ART	Antiretroviral Therapy
CCRP	Client Centered Representative Payee
DSMB	Data and Safety Monitoring Board
NIH	National Institutes of Health
NIMH	National Institute of Mental Health
PLWHA	People Living with HIV/AIDS
RCT	Randomized Controlled Trial
SES	Socioeconomic Status
SSA	Social Security Administration
SSDI	Social Security Disability Insurance
SSI	Supplemental Security Income

all study participants, we have measures in place to provide CCRP to control arm participants once their study periods have concluded.

In addition, in the initial years of this study we observed that the RCT design created a barrier for some eligible clients, specifically those who experience significant health and practical challenges and required a representative payee in order to stabilize their housing and health. Study recruiters and the Data and Safety Monitoring Board agreed the possibility of randomizing these individuals to the control created an ethical risk. For this reason, choice arms have been added to the study. Participants (n=25) who demonstrate significant need or who are mandated to receive representative payee services by Social Security will be able to enter the choice intervention arm. To determine if immediate assignment to rep payee via the choice intervention arm is warranted, the following questions will be used to guide discussions with clients and their providers:

- Is there risk of housing loss, as evidenced by multiple evictions, eviction notices, and/or utility shut-offs in the past year?
- Is there risk of money mismanagement because the client is being persuaded to use money in ways they don't want to?
- Would it be unethical to wait to provide Rep Payee services? (Given all participants can get Payee within 12 months.)

Additionally, 25 clients who meet study inclusion criteria will be recruited to the choice control arm. These clients will receive care as usual.

The study population is limited to PLWHA who are 18 years of age and older, English- or Spanish-speaking, recipients of Social Security entitlements (SSI and/or SSDI), not currently receiving representative payee services nor having received them in the past 12 months, income below 138% of the federal poverty level, and one or more of the following: not virally suppressed (>200copies/ml), unsustained viral suppression over the past 12 months, or poor ART adherence. As its standard of care, providers at study sites currently use either the CASE Adherence Index (poor adherence is indicated by a CASE Index score of ≤10) or by a single question to assess the percentage of missed dosages in the past week (poor adherence is indicated by a score of less than 90%)**.** When using the CASE Index for screening eligibility the most recent CASE score must be used and the score cannot be more than 6 months old. These measures will be used to assess eligibility for this study, along with counts of unsuppressed viral load or unsustained viral suppression. New clinic clients who do not have historical viral load data but are not suppressed at baseline or who meet other inclusion criteria (poor self-reported adherence) will be eligible for the study.

These inclusion criteria will enable us to provide services to a population that historically struggles with ART adherence and low rates of viral suppression. We will also be able to assess the extent to which CCRP helps stabilize clients who may be virally suppressed at baseline but are not likely to stay that way due to poor adherence history. Including clients who have viral suppression at baseline but have poor adherence or have not sustained suppression over time is critical; a recent study that followed clients over a three-year period found that of those who had viral suppression at baseline, 20-25% subsequently had viral failure or were lost to follow up (37).

4.0 Potential Risks and Benefits

4.1 Risks to Human Subjects

In order to test the impact of Client-Centered Rep Payee services on ART adherence of people living with HIV/AIDS (PLWH), we will randomize 160 individuals to intervention or control arms and recruit 50 non-randomized individuals to the choice arms. Inclusion criteria are living with HIV/AIDS, 18 years of age and older, English- or Spanish-speaking, recipient of Social Security entitlements (SSI or SSDI), not currently receiving representative payee services nor having received them in the past 12 months, income below 138% of the federal poverty level, and one or more of the following: not virally suppressed, unsustained viral suppression over the past 12 months, or poor ART adherence. To assess poor

substance dependency or substance use disorder). (Modified from the definition of serious adverse drug experience in FDA regulations at 21 CFR 312.32(a).)

Unanticipated Problems: OHRP considers unanticipated problems, in general, to include any incident, experience, or outcome that meets *all* of the following criteria:

1. Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
2. Related or possibly related to participation in the research (in this guidance document, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and,
3. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

This trial is designed to test the effect of CCRP on viral load and other clinical markers among persons with HIV. The risks in this study are minimal, and we do not expect any adverse events to occur as a consequence of participation in this research study. This study, however, involves a high-risk patient population, and the natural progression of HIV/AIDS does include a large number of expected adverse events unrelated to participating in this research study. Given these circumstances, the trial investigators propose to limit the tracking and submission of adverse events to those that are:

1. Related to the attendance of a study visit, or,
2. Related to the study intervention.

Below is a description of the expected adverse events and other expected incidents, experiences and outcomes that are related to this trial.

