
Funding Agencies:

Protocol Chair:

Version X.X

DD MMM YYYY
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ABBREVIATIONS

AGYW   Adolescent Girls and Young Women
AHI    Acute HIV Infection
ART    Antiretroviral Treatment
ARV    Antiretroviral
CDC    Centers for Disease Control and Prevention
DBS    Dried Blood Spot
DR     Drug Resistance
FSW    Female Sex Worker
HIV    Human Immunodeficiency Virus
MSM    Men who have sex with men
PK     Pharmacokinetics
PrEP   Pre-exposure Prophylaxis
RNA    Ribonucleic Acid
SOP    Standard Operating Procedure
TDF/FTC Tenofovir disoproxil fumarate/Emtricitabine
TDF/3TC TDF/lamivudine
TDR    Transmitted drug resistance
TFV    Tenofovir
WHO    World Health Organization
PROTOCOL INVESTIGATORS

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[Tel Number]
[Email]

**Co-Investigators**
[Name]
[Title]
[Institution]
[Address]
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[Email]

**Collaborating institution(s)**
1. PROTOCOL SUMMARY

Short Title: HIV Drug Resistance Assessment in PrEP Seroconverters

Funder: [insert funding source]

Protocol Chair: [insert name]

Sample Size: Approximately [insert sample size] clients

Client Population: Clients who acquire HIV-1 infection while using TDF, TDF/FTC or TDF/3TC for PrEP

Study Design: Cross-sectional/Surveillance

Study Duration: One time visit per participant with enrollment continuing through [MM/YYYY] or [insert sample size] participants are enrolled

Study Methods: PrEP clients who have a reactive HIV test will have blood drawn for dried blood spot (DBS) collection to assess HIV drug resistance. The DBS sample will be collected only once for each seroconverter, 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: HIV-1 drug resistance mutations among seroconverters on PrEP

Exploratory Objectives: 1. To explore the relationship between HIV drug resistance and PrEP adherence in individuals who seroconvert on PrEP

Exploratory Endpoints: 1. Individual self-reported adherence or factors that may be associated with HIV drug resistance

2. Proportion of seroconverters with drug resistance that have detectable drug levels in blood
3. KEY ROLES

**Funding Agencies:** [Include name and address]

**Laboratories:** [Include name and address]

**Data Center:** [Include name and address]

**Study Operations:** [Include name and address]

4. INTRODUCTION AND BACKGROUND

Primary HIV prevention is an important component of efforts towards UNAIDS goal of elimination of HIV by 2030\(^1\). High incidence of HIV infection has been reported among high risk populations such as men who have sex with men (MSM), female sex workers (FSWs), HIV serodiscordant couples, and adolescent girls and young women (AGYW)\(^2\). Interventions to prevent HIV infection include mutual monogamy, male circumcision, consistent condom use, and antiretrovirals (ARVs) as pre-exposure prophylaxis (PrEP).

The World Health Organization (WHO) recommends the use of PrEP with daily oral emtricitabine plus tenofovir disoproxil fumarate (FTC/TDF) or TDF alone as a prevention strategy for HIV uninfected individuals at substantial risk of HIV\(^3\). PrEP has been shown to substantially reduce the risk of HIV acquisition, especially when used in combination with other behavioral preventive methods\(^3\). PrEP efficacy trials in different populations have reported an HIV seroconversion incidence ranging from 0.3%\(^4\) to 6.5%\(^5\) [see Table 1]. In the Partners PrEP study, TDF/FTC provided 75% protection, while use of tenofovir alone offered 67% protection\(^6\). Although some PrEP users may still acquire HIV infection, protection against infection increased as adherence increased in TDF/FTC PrEP efficacy trials\(^7,8\).

