Evaluating a Group-Based Intervention to Improve Mental Health and ART Adherence in HIV-Infected Adolescents in Low Resource Settings

Manual of Procedures

Final Version 1.0
19 July 2019
## Overview of Section Contents and Identification of Current Section Versions

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1.0 Study Overview

IMPAACT 2016 is a multi-site, two-arm, individually randomized controlled trial to evaluate whether a trauma-informed cognitive behavioral therapy (TI-CBT) group intervention delivered by Indigenous Youth Leaders (IYL) is associated with improved mental health outcomes and ART adherence in youth 15 - 19 years old living with HIV in sub-Saharan Africa.

The randomized trial is preceded by an adaptation process to ensure that the TI-CBT Youth Intervention Manual (used by IYL) and Caregiver Intervention Manual (used by adult study staff) to deliver the TI-CBT group intervention are relevant and acceptable per the local culture of each of the eight participating sites: Gaborone Prevention/Treatment Trials CRS 12701 (Botswana); Molepolole Prevention/Treatment Trials CRS 12702 (Botswana); University of North Carolina Lilongwe CRS 12001 (Malawi); College of Medicine JHU CRS 30301 (Malawi); St Mary’s CRS 30303 (Zimbabwe); Seke North CRS 30306 (Zimbabwe); Harare Family Care CRS 31890 (Zimbabwe); and Soweto IMPAACT CRS 8052 (South Africa).

The adaptation process includes Focus Groups at select sites within a participating country and Pilot Testing of the intervention at each site. The TI-CBT Youth and Caregiver Intervention Manuals will be updated at each site to incorporate site-specific adaptations based on the Focus Groups and Pilot Testing, as needed. For guidance on the adaptation process, refer to the Guidance Document: Preparation and Adaptation of the Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention.

Pilot Testing of the intervention will be conducted with up to 8 youth and up to 8 caregivers at each site. After successful completion of a Pilot test, the Randomized Trial will be initiated at each site. Collectively across all sites, approximately 192 - 256 youth participants will be enrolled and randomized to the TI-CBT Intervention or Discussion Control arm. Caregivers (as available and with youth permission) will be assigned to the same study arm as their youth. While on study, youth will meet as a group for six 2-hour group sessions (or an equivalent) led by IYL plus one booster session during follow-up, and caregivers will meet as a separate group for two 2-hour group sessions led by adult study staff plus one booster session during follow-up.

2.0 Preparing for the Study

2.1 Investigator Responsibilities

IMPAACT 2016 must be conducted in accordance with the United States (US) Code of Federal Regulations (CFR) and the International Conference on Harmonization (ICH) Consolidated Guidance for Good Clinical Practice (GCP). The Division of AIDS (DAIDS) policies on Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials and Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials are useful for interpreting and operationalizing the regulations and guidelines in accordance with DAIDS expectations. These policies are available at the following website and must be followed throughout implementation of IMPAACT 2016:

https://www.niaid.nih.gov/research/daids-clinical-site-implementation-operations

IMPAACT 2016 also must be conducted in accordance with the IMPAACT Manual of Procedures and all site-specific policies, procedures, and guidelines applicable to human subjects research in general and/or the conduct of study procedures in particular. Copies of all applicable regulations, policies, procedures and guidelines should be maintained in on-site essential document files.
The IMPAACT Manual of Procedures is available at:

http://impaactnetwork.org/resources/policies-procedures.htm

The Investigator of Record (IoR) at each site must sign a DAIDS Investigator of Record Agreement form to formally indicate his/her agreement to conduct the study in accordance with the protocol and all applicable regulations, policies, and guidelines. The obligations and responsibilities assumed by the IoR when signing this form are listed on the form, which is available on the DAIDS Regulatory Support Center (RSC) website:

http://rsc.tech-res.com/protocolregistration/

2.1.1 Protocol Signature Page (PSP)

The Investigator of Record (IoR) at each site must sign both a Protocol Signature Page (PSP) to formally indicate his/her agreement to conduct the study in accordance with the protocol and all applicable regulations, policies, and guidelines. A copy of the PSP can be found in the IMPAACT 2016 protocol.

A PSP must be signed by the IoR and uploaded to the DAIDS Protocol Registration System (DPRS) for all initial protocol versions, all full protocol amendments, and all letters of amendment (LOAs).

If there is a change in IoR, a new PSP should be submitted to the DAIDS PRO. Sites should follow guidance in the current Protocol Registration Manual regarding procedures for a change in IoR with the DAIDS PRO.

2.1.2 Delegation of Duties

IoRs may delegate their obligations and responsibilities for conducting this study to other study staff; however, delegation does not relieve the IoR of his/her ultimate responsibility for all study procedures performed and all study data collected. Delegation of IoR responsibilities must be formally documented on the site’s study-specific delegation of duties log described below throughout the period of study implementation per the DAIDS Delegation of Duties Log (DoD Log) Instructions and DoD Log Policy, which are available on the DAIDS Clinical Site Implementation and Operations website:

https://www.niaid.nih.gov/research/daids-clinical-site-implementation-operations

Per DAIDS process requirements for documenting study staff responsibility of obtaining informed consent (guidance document New DAIDS Requirements: Informed Consent Process, distributed to IMPAACT sites on September 5, 2017), a study-specific delegation of duties log must be completed as a requirement for site-specific study activation and maintained throughout the conduct of the study. To comply with this requirement, all key site staff involved with the IMPAACT 2016 study must be listed on a study-specific delegation of duties log. For IMPAACT 2016, sites hosting and conducting the Focus Groups in addition to the Pilot Test and Randomized Trial may complete two delegation of duties logs: one for the Focus Group conduct and one for the Pilot Test and Randomized Trial combined. All other sites not conducting Focus Groups only need to complete one delegation of duties log for the Pilot Test and Randomized Trial combined. A template log is provided on the DAIDS Clinical Site Implementation and Operations website and should be adapted for each CRS:

https://www.niaid.nih.gov/research/daids-clinical-site-implementation-operations
Study-specific delegation of duties logs must be filed in the study essential files and should only be sent to DAIDS PRO or to the IMPAACT Operations Center upon request. Should the IoR change during the course of the study, it is suggested that the current delegation log at the site be closed out and a new log implemented, including study staff signatures. Additional information regarding study-specific delegation of duties logs are available in the IMPAACT Network MOP.

2.1.3 IRB/EC Submissions

Consistent with the regulations, guidelines, and policies cited above, the IoR at each site must obtain all applicable regulatory and ethical review approvals for IMPAACT 2016 prior to study initiation; the IoR must also maintain these approvals in good standing throughout the period of study implementation. With regard to institutional review boards and ethics committees (IRBs/ECs), further guidance on initial and continuing review requirements is available in 45 CFR 46 and the ICH GCP guidance, as well as on the website of the US Office for Human Research Protections (OHRP):

http://www.hhs.gov/ohrp/

All sites are encouraged to request an acknowledgement of receipt for all documents submitted to their IRBs/ECs and to request that IRBs/ECs note the effective and expiry dates of all approvals. Because IMPAACT 2016 involves pediatric participants, IRBs/ECs must consider the potential benefits, risks, and discomforts of the study to children and assess the justification for their inclusion in the study. As part of this assessment, IRB/ECs must assess the level of risk to participants as described in protocol Section 12.2. Complete documentation of all correspondence to and from all responsible IRBs/ECs (i.e., complete copies of all submissions, responses, and approvals) must be maintained in on-site essential document files. All submission letters should list the date of the submission, the contents of the submission, and the version number and/or version date of each document submitted.

2.2 Protocol Registration

After obtaining all required IRB/EC approvals, each participating study site is responsible for submitting documentation of the approvals, and other required documentation, to the DAIDS Protocol Registration Office (PRO). Further information on the protocol registration process can be found in protocol Section 13.2 and the DAIDS Protocol Registration Manual, which is available at:

http://rsc.tech-res.com/clinical-research-sites/protocol-registration/form

Upon confirming receipt of all required documentation, the PRO will issue an Initial Registration Notification that indicates successful completion of the process. Site staff are responsible for maintaining documentation of all submissions for the study, along with all associated approvals, notifications, and other correspondence from the PRO. Sites must obtain an Initial Registration Notification for protocol Version 1.0 as a condition for study activation (described below).
2.3 Site-Specific Focus Group Implementation and Study Activation

Site-Specific Focus Group Implementation

Prior to Focus Group conduct, a site must be protocol registered, complete Focus Group-specific implementation requirements, and receive an Implementation Notice prior to proceeding with the Focus Group activities. To help ensure readiness for the Focus Group, the Protocol Team has specified a set of Focus Group requirements that must be met in order to obtain the Implementation Notice. These requirements are listed on the IMPAACT 2016 Site-Specific Study Activation Checklist, which is available on request from the IMPAACT Operations Center Clinical Trial Specialists. For details on site-specific Focus Group implementation, refer to Section 3.3.2 in the Guidance Document: Preparation and Adaptation of the Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention.

Site-Specific Study Activation

Prior to any Pilot Test and Randomized Trial conduct, each site must obtain all required approvals (as described above) and must complete study-specific activation procedures with the Protocol Team. To help ensure site readiness for study initiation, the Protocol Team has specified a set of study activation requirements that must be met in order to obtain approval to begin Pilot Test and Randomized Trial implementation. These requirements are listed on the IMPAACT 2016 Site-Specific Study Activation Checklist, which is available on request from the IMPAACT Operations Center Clinical Trial Specialists.

Any questions related to the study activation process should be directed to the IMPAACT Operations Center Clinical Trials Specialists. On a site-by-site basis, when all activation requirements have been met, the Operations Center will issue a Site-Specific Study Activation Notice. At each site, no Pilot Test and Randomized Trial study procedures may be performed prior to receipt of the activation notice.

2.4 Adaptation of TI-CBT Intervention

For guidance on how to adapt the TI-CBT Intervention using community stakeholder engagement, Focus Groups and Pilot Test, refer to the Guidance Document: Preparation and Adaptation of the Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention.
2.5 Study-Specific Personnel

A definition list for personnel is included in Figure 2-1 below.

**Figure 2-1**
Personnel Definitions

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<tr>
<th>Personnel</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Study Staff</td>
<td>Study staff designated to facilitate or observe the caregiver TI-CBT group sessions OR the caregiver Discussion Control group sessions.</td>
</tr>
<tr>
<td>Indigenous Youth Leader (IYL)</td>
<td>21-30 year-old IYL from local HIV clinics designated to facilitate or observe the youth TI-CBT group sessions OR the youth Discussion Control group sessions.</td>
</tr>
<tr>
<td>Facilitator</td>
<td>An individual leading community engagement, a Focus Group, or TI-CBT or Discussion Group sessions (Pilot Test and Randomized Trial) as follows:</td>
</tr>
<tr>
<td></td>
<td>• Facilitators leading community stakeholder engagement or a Focus Group may be an adult study staff (not designated to the Discussion Control Arm), local supervisor, site Investigator of Record (IoR), or other designee – excluding IYL.</td>
</tr>
<tr>
<td></td>
<td>• Facilitators leading a youth group session or caregiver group session will be an IYL or adult study staff, respectively.</td>
</tr>
<tr>
<td>Observer</td>
<td>An individual observing a Focus Group, or an individual observing a youth group session or caregiver group session who will be an IYL or adult study staff, respectively. May take the place of a facilitator should a facilitator be unavailable to lead a youth or caregiver group session.</td>
</tr>
<tr>
<td>Local Supervisor</td>
<td>An individual (e.g. psychologist, nurse, IoR, other) with a working relationship with the site who is designated to supervise IYL or adult study staff.</td>
</tr>
<tr>
<td>On-site Study Clinician</td>
<td>An individual who is qualified and designated to address safety concerns and intervene as needed to maintain safety of youth and staff (refer to protocol Section 8.1). The local supervisor and/or IoR can also serve as the on-site study clinician.</td>
</tr>
<tr>
<td>Expert Trainer</td>
<td>An individual selected and provided by the Protocol Team to conduct on-site TI-CBT intervention training for the IYL, adult study staff and local supervisors, and conduct supervision with site IoRs and local supervisors.</td>
</tr>
</tbody>
</table>

**Indigenous Youth Leaders, Adult Study Staff and Local Study Supervisor**

For guidance on recruiting, selecting, and training study-specific personnel including Indigenous Youth Leaders (IYL), adult study staff, and local study supervisors, refer to the Guidance Document: Preparation and Adaptation of the Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention.