Expected Adverse Events: None. The risks in this study are minimal and adverse events related to participating in this research study are not expected to occur.

Expected Incidents, Experiences or Outcomes: Based on prior experience with the Social Security Administration and Rep Payee services, the following issues may occur. These do not meet the definition of an adverse event (i.e., are not untoward or unfavorable medical occurrences). If such issues occur during this study, they will be evaluated to determine if they meet the criteria for unanticipated problems.

- Social Security Administration fails to deposit participant's Social Security entitlements.
- Social Security Administration deposits a lower-than-expected amount of Social Security entitlements.
- Checks or electronic transfers for rent/utilities/other expenses are delayed or not received.
- Expendable funds are delayed or not transferred to the participant.

8.5 Reporting Policy and Timeframe

In keeping with NIMH Policy, the written notice of reportable events will be provided to the NIMH Program Official in keeping with the following timeframes.

- IRB/DSMB suspension or termination – within 3 business days of receipt (Regulatory entity and PI)
- Deaths related to study participation – within 5 business days of the PI first learning of the death (PI)
- Unexpected SAEs related to study participation – within 10 business days of the study team becoming aware of the SAE (PI)
- Unanticipated problems involving risks to participants or others – within 10 business day of the PI learning of the event (PI)
- Serious or continuing noncompliance – within 10 business days of IRB determination (Institution)

constructed with the follow-up outcome measures as dependent variables, with the randomized and choice intervention group, follow-up time, and corresponding baseline measure as independent variables, and with a random intercept term to account for within-subject correlation. All clients with at least one outcome value will be included in the models since linear mixed models account appropriately for data missing at random (MAR). We will compare both baseline characteristics as well as intermediate outcome values between clients with missing outcome data and those with complete outcome data. We anticipate that some patient factors will be significantly associated with missing data, and thus, that the data will not be missing completely at random (MCAR). It is difficult to distinguish whether outcome data are missing at random (i.e., missing at random conditional on known and observed factors, MAR), or the data are missing not at random (MNAR). We will conduct a propensity analysis to control for confounding variables in estimating our intervention effect. Also, we will take precautions to adjust for the observed factors associated with the missing data patterns in the primary analyses and will use models that appropriately account for data missing at random. If concerns about missing data remain, pattern mixture models will be used to account for the various observed missing data patterns.

Non-linear mixed models using a binomial link will be used for binary outcome measures. The significance of the coefficient of the intervention term is the primary test of the intervention main effect. Adjustment for the baseline level of the measure effectively means that we are comparing the “changes” from baseline. An interaction (i.e., the product term) between follow-up time and intervention group will be added to test whether the effect of the intervention differs over the follow-up course. Mixed models accounting for confounding factors and moderating factors will be conducted as secondary analyses based on the initial exploratory data analyses.

9.2.1 Sample Size and Power Calculations

In HIV-infected clients, ART has been shown to have a dramatic effect on viral load and CD4 cell counts (53). Since the control group will also have access to treatment, we conservatively estimate that the observed between-group standardized effect size in this trial will be between 0.33 and 0.50 [i.e. Platten, et. al. showed that treatment with ART increased CD4 cell counts from 210 /µL to 410 /µL, a 95% increase, and viral load was reduced (to under 50 copies /mL) in 91% of clients.] Based on the data presented in that paper, an effect size of 0.50 is reasonable for ART therapy in a broad population. Moreover, an effect size of 0.5 is generally considered medium (61), and we designed our trial to have power to detect modest effects for this intervention. Using a two-sided inequality hypothesis test and a two-sample t-test with alpha=0.05, we determined the samples sizes required to provide 80% and 90% power to detect varying effect size differences between the two assigned treatment groups (Table 3).

Table 3. Sample Size Required to Detect Specified Effects

Effect Size	Sample Size for 80% Power	Sample Size for 90% Power
0.40	200	266
0.45	158	211
0.50	128	171
0.55	106	141

Based on these estimates, we plan to enroll a sample of 160 participants in the randomized study arm. If greater than 80% of participants contribute at least some follow-up data, the trial would have 128 clients with analyzable outcome data. This study would then have 80% power to detect a difference between the intervention and control groups of 0.5 SDs. For other outcomes where analyses are based on an alpha=0.01, the study would have 80% power to detect an effect size of 0.608. Since 0.50 is considered a medium effect size, the trial is powered to detect medium effect sizes between the intervention groups for these key outcome measures.