### Table 1
HIV Incidence in PrEP Efficacy Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Population(^a)</th>
<th>TDF/FTC Arm Only</th>
<th># Enrolled</th>
<th># Infected</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEM-PrEP(^9)</td>
<td>Women</td>
<td>1062</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>iPrEX(^10)</td>
<td>MSM</td>
<td>1252</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>TDF2(^11)</td>
<td>HS Men and Women</td>
<td>611</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Partners PrEP(^6)</td>
<td>HS Discordant Couples</td>
<td>1579</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>VOICE(^12)</td>
<td>Women</td>
<td>1003</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>PROUD(^13)</td>
<td>MSM</td>
<td>544</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>IPERGAY(^5)</td>
<td>MSM</td>
<td>31</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>USA DEMO Project(^4)</td>
<td>MSM/TW</td>
<td>557</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td><strong>6638</strong></td>
<td><strong>184</strong></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)HS = heterosexual; MSM = men who have sex with men; TW = transgendered women
Factors linked to risk of HIV seroconversion include social-behavioral, adherence and possible infection with TDF resistant strains\textsuperscript{14}. The potential for overlapping resistance and cross-resistance between ARVs used for prevention and for treatment is an important concern for the large-scale roll-out 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 (TDR) in the regions where PrEP roll-out is planned.

Resistance to tenofovir (TFV) or FTC is infrequently selected if TDF/FTC PrEP is started before HIV-1 infection has occurred, but is more common when PrEP is inadvertently started during undiagnosed acute infection [see Table 2]. FTC resistance from M184V/I occurs more frequently than TFV resistance with K65R in seroconverters from clinical trials of TDF/FTC PrEP. Studies in macaques show that TFV-resistant virus but not FTC-resistant virus can cause breakthrough infection despite TDF/FTC PrEP. Mathematical modeling suggests that the number of HIV-1 infections averted by the use of PrEP exceeds the increase in drug-resistant infections that could occur from PrEP\textsuperscript{14,15}. Clinical identification of acute HIV infection will be an important component of PrEP programs to prevent development of drug resistance. However, acute infection is often either overlooked or misdiagnosed at outpatient care settings\textsuperscript{16-18}.

### Table 2.

**HIV-1 resistance to tenofovir or FTC in oral TDF/FTC PrEP trials\textsuperscript{15}**

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Seroconverters in TDF/FTC Arm</th>
<th>TFV Resistance</th>
<th>FTC Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Standard</td>
<td>Sensitive</td>
</tr>
<tr>
<td>Infection After Enrollment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEM-PrEP</td>
<td>33</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>iPrEX</td>
<td>36</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TDF2</td>
<td>9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Partners PrEP</td>
<td>21</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>VOICE</td>
<td>61</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>160</td>
<td>0 (0%)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Acute Infection at Enrollment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEM-PrEP</td>
<td>1</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>iPrEX</td>
<td>2</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>TDF2</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Partners PrEP</td>
<td>4</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>VOICE</td>
<td>9</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>TOTAL</td>
<td>17</td>
<td>1 (6%)</td>
<td>-</td>
</tr>
</tbody>
</table>

Currently, WHO recommends immediate initiation of antiretroviral therapy (ART) for all individuals diagnosed as HIV infected regardless of WHO clinical stage or CD4 count\textsuperscript{3}. Early initiation of ART has several benefits that include fewer events of severe HIV morbidity and disease progression, improved uptake and initial linkage to care, better immune recovery and reduction in HIV transmission to negative
partners\textsuperscript{19}. In line with these guidelines, individuals who seroconvert while on PrEP will be advised to initiate ART immediately. However, it is uncertain if the failed PrEP prevention method would be associated with blunted response to ART due to the presence of drug resistant HIV strains.

Therefore, as countries implement national PrEP programs, it is important to assess individuals who seroconvert to determine the frequency of those seroconverters with HIV drug resistance mutations. These data will inform national PrEP programs and can help to ensure long-term effectiveness of both PrEP and ART.

5. RATIONALE FOR STUDY DESIGN

The primary objective of the study is to assess the frequency of HIV drug resistance with PrEP use. 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. However, there is currently a paucity of data on the risk of HIV drug resistance in the context of PrEP, all of which is based on limited data from completed PrEP clinical trials and not from real-world PrEP implementation. These clinical trials differed in many ways from current strategies for PrEP roll-out, including different intervals for HIV testing and adherence support strategies.

This study is designed to measure the frequency of HIV drug resistance through a cross-sectional, surveillance method. This design allows for a one-time measurement of drug resistance following seroconversion on PrEP, limiting clinic and participant burden. Results will provide an overall prevalence of drug resistance in clients that seroconverted while taking PrEP. These data may help assess the quality of the PrEP program. A high rate of observed resistance may indicate changes needed to the timing of PrEP provision or improved diagnosis of acute infection. A low rate of observed resistance with a high rate of infection may indicate adherence issues. The specific mutations observed may indicate if resistance is predominantly transmitted or potentially unrelated to PrEP use. This drug resistance surveillance technique will also contribute to local capacity building to incorporate pre-treatment, and acquired drug resistance surveillance as per WHO recommendations.