For details on roles and responsibilities of IYL and adult study staff for the delivery of group sessions, refer to Section 5.6 of this MOP.

For details on roles and responsibilities of local study supervisors for regularly supervising IYL and adult study staff, refer to Section 5.7 of this MOP.

**On-site Study Clinician**

The on-site study clinician may be the local study supervisor, IoR or other designee who serves to supervise the IYL and help monitor and evaluate youth participants’ mental health risk and safety per
protocol Section 8.1 and intervene as needed to address a safety concern or remove disruptive youth from the current group session per protocol Section 4.8.

For details on monitoring and evaluating youth mental health risk and safety, refer to Section 6.0 of this MOP.

**Expert Trainer**

The expert trainer will conduct on-site study-specific TI-CBT intervention training for the IYL and adult study staff designated to deliver or observe the youth and caregiver group sessions, respectively. Sites do not identify and select an expert trainer; the Protocol Team will identify and select the expert trainer for each site.

Once the IYL and adult study staff have been selected and designated to the TI-CBT Intervention or Discussion Control group, as outlined in the Guidance Document: Preparation and Adaptation of the Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention, the Protocol Team, Operations Center, and expert trainer will work with sites to schedule the training.

For details on the roles and responsibilities of the expert trainer related to the training of IYL and adult study staff, refer to the Guidance Document: Preparation and Adaptation of the Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention.

### 3.0 Study Resources

This section specifies the resources available to IMPAACT 2016 study site staff, including study-related communication and informational resources, the Data Management Center (DMC) IMPAACT Portal, Computer Assisted Self Interview (CASI) and other essential documents.

#### 3.1 Study-Related Information and Communications

All IMPAACT 2016 visits and procedures must be conducted in accordance with the study protocol. The purpose of this manual is to supplement the protocol, not to replace or substitute it. In the event this manual is inconsistent with the protocol, the specifications in the protocol take precedence. Please notify the IMPAACT Operations Center Clinical Trial Specialists of any such inconsistencies.

This manual will be reviewed with each protocol modification (clarification memorandum, letter of amendment, or full protocol amendment), and approximately annually, for any indicated updates. Operational guidance will be released as study-wide communications between these planned updates, as needed.

The IMPAACT 2016 protocol and related protocol documents including the study-specific Laboratory Processing Chart (LPC) and Guidance Document: Preparation and Adaptation of Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention are available on the study-specific web page:

http://impaactnetwork.org/studies/IMPAACT2016.asp

The Protocol Team has developed study-specific contacts for various types of issues and questions, as shown in Figure 3-1. For issues and questions directed to the Protocol Team, a response from the appropriate team member can generally be expected within 24 hours. Always retain a copy of correspondence with the team in the relevant participant’s study chart.
**Figure 3-1**
IMPAACT 2016 Study-Related Communications

<table>
<thead>
<tr>
<th>Topic</th>
<th>Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>User Support</strong></td>
<td></td>
</tr>
<tr>
<td>Adding site staff to protocol email group (<a href="mailto:IMPAACT.prot2016@fstrf.org">IMPAACT.prot2016@fstrf.org</a>)</td>
<td>User Support <a href="mailto:user.support@fstrf.org">user.support@fstrf.org</a> (include the protocol number in the subject line of your email message)</td>
</tr>
<tr>
<td>Data management computer and screen problems</td>
<td>User Support (FSTRF) <a href="mailto:user.support@fstrf.org">user.support@fstrf.org</a> or by phone: +716-834-0900, ext. 7302</td>
</tr>
<tr>
<td><strong>General</strong></td>
<td></td>
</tr>
<tr>
<td>Protocol interpretation or study implementation, including administrative, ethical, regulatory, counseling, data, and laboratory operation</td>
<td>IMPAACT 2016 Protocol Team <a href="mailto:impaact.team2016@fstrf.org">impaact.team2016@fstrf.org</a></td>
</tr>
<tr>
<td><strong>Screening, Enrollment, and Data Management</strong></td>
<td></td>
</tr>
<tr>
<td>Participant eligibility, potential enrollment of an ineligible participant, and/or deviation from protocol requirements for eligibility determination and/or enrollment</td>
<td>IMPAACT 2016 Protocol Team <a href="mailto:impaact.team2016@fstrf.org">impaact.team2016@fstrf.org</a></td>
</tr>
<tr>
<td>Co-enrollment and concurrent waves</td>
<td>IMPAACT 2016 Core Team <a href="mailto:impaact.core2016@fstrf.org">impaact.core2016@fstrf.org</a></td>
</tr>
<tr>
<td>Subject Enrollment System</td>
<td>DMC Randomization Support Office <a href="mailto:rando.support@fstrf.org">rando.support@fstrf.org</a> or by phone: +716-834-0900, ext. 7301</td>
</tr>
<tr>
<td>Adding designated site staff (limited to site IoR, study/nurse coordinator, and local supervisor) to CASI alert email group for receiving mental health eligibility determination and safety alerts (email the staff name(s), title/role(s), and email(s)) eCRF and data management issues and questions</td>
<td>IMPAACT 2016 Protocol Data Managers <a href="mailto:impaact.dm2016@fstrf.org">impaact.dm2016@fstrf.org</a></td>
</tr>
<tr>
<td><strong>Participant Safety, Monitoring, and Study Management</strong></td>
<td></td>
</tr>
<tr>
<td>Expedited Adverse Event (EAE) Reporting</td>
<td>DAIDS RSC Safety Office <a href="mailto:DAIDSRSCSafetyOffice@tech-res.com">DAIDSRSCSafetyOffice@tech-res.com</a> or by phone: 800-537-9979 or +301-897-1709 or by fax: 800-275-7619 or +301-8977-1710</td>
</tr>
<tr>
<td>DAIDS Adverse Experience Reporting System (DAERS)</td>
<td>DAIDS DAERS Support <a href="mailto:CRMSsupport@niaid.nih.gov">CRMSsupport@niaid.nih.gov</a> (questions also may be submitted from within the DAERS application)</td>
</tr>
<tr>
<td>Concerns regarding mental health questionnaires including questions related to flagged high-risk response email notifications</td>
<td>IMPAACT 2016 Core Team <a href="mailto:impaact.core2016@fstrf.org">impaact.core2016@fstrf.org</a></td>
</tr>
<tr>
<td>Participant safety assessment, monitoring, psychiatric adverse events, reporting including social harms, and/or contamination concerns</td>
<td></td>
</tr>
<tr>
<td>Any other aspect of participant management, protocol interpretation, or study implementation not listed above</td>
<td>IMPAACT 2016 Protocol Team <a href="mailto:impaact.team2016@fstrf.org">impaact.team2016@fstrf.org</a></td>
</tr>
</tbody>
</table>
Active communication is expected between site staff, IYL, designated on-site study clinicians, and local study supervisors to monitor and manage youth mental health risk and safety (refer to protocol Section 7 and 8). The IMPAACT 2016 Core Protocol Team is composed of study team members who have been designated to provide as needed guidance to sites regarding all aspects of participant management, including but not limited to site questions pertaining to 1) clinical and mental health risk management questions and notifications, and 2) youth participant self-reported flagged high-risk responses sent via email notifications (refer to Sections 6.1 and 6.1.1 of this MOP; refer to protocol Section 7.1.2, 8 and 8.1.)

When submitting questions and notifications to the Core Protocol Team, please address each of the points listed in Figure 3-2 and include in the email subject line the protocol, site, and PID numbers to help ensure that members have adequate information to respond in a timely manner. Always retain a copy of correspondence with the Core Protocol Team in the relevant participant’s study chart.

### Figure 3-2

**Communications with IMPAACT 2016 Core Protocol Team**

<table>
<thead>
<tr>
<th>Questions and notifications for IMPAACT 2016 Core Protocol Team: Copy and paste this listing into the body of your email message to <a href="mailto:IMPAACT.core2016@fstrf.org">IMPAACT.core2016@fstrf.org</a> to ensure that all required information is included.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Include the protocol number, site number and PID in the subject line of your email.</td>
</tr>
<tr>
<td>1. Site name and number:</td>
</tr>
<tr>
<td>2. Name of person submitting query:</td>
</tr>
<tr>
<td>3. PID(s):</td>
</tr>
<tr>
<td>4. Study Component: Pilot Test <em>or</em> Randomized Trial</td>
</tr>
<tr>
<td>5. Study Arm: Youth TI-CBT Intervention, Youth Discussion Control, Caregiver TI-CBT Intervention <em>or</em> Caregiver Discussion Control</td>
</tr>
<tr>
<td>6. For consultation on (choose one):</td>
</tr>
<tr>
<td>a. Eligibility or enrollment (describe in case description)</td>
</tr>
<tr>
<td>b. Adverse event (specify severity grade in case description)</td>
</tr>
<tr>
<td>c. Mental health risk and Safety Concern (e.g. youth participant flagged high-risk response, social harm, group session disruption)</td>
</tr>
<tr>
<td>d. Other (specify in case description)</td>
</tr>
<tr>
<td>7. Current week on study:</td>
</tr>
<tr>
<td>8. For adverse events, mental health risk, or queries related to a specific group session, indicate the specific group session (e.g. Session 1, 2, 3, 4, 5, 6, or booster for youth, and Session A, B or booster for caregiver) and Group Identification Number (refer to Section 5.5 of this MOP for details on Group Identification naming convention):</td>
</tr>
<tr>
<td>9. Case description and question or notification for Core Protocol Team:</td>
</tr>
</tbody>
</table>

File a copy of the email exchange in the participant’s study chart.

The IMPAACT 2016 protocol also details the circumstances in which IoRs, study coordinators, on-site clinician/supervisors, and/or designee must consult with the Core Protocol Team. All protocol requirements must be followed. For ease of reference, a summary of issues requiring consultation with the IMPAACT 2016 Core Protocol Team, is provided below in Figure 3-3. IoRs, study coordinators, local supervisors (or on-site study clinician), and/or designee receiving flagged safety alert emails are also encouraged to contact the Core Protocol Team with any other issues, questions, or concerns related to questionnaire responses from study participants.
For details on participant safety and management, refer to the following sections in the protocol:

- **Section 4.8**: Participant Withdrawal or Termination from the Study (Pilot Test/Randomized Trial)
- **Section 7.1**: Safety-Related Roles and Responsibilities
- **Section 8**: Participant Management

### Study Implementation

- Request approvals for co-enrollment in observational or other studies (refer to protocol Section 4.5).
- A participant fails to comply with study requirements and/or is disruptive, so as to cause harm to self or others, seriously interfere with the validity of the study results, or otherwise acts in ways such that continuing in the group is not in the best interest of the participants and study site staff so that the site investigator or designee determines permanent discontinuation is warranted (refer to protocol Section 4.8).
- Site investigator or designee request for resumption of follow-up for a participant whose circumstances that led to his/her withdrawal or termination change, e.g., he/she returns to the study site area after relocating (refer to protocol Section 4.8).