APPENDICES

Appendix A. Data Security Assessment Form

Principal Investigator: Mary Hawk **IRB#: PRO17080613**

Investigators must complete this form when data is collected, transmitted, or stored electronically. Upload the completed form into Section 5, question 5.15 of the IRB application or in the Supporting Documentation section if the upload button is not available. We highly recommend the Data Security Guidance document available in the A-Z Guidance of the HRPO website be reviewed before answering the questions. The IRB may request a consultation from data security experts from either Pitt or UPMC to ensure risks to research participants are minimized and appropriate safeguards are in place. **It is important that all relevant questions are addressed to prevent a delay in review.** If you have any questions, email us at irb@pitt.edu.

- It is important to remember that the research data belongs to the University of Pittsburgh
- All purchase agreements should be processed by the University Purchasing Office. Contact the Pitt Purchasing Office at 412-624-3578 or http://cfo.pitt.edu/pexpress/CustomerService/inquiry.php

Part A – Identifiers to be collected (check all that apply):

Resource: http://technology.pitt.edu/security/security-guideline-de-identifying-health-information

☐ Anonymous data – at no time will any identifiers be collected including IP addresses

Check all identifiers that will be collected below:
(If any identifiers will be collected, a data security review may be required)

☐ Name	☐ Biometric identifiers, including finger and voice prints
☐ Electronic mail address	☐ Full face photographic images and any comparable images
☐ Social security number	☐ Health plan beneficiary numbers
☐ Telephone number	☐ Account numbers
☐ Fax number	☐ Certificate/license numbers
☐ Internet protocol (IP) address	☐ Vehicle identifiers and serial numbers, including license plate numbers
☐ Medical record number	
☐ Device identifiers/serial numbers	
☐ Web Universal Resource Locators (URLs)	

Certain dates, age, zip codes or other geographic subdivision that could be personally identifiable per the standards below.
☐ All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes.
☒ All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older

☒ **List any other unique identifying number, characteristic, or code to be collected:** Identifiers are only collected at the study site and will not be collected at study center. Because interviews could potentially include identifiable data, these will be recorded on an Olympus DS-3500 portable recorder with 256-bit file encryption and device PIN locking to ensure data security. Once interviews are complete, any identifying information will be deleted from these files, and the audio tapes will

Action taken. *If the action taken was inpatient hospitalization, an SAE form (not an AE form) must be completed in the data management system.*

☐ None
☐ Out-patient evaluation
☐ Other, specify _____

What is the status of this event?

☐ Ongoing
☐ Resolved

Date of resolution __ __ / __ __ / 2 0 __ __

Reporting

1. Was this AE reported to the Pitt IRB?
   ☐ Yes, date reported to Pitt IRB: __ __ / __ __ / 2 0 __ __
   ☐ No, did not meet reporting criteria

2. Was this AE reported to the Philadelphia IRB?
   ☐ Yes, date reported to Philadelphia IRB: __ __ / __ __ / 2 0 __ __
   ☐ No, did not meet reporting criteria

3. Date reported to NIMH: __ __ / __ __ / 2 0 __ __

General description of event:

Other relevant history, including preexisting medical conditions

What is the status of this event?

☐ Ongoing
☐ Resolved

Date of resolution __ __ / __ __ / 2 0 __ __

☐ Death

Date of death: __ __ / __ __ / 2 0 __ __ ☐ Unknown

Report Dates

Date reported to Pitt IRB: __ __ / __ __ / 2 0 __ __

Date reported to Philadelphia IRB: __ __ / __ __ / 2 0 __ __

Date reported to NIMH: __ __ / __ __ / 2 0 __ __

Statement of Compliance

The trial will be conducted in accordance with the ICH E6, the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), and the NIH/NIMH Terms of Award. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection Training.

I agree to ensure that all staff members involved in the conduct of this study are informed about their obligations in meeting the above commitments.

Mary E. Hawk
Principal Investigator

Signature

February 27, 2017
Date

adherence, providers will use the CASE Adherence Index (poor adherence is indicated by a CASE Index score of ≤10) or a single question to assess the percentage of missed dosages in the past week (poor adherence is indicated by a score of less than 90%). When using the CASE Index for screening eligibility the most recent CASE score must be used and the score cannot be more than 6 months old. New clinic clients who do not have historical viral load data but are not suppressed at baseline are eligible for the study if they meet other criteria. These inclusion criteria will enable us to provide services to a population that historically struggles with ART adherence and low rates of sustained viral suppression.