Data from this study will inform the global community on the risk of HIV drug resistance on PrEP seroconverters. It will importantly inform PrEP implementation programs, by providing recommendations on HIV testing frequencies, and PrEP adherence strategies. Ultimately, it will help to ensure the long-term effectiveness of both PrEP and ART.

6. 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: HIV-1 drug resistance mutations among seroconverters on PrEP
Exploratory Objectives:
1. To explore the relationship between HIV drug resistance and PrEP adherence in clients who seroconvert on PrEP
2. To assess drug levels at time of seroconversion

Exploratory Endpoints:
1. Individual self-reported adherence or factors that may be associated with HIV drug resistance
2. Proportion of seroconverters with drug resistance that have detectable drug levels in blood

7. STUDY DESIGN AND METHODOLOGY

Study design

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 adherence factors associated with HIV seroconversion, will be collected.

Throughout the study period, PrEP users who acquire HIV-1 will be provided information about this study by healthcare providers. If the PrEP user consents, the client will have blood drawn for preparing a dried blood spot (DBS) sample for HIV drug resistance testing and pharmacokinetic (PK) testing. Procedures (detailed in Section 9) are scheduled to all be completed at the visit that seroconversion is identified. However, if for some reason procedures are not completed on the day of seroconversion, clients will be asked to return to the clinic to complete the procedure.

Study area description

The study will be conducted at facilities providing PrEP, with capacity for DBS sample collection.

Study population

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

Inclusion criteria
1. Current PrEP user - defined as an individual who has collected an initial supply of PrEP agents or a resupply of PrEP agents in the last three months, independent of self-reported adherence
2. Identified as HIV infected, by two positive rapid HIV test kits from different manufacturers or by detectable HIV RNA in cases of suspected acute HIV infection
3. Willing to participate in the study and provide a blood sample

Sample size and power calculations

The primary objective will be measured via the proportion of HIV-infected individuals with evidence of drug resistance. Assuming a population of approximately [insert] PrEP users, an HIV incidence rate of
[insert] per 100 person years, an average of [insert] years of follow up for each PrEP client, and a 10% refusal rate, the study should be able to enroll [insert] seroconverters over [insert] years. The proportion of those with drug resistance is expected to be low and less than 10% of the 100 seroconverters.

As a means to characterize the statistical properties of this study Table 3 below presents the probability of observing zero, one or more and two or more safety events among the 100 participants given a true event rate [note: Tables below are illustrative of 100 seroconverters; will need to be adapted for varying sample size]. For example, if the true rate of resistance is 10%, then the probability we will see 1 or more cases of resistance is 99%.

### Table 3
**Analysis of Resistance Frequency**

| “True” Event Rate | P (0 events | n=100) | P (≥1 events | n=100) | P (≥2 events | n=100) |
|-------------------|-----------|-----------|-----------|-----------|-----------|
| 1%                | 0.37      | 0.26      | 0.08      |
| 5%                | <0.01     | 0.96      | 0.88      |
| 10%               | <0.01     | >0.99     | >0.99     |

An alternative way of describing the statistical properties of the study design is in terms of the 95% confidence interval (95% CI) for the true rate based on the observed data. Table 4 below shows the exact 2-sided 95% CIs for the probability of an event based on a particular observed rate. If none of the 100 participants has resistant virus, the 95% exact 2-sided upper confidence bound for the true rate of resistance is 3.6%. Similarly, if 10 of the 100 participants have resistant virus, the 95% exact 2-sided lower confidence bound for the true rate of resistance is 4.9% and the upper bound is 17.6%.