### General Participant Management

- Consultation with the Core Protocol Team by site investigators is required for the following as soon as possible and within three days of site awareness of event (refer to protocol Sections 7.1.1 and 8):
  - Psychiatric adverse events resulting in hospitalization
  - Adverse events involving suicide attempts
  - Any other occurrence that, in the opinion of the site investigator, could cause harm to a participant or others
  - Any unexpected concerns
- Consultation with the Core Protocol Team regarding management of psychiatric adverse events resulting in hospitalization and/or involving suicide attempts that include premature discontinuation of the study intervention.
- Social harms

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### 3.2 Data Management Center (DMC) IMPAACT Portal

The IMPAACT Portal of the DMC website provides information, documents and tools to assist site staff with the data management aspect of conducting IMPAACT studies, including the eCRF Completion Guide which includes the Case Report Forms (CRFs) and forms instructions, as well as the Data Collection Forms Schedules (DCFS), Forms Management Utility for participant questionnaires, links to required Computer Assisted Self-Interview (CASI) surveys, and Subject Enrollment System (SES). The IMPAACT Portal can be accessed from the Frontier Science and Technology Research Foundation (FSTRF) webpage at: [https://www.frontierscience.org/](https://www.frontierscience.org/)

Site staff members apply for access to the Portal by submitting a registration form located on the Frontier Science and Technology Research Foundation (FSTRF) home page. All requests for Portal access are subject to review and verification by User Support before processing. The site leader or site coordinator will be contacted by the DMC to ensure legitimate affiliation of the applicant.

To request for DMC IMPAACT Portal access, complete the form located at:


Confirmation of registration will be sent via email from User Support. Click on the IMPAACT project link to enter the project website. A log-in screen appears. Enter your username (format: lastname.firstname) and the password that you set up when you registered for DMC web access.
For clinical user support, send an email message to impaact.support@fstrf.org or call +1 (716) 834-0900 x 7302. If you experience problems or have questions about the IMPAACT portal in the Frontier Science website, please contact the Webmaster at webmaster@fstrf.org and include a detailed description of your question or the problem you encountered.

3.3 Electronic Case Report Form (eCRF) Completion and Data Entry

The DMC has developed an eCRF Completion Guide to assist site staff in the accurate completion of electronic Case Report Forms (eCRFs) used for DAIDS-sponsored Clinical Trials. Additionally, a print matrix of the 2016 eCRFs is available. The 2016 eCRF Completion Guide and the 2016 Print Matrix are located in the DMC IMPAACT Portal under the Site Support heading and the Medidata Rave Resources link. The eCRF Completion Guide and Print Matrix may be used as guides for source documentation purposes.

The eCRF Completion Guide contains the data collection forms schedules and all the eCRFs with instructions and help text. These documents outline standards and guidelines which, when followed, will result in fewer queries, shorter delinquency lists, and most importantly, straightforward and timely analyses.

The participant questionnaires have been posted in English, and other needed language translations have been posted in the Forms Management Utility, located on the DMC IMPAACT Portal under the Case Report Form heading.

Additionally, the eCRFs may also be accessed through the Medidata RAVE system.

3.4 Computer Assisted Self-Interview (CASI) Set Up

Youth - Screening/Enrollment

- As part of the youth screening process, a study-specific Screening Checklist/Log will be used (PS2016) via the SES. Upon successful completion of the study-specific Screening Checklist, sites will receive a participant-specific Tracking Number. Within CASI, site staff will complete the log-in questions for potential youth participants prior to having the youth begin their questionnaires. Sites will enter the Tracking Number in CASI when logging into the CASI screening/pre-entry questionnaires for each potential participant.
- When it has been determined that the youth meets eligibility criteria and the Eligibility Checklist is successfully completed via the SES, sites will receive a Study ID (SID) number for each successfully enrolled participant. Within CASI site staff will complete the log-in questions for youth participants prior to having the youth begin their questionnaires. These participant-specific SID numbers will be entered in CASI and used to log into all post-screening/pre-entry CASI questionnaires during the course of the study.

Caregiver - Enrollment

- Caregivers will not be using the Screening Checklist and do not have CASI screening questionnaire requirements.
- Caregivers will receive a participant-specific SID number after successful completion of the Eligibility Checklist via the SES. Within CASI, site staff will complete the log-in questions for caregiver participants prior to having the caregivers begin their questionnaires. These participant-specific SID numbers will be entered in CASI and used to log into all CASI questionnaires during the course of the study beginning with the entry visit.
Fidelity – Facilitator

- Each group session facilitator for IMPAACT 2016 will receive a Facilitator ID (FCID) from a pre-generated list provided to the site by the DMC. Site Supervisors will assign each facilitator a unique FCID from this list. These facilitator-specific FCID numbers will be entered in CASI and used to log into all CASI fidelity questionnaires during the course of the study (refer to Section 5.5 for guidance on completing the fidelity questionnaire).

Fidelity – Observer

- Each group session observer for IMPAACT 2016 will receive an Observer ID (FOID) from a pre-generated list provided to the site by the DMC. Site Supervisors will assign each observer a unique FOID from this list. These observer-specific FOID numbers will be entered in CASI and used to log into all CASI fidelity questionnaires during the course of the study (refer to Section 5.5 for guidance on completing the fidelity questionnaire).

3.5 Study Webpage

A variety of IMPAACT 2016 study-related materials and information can be found on the study-specific webpage: [http://www.impaactnetwork.org/studies/IMPAACT2016.asp](http://www.impaactnetwork.org/studies/IMPAACT2016.asp)

Resources available on this site include, but are not limited to:

- Current version of the protocol, including any Clarification Memoranda (CMs) and/or Letters of Amendment (LoAs)
- Study contacts
- List of participating sites
- Current study implementation materials, including this Manual of Procedures (MOP), the Laboratory Processing Chart (LPC), and the Guidance Document: Preparation and Adaptation of the TI-CBT Intervention
- Study training materials

4.0 Participant Accrual

Accrual for the Pilot Test and Randomized Trial differ as outlined below.

**Pilot Test only:** Each site will enroll one group of 5 - 8 youth and one group of up to 5 - 8 caregivers of the enrolled youth to participate in the TI-CBT Intervention Group Sessions. Potential youth and caregivers will be consented during the screening process. Once a sufficient pool of eligible youth exist based on prior screening to fill one group (range of 5 - 8 youth), all youth will be enrolled on the same day. Participant accrual at a given site is expected to be completed within 60 days of the first screened eligible youth. The same timing of screening and enrollment applies to caregivers. Refer to Section 4.5 for screening procedures.

**Randomized Trial only:** Approximately 192 - 256 youth participants (96 - 128 per arm), plus their caregivers (as available and with youth permission), will be enrolled into the Randomized Trial collectively across all sites. Enrolled youth and their caregivers will be randomized to the same arm, either to the TI-CBT Intervention Arm or Discussion Control Arm. Each arm will have 12 - 16 groups collectively across all sites, with an average of eight youth (and their caregiver) participants per group (range 6 - 10). Each site is expected to conduct at a minimum one group per arm.
Potential youth and caregivers will be consented during the screening process. Once a sufficient pool of eligible youth (range of 12 - 20 youth) exists based on prior screening to fill two groups (one group per arm), all youth will be enrolled and randomized to an arm on the same day. Participant accrual for two groups at a given site is expected to be completed within 60 days of the first screened eligible youth. Refer to Section 4.5 for screening procedures.

For the purpose of this manual, in the Randomized Trial, a set of two youth groups (one group per arm) and two caregiver groups (one group per arm) equals one wave.

At a given site, at least one wave will be accrued for the duration of the study. Some sites may accrue two or more waves following the Pilot Study, as determined by the Core Protocol Team, to meet the total Randomized Trial accrual of 192 - 256 youth participants. Sites may have the option to conduct concurrent waves, and this will be assessed on a site-by-site basis dependent on site readiness, feasibility, accrual pace, timely completion, and site supervisor input. At a minimum, the following will be considered by the Protocol Team for site readiness and feasibility:

- Supervisor confirmation of IYL and adult study staff readiness to facilitate concurrent waves
- Assessment that IYLs, adult study staff and local supervisors have sufficient time, training, and resources
- Ability to schedule groups sessions of different waves at different times to prevent cross contamination (refer to Section 5.6 for guidance on scheduling group sessions)
- Accrual pace

Refer to Section 5.6.3 for guidance on conducting multiple concurrent waves.

### 4.1 Site-Specific Accrual

For each site, accrual will begin after all required approvals are obtained and a site-specific study activation notice is issued by the IMPAACT Operations Center. As a condition for site activation, each site will establish a study-specific SOP for participant accrual, which must be submitted to the protocol chairs and clinical trials specialists for review and approval. This SOP should minimally contain the following elements:

- Recruitment methods and materials (i.e., scheduling)
- Screening procedures
- Considerations for recruitment of minors and caregivers
- Methods for tracking recruitment
- Participant retention
- Ethical and human subjects considerations
- Staff responsibilities for all of the above (direct and supervisory)
- QC/QA procedures (if not specified elsewhere)

All sites are responsible for following the participant accrual SOP and updating the document if needed to meet site-specific accrual projections, throughout the study accrual period. Following the participant accrual SOP approval by protocol chairs and clinical trials specialists, if changes are made to the participant accrual SOP in connection with protocol requirements, it is not required to submit the SOP for an additional review after the site has been activated.
Once accrual is initiated, the DMC will report the number of participants enrolled to the Protocol Team at least monthly. Throughout the accrual period, the Protocol Team will review accrual and other performance data across sites to determine whether accrual targets should be adjusted across sites to achieve the study objectives most efficiently and to determine when to discontinue accrual at each site. Findings and recommendations from these reviews will be communicated to all sites, and all sites will adjust their accrual efforts accordingly. Similar adjustments may be made after IMPAACT Study Monitoring Committee (SMC) reviews of the study, which are expected at least annually, and at 6 months following the first participant enrollment plus every 6 months or as needed during the enrollment period.

Selected operational considerations related to the recruitment, screening, and enrollment process are provided in the remainder of this section.

### 4.2 Participant Recruitment, Screening, and Enrollment Processes

Refer to protocol Section 4.6 for an overview of the participant recruitment, screening, and enrollment process for this study. Recruitment methods may vary across sites but are generally expected to rely on outreach to populations of 15 - 19 year-old youth living with HIV in care at participating study sites and local clinics, and their caregivers, as applicable.

Provided below is a reminder on the importance of rapid recruitment, screening, and enrollment.

> Enrollment/randomization must occur within 60 days of each youth participant initiating the screening process.

> Eligibility is subsequently confirmed and the potential participant’s availability to return to the clinic to complete Pre-Entry and Entry procedures followed by the first group session are documented for scheduling purposes. From the day the first participant is screened the remaining pool of eligible youth (5 – 8) for the Pilot Test and (12 – 20) for the Randomized Trial must be rapidly identified, screened, complete Pre-Entry visit procedures and enrolled during the Entry visit within 60 days to prevent the need for re-screening.

