, 18 of 35 (51 percent) had HIV-1 with mutations associated with TDF or FTC resistance (K65R and/or M184I or V). A total of 313 individuals became HIV positive after starting PrEP; of these, 19 of 313 (6 percent) had TDF- and/or FTC-associated mutations.(13-15) Results from the Global Evaluation of Microbicide Sensitivity (GEMS) project further demonstrated the risk of HIVDR with oral PrEP use in a real-world setting across Eswatini, Kenya, South Africa, and Zimbabwe. Of the 118 individuals who seroconverted and were tested for HIVDR through GEMS, 23 percent had PrEP-associated resistance mutations, with the majority having TDF-diphosphate levels associated with four or more doses per week.(15)

***[Insert Country-specific data as applicable.]***

The PrEP ring efficacy trials (ASPIRE and The Ring Study) demonstrated that rates of resistance did not differ between the placebo ring and PrEP ring arms, indicating that resistance was likely transmitted and not selected by dapivirine ring use (Table 1). Of 71 women from the PrEP ring arm who seroconverted in ASPIRE, eight (11 percent) had one or more non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance mutations; of the 77 women from the PrEP ring arm who seroconverted in The Ring Study, 14 (18 percent) had one or more NNRTI resistance mutations. Similar levels of drug resistance were observed in placebo arms.(6, 9, 10) The risk of transmission or selection of high-level NNRTI-resistant virus in rollout settings is not yet known.

table 1. NNRTI resistance from Phase 3 and open-label studies of the PrEP ring (18)

|  |  |  |
| --- | --- | --- |
| Study | PrEP ring arm: number with NNRTI resistance/number seroconverted (%) | Placebo ring arm: number with NNRTI resistance/number seroconverted (%) |
| MTN-020 (ASPIRE) | 8/71 (11%) | 10/96 (10%) |
| IPM 027 (THE RING STUDY) | 14/77 (18%) | 9/56 (16%) |

The CAB PrEP efficacy trials identified 20 seroconversions, five of which involved integrase strand transfer inhibitor (INSTI) resistance (Table 2). (4, 5) These trials demonstrated that diagnosis of HIV could be delayed for individuals who become HIV positive while taking CAB PrEP, and there is a risk of CAB resistance selection during undiagnosed infection. More research is needed to understand the risk of resistance among individuals who acquire HIV after missing doses or discontinuing CAB PrEP. Resistance is a potential concern with CAB PrEP due to its long pharmacokinetic (PK) tail, which remains at subtherapeutic concentrations for up to a year or longer after the last injection.(4, 5, 18-20) Despite significant progress in controlling HIV, the incidence of HIV among adolescent girls and young women in many parts of sub-Saharan Africa remains excessively high: Among 15- to 19-year-olds, four in five new infections occur in females. Numerous factors contribute to this high incidence rate and subsequent complications.

table 2. HIV drug resistance from individuals from HPTN 083 who seroconverted on CAB PrEP (23)

|  |  |  |  |
| --- | --- | --- | --- |
| Case | Visit | NRTI/*NNRTI* | INSTI |
| A2 | Enrollment | – | Not detected |
|  | Week 6 | – | E138K, Q148K |
| C1 (oral) | Week 9 | – | Q148R |
|  | Week 10 | – | E138E/K, G140G/S, Q148R |
| C3 (oral) | Week 9 | – | E138, Q148R |
| D3 (IM) | Week 17 | *K103N* | – |
|  | Week 33 | *K103N* | R263K |
| D4 (IM) | Week 12 | – | G140A, Q148R |

As countries implement national PrEP programs, it is important to assess individuals who seroconvert to determine the frequency of HIV drug resistance mutations. These data will inform national PrEP programs and can help to ensure long-term effectiveness of both PrEP and antiretroviral treatment (ART).