### Table 4
**Precision of Exact 2-sided 95% CIs for Observed Event Rates**

<table>
<thead>
<tr>
<th>Observed Event Rate</th>
<th>Exact 2-sided 95% CI (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20/100 (20%)</td>
<td>12.7%, 29.2%</td>
</tr>
<tr>
<td>15/100 (15%)</td>
<td>8.7%, 23.5%</td>
</tr>
<tr>
<td>10/100 (10%)</td>
<td>4.9%, 17.6%</td>
</tr>
<tr>
<td>5/100 (5%)</td>
<td>1.6%, 11.3%</td>
</tr>
<tr>
<td>1/100 (1%)</td>
<td>&lt;0.1%, 5.5%</td>
</tr>
<tr>
<td>0/100 (0%)</td>
<td>0%, 3.6%</td>
</tr>
</tbody>
</table>

### 8. STUDY PROCEDURES

This is a cross-sectional study conducted with PrEP clients who acquire HIV infection. Accrual will continue until approximately [insert sample size] HIV-positive participants have been enrolled or until [MM/YYYY]. Blood collection for dried blood spots (DBS) is expected to be completed at one visit. Figure 1 presents the operational flow that will be repeated each time a PrEP client returns for an HIV test. Samples will be shipped to [insert laboratory name] for drug resistance testing.
9a. Recruitment

Consecutive PrEP users who seroconvert will be recruited until the sample size is reached, or the study closes. PrEP users identified as HIV infected by the healthcare worker will be informed about the study and referred to the designated study coordinator, which may be a Nurse, Clinical officer, or Medical officer. The study coordinator will inform the potential participant about the study, and assess eligibility.

9b. Informed Consent

Written informed consent will be sought from eligible clients who initiated PrEP and have an HIV positive rapid test to collect a blood specimen for DBS for HIV resistance testing and PK testing. The informed consent process and form will comply with ICH GCP regulations. The original consent form will be filed in the clinic and a copy of the form will be offered to the client.

Figure 1
Study Procedure Flowchart
9c. DBS Collection

After HIV infection is confirmed and the participant consents, the study coordinator, or designee, will collect the DBS sample according to standard operating procedures for DBS preparation by venipuncture. Blood will be pipetted onto two DBS cards, of 5 spots each. Once the DBS is collected and dried, it will be individually packaged and shipped to the laboratory. The first card will be used for drug resistance testing and the second card will be sent to the laboratory for PK testing. DBS cards may be stored at ambient temperature for up to 5 days total including the time needed for shipping. After 5 days, cards must be stored at -80°C, or temporarily at -20°C until long-term storage at -80°C is available.

The blood collection and DBS preparation procedure 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 to complete the procedure.

9d. Data Collection

The study coordinator, or designee, will complete the laboratory requisition form, data collection form, or other document as appropriate by reviewing the client’s medical file as well as interviewing the client to determine self-reported adherence level.

9e. DBS Testing

Drug resistance testing will be performed at the laboratory. All information received by the testing laboratory will be unlinked and the laboratory staff will remain blinded to the client apart from gender and date of birth. The sample and results will be tracked only by a sample specific barcode.

>Note: update testing method as needed per laboratory SOP] The laboratory will perform the resistance test using a laboratory developed DBS-based population genotyping resistance assay, per laboratory standard operating procedures. Briefly, a 1.5kb fragment of protease and reverse transcriptase will be reverse transcribed for extracted viral RNA. The amplicon that has been generated will be purified and sequenced using the BigDye® Terminator v3.1 Cycle Sequencing Kit (Applied Biosystems, Foster City, CA), and analyzed on the ABI Prism™ 3500 Genetic Analyzer (Applied Biosystems). The SeqScape software program (Applied Biosystems) will be used to edit the raw sequences and generate consensus sequences. HIV DRMs and drug susceptibility profiles (HIVd algorithm) will be determined using the Stanford University Drug-Resistance Database (Palo Alto, CA).

>Note: update testing method as needed per laboratory SOP] PK testing will be performed at the laboratory using one DBS card. All information received by the testing laboratory will be unlinked and the sample and results will be tracked only by a sample specific barcode. The laboratory will perform the test using a laboratory developed PK assay, per laboratory standard operating procedures. Briefly, TFV-DP in dried blood spots (DBS) will be quantified by a validated liquid chromatography tandem mass spectrometry assay. TFV-DP steady state concentration (Css) in DBS
will be determined with a one-compartment first-order model fit to all available concentration data and compared to pharmacologic standards that estimate adherence as high, moderate or low/no adherence.

9f. Provision of test results

Once the resistance test is completed, the [insert name of laboratory] will provide the resistance test results in an easy to understand format to the clinic where the DBS was collected. The clinic staff will retrieve the result and confirm client identification as per the barcode sticker. The clinician, or other designee, will either counsel the client on their results and implications for future treatment, or forward the results directly to the client’s ART provider upon request.