> Youth who are screened more than 60 days prior to enrollment must be re-screened for all inclusion and exclusion criteria prior to enrollment.

**Contact the Protocol Team with any questions involving the recruitment, screening, and enrollment process.** While recruitment methods may vary across sites, screening and enrollment methods will be more standardized across sites, consistent with the requirements of protocol Sections 6.1.1-6.1.3, 6.2.1, 6.3.1-6.3.3.

A schematic overview of the recruitment, screening, and enrollment process is provided in Figure 4-1 for youth and Figure 4-2 for caregivers.
Figure 4-1
IMPAACT 2016 Recruitment, Screening, and Enrollment Process for Youth

START

Informed Consent/Assent Obtained?

no

yes

STOP

Assign PIDs
- Obtain screening number from SES
- Enter youth permission for caregiver participation in eligibility checklist

Eligible?

no

yes

Hold for Entry Visit

Pool of 12-20 eligible youth?

no

yes

Sufficient pool of eligible youth NOT met within 60 days of screening date; repeat youth screening for eligibility

Sufficient pool of eligible youth MET within 90 days of screening date

Conduct Pre-Entry Procedures (on or within 14 days of Entry Visit)

Conduct Entry Visit:
- Enroll in SES
- Randomize (Randomize Trial only)

Start first group session

Enter SCR 10003 and SCR 10004 eCRF to record screen failure

STOP

Figure 4-2
IMPAACT 2016 Recruitment, Screening, and Enrollment Process for Caregivers

START

Youth Permission per youth’s eligibility checklist?

no

STOP

yes

Contacted caregiver?

yes

no

STOP

Informed Consent Obtained?

yes

no

STOP

Eligible?

yes

no

STOP

Assign PIDs
- Complete eligibility determination
- Enter eligibility checklist data to youth’s eligibility checklist linking the PIDs of youth and caregiver

Complete Screen/Entry Visit:
- Enroll in SES
- Randomize based on youth’s randomization (Randomize Trial only)
- Complete screening/entry procedures
- Start caregiver Group Session A on same day or separate day
4.3 Obtaining Informed Consent and Assent

Youth Participant

Inclusion criterion 4.1.2 specifies requirements for obtaining informed consent and assent from youth for this study, with two options depending on age of the potential youth participant listed below and additional details outlined in protocol Section 12.3.

- **If of legal age and able to provide independent informed consent as determined by site SOPs and consistent with site IRB/EC policies and procedures:** Willing and able to provide written informed consent for study participation. Under this option, the potential participant must undergo the study informed consent process.

- **If not of legal age to provide independent informed consent:** Parent or legal guardian, or other legally authorized representative is willing and able to provide written informed consent for study participation and potential participant is willing and able to provide written assent for study participation. Under this option, the potential participant’s parent, legal guardian, or other legally authorized representative must undergo the study informed consent process and the potential participant must undergo the study assent process. If the legal age of consent is reached any time following entry, the participant must undergo the study informed consent process at the next scheduled visit after the legal age is reached.

For each potential youth participant, study site staff will be required to determine which of the two above-listed options apply, and to conduct informed consent and assent processes accordingly.

Each site must have on file a study-specific SOP or study-specific addendum to an existing SOP for obtaining informed consent and assent that addresses all aspects of the informed consent and assent processes for this study consistent with all applicable regulations (e.g. 45 CFR 46), DAIDS policies, IRB/EC policies and procedures, and protocol specifications. Site staff involved in conducting informed consent and assent processes must follow these SOPs consistently. These staff must be designated on the study-specific delegation of duties log and must also be listed on the DAIDS Investigator of Record Form for the study.

Research regulations require that informed consent and assent be documented through the use of a written informed consent and assent form approved by the IRB/EC and signed and dated by the participant or the participant’s legally authorized representative at the time of consent. The DAIDS policy on Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials lists detailed requirements and suggestions for documenting the informed consent and assent process. Study sites must comply with all requirements and are encouraged to comply with all suggestions. To assist with compliance, site staff may use informed consent and assent coversheets or other similar materials. Each informed consent and assent process should also be documented in a signed and dated chart note. The note should document that informed consent or assent was obtained before conducting any study procedures. The note should also meet the requirements of the DAIDS policy referenced above. However, if an informed consent or assent coversheet is used, it is not necessary to transcribe or otherwise duplicate information recorded on the coversheet in the chart note.

**Caregiver Participant**

Inclusion criterion 4.3.2 specifies requirements for obtaining informed consent from caregivers for this study, with only one option: caregivers must be of legal age and able to provide informed consent to participate. Additional details outlined in protocol Section 12.3.
Youth and Caregiver Participants

See Section 4.5.2 of this MOP for further guidance on adequate documentation of informed consent and assent to fulfill protocol inclusion criterion 4.1.2 and 4.3.2 for youth and caregivers, respectively. Figure 4-3 and Figure 4-4 provide instructions for entering informed consent and assent data into eCRFs.

Figure 4-3
Youth and Caregiver Participants Who Can Provide Independent Informed Consent

<table>
<thead>
<tr>
<th>Informed consent for study participation (Youth and Caregiver)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Enter the outcome of this informed consent process into the LGW10025 eCRF.</td>
</tr>
<tr>
<td>• Complete a log line entry for “protocol version” and select the protocol version number.</td>
</tr>
<tr>
<td>• For the date of consent, enter the date when informed consent was provided.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Informed consent for non-protocol defined specimen storage and future use — research on HIV, the immune system, and other diseases (Youth only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Enter the outcome of this informed consent process into the TRK10000 eCRF, item 2.</td>
</tr>
<tr>
<td>• Enter “yes” or “no” in item 2.</td>
</tr>
<tr>
<td>• Enter the date when this informed consent decision was made in item 2a.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Informed consent for non-protocol defined specimen storage and future use — research involving genetic testing (Youth only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Enter the outcome of this informed consent process into the TRK10000 eCRF, item 1.</td>
</tr>
<tr>
<td>• Enter “yes” or “no” in item 1.</td>
</tr>
<tr>
<td>• Enter the date when this informed consent decision was made in item 1a.</td>
</tr>
</tbody>
</table>

Figure 4-4
Youth Participants Who Cannot Provide Independent Informed Consent

<table>
<thead>
<tr>
<th>Informed consent and assent for study participation (Youth only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Enter the outcome of this informed consent and assent process into the LGW10025 eCRF.</td>
</tr>
<tr>
<td>• Complete a log line entry for “protocol version” and select the protocol version number.</td>
</tr>
<tr>
<td>• For the date of consent, enter the date when informed consent and assent were provided. If informed consent and assent were provided on different dates, enter the later of the two dates.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Informed consent and assent for non-protocol defined specimen storage and future use — research on HIV, the immune system, and other diseases (Youth only)</th>
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</thead>
<tbody>
<tr>
<td>• Enter the outcome of this informed consent and assent process into the TRK10000 eCRF, item 2.</td>
</tr>
<tr>
<td>• Enter “yes” or “no” in item 2.</td>
</tr>
<tr>
<td>• Enter the date when the informed consent and assent decisions were made in item 2a. If these decisions were made on different dates, enter the later of the two dates.</td>
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<tr>
<td>• Enter the outcome of this informed consent and assent process into the TRK10000 eCRF, item 1.</td>
</tr>
<tr>
<td>• Enter “yes” or “no” in item 1.</td>
</tr>
<tr>
<td>• Enter the date when the informed consent and assent decisions were made in item 1a. If these decisions were made on different dates, enter the later of the two dates.</td>
</tr>
</tbody>
</table>
Regulations require that persons providing informed consent or assent be given a signed copy of their informed consent or assent form. If the copy is declined, this should be documented, and the person should be offered an alternate form of study contact information (e.g., a contact card or appointment card) in lieu of the full informed consent or assent form.

4.4 Assigning Participant Identification Numbers

A participant identification (PID) number must be assigned to each potential participant for whom informed consent for study participation is obtained. The only exception to this requirement applies when a participant has previously been assigned a PID for another IMPAACT or ACTG study. In that case, the previously-assigned PID would be used for IMPAACT 2016. Study site staff should assign PIDs from lists provided by the DMC and should contact the DMC with any questions related to use of PID lists.

4.5 Screening for Eligibility

Participant eligibility criteria are provided in protocol Sections 4.1 and 4.2, and eligibility screening procedures are provided in protocol Section 6. Operational guidance related to selected eligibility criteria is provided in the remainder of this section. Sites are encouraged to perform procedures that are least burdensome and/or most likely to identify ineligibility first. Note that all screening procedures, must occur within 60 days prior to entry.

As described in protocol Section 4.6, a PID will be assigned to all potential participants for whom informed consent or assent for study participation is obtained. A study-specific screening number will also be obtained for youth only through the DMC’s Subject Enrollment System (SES). Potential youth and caregiver participants found to meet all eligibility criteria will be enrolled in the study using the SES as described in protocol Section 4.6 and Section 4.6 of this MOP.

For potential youth participants who are found to be ineligible, or who do not enroll in the study for any reason, the IMPAACT 2016 Screening Failure (SCR10003) electronic case report form (eCRF) must be entered to record the screening outcome. If indicated on the SCR10003 that the reason for non-enrollment is due to the participant not meeting the inclusion/exclusion criteria, the eCRF IMPAACT 2016 Screen Failure Inclusion/Exclusion (SCR10004) eCRF must be entered to record the criteria not met.

It is the responsibility of the IoR and other designated study site staff to ensure that all required screening procedures are performed and adequately documented, and that only participants who meet the study eligibility criteria are enrolled. Each study site must have on file a study-specific SOP for eligibility determination that describes how study site staff will fulfill this responsibility; all sites must follow their SOPs when assessing eligibility for all potential participants.

In the event that study site staff identify that an ineligible participant has been enrolled, the Protocol Team must be consulted as soon as possible and ideally within 24 hours of site awareness per the communication procedures described in Section 3.0 of this MOP.

Re-Screening for Eligibility

The term “screening attempt” is used to describe each time a participant screens for the study, ending at the time the screening window for that participant closes. A total of two screening attempts for the Pilot Test and two screening attempts for the Randomized Trial are allowed (i.e., participants may re-screen once per Pilot Test or Randomized Trial).
If all screening and enrollment procedures are not completed within 60 days of obtaining written informed consent or assent for screening, the participant must repeat the entire screening process except:

- A new PID should not be assigned (Note: For youth only, obtain a new screening number from SES for second screening attempt)
- For youth only, if HIV infection is documented, a repeat test is not required
- For youth only, previously documented medical and medications history information should be reviewed and updated through the date of re-screening (it is not necessary to re-record history information that was previously documented)

Informed consent or assent is required for each screening attempt, and previously provided consent or assent does not “roll over” to a subsequent screening attempt/window.

4.5.1 Screening Medical History and Chart Reviews

For youth, the listing of Eligibility Screening Procedures in protocol Section 6.1.1 and 6.3.1 requires site staff to “review medical records to assess study requirements related to HIV infection per inclusion criterion 4.1.3 and ARV history per inclusion criterion 4.1.5.”

Some of the study eligibility criteria require consideration of medical history information to be obtained from potential youth study participants, as well as detailed review of youth participants’ medical records. Study sites are encouraged to develop operational tools to guide and document this process. These may include a structured medical history source document, with medical history questions to be asked and fields to record participant responses and/or a medical record review tool to record medical record review findings.