Action Wellness, The Open Door, and Birmingham AIDS Outreach (BAO) will serve as the intervention sites for this study. In addition, Allies for Health + Wellbeing (Allies) will support recruitment, consenting, and data collection efforts in Pittsburgh, PA, referring participants to The Open Door for intervention activities.

Action Wellness is a community-based organization that provides comprehensive health services to PLWHA including clinical care, adherence support, supportive services, consumer education, research, and advocacy. Action Wellness provides clinical care to 2,100 PLWHA annually.

The Open Door, Inc. is a grassroots, 501(c)3 non-profit organization located in Pittsburgh city limits. The program has been serving chronically homeless PLWAH since 2006 and is the organization that developed the CCRP intervention. The Open Door (TOD) has served hundreds of marginalized individuals in the past decade, and provides representative payee services to nearly 100 people at any point in time. TOD works to both **solve** the homeless problem for those already on the streets with its supportive homes and **prevent** others from becoming homeless with representative payee services.

Birmingham AIDS Outreach is a 501(c)3 non-profit organization located in Birmingham, Alabama. The organization works in collaboration with the University of Alabama 1917 clinic. They provide free services to HIV positive individuals as well as free HIV testing and prevention services in the greater Birmingham and surrounding areas. the organization provides case management, counseling, and legal services. The mission of the organization is to provide financial, emotional, and home health support to individuals with HIV and AIDS and to provide educational information to the community with the goal of reducing the spread of AIDS. Birmingham AIDS Outreach will work in collaboration with the 1917 Clinic at the University of Alabama for retrieval of the clinical data of enrolled participants.

Allies for Health + Wellbeing is a 501(c)3 non-profit organization located in Pittsburgh, PA. Allies' services include a medical clinic, behavioral health services, PrEP services, medical case management, HIV, hepatitis and STI testing and counseling, a food pantry, transportation, and emergency financial assistance, housing, and prevention and educational outreach. Allies serves approximately 1300 unique clients each year and has been in operation since 1985. The role of Allies' staff on this study is limited to participant recruitment, consenting, and data collection. All representative payee intervention activities in Pittsburgh will be provided by The Open Door, which currently collaborates closely with Allies in providing services to clients that are comprehensive but not duplicative.

Staff from the study sites will recruit and consent participants, implement the intervention, and provide data for analysis to the University of Pittsburgh. Study participants will be assigned a unique identifier. The study sites will provide de-identified participant data to the University of Pittsburgh team for analysis. All materials with identifying information, including consent forms, will be kept in double-locked filing cabinets at the study intervention site, or within a password-protected electronic database with no potential access by modem or other means.

4.1.1 Sources of Materials

Data collected from study participants will include that which is biological (CD4, viral load); behavioral, captured via self-report (collected electronically via use of tablets); and electronic data abstracted from Action Wellness and Birmingham AIDS Outreach's electronic health record (appointment adherence, exposure to services, and retention in care.) Birmingham AIDS Outreach will work in collaboration with the 1917 clinic at the University of Alabama to retrieve the

- Adverse event – summary provided in annual progress report (PI)
- Protocol violations – annual progress report (PI)

8.6 Data Management

Data that is abstracted from patient records at the study sites will be collected by the study sites and provided to the Coordinating Center via a scheduled transfer using PittBox as a temporary transfer vehicle. Data will be deleted from Pittbox within 24 hours of scheduled transfer then uploaded to a Pitt department managed server. Client self-report data and tracking forms (off protocol, events) collected through computerized tablets will be stored on Pitt department managed servers. To minimize loss of confidentiality, we will ensure that participant ID numbers are used to identify study materials. All materials with identifying information, including consent forms, will be maintained separately from the study materials and will be secured per the study site's security policy and approved per the local IRB. Additional information regarding protection against risk is discussed in section 4.2 of the study protocol.

Qualitative data will be collected by researchers from the Coordinating Center. An Olympus DS3500 portable recorder with 256bit file encryption and device PIN locking will be used to record the semi-structured interviews (n=40 eligible clients and 15 providers). The audio recording will be transferred to a Pitt desktop, transcribed, and imported into qualitative analysis software. The Pitt desktop utilizes encryption software. The audio recording will be permanently erased from the portable recorder. The study site will link abstracted and self-report data to participants recruited to the qualitative interviews so that that these data can inform the interview questions.