# Rationale for study design

The primary objective of this study is to assess the frequency of HIVDR in individuals who seroconvert while using PrEP as part of national PrEP rollout. The potential for overlapping HIV drug resistance and cross-resistance between ARVs used for prevention and for treatment is an important global concern for the large-scale implementation of PrEP products. The GEMS project showed low rates of seroconversion but high rates of NRTI and NNRTI resistance in individuals who seroconverted on oral PrEP during the first three to five years of oral PrEP introduction and rollout in four countries in sub-Saharan Africa.(15) The data on the risk of HIVDR in the context of newer PrEP modalities (the PrEP ring and CAB PrEP) are limited to clinical trials or open-label studies, and it is important to assess resistance risk in seroconversions with the introduction of these products nationally. Implementation of PrEP rollout differs from clinical trials in many ways, including different intervals for HIV testing and adherence support strategies. For CAB PrEP, they also include differences in strategies of using nucleic acid testing for detection of acute infection and the addition of oral PrEP to help prevent HIV acquisition and drug resistance after discontinuation of CAB PrEP.(4),(5)

This cross-sectional study allows for a one-time measurement of drug resistance following seroconversion on any PrEP method or strategy that has been approved in country, limiting clinic and participant burden. The results will provide an overall prevalence of drug resistance in clients who seroconverted while receiving PrEP. These data may assist in the assessment of the quality of the PrEP programs, contribute to overall pretreatment surveillance data, and inform our understanding of the potential impact of HIVDR on first-line ART regimens. Ultimately, collecting and analyzing these data will help ensure the long-term effectiveness of both PrEP and ART.

# Study objectives

**Primary Objective:**

To assess the frequency of HIV-1 drug resistance mutations among PrEP clients who test HIV- positive after initiating PrEP

**Primary Endpoint:**

Mutations in HIV-1 reverse transcriptase and/or integrase known to be associated with drug resistance

**Exploratory Objectives:**

To explore the relationship between HIV drug resistance and PrEP adherence in individuals who seroconvert on PrEP

**Exploratory Endpoints:**

Proportion of individuals with drug resistance mutations, by PrEP exposure status

# Study design and methodology

This study is a multi-site, cross-sectional study in facilities providing PrEP. The study will provide an estimate of the frequency of ARV resistance in the population of PrEP users who test HIV positive after initiating PrEP. Descriptive demographic characteristics, including gender and age, as well as factors associated with HIV seroconversion, will be collected.

Throughout the study period, PrEP users who seroconvert will be provided information about this study by health care providers. The clinic staff will have records of PrEP provision to assess participant eligibility. If the PrEP user consents, the client will have blood drawn for HIVDR testing and PK testing. ***[Insert as applicable: PrEP ring users will also have their most recently used ring(s) collected for residual drug level testing.]*** All procedures are scheduled to be completed during the same visit when seroconversion is identified. However, if for some reason procedures are not completed on the day of seroconversion, the clinic staff will contact clients to request that they return to the clinic to complete them as soon as possible.

## Study area description

The study will be conducted at facilities providing PrEP that have the capacity for sample collection. The protocol team will work with the ***[Insert as applicable: such as, Ministry of Health, PrEP implementing partners]*** to identify a current listing of all PrEP facilities. As that list is updated during the study, new trainings will be conducted as needed.

## Study population

PrEP users who present for any visit and are identified as HIV positive during that visit will be eligible for participation in the study if they meet the criteria listed below.

Inclusion Criteria

* 1. Current PrEP user – defined as an individual who has collected a supply of oral PrEP or PrEP ring in the last three months or has received a CAB PrEP injection in the last 12 months
  2. Identified as HIV positive, as per the HIV testing algorithm in national guidelines
  3. Willing to participate in the study and provide a blood sample
  4. Age ≥ ***[Insert # based on eligible age of PrEP users in country]*** years

## Sample size and event estimation

We expect to enroll ***[XXX-YYY]*** individuals who seroconverted while using PrEP. This calculation assumes a population of ***[XXX]*** PrEP users are followed for an average of one year, an HIV-1 seroconversion rate of 0.2-0.5 per 100 person-years, and that half of the individuals who seroconvert consent to participate. However, the study will continue to enroll throughout the protocol accrual period, and the final enrollment numbers may differ. Assuming a minimum of 100 participants are available for a particular analysis, the probability of observing at least one participant with a specific resistance mutation will exceed 87 percent if the true prevalence of that mutation exceeds 2 percent. Similarly, the probability of observing at least three participants with one or more resistance mutations of any type will exceed 88 percent, so long as the prevalence of one or more mutations exceeds 5 percent. (See bolded cells in Table 3.)

### Table 3. Probability of observing participants with resistance mutations

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Number of participants available for analysis | True prevalence of mutation(s) | Number of participants with mutation(s) | | |
| 1 or more | 2 or more | 3 or more |
| 100 | 1% | 0.63 | 0.26 | 0.08 |
|  | 2% | ***0.87*** | 0.60 | 0.32 |
|  | 5% | 0.99 | 0.96 | ***0.88*** |
|  | 10% | >0.99 | >0.99 | >0.99 |
|  |  |  |  |  |
| 200 | 1% | 0.87 | 0.60 | 0.32 |
|  | 2% | 0.98 | 0.91 | 0.76 |
|  | 5% | >0.99 | >0.99 | >0.99 |
|  | 10% | >0.99 | >0.99 | >0.99 |

The expected precision of two-sided 95 percent confidence intervals (CIs) for the probability of resistance mutations is shown in Table 4. For example, if the true prevalence of one or more mutations is 10 percent, the expected 95 percent CI for the probability of resistance is [4.9, 17.6] for any subset of 100 participants and [6.2, 15.0] if 200 participants are available for analysis. There is also at least a 70 percent chance of concluding that the prevalence of one or more mutations is less than 20 percent, so long as the true prevalence is no more than 10 percent and at least 100 participants are available for analysis.

### Table 4. Expected 2-sided 95% CI for the prevalence of resistance mutation(s)

|  |  |  |  |
| --- | --- | --- | --- |
| Number of participants available for analysis | True prevalence of mutation(s) | Expected 95% CI | Chance of ruling out a 20% prevalence |
| 100 | 1% | [0.0, 5.4] | >99 |
|  | 2% | [0.2, 7.0] | >99 |
|  | 5% | [ 1.6, 11.3] | >99 |
|  | 10% | [ 4.9, 17.6] | ***70*** |
|  | 15% | [ 8.6, 23.5] | 16 |
|  | 20% | [ 12.7, 29.2] | 3 |
|  |  |  |  |
| 200 | 1% | [ 0.1, 3.6] | >99 |
|  | 2% | [ 0.5, 5.0] | >99 |
|  | 5% | [ 2.4, 9.0] | >99 |
|  | 10% | [ 6.2, 15.0] | 97 |
|  | 15% | [ 10.4, 20.7] | 39 |
|  | 20% | [ 14.7, 26.2] | 3 |

# Study procedures

Accrual will continue until ***[Insert Date]*** or until the approximate sample size is reached, whichever comes first. Blood collection is expected to be completed at one visit, at the time of enrollment. Figure 1 presents the operational flow that will be repeated each time a PrEP client returns for an HIV test. Samples will be transported to the laboratories listed under Key Roles for drug resistance testing and drug level testing. Blood samples will be shipped to the backup laboratories listed in the Key Roles section in the event of testing problems at the primary laboratories and/or for quality control measures.

### Figure 1. Study procedure flowchart

**Client consents**

**Client DOES NOT consent**

**No further evaluation needed.**

**If HIV POSITIVE**

**If HIV NEGATIVE**

## Recruitment

Consecutive PrEP users who seroconvert will be recruited until the study closes. PrEP users identified as HIV positive by any health care worker (HCW) at a participating clinic will be referred to a study-trained nurse or other applicable clinician, who will inform the potential participant in a private setting about the study and assess eligibility and interest in participation.

## Informed consent

***[Insert: Oral or written]*** informed consent will be sought from eligible clients who initiated PrEP and are identified as HIV positive, to collect specimens for HIV drug resistance testing and, if applicable, drug level testing. The informed consent process and form will comply with International Council for Harmonisation Good Clinical Practice (GCP) regulations. A copy of the form will be offered to the client. *[****Insert if applicable: In the event a PrEP client does not agree to participate in the study, only de-identified demographic information, which may include age, gender, and population group, will be collected****.]*

## Specimen collecting and processing

For participants who have confirmed HIV-positive status and documented consent, an HCW trained in phlebotomy will collect a blood sample according to local standard operating procedures for safe collection by venipuncture. The blood samples will be processed and/or packaged and transported to the testing laboratory per the MOSAIC HIVDR Manual of Procedures (MOP). If applicable and feasible, the most recently used ring will be collected from the client, washed, packaged, and transported to the testing laboratory. All specimen processing and chain-of-custody must be done according to Good Clinical Laboratory Practices and the MOSAIC HIVDR MOP.

Samples will be tested at the laboratories or backup laboratories listed in the Key Roles section. Any leftover specimens may be temporarily stored for retesting of samples as needed due to test failure or for quality control. Sample testing will be prioritized to occur at the designated laboratory. Samples will be shipped to the backup laboratory only if necessary.

Blood collection is expected to be completed at the time of HIV seroconversion confirmation. However, if for some reason the sample collection is not completed on the day of seroconversion confirmation, clients will be asked to return as soon as possible, and within a five-day window of their HIV diagnosis, to complete the procedure. Samples may be collected after five days on a case-by-case basis and in consultation with the ***[Country]-***based MOSAIC project manager.

## Data collection

The HCW will be trained to complete the case report form (CRF) on paper by reviewing the client’s medical file as well as interviewing the client. The PrEP identification number will be entered on the CRF, along with data on demographics, client population classification, dates and history of PrEP methods, and date and testing information for HIV diagnosis. The CRF will be sent to the testing laboratory with the collected blood samples, for return to the ***[Country]-***based MOSAIC project manager.

## Drug resistance testing

All information received by the testing laboratories will be unlinked, and the laboratory staff will remain blinded to clients’ information. The sample and results will be tracked only by a sample-specific barcode.

The laboratories will perform the resistance test using an approved genotyping assay that is validated for sequencing the HIV-1 reverse transcriptase and/or integrase gene, per laboratory standard operating procedures.

## Drug level testing

All information received by the testing laboratory will be unlinked, and the sample and results will be tracked only by a sample-specific barcode. Drug level results will not be returned to the participant. The laboratory will perform tests using an approved and validated PK assay, per laboratory standard operating procedures. For oral PrEP, tenofovir–diphosphate (TFV–DP) will be quantified by a validated liquid chromatography tandem mass spectrometry assay. For the PrEP ring, residual drug testing will be performed using acetone extraction and high-pressure liquid chromatography. The peak area ratio will be used to determine the amount of drug remaining in the ring. For CAB PrEP, samples will be extracted using protein precipitation and tested by high-pressure liquid chromatography. [***Methods equivalent to those described here may be used***.]

## Provision of test results

Once the resistance test has been completed, the applicable laboratory will provide the resistance test results to the ***[Country]-***based MOSAIC project manager in an easy-to-understand electronic format. The results will then be distributed to the relevant facility. The clinic staff will retrieve each result and confirm client identification through the barcode sticker. The clinician or other designee will either counsel the client on their results and the implications for future treatment or forward the results directly to the client’s ART provider upon request.

# Data management

The CRF will be developed by the protocol team. The laboratory will send a copy of the CRF to the ***[Country]-***MOSAIC project manager, who will enter the de-identified CRF and HIVDR data into a centralized database, such as REDCap, developed by MOSAIC headquarters (HQ) research staff. The ***[Country]-***based MOSAIC project manager will conduct ongoing quality control to confirm the accuracy of the study data. In addition, MOSAIC HIVDR HQ research staff will conduct a quarterly quality assurance process for the information included in the central database. Any inconsistencies or deviations will be sent to the PrEP clinic site or laboratory for verification and resolution. Documentation of source verification will be required for data changes.

Every effort will be made to protect participant privacy and confidentiality. All study-related information will be stored securely at the applicable PrEP clinic, in the project office in ***[Country],*** and in the HQ research office. Informed consent forms will be stored separately at the clinic and will not combined with CRF and testing results data. All laboratory specimens and data collection forms will be identified by coded number only to maintain participant confidentiality. All databases will be secured with password-protected access systems. Only the project office staff in ***[Country]*** and HQ will have access to the electronic database.

# Data analysis

Basic sociodemographic data for participating clients will be summarized using the mean, the median, standard deviation, quartiles, and range (minimum and maximum) for continuous variables and frequency tables for categorical variables.

The proportion of HIV-positive PrEP clients with any major drug resistance mutation, as defined by the current Stanford HIV Drug Resistance Database, will be computed along with exact (Clopper-Pearson) 95 percent CIs.(22) In addition, frequencies, proportions, and exact 95 percent CIs of specific mutations will be computed and presented. Drug resistance analysis will be disaggregated by PrEP regimen. In rare situations, a sample may be collected after ART initiation. In those cases, ART initiation dates and regimen will be collected, and results may be analyzed separately.

For the exploratory objectives, we will estimate the proportion of participants with drug resistance who have detectable levels of the PrEP drug prescribed (TDF–DP, dapivirine, and/or CAB). We will also assess whether the presence of PrEP drug is associated with a different rate of resistance, separately by PrEP method and stratified by method.

# Study monitoring

MOSAIC [Country]-based program staff will confirm with the applicable laboratory that samples were received, along with the required CRF. The program staff and HQ project staff may review study records at clinics and laboratories during the course of the study; however, no formal clinical monitoring will be conducted. MOSAIC project staff may perform the following:

* Review informed consent forms and documentation
* Assess compliance with the protocol
* Review source documents to ensure accuracy of study data

The participating PrEP clinic will allow inspection of study documentation by MOSAIC project staff, USAID, and authorized representatives of regulatory authorities, including institutional review boards/ethics committees (IRBs/ECs). The ***[Country]-***based MOSAIC project manager, in coordination with the applicable clinic or laboratory staff, will document and mitigate any identified protocol deviations. Protocol deviations will be reported to the IRBs/ECs per policy.

# Ethical considerations

The health care facilities participating in this study will make efforts to minimize the risks of study procedures to participants. Before beginning the study, the MOSAIC study team will have obtained IRB/EC approval. Potential risks and benefits include the following:

**Risks**

Participants may become worried about their privacy and confidentiality. Every effort will be made to protect privacy and confidentiality. Participant visits will take place in private.

Phlebotomy may lead to discomfort or pain, feelings of dizziness or faintness, bruising, swelling, small clots, and/or infection.

**Benefits**

Participants may experience no direct benefits from participation in this study. However, they may appreciate the opportunity to contribute to the field of HIV research.

**Informed Consent Process**

Before each participant enrolls in the study, informed consent will be obtained to collect samples for laboratory testing and data collection. The informed consent process will be documented and stored in the clinic records. Participants will be offered a copy of the informed consent form. The informed consent will cover the following elements:

* + - Information about the rationale for the study and the participant’s role in the study
    - Potential risks and benefits
    - Alternatives to participation
    - Efforts to maintain confidentiality

**Confidentiality**

All study-related information will be stored securely at the health care facilities. To maintain confidentiality, all blood specimens, reports, and data will be identified by a coded number. Materials that link participant barcoded numbers to other identifying information will be stored in an area with limited access. After all testing has been completed, any leftover specimens will be destroyed.

# Publication policy and results dissemination

Representatives from partner organizations will be invited to co-author any presentation, abstract, or manuscript that utilizes study data. All partner organizations will review and approve all abstracts and manuscripts prior to submission to a conference or journal. In accordance with the USAID Automated Directives System (ADS) 579, the dataset and relevant documentation will be made available publicly in an open data repository, to the extent permissible by each country’s data privacy regulations, after acceptance of any knowledge product presenting study findings and after being cleaned of any information that could be used to personally identify participants.

# 

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# Appendices

## Appendix 1. Template informed consent form (English)

**Title**: **An Assessment of HIV Drug Resistance among PrEP Users in *[Insert Country name]***

**Funded by:** United States President's Emergency Plan for AIDS Relief (PEPFAR) and United States Agency for International Development (USAID); 7200AA21CA00011 (MOSAIC)

**Project Partners**: ***[Insert Local partners],*** MOSAIC

**Introduction:** You are being asked to join a research study for all people who acquire HIV while using pre-exposure prophylaxis (otherwise known as PrEP). PrEP may include oral tablets, a monthly vaginal ring, or a long-acting injection. With whatever PrEP method you are using, we want to better understand why you acquired HIV. We also want to know if your HIV virus has developed drug resistance. Drug resistance is when one or more medicines that usually work to treat HIV, called antiretrovirals or ARVs, no longer work as well.

**Information about the project:** This project will take place in different health facilities that are providing PrEP in ***[Insert Country name].*** We expect to enroll about ***[X]*** people across all the health facilities.

**Your role in the project:** We would like to take approximately 10 ml (about two teaspoons) of blood from you at the time that you have a positive HIV test. If you are using the PrEP ring, we would also like to collect the used ring from you at the time that you have a positive HIV test. We will be asking a few questions about you, such as your age and how you have been using PrEP up until this point. We may also look for this information in the records that the health center already collects. The time for us to take the blood sample and ask you a few questions is not expected to exceed 30–60 minutes. If you agree to this blood test, we will check for drug resistance in your blood ***[Insert if applicable: and then let you know when the results are ready to share with you or your health care worker***]. We will also check for the amount of drug in your blood or the ring, but this information will not be shared with you because it is for research purposes only and is not important for your medical care. Lab testing for this study will be done in either ***[Insert Country name]*** or, in some cases, in the USA. After all testing has been completed, any leftover blood specimens will be destroyed.

**Possible risks:** There is minimal risk in this project, but it is possible that the blood draw could lead to discomfort or, very rarely, an infection. There is also a risk that others may learn that you participated in this project. Every effort will be made to keep information about you safe; however, this cannot be guaranteed.

**Possible benefits:** You may get some personal satisfaction from helping us understand if people who get HIV while using PrEP may have drug resistance.

**If you decide to not participate:** You are free to participate or not in this study. If you decide not to participate, you can continue to get your health care at this facility or other facilities, but we will not be able to take your blood for resistance testing. If you decide to participate but later change your mind, you can stop participating, and your rights to receive services at health centers will not be affected.

**Confidentiality:** Your name will not be recorded in the computer that we will use to look at your drug resistance results. Your name will not appear in any reports or publications. All information collected for this project will be kept in a locked cabinet or room. Study information may be posted online for other researchers to use, but no one will know it was your information. When we post the information, to protect your privacy, we will not include your name or the name of this health clinic.

**Compensation:** Your participation is voluntary; no monetary or other compensation will be given.

**If you have questions,** you can call: ***[Insert Name/phone number]***

**Volunteer Agreement:** If you have read this consent form (or had it explained to you), all your questions have been answered, and you agree to take part in this project and for your blood sample to be taken, please sign your name below.

|  |  |  |  |
| --- | --- | --- | --- |
| Client Name (Print) |  | Client Signature | Date |
| Clinic Staff Conducting Consent Process Name (print) |  | Clinic Staff Signature | Date |
|  |  |  |  |
| Witness Name (Print) |  | Witness Signature | Date |