Adequate source documentation must be available in each potential participant’s study record to substantiate his/her eligibility for the study in relation to the protocol-specified eligibility criteria. Monitors and auditors may request original source documents or certified copies to verify eligibility in relation to each inclusion and exclusion criterion. Further guidance related to these documentation requirements can be found in the following sections of the DAIDS policy on Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials: Certified Copies, Entry Criteria, Medical History, Medical Records, Screening.

4.5.2 Guidance on Adequate Documentation of Provision of Informed Consent and Assent (Inclusion Criteria 4.1.2 and 4.3.2)

Protocol inclusion criteria 4.1.2 (youth) and 4.3.2 (caregivers) specify requirements for obtaining informed consent and assent for this study, with two potential options depending on the age of the potential participant, as specified in Section 4.3 of this MOP. The protocol refers site staff to the study-specific MOP for guidance on adequate documentation of these criteria. Adequate documentation should include the following:

- Copies of (blank) study-specific informed consent (for potential youth and caregiver participants as applicable) and assent (for potential youth participants as applicable) forms approved by the site IRB/EC as well as the IRB/EC risk determination for the study, and any other directives provided by the IRB/EC pertaining to obtaining informed consent and assent for this study. It is generally expected that this documentation will be maintained in study-specific essential document files.
• Copies of IRB/EC policies and procedures pertaining to the legal age of consent for research, and expectations for obtaining assent from underage research participants. It is generally expected that this documentation will be maintained in study-specific essential document files.

• Copies of site SOPs for obtaining informed consent (for potential youth and caregiver participants as applicable) and assent (for potential youth participants as applicable) for IMPAACT 2016, including documentation of whether the youth or caregiver participant is of legal age to provide independent informed consent. It is generally expected that this documentation will be maintained in study-specific essential document files.

Note: Per protocol Section 4.6, the informed consent process “will include detailed review of the study informed consent and assent forms (as applicable), time to address any questions or concerns the potential participant, parent, or guardian may have, and an assessment of understanding before proceeding to informed consent and assent decisions.” Site SOPs should describe how understanding will be assessed and documented.

• For each potential youth participant who is not able to provide independent informed consent, documentation of the name of the parent, guardian, or other legally authorized representative who took part in the study informed consent process and the relationship of this person to the potential participant. It is generally expected that this documentation will be maintained in individual participant research records.

• For each potential youth participant, documentation of the conduct of the informed consent and assent processes, as applicable, consistent with site SOPs and the DAIDS policy on Requirements for Source Documentation in DAIDS Funded and/or Sponsored Studies. See also Section 4.3 of this MOP.

• For each potential caregiver participant, documentation of the conduct of the informed processes, consistent with site SOPs and the DAIDS policy on Requirements for Source Documentation in DAIDS Funded and/or Sponsored Studies. See also Section 4.3 of this MOP.

• For each potential youth participant for whom informed consent and/or assent is provided, signed and dated informed consent and assent forms. It is generally expected that this documentation will be maintained in individual participant research records.

• For each potential caregiver participant for whom informed consent is provided, signed and dated informed consent forms. It is generally expected that this documentation will be maintained in individual participant research records.

4.5.3 Guidance on Indicators of Moderate to Severe Mental Health symptomology per Inclusion Criterion 4.1.6

Per inclusion criterion 4.1.6, potential youth participants must demonstrate a mental health symptomology to be included in the study. As part of the study eligibility determination and confirmation process, the three participant self-reported mental health questionnaires must be administered to youth to assess for symptoms related to depression (Patient Health Questionnaire-9 or PHQ-9), anxiety (General Anxiety Disorder or GAD-7) and trauma (UCLA PTSD Reaction Index). The questionnaires will be administered as computer-administered self-interview (CASI) questionnaires on an electronic device (e.g. laptop, desktop, tablet) in the participant’s chosen language that would maximize the participant’s performance on the tests. Refer to Section 5.3 below for details on how to administer CASI questionnaires.
For a youth to meet inclusion criterion 4.1.6, a minimum score must be obtained on at least one of the three mental health questionnaires. Email alerts indicating whether or not a given participant obtained a minimum score on at least one of the three required questionnaires will be sent in real-time to a site email group with designated site staff (limited to the site IoR, study and/or nurse coordinator, and local supervisor who may also be serving as the on-site study clinician and/or IoR). One email alert will be sent for each participant noting whether minimum score requirements were met for at least one questionnaire, however the scores and questionnaire names will not be provided in these emails.

As outlined in Figure 3-1, sites should email the Protocol Data Managers the name(s), email(s), and title(s) (i.e. IoR and local supervisor) of designated site staff to receive the email alerts. Recipients of the alerts should forward the eligibility alerts as needed to site staff designated to complete participant eligibility checklists. Such site staff must enter ‘yes’ or ‘no’ into designated item (refer to Figure 4-5) on the participant’s eligibility checklist to confirm the participant’s eligibility per inclusion criterion 4.1.6.

**Figure 4-5**

<table>
<thead>
<tr>
<th>Item in the IMPAACT 2016 Eligibility Checklist</th>
</tr>
</thead>
<tbody>
<tr>
<td>At screening, does the youth participant have a qualifying score for mental health symptomatology based on at least one of the following questionnaires:</td>
</tr>
<tr>
<td>- Patient Health Questionnaire-9 (PHQ-9)</td>
</tr>
<tr>
<td>- General Anxiety Disorder-7 (GAD-7)</td>
</tr>
<tr>
<td>- UCLA Post-Traumatic Stress Disorder-Reaction Index (UCLA PTSD-RI)</td>
</tr>
<tr>
<td>Note: Severe distress or suicidal ideation is not exclusionary.</td>
</tr>
<tr>
<td>1. Yes</td>
</tr>
<tr>
<td>2. No [FAIL]</td>
</tr>
<tr>
<td>3. Unknown [FAIL]</td>
</tr>
</tbody>
</table>

**4.5.4 Guidance on obtaining and documenting youth written permission for caregiver participation per Inclusion Criterion 4.3.1**

Per protocol Section 4.6, as part of the youth informed consent or assent process, youth will be asked whether they are willing to identify a caregiver and provide written permission for the caregiver to participate in the study. Written permission is source documented on the youth’s informed consent or assent form by the youth writing an ‘X’ to indicate her/his decision as shown in Figure 4-6 below.

**Figure 4-6**

<table>
<thead>
<tr>
<th>Written Permission Excerpt from the Sample Youth Informed Consent Forms</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Youth Participants Only]</td>
</tr>
<tr>
<td>For the optional caregiver participation, write a ‘X’ to indicate your decision.</td>
</tr>
<tr>
<td>_______ Yes, I agree to have my caregiver join the study</td>
</tr>
<tr>
<td>_______ No, I don’t want to have my caregiver join the study</td>
</tr>
</tbody>
</table>

Site staff must enter the decision into the youth participant’s eligibility checklist.

*For youth who write an ‘X’ to indicate yes*, he/she agrees to have her/his caregiver join the study, site staff should ask the youth for their caregiver’s name, phone number, and email to be able to contact the
caregiver. A youth’s decision regarding caregiver participation will also be reported on the EVW10053: IMPAACT 2016 Report of Caregiver Participation eCRF within Medidata Rave.

If the identified caregiver agrees to participate, he/she will be introduced to the study and asked to provide informed consent for his/her own participation. Caregivers may be contacted, introduced to the study and provide consent at any point between youth screening and the first caregiver group session unless either the youth or caregiver is determined ineligible to participate in the study.

If the identified caregiver does not agree to participate, he/she will not be asked to provide informed consent. Sites should establish a mechanism to track the number of caregivers identified who do not agree to participate; this data will be requested by the Protocol Team.

*For youth who write an ‘X’ to indicate no,* site staff should explain to the youth that their caregiver will not be contacted on their behalf. However, if another youth who is under the care of the same caregiver agrees to invite the caregiver to join study, the caregiver will be contacted ONLY on behalf of the youth who provided permission for caregiver participation. Further explain to the youth that their caregiver will only engage in the study with any other youth who agreed to the caregiver participation, and their caregiver will not be told that he/she (the youth) did not agree to the caregiver’s participation.

### 4.6 Enrolling Eligible Participants

*Contact the Protocol Team with any questions about eligibility, and adequate documentation thereof, prior to enrollment.*

Participants will be considered enrolled in this study upon successful entry of eligibility checklist data into the SES, which will result in generation of a Study ID Number (SID). Youth and their caregivers (if applicable) will be enrolled through the same eligibility checklist that will link the PID number of the youth and the caregiver through additional questions in the eligibility checklist. While the caregiver may provide informed consent for his/her own participation at any point between the youth screening and the first caregiver group session, the caregiver should only be enrolled after the youth who consented for the caregiver’s participation is enrolled.

### 4.7 Screening and Enrollment Logs

Per the DAIDS policy on *Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials,* study sites are required to document screening (including screening failures) and enrollment activity on screening and enrollment logs. These logs may be maintained electronically but must be 21 CFR Part 11 compliant if the log is considered a source document. Screening and enrollment logs may be maintained separately or combined into one log. Screening and enrollment logs should be updated in real time and completed after a participant provides informed consent for screening.

### 4.8 Participant Retention

Per protocol Section 4.7, each site must establish and implement SOPs that target retention rates that are sufficient to reliably estimate the primary study outcomes. Such SOPs may be included in the required participant accrual SOP listed on the site-specific study activation checklist (refer to Section 4.1 of this manual). The following guidance provide suggested retention procedures sites may incorporate into the participant accrual SOP and implement when feasible and acceptable per local regulations. Sites are not limited to only the following suggested retention procedures and are encouraged to incorporate best practices per local regulations.
At the Screening and Pre-Entry visit, youths’ birthdate, email, phone numbers, and home address should be obtained to help us locate participants in the future. If the youth has a social media account he/she would like to communicate with, such as Instagram, SnapChat, WhatsApp, or Facebook, obtain the name and/or number of the account. Collect the same contact information for caregivers. In addition to the youth and caregiver information, collect the name and contact information for at least two other individuals who “will always know where the youth/caregiver is in the event that their contact information has changed.” Youth and caregivers should indicate how they would like the site staff to refer to themselves should they contact the “other” individuals.

Contact information for the youth, caregiver, and “others” should be updated as needed at each study visit, and youth and caregivers should be telephoned/emailed/texted monthly to update information during the follow-up study period. The contact information should be used to enable scheduling, address scheduling issues and barriers, and remind participants of when their study visits and group sessions will be conducted.

Youth (and caregivers where relevant) should be contacted the day before group sessions and study visits to confirm attendance.

Phone calls, text messages, emails, or other methods intended as retention techniques may be provided following each study visit to demonstrate the team’s appreciation of participation. The same methods could be used prior to the next session as reminders and incentive to return. Other methods may be implemented at the discretion of the site IoR or designee such as acknowledging a participant’s birthday by phone call, text message or email.

Confirm with the IRB on any materials and/or methods that may be provided to participants per site standards, including but not limited to social media accounts, phone calls, text messages, emails, or other methods.

5.0 Study Procedures

5.1 Mock Procedures (Pilot Test only)

Per protocol Section 6.1.2, youth participants will perform mock procedures for hair and blood collection, and per protocol Sections 6.1.2 and 6.2.1, youth and caregiver participants will perform mock procedures for completing the questionnaires. The purpose of the mock procedures is for each site to assess the logistical feasibility and duration to complete all youth procedures on the same day or up to 14 days prior to the Group Session 1, and all caregiver procedures on the same day or up to 60 days prior to the Group Session A.