The data analysis plan for this study is described in section 9.0 of this protocol.

A plan for quality assurance and control is described in section 10.0.

9.3 Semi-Structured Qualitative Interviews

Semi-structured interviews with 40 eligible clients (study participants and non-participants) and 15 providers (physicians, nurse practitioners, medical social workers, CCRP (case manager and financial manager) will be conducted by the University of Pittsburgh team (PI: Hawk, Project Coordinator and doctoral student) to further contextualize findings from the mediation analysis. Interviews will take place in year 3 of the study, providing sufficient time to contextualize initial findings from the mediation analysis and to provide a large enough pool of participants who have completed 12-month follow-up assessments. Information regarding recruitment methods and confidential nature of data are described in sections 5.2 and 4.2.2.

Semi-structured interview guides will be developed for providers and eligible clients using the theoretical framework described above. Drafts of the interview guides are attached as Appendix C. Theinterviews with providers and study participants will explore factors perceived to contribute to ART adherence, specifically examining for the effects of our hypothesized mediators as shown in Figure 1 (housing stability, retention in care, perception of social support, decreased financial stress, etc.). In addition, interviews with eligible clients who did not want to participate in the study will elicit their perception of the study and the intervention. We will purposively sample study participants for interviews based on their success or lack of success in improving ART adherence as well as improved biological measures. In addition, we will interview control arm participants to gain contrasting information regarding our hypothesized mediators. We also seek to understand participants' acceptance of and satisfaction with CCRP and the degree to which these change over time, given that it is likely that the intervention will become easier for clients after an adjustment period is over. Additional information regarding recruitment for qualitative interviews and confidentiality of qualitative data is documented in sections 5.2 and 4.2.2 respectively.

Our sampling approach for qualitative interviews will enable us to assess the degree to which the intervention contributed to adherence changes, as well as mechanisms underlying change. One-on-one interviews will be held in a private space, last 60-90 minutes, and will be audio recorded and professionally transcribed. Participants will receive $40 in incentives via gift cards to honor their time. Interviews will be digitally recorded and transcribed. Content will be analyzed in NVivo 11 using contextualizing and categorizing strategies. First, the interviews will be explored for major themes to contextualize the data. Then we will develop a set of analytic codes, derived from the exploration of themes as well as a priori hypotheses. All of the interviews will be coded, and at least five interviews will be coded by two researchers and compared for consistency. Results will be discussed with the research team to triangulate and validate the findings.

9.4 Economic Analysis

We will assess the cost, cost threshold, and cost-utility of the CCRP model (Aim 3). This will be accomplished by conducting an economic analysis to estimate the cost of delivering services and the cost thresholds for cost-effectiveness and cost savings. We will also determine if the intervention is cost-effective. The cost-effectiveness analysis will use de-identified data from the study sites including those collected via participant self-report (time spent by clients traveling to and from services, transportation costs to and from services, and HIV risk behavior) as well as those abstracted from the study site, (number of participants enrolled, number of client contacts, time spent by clients in service, wage level for clients, staff personnel costs, materials and consumables, and viral suppression.)

The cost analyses will estimate the cost of delivering the program locally and will be conducted from both the payer perspective (the cost to the party implementing the program; i.e., study sties), and the societal perspective (the cost to the party implementing the program + the cost to the participant for participating in the program). The cost analysis will calculate the overall cost of implementing the program, the cost per client, and the cost per contact. The threshold analysis will assess two things: 1) the number of quality-adjusted life years (QALY) that would need to be averted to

be transferred to a Pitt Desktop for transcription using local transcription software. No identifable data will be transcribed, and once transcripion is complete the audio recording will be deleted. Qualitative analysis will therefore be limited to de-identified data.

(DSR required if any identifiers checked above and data is not coded)

For **ALL** of the identifiable data collected above, will you be coding the data by removing the identifiers and assigning a unique study ID/code to protect the identity of the participant? ☐ Yes ☒ No

Indicate how the coded data will be stored separately from the identifiable data: The dates collected will not be stored separately from other study data. Participants will be assigned a unique study ID at time of randomization. Only authorized site personnel will be able to link study ID to participant name.