9. STATISTICAL CONSIDERATIONS

The proportion of drug resistance among the 100 HIV-infected PrEP clients will be computed along with (exact) 95% confidence intervals (using the Clopper-Pearson method). In addition, frequencies, proportions, and exact 95% confidence intervals of specific mutations (e.g., K65R, K70E, M184I and M184V) will be computed and presented.

Basic socio-demographic data for participating clients will be summarized using the mean, the median, standard deviation, quartiles, and range (minimum and maximum) for continuous variables, proportions for binomial responses, and contingency tables for categorical variables. Logistic regression models will be used to explore differences (e.g., adherence levels, age, and gender) between HIV-positive participants who are drug resistant or not drug resistant if the sample size in each category is sufficient to perform such analyses. Exploratory analyses may be done on resistance data obtained from standard resistance testing to identify polymorphic or subtype-specific sequence changes in HIV-1 that may be associated with ARV resistance.

10. ETHICAL CONSIDERATIONS

The healthcare facilities participating in this study will make efforts to minimize risks of study procedures to participants. 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, and/or bruising, swelling, small clot and/or infection.

**Benefits**

Participants may experience no direct benefit from participation in this study. However, they may appreciate the opportunity to contribute to the field of HIV research. Resistance test results may also provide important clinical information for the PrEP client and their clinician.
Confidentiality

All study-related information will be stored securely at the healthcare facilities. To maintain confidentiality a coded number will identify all DBS specimens, reports, and data collection. Materials that link participant barcoded numbers to other identifying information will be stored in an area with limited access.

11. DATA ANALYSIS

After performing the resistance test assay, the [insert name of laboratory] will upload the AB1 files and the data collection forms associated with the resistance test results into a secure database at [insert name of coordinating or data center]. All samples, original files, and forms will remain onsite at [insert name of laboratory]. A subset of de-identified AB1 files that do not include client names or any other personal identifying client information may be securely sent to [insert location for QC review] to conduct quality assurance and for cohort analysis. Adherence will be measured by detectable drug levels in blood. The de-identified test results will be sent via secure electronic transfer to the GEMS laboratory at the University of Pittsburgh. Results will be analyzed across all clients and presented in annual outcome reports. [Insert coordinating or data center] will analyze the results across all clients and present the results and recommendations in [insert report/conference abstract/manuscript as applicable].

12. REFERENCES

3. WHO. GUIDELINE ON WHEN TO START ANTIRETROVIRAL THERAPY AND ON PRE-EXPOSURE PROPHYLAXIS FOR HIV. Geneva, WHO. 2015, September.
Appendix I
Template Informed Consent Form

Title: A Comprehensive Assessment of HIV Drug Resistance among PrEP Users
Funded by: [insert]
Project Partners: [insert]

Introduction: My name is ___________ and I am talking to all people who became infected with HIV while using pre-exposure prophylaxis (otherwise known as PrEP). We want to better understand why you became infected with 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]. We expect to enroll about [insert number] people across all the health facilities.

Your role in the project: We would like to take approximately 4 ml (about a teaspoonful) of blood from you at the time that you have a positive HIV test. We will also be asking a few questions about you, such as your age and how often 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. If you agree to this blood test, we will check for drug resistance in your blood and then let you know when the results are ready to share with you or your doctor. We will also check for the amount of drug in your blood [remove if PK testing not performed].

Possible risks: There is minimal risk in this project, but it is possible that there could be discomfort, or very rarely an infection, from the blood draw. There also is the 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 will find out if you have any drug resistance and this information can be used by your doctors to know which ARV medication might work best for you. You may also 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 healthcare at this facility or other facilities. If you decide to participate but later change your mind, you can, 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.

Compensation: Your participation is voluntary; no monetary or other compensation will be given.
If you have questions, you can call: [health clinic coordinator/clinician name and telephone 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, please sign your name below.

<table>
<thead>
<tr>
<th>Client’s Name (Print)</th>
<th>Client’s Signature</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinic Staff Conducting</td>
<td>Clinic Staff Signature</td>
<td>Date</td>
</tr>
<tr>
<td>Consent Process Name (print)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Witness Name</td>
<td>Witness Signature</td>
<td>Date</td>
</tr>
</tbody>
</table>