As part of the mock procedures, site staff should conduct the following:

- Complete each step of the blood collection procedure outlined in Section 7.1 and LPC excluding the actual needle stick of drawing blood with each youth participant.
- Complete each step of the hair collection procedure outlined in Section 7.2 excluding Step 3 (cutting of hair) and Step 8 (complete/entering into LDMS) with each youth participant.
- Have each youth and caregiver participant complete all CASI-administered questionnaires designated for their Pre-Entry Visit (youth) or Screening/Entry Visit (caregiver).

Information entered into CASI-administered questionnaires will not be downloaded by the Protocol Data Managers from the CASI system to the study database.
5.2 Targeted Medical and Medication History

Targeted medical and medication history information, focused on psychiatric history and medication, will be collected per the schedule of evaluations as described in protocol Section 6.5.

Site staff will review available medical records in advance of a youth’s scheduled visit during which targeted medical and medication history is to be collected per the schedule of evaluations (Pre-Entry and Follow-up Study Visits) to identify new information. During the youth’s scheduled visit, site staff will query youth and/or their caregivers on an individual basis in a private setting separate from other participants. Adequate source documentation of information collected must be maintained in the participant’s study record and entered into eCRFs as listed in Figure 5-1.

**Figure 5-1**

**IMPAACT 2016 Targeted Medical and Medication History Documentation**

<table>
<thead>
<tr>
<th>Assess for and Source Document</th>
<th>Enter into eCRF**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Been diagnosed with a mental illness (if yes, diagnosis and dates of diagnosis)</td>
<td>MHW10000: Medical History Log</td>
</tr>
<tr>
<td>Attempted suicide (if yes, number of times; dates of all attempts)</td>
<td>MHW10000: Medical History Log (if prior to enrollment)</td>
</tr>
<tr>
<td></td>
<td>ADE10000: Adverse Events Log (if new events on day of enrollment or visits following enrollment)</td>
</tr>
<tr>
<td>Received non-study mental health services (if yes, what kind of services – record any diagnosis resulting from the service; dates provided)</td>
<td>MHW10000: Medical History Log</td>
</tr>
<tr>
<td>Received referral from study site staff to non-study mental health services (if yes, date and outcome of referral)</td>
<td>EVW10049: IMPAACT 2016 Youth Referrals (only for IPL, 6- and 12-month Follow-up Visits in Randomized Trial)</td>
</tr>
<tr>
<td>Received psychiatric medications (if yes, medications received and dates of use)</td>
<td>CMW10000: Concomitant Medications Log</td>
</tr>
<tr>
<td>Occurrences of insomnia, psychiatric disorders, and suicidal ideation meeting adverse event criteria specified in protocol Section 7.2</td>
<td>ADE10000: Adverse Events Log (only for new events at visits following enrollment)</td>
</tr>
</tbody>
</table>

In addition to information collected and entered into eCRFs, youth will also self-report information using CASI; refer to Section 5.3 for details on CASI administration. Any response(s) suggesting a safety concern or risk will generate a safety email alert to the site’s CASI alert email group composed of designated study site staff (refer to Section 6.0 for details on designating staff and managing safety alerts); study site staff should review relevant information with the on-site study clinician, or IoR and/or designee in advance of a participant’s scheduled visit and enter relevant information into eCRFs per Figure 5-1.

5.3 CASI-Administered Questionnaire Data Collection

All questionnaires for youth and caregiver participants are administered as computer-assisted self-interview (CASI) questionnaires to the participants to enable assessments for eligibility and/or study outcomes for analyses. Refer to protocol Sections 5.5 and Schedule of Evaluations in protocol Appendices I-A, I-B, II-A and II-B for details on when questionnaires are administered to youth and caregivers.
All questionnaires should be completed by the participants in a quiet, private space using an electronic device, such as a computer, laptop, or tablet, unless CASI is inaccessible for an unforeseen cause, in which case paper versions of questionnaires will be administered by designated study site staff. Designated study site staff will log in each participant’s information into CASI. The questionnaires are available in English and local languages. The study site staff will ask each participant to choose which language they prefer the questionnaires to be administered in to him/her, then the staff will select the participant’s chosen language. A reminder to study site staff will appear after login, which instructs study site staff to read the instruction paragraph to the participant before the participant begins completing the questionnaires.

Participants should be instructed to carefully read and follow the directions provided at the beginning of each questionnaire as directions for each questionnaire may differ. The study site staff who initiated the questionnaire should remain in the room while the participant completes the CASI questionnaires, to answer the participant’s questions as needed.

Completion of the questionnaires involves a significant time commitment for the participants. Before beginning questionnaire administration, the designated study site staff should assess whether the participant is rested, alert, and how he/she is feeling. Snacks and water should be available in case the participant has not eaten prior to the visit. Short breaks are acceptable although they should be brief and only as needed to increase response validity.

Refer to Section 6.1 for guidance on monitoring and addressing mental health risks and safety concerns identified in a youth’s responses to one or more questions suggesting a risk of suicide, suicidal ideation, or other safety concerns.

**Multiple youth under the care of the same caregiver**

Should there be more than one youth participating in the study under the care of the same caregiver, the caregiver will be instructed by the site to only complete questionnaires for one youth as follows:

- **If more than one enrolled youth are under the care of the same caregiver, and more than one youth agreed to the same caregiver participation:** the caregiver will be randomly* assigned to complete questionnaires for only one of the enrolled youth throughout the duration of the study.

  *Each site will be responsible for establishing a mechanism to randomly assign each enrolled caregiver to the PID number of the appropriate enrolled youth. Each assignment will remain effective for the duration of the study so that a given caregiver completes all questionnaires for the same youth PID throughout the entire study. Documentation of the assignments should be securely stored on-site.

- **If more than one enrolled youth are under the care of the same caregiver, but only one youth agreed to the caregiver participation:** the caregiver will complete questionnaires for the enrolled youth who agreed to their participation. The site will not disclose which youth agreed or did not agree to the caregiver participation.

5.4 **Fun Had, Knowledge Learned, and Logistical Data Collection**

During the Pilot Test and Randomized Trial, study site staff will enter data collected on study participant group session attendance and study participant perception of fun had and knowledge learned from attending each group session into the IMPAACT 2016 Group Session Feedback Form (EVW10048).
**Participant Reported Fun Had and Knowledge Learned Data**

Per protocol Sections 3.1 and 5.5.5, following each group session and before participants leave the session, each youth and caregiver will report on a paper form their perception of 1) how much fun they had at the given group session, and 2) how much they learned at the given session, both on a scale from 1-10, with 1 representing ‘no fun’/‘learned nothing’ and 10 representing ‘a lot of fun’/‘learned a lot.’

English and translated versions of the paper EVW10048 form are accessible on the DMC IMPAACT Portal within the Forms Management Utility (FMU). Sites are responsible for printing the paper version of the IMPAACT Group Session Feedback Form (EVW10048) to serve as a place for the youth and caregivers to report their responses; example of the paper version of EVW10048 shown below in Figure 5-2.

**Figure 5-2**

**English Paper Version of IMPAACT 2016 Group Session Feedback eCRF (EVW10048) in FMU for Participants**

![Figure 5-2](image-url)

Study site staff **who are not the group leaders** should distribute the form to participants and reassure them that their individual answers will not be shared with the IYL and adult study staff group leaders.
Study site staff will read the following questions aloud to youth and caregiver participants while showing a response cue card (1 = ‘no fun’/’nothing learned’ to 10 = ‘a lot of fun’/’a lot learned’) at the end of each group session:

- How much fun did you have at the group session? Youth and caregivers will then write down their response from 1 – 10.
- How much did you learn at the group session? Youth and caregivers will then write down their response from 1 – 10.

Study site staff will ask participants to complete the paper form and will collect the completed forms from all participants at the end of the session. Study site staff will not share participant responses with IYL and adult study staff, and IYL and adult study staff group leaders should not review youth and/or caregiver reports to preserve confidentiality and avoid youth and caregivers responding in a way to please the group leaders.

Immediately following the end of the session, site staff will enter the responses into the IMPAACT 2016 Group Session Feedback eCRF (EVW10048) within Medidata Rave; example of the eCRF (EVW10048) shown below in Figure 5-3.

Figure 5-3
IMPAACT 2016 Group Session Feedback eCRF (EVW10048) in Medidata Rave for Site staff
**Logistical Data**

Per protocol Section 5.5.5, during each group session, the IYL and adult study staff should be the designated study site staff to collect logistical data on study participant attendance and punctuality. The IYL and adult study staff will confirm the answer to the following questions for each participant at each group session:

- Did the study participant attend the scheduled group session?
- Did the study participant stay for at least half of the group session?

Immediately following the end of the group session, IYL and adult study staff observers should provide designated study site staff with participant logistical data to enter into the IMPAACT 2016 Group Session Feedback eCRF (EVW10048) within Medidata Rave in Figure 5-3 above.

### 5.5 Intervention Fidelity Assessment (IYL and Adult Study Staff)

Refer to protocol Section 5.4 for details on the assessment of the TI-CBT intervention fidelity.

In the TI-CBT arm only, IYL and adult study staff facilitators will self-report, and IYL and adult study staff observers will provide observer ratings, on the fidelity of intervention delivery using paper versions of the IMPAACT 2016 Treatment Fidelity-Facilitator Evaluation (QLW10129) or IMPAACT 2016 Treatment Fidelity-Observer Evaluation (QLW10130) checklist, respectively. Forms will be available in English and local language(s), and paper forms are completed at the end of each youth and caregiver group session (Pilot Test and Randomized Trial).

To identify which group session an individual form submission is associated with, IYL and adult study staff must enter a Group Identification Number on each form; example shown below in Figure 5-4.

**Figure 5-4**

**IMPAACT 2016 Group Session Feedback eCRF (EVW10048) in Medidata Rave for Site staff**

The **Group Identification Number** naming convention is Site #-[Y or C][T or D][Pilot, 1, 2 or 3…], where:

- Y = Youth group
- C = Caregiver group
- T = TI-CBT Intervention
- D = Discussion Control
- P = Pilot Test
- 1 = 1st wave in Randomized Trial
- 2 = 2nd wave in Randomized Trial
- 3 = 3rd wave in Randomized Trial
Examples include (refer to Section 4.0 of this MOP for definition of a wave):

111111-YT1 = At site 111111, a Youth group in TI-CBT of the 1st wave in the Randomized Trial
222222-YD2 = At site 222222, a Youth group in Discussion Control of the 2nd wave in the Randomized Trial
333333-YTP = At site 333333, a Youth group in TI-CBT of the Pilot Test
444444-CTP = At site 444444, a Caregiver group in TI-CBT of the Pilot Test
555555-CD1 = At site 555555, a Caregiver group in Discussion Control of the 1st wave in the Randomized Trial

All completed paper forms are to be immediately provided to the local supervisor(s) who will review and enter all data into CASI. All data entered into CASI must be entered in English, regardless of the language they were completed in. The local supervisor(s) or designee is responsible for translating any data reported in the local language to English before or while entering the responses in CASI. The local supervisor(s) will use the forms to guide discussions during the supervision meetings with IYL and adult study staff; refer to Section 5.7 of this MOP. Forms should be securely stored on site.

5.6 Group Sessions

5.6.1 Preparation

Practice for the TI-CBT Intervention Group Sessions

After IYL and adult study staff are fully trained to competence as determined by the expert trainer, IYL and adult study staff will continue to practice delivering the group sessions during their supervision as described in Section 5.7 of this MOP. IYL and adult study staff will specifically practice the next upcoming session during the week prior to that session. The practice will occur with the local supervisor and other IYL or adult study staff who will provide feedback to ensure fidelity to the intervention manual and comfort delivering the content.

Notes from the practice sessions may be kept for training purposes and further reviewed during the debrief supervision meeting that occurs between the local supervisor and the IYLS or adult study staff within one week after each intervention session and/or reviewed during the weekly meeting between the local supervisor and expert trainer (refer to protocol Section 5.3.1). IYL and adult study staff trained on the TI-CBT intervention should ONLY practice with other facilitators and observers assigned to the TI-CBT intervention and NOT with those assigned to the discussion control group.

Supplies for the TI-CBT Intervention Group Sessions

Sites are advised to have all necessary supplies available for the practice as well as prior to administering the TI-CBT intervention group sessions to participants. The existence of these materials should be re-checked prior to each session to ensure none have been lost. This will ensure all materials are available before the intervention begins and prevent duplicate orders of supplies that may be re-used in subsequent sessions. Practice sessions should be conducted in the actual study intervention space to ensure it provides adequate space and privacy.

Flip chart paper, markers, pens, and handouts should be ready before each intervention session. Refer to Appendix 1 of this MOP and the first page of the TI-CBT Youth and Caregiver Intervention Manuals for each group session to find what materials are needed for that session.
Logistical Considerations

For both the TI-CBT intervention and discussion control groups, the rooms should be reserved in advance with adequate chairs, tables, and working space. On the day of the group session, the materials should be set up in advance of participant arrival so IYL and adult study staff can interact with participants as they arrive and help them feel at ease. Participants should be given a reminder the day prior to the session, in order to maintain session attendance.

Drinks and snacks should be ordered in advance and provided at the end of the group session. Transport compensation and tracking should also be confirmed at each session and available prior to session start.

It is recommended that sites have an SOP with designated responsibilities for IYL, adult study staff, and local supervisor(s) to ensure study sessions and discussion control groups occur smoothly. The designated on-site study clinician, who may also be the local supervisor, should be available on-site during participant sessions in case of any emergency or safety concern (refer to Section 6.1 of this MOP for guidance on managing emergency or safety concerns).

5.6.2 Conducting Group Sessions

Attendance

The local supervisor and on-site study clinician (the same individual may serve as both the local supervisor and on-site study clinician) should be on site in a separate room from the participants for all group sessions (TI-CBT Intervention and Discussion Control) to address safety concerns or other emergency situations. All group sessions will be delivered by two trained and designated IYL (youth sessions) or adult study staff (caregiver sessions) facilitators and observed by a third trained IYL (youth sessions) or adult study staff (caregiver sessions).

If one of the two group facilitators is unable to attend the session, the observer will take his/her place. If this occurs, the local supervisor will become the designated observer, and he/she will complete the fidelity ratings and note taking during the session.

Arrival and Set-Up

IYL and adult study staff group leaders and observers should arrive 30 minutes prior to the start of the group session to set up the space with chairs in a half circle for participants; additional chairs for group leaders will be at the front, and chairs for observers will be to the side or back of the room.

For the TI-CBT group sessions only, in advance of a scheduled session (e.g. a few days prior to a session), IYL and adult study staff designated to the TI-CBT Intervention group should re-check to ensure that all materials are present as described in Section 5.6.1 of this MOP according. If any materials are missing, IYL and adult study staff should immediately inform the local supervisor or designated site staff so he/she can replace the missing materials. IYL and adult study staff should set up TI-CBT intervention materials in advance of participant arrival, including the flip chart, handouts, and writing utensils.

Greet Participants and Track Attendance

Once the room is prepared for the group session, IYL and adult study staff should warmly greet participants as they arrive and help participants feel comfortable and at ease. IYL and adult study staff should encourage participants to sit where they like and continue to engage with participants in a friendly and open manner as the group waits for everyone to arrive.
As is often the case, participants may arrive late to the session. IYL and adult study staff, in consultation with the local supervisor, should use discretion regarding how long to wait for all participants to arrive. As a general rule, once there are at least five participants present, the group session should begin, although not before the stated start time. The group session can begin early if all participants are present. The local supervisor should be aware when all participants are present and the group session begins.

In the event a participant has not arrived but is expected to attend (i.e., the participant confirmed attendance the day before the group session), the local supervisor and/or IYL/adult study staff should attempt to reach the participant following the group session to encourage attendance at future group sessions. Participants should be invited to arrive late rather than miss the full group session. Similarly, if a participant needs to leave early, he/she should be encouraged to attend as much of the group session as possible.

Late arrivals (>15 minutes after the session begins) and early departures (>30 minutes before the session ends) should be noted on the participants’ study files for the local supervisor and/or IYL/adult study staff to reference if reaching out to participants to encourage full attendance. Refer to Section 5.4 and Figure 5-3 for guidance on documenting attendance in an eCRF.

**Delivering the TI-CBT Intervention**

For the TI-CBT Intervention group sessions only, IYL and adult study staff should follow the structure and script provided in the TI-CBT Youth and Caregiver Intervention Manuals, respectively, but avoid reading it word-for-word. This will be emphasized in the training of IYL and adult study staff. IYL and adult study staff should be comfortable with the content and materials to be able to deliver the activities smoothly.

The IYL and adult study staff observers should monitor the timing of each activity, take notes throughout the group session for later use during weekly supervision to enhance delivery, and address concerns that arise. The observers do not take part in the group unless indicated in the TI-CBT Youth and Caregiver Intervention Manuals, or if a primary facilitator is absent. The IYL and adult study staff observers should also complete the IMPAACT 2016 Treatment Fidelity Evaluation form for each specific activity, and at the end of the group session, they should complete the more general questions (refer to Section 5.5 of this MOP for guidance on completing and processing the form).

**Ending Each Group Session**

At the end of the group session, the IYL and adult study staff should distribute the snacks. During the snack, IYL and adult study staff should leave the room so designated site staff such as the local supervisor can implement the procedures described in Section 5.4 of this MOP. Site staff will collect the completed forms and not share individual responses with IYL and adult study staff.

At the conclusion of the group session, IYL and adult study staff should put away all materials and notify the local supervisor or designated study site staff if any materials need replacement in preparation for the next group session.

**5.6.3 Concurrent Waves of Group Sessions**

Given the complexity of the study, concurrent waves of the intervention are not expected. However, should a site enroll enough participants for concurrent waves, the local supervisor will consult with the Protocol Team to determine whether a concurrent wave is feasible. This determination will depend in part on the supervisor’s opinion whether the IYL and the site have the capacity and time to implement the
intervention, conduct supervision, and key all forms for two waves simultaneously. Any intent to run concurrent waves will be considered on a case by case basis. Refer to Section 4.0 of this MOP for additional guidance on concurrent waves.

If multiple waves are initiated, the concurrent waves may maintain the same schedule or different schedules, depending on site resources and staff availability. Timing should be discussed with the Protocol Team to ensure smooth processing. The same preparation (refer to Section 5.6.1 of this MOP) and conduct (refer to Section 5.6.2 of this MOP) will be required. Supervision will proceed as usual per Section 5.7 of this MOP.

5.7 Supervision of Indigenous Youth Leaders and Adult Study Staff

Per protocol Section 5.3, the expert trainer will conduct supervision of the local supervisors in the form of weekly SKYPE meetings, per country or per site, as agreed upon by the local supervisors and expert trainer. The local site IoR and/or local supervisors as designated will then provide direct supervision to the IYL and adult study staff.

5.7.1 TI-CBT Intervention Arm

Prior to the Pilot Test, the local supervisor who took part in the training for IYL and adult study staff for delivering the TI-CBT intervention will continue to oversee IYL and adult study staff practice of the TI-CBT Intervention delivery. Practice will continue until IYL and adult study staff are deemed competent by the expert trainer and local supervisor, express confidence and familiarity with the material, and demonstrate the ability to deliver the intervention smoothly to participants, as described in Section 3.5 of the Guidance Document: Preparation and Adaptation of the Trauma-Informed Cognitive Behavioral Therapy (TI-CBT) Intervention.

Ongoing Supervision of IYL and Adult Study Staff during Pilot Test and Randomized Trial

After each group session, the local supervisor will review the completed IMPAACT 2016 Treatment Fidelity Evaluation forms (refer to Section 5.5 of this MOP for guidance on completing and processing the form) and observer notes to identify any challenges and/or concerns with intervention delivery. These forms and notes will be used in supervision with IYL and adult study staff to facilitate improvement and/or remediate concerns as needed. If additional training is determined to be needed, the local supervisor will provide additional training until the IYL and/or adult study staff meets competency requirements.

IYL and adult study staff will meet with local supervisors twice weekly during the Pilot Test and the Randomized Trial. In the first meeting of the week, IYL and adult study staff will review the prior session, facilitator fidelity forms, and observer fidelity forms. In the second meeting of the week, IYL and adult study staff will practice the upcoming group session.

The local supervisor should take notes regarding IYL and adult study staff performance to review with IYL and adult study staff during the supervision session and with the expert trainer during weekly SKYPE meetings. Local supervisors should not disclose which IYL and/or adult study staff the information within the fidelity form is about, however general themes can be shared with facilitators to help improve the administration of the intervention.
Local Supervisor and Expert Trainer Meetings

The expert trainer will conduct supervision of the local supervisors in the form of weekly SKYPE meetings, per country or per site, as agreed upon by the local supervisors and expert trainer. During these meetings, local supervisors will discuss the observers’ notes, the facilitator and observer fidelity forms, and other issues that arise during supervision with IYL and adult study staff. Ideally, these meetings will occur with all local supervisors across all participating sites within one country simultaneously to build capacity of sites to work together. These meetings should be scheduled at a time that works for all parties involved.

5.7.2 Discussion Control Arm

The local supervisor, or other designee who is not exposed to the TI-CBT group sessions, will meet weekly with IYL and adult study staff leading the Discussion Control Group. Meetings will be unstructured and IYL and adult study staff should be encouraged to discuss and trouble shoot any concerns or issues that arise during the groups. It is ideal that a designee who is not exposed to the TI-CBT group sessions meet with the IYL and adult study staff if site resources allow for it to prevent contamination; sites may consult with the Core Protocol Team if the same person (i.e. local supervisor) will supervise both arms.

Care should be taken NOT to bring in content from the TI-CBT intervention during these meetings.

6.0 Participant Monitoring, Management, and Safety-Related Reporting

6.1 Youth Participant Safety Monitoring and Management

Refer to protocol Sections 6.6, 6.7, 7, and 8.1 for details on procedures addressing potential psychiatric concerns, social harms and suicidal ideation among youth participants, information on safety monitoring and reporting, and monitoring safety concerns among youth participants.

During the consent process, potential youth and caregiver study participants are informed that their participation in the study and responses to assessments will be kept private and confidential except in the cases of child abuse or risk of self-harm or harm to others. Occasionally, site staff must balance their concerns about the well-being of the participants with the promise to keep their responses and comments confidential. In some cases, such disclosures are required by law to be reported in order to maintain individual safety. In these cases, participants should be informed if the report is disclosed to the Protocol Team and/or local supervisor for further review.

Any participant information should only be discussed in a clinical or research setting unless referrals are made per site standard of care. Where a youth participant discloses any safety concerns or risks, the on-site study clinician may need to involve the caregiver to plan for youth safety. In these cases, the on-site study clinician should inform the youth that the on-site study clinician will be speaking with the caregiver to plan for safety. Additional training will be provided to on-site study clinicians, should they need/request it.

It is the site staff’s responsibility to share their awareness of safety concerns with the site IoR, local supervisor, and on-site study clinician so that together the study site staff can make the best decisions on how to assist the youth participant responsibly, attempting to ensure participant’s current safety. Study site staff, including but not limited to IYL and adult study staff, will be trained to identify and respond appropriately to youth participants who report safety concerns and will be encouraged to communicate
with the IoR, local supervisor, and/or on-site study clinician for guidance as needed. Refer to Sections 6.1.1, 6.1.2, and 6.1.3 of this MOP for guidance on managing CASI safety email alerts, social harms and suicidal ideations/attempts, respectively.

Participants (or their parent/guardian/caregiver) may discuss sign(s) or symptom(s) experienced by the youth participant(s) suggesting a safety concern to study site staff, including but not limited to:

- Youth expresses safety concern for self or others, or caregiver expresses safety concerns for youth, during group sessions or follow-up visits.
- Youth expresses safety concern for self or others, or caregiver expresses safety concern for youth, by phone.
- Youth response to a pre-specified CASI-administered questionnaire item is flagged for safety concern and a safety email alert is sent to designated site staff.

If a participant reports or exhibits a safety concern, the following steps will occur to ensure participant safety:

1. Upon site staff awareness of a safety concern, the site staff will immediately contact the on-site study clinician and share any safety concern(s) received.
2. The on-site study clinician will further evaluate the participant before the participant leaves the clinic/site to provide appropriate care, treatment, and support that is consistent with their study-specific roles and responsibilities, and according to standard of care. Refer to Appendix II of this MOP for example questions to ask youth participants during an evaluation to help determine imminent risk.
3. The on-site study clinician will notify the site IoR or designee of information collected and will follow local policies for management of such situations including engaging immediate/first responders as applicable.
4. The on-site study clinician and IoR or designee will also follow local reporting policies and legal statutes, including reporting to child protection or other appropriate agencies, as well as arranging referrals to appropriate support, counseling or treatment resources.

After the safety of the participant is ensured according to the steps above, the IoR or designee will notify the Core Protocol Team per Figure 3-2 and source document the event, as applicable per protocol Sections 7 and 8. All reported safety concerns/social harms will be source documented and will be managed consistent with the guidance provided in protocol Section 8. Follow-up contacts will also be conducted as needed to document resolution of reported signs and symptoms.

To facilitate rapid communications, the on-site study clinician and local supervisor should be on-site during study visit evaluations and group sessions as well as provide up-to-date contact information to the protocol site staff.
6.1.1 CASI-Administered Questionnaire: Safety Concerns

The questionnaires administered via CASI include questions surrounding feelings, behaviors, or situations that could be upsetting to youth. Some questions are about feelings of sadness and/or depression, symptoms of anxiety, and traumatic experiences and violence. Some questions are about risky behaviors, such as drinking too much alcohol, using drugs, and sexual activities. As described in the protocol, the purpose of the questionnaires is to evaluate how TI-CBT may decrease mental health symptoms. There is a wealth of research that shows that asking youth these types of questions does not increase the likelihood or risk of self-harm or harm to others. However, sometimes youth reveal concerning symptoms or signs of distress during psychosocial or mental health evaluations when directly asked.

Safety concerns could arise from a participant’s response to one or more question(s) in the questionnaires, if participant answer(s) suggest a risk for suicide, recent suicidal ideation, any past suicide attempt, or other safety concerns (e.g., youth reports risk of harming themselves or others, or physical and/or sexual abuse). It is important that the on-site study clinician is available for immediate consultation and referral/intervention if recent suicidal ideation is considered or an attempt is reported by participants, refer to Section 6.1.2 of this MOP for additional guidance on social harms.

Any response suggesting a safety concern or risk will generate a safety email alert, which will be sent in real-time to a site email group with designated study site staff (limited to the site IoR, study and/or nurse coordinator, and local supervisor who may also be serving as the on-site study clinician and/or IoR).

**Study site staff (if not the on-site study clinician) in receipt of safety email alerts must notify the on-site study clinician(s) of every safety alert immediately upon receipt.** As outlined in Figure 3-1, sites should email the Protocol Data Managers the name(s), email(s), and title(s) (i.e. IoR and local supervisor) of designated site staff to receive the email alerts.

The on-site study clinician and/or counselor will follow the guidelines in Section 6.1 of this MOP, starting with further evaluating the participant before the participant leaves the clinic/site to ensure immediate safety and to provide appropriate care, treatment, and support consistent with their study-specific roles and responsibilities, and according to standard of care.

As a condition for site activation, each site is required to create a study-specific SOP or addendum for Safety Monitoring and Adverse Event Reporting requirements. This document should include, as described in protocol Section 8.1, the following elements:

- Emergency response guidance,
- Describe procedures to evaluate imminent risk and next steps,
- Specific referral information and lines of communication (e.g. inpatient hospital contact detail, other standard of care resources), and
- Roles, and responsibilities for site staff to respond to participants in crisis.

6.1.2 Social Harms

Refer to protocol Section 6.6 and guidelines in Section 6.1 of this MOP for details on procedures and steps for responding to potential youth social harms.

Upon site awareness of a social harm(s), defined as a non-medical adverse consequence(s) of their study participation (e.g., unintentional or unwanted disclosure of HIV-status to others, verbal bullying, physical bullying, and/or other social harm), designated study site staff and IYL should source document the social
harm(s). Each social harm occurrence should be entered into the IMPAACT 2016 Youth Social Harms Log eCRF (LGW10018).

Per protocol Section 6.6 and in accordance with local standard of care and site SOPs, designated study site staff will make every effort to provide follow-up support and counseling to the participant as necessary, and/or refer participants to non-study resources.

In addition, the following steps should be taken:

1. Designated study site staff should provide appropriate follow-up with the participant as soon as possible to determine if there are changes in the social harm occurrence and impact on the participant; changes in the social harm occurrence should be source documented and a new social harm(s) should be entered into the eCRF LGW10018.
2. Per protocol Section 6.6, while maintaining participant confidentiality, study sites may engage their CAB members in exploring the social context surrounding instances of social harms, to minimize occurrence and identify appropriate follow-up actions to be taken.
3. It is suggested that sites develop SOPs to minimize and prevent a social harm from re-occurring.

Sites may consult with the IMPAACT 2016 Core Team as needed.

6.1.3 Suicidal Ideation/Attempts

Grade 2 or higher suicidal ideation should be entered into the Adverse Events Log eCRF (ADE10000); refer to protocol Section 6.7 and guidelines in Section 6.1 of this MOP for details on responding to and documenting new suicidal ideation events expressed in youth participants at visits following enrollment.

Immediate on-site evaluation

In the event that a participant (youth or caregiver) reports a youth’s recent or current suicidal ideation or any prior suicide attempts, the on-site study clinician should evaluate the youth immediately following the group session and/or study visit procedures, depending on when the disclosure occurs, as outlined in step 2 in Section 6.1 of this MOP. The group session and/or study visit procedures should be completed prior to further evaluation. If the disclosure is made during a group session, group leaders will be trained to respond to such disclosures. For example, group leaders will let the participant know they are concerned about the disclosure and will follow up with him/her at the end of the session.

Each site should have a standard procedure to evaluate if a participant is at imminent risk, per protocol Section 6.7.

One approach is provided in Appendix II of this MOP in which the on-site study clinician determines the recency of the ideation/attempt, if there is a plan to carry it out, and whether the participant has the means to carry out the plan. Special training will be provided to on-site study clinicians to conduct these evaluations. If a participant is determined to be at imminent risk, the on-site study clinician should follow the standard of care at the site. This may include hospitalization and/or contacting authorities.
6.2 Expedited Adverse Event Reporting

Per protocol Section 7.3.2, serious adverse events assessed as related to study participation must be reported as expedited adverse events (EAEs) for this study. Consistent with the DAIDS EAE Manual, a serious adverse event is an untoward medical occurrence that result in psychiatric adverse events (e.g., insomnia, psychiatric disorders [including anxiety, depression, mania, and psychosis] and suicidal ideation or attempt) occurring among youth participants.

Serious adverse events are not expected to occur commonly in this study; nonetheless, each adverse event that does occur must be assessed by the IoR or designee for seriousness (per the definition shown above) as well as relationship to study participation (per the definitions provided in protocol Section 8), with the outcome of these assessments documented in the participant’s study chart. The severity of each event should also be similarly assessed (per the DAIDS AE Grading Table) and documented. Site IoRs are encouraged to contact the Protocol Team with any questions or concerns related to assessing seriousness and/or reporting events as EAEs.

For each participant, the EAE reporting period begins at enrollment and ends 30 days after the last study procedure is performed.

Events meeting EAE reporting criteria should be reported using the DAIDS Adverse Experience Reporting System (DAERS) following procedures specified in Version 2.0 of the DAIDS EAE Manual and other associated instructional and operational resources, which are available at:

http://rsc.tech-res.com/clinical-research-sites/safety-reporting/manual

DAERS incorporates a report printing function that should be used to print all EAE reports—including modifications and updates—for filing in participant study records. Automated email messages confirming submission of EAE reports also should be printed and filed with the print-out of the associated EAE report.

Note: Per protocol Section 7.2, safety-related data collection for this study will be limited to psychiatric adverse events and/or social harms, and any such conditions meeting the definition of an adverse event will be entered into the Adverse Events Log eCRF (ADE10000). Any event reported as an EAE through DAERS must also be entered into an Adverse Event Log eCRF.
7.0 Laboratory Considerations

Protocol Section 6, the Schedule of Evaluations (SoE) and Laboratory Processing Chart (LPC) are the primary sources of information on specimen collection, processing, testing, storage, and shipping for this study; both clinic and laboratory staff should routinely refer to these documents for further operational guidance as needed.

The remainder of this section provides detailed operational instructions for youth blood and hair collection. FAQs and other operational guidance will be added to this section as needs for such guidance are identified.

7.1 Blood Collection

Refer to the listing of On-Study Procedures in protocol Section 6 and additional guidance for blood collection in protocol Section 6.8.1.

Refer to the LPC for detailed blood collection, processing, testing, storage, and shipping instructions.

7.2 Hair Collection

Approximately 50-60 strands of hair will be collected from enrolled study youth participants. Hair should be collected from the head (scalp) only, and not from other anatomical locations; hair collection is not required from youth participants who are bald. A sample of 50-60 strands is about the same diameter as a standard pencil eraser or drinking straw.

Hair samples should be collected consistent with the “hair collection protocol” shown in this section. Following collection, hair samples should be logged into the LDMS, and the zipper bags should be labeled with LDMS-generated labels. Hair samples should be kept at room temperature and in a dark place at each site until a request is received to ship the samples for testing.

### Hair Collection Protocol

<table>
<thead>
<tr>
<th>Materials Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piece of aluminum/tin foil</td>
</tr>
<tr>
<td>Desiccant packets</td>
</tr>
<tr>
<td>Scissors/Razors/Hair clips</td>
</tr>
<tr>
<td>Zipper bags</td>
</tr>
<tr>
<td>Alcohol swabs/pads</td>
</tr>
<tr>
<td>2 – Patient labels