Will you be collecting any **sensitive data**? ☐ Yes ☒ No (DSR required if identifiable, limited data set, or coded sensitive data)

Data is considered to be sensitive when the disclosure of identifying information could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation.

Part B – What technologies will be used to collect data?

Mobile App ☒ Not applicable

(DSR required)

1. Name of the app:
2. Identify the mobile device platform(s) (IOS/Android/Windows)to be used:
3. Identify who created the app:
4. Whose device will be used: ☐ Personal phone ☐ Researcher provides phone
5. Address how the app is downloaded to the device:
6. Will data be stored on device for any period of time? ☐ Yes ☐ No
    a. If yes, please describe (e.g. queue on phone and then transmit to server, stored on device indefinitely)?
    b. Is the data encrypted on device? ☐ Yes ☐ No
7. How is the app secured on the device:
    a. Is a password or PIN for app required? ☐ Yes ☐ No
    b. Is a password or PIN for the device required? ☐ Yes ☐ No
8. Will the app be able to access other device functionality such as Location, Contacts, Notifications, etc.?
9. Where is data transmitted by device?
    a. How is it encrypted in transit?
10. Address how the data is coded:
    a. Are phone numbers or mobile identification numbers stored with data: ☐ Yes ☐ No
11. When data is transmitted from the device, please list all locations where it will reside (even temporarily):
12. Provide any additional information**:**

Web-based site, survey or other tool ☐ Not applicable

(DSR required except if all data recorded is anonymous)

ou select any of the first 4 options, jump to question 6:

☐ Pitt licensed Qualtrics ☒ CTSI REDCap

WebDataXpress ☐ TrialSpark

CCRP Serious Adverse Events Form

Participant ID:__ __ __ __

Date of Completion: <system date>

Instructions: An adverse event will be deemed a Serious Adverse Event (SAE) if it is fatal or life-threatening; requires or prolongs hospitalization; produces a disability; results in a congenital anomaly/birth defect; or may require medical intervention to prevent any of the preceding.

Date of event onset: __ __ / __ __ / 2 0 __ __
mm dd yyyy

Date site became aware of event: __ __ / __ __ / 2 0 __ __
mm dd yyyy

Event Criteria (check all that apply):

- ☐ Death
- ☐ Life threatening (immediate risk of death)
- ☐ Inpatient hospitalization or prolongation of existing hospitalization
- ☐ Persistent or significant disability/incapacity
- ☐ Congenital anomaly/birth defect
- ☐ Other adverse event that may require medical or surgical intervention to prevent one of the above

Was this event unexpected (not documented prior to study recruitment as a possible event related to the study visit and/or intervention and is not recognized as part of the natural progression of HIV/AIDs)?

- ☐ Expected
- ☐ Unexpected

What is the severity of the event?

- ☐ Mild (easily tolerated condition or symptom)
- ☐ Moderate (discomfort interferes with usual activity)
- ☐ Severe (incapacitating or causes inability to work or undertake usual activity)
- ☐ Life threatening
- ☐ Death

Was the event related to this research study?

- ☐ Definitely related (would not have occurred outside of the study visit and/or intervention)
- ☐ Probably related (likely to have occurred due to the study visit and/or intervention)
- ☐ Possibly related (may have occurred due to the study visit and/or intervention)
- ☐ Not related (would have occurred regardless of the study visit and/or intervention)

CCRP Unanticipated Problem Form

Participant ID:__ __ __ __

Date of Completion: <system date>

Instructions: Complete this form in the data management system if any incident, experience or outcome is unexpected, and related or possibly related to participating in the research and suggests that the research places subjects or others at greater risk of harm than was previously known or recognized.

1. What participant(s) are affected by the event (check one)?
   ☐ Single participant specific problem, ID: _____

   ☐ Problem affected multiple subjects

List the participant IDs of subjects affected:		
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____

   ☐ Problem affected all subjects at the site in the following date range:
   Start Date: __ __ / __ __ / 2 0 __ __ (*mm dd yyyy*) End Date: __ __ / __ __ / 2 0 __ __ (*mm dd yyyy*)

2. Date of event onset: __ __ / __ __ / 2 0 __ __

3. Date site became aware of event: __ __ / __ __ / 2 0 __ __

4. Type of unanticipated problem (check all that apply):
   ☐ Protocol Deviation (also requires completion of off protocol form)
   ☐ Non-Compliance
   ☐ Unanticipated medical issue
   ☐ Unanticipated issue related to representative payee process
   ☐ Other, specify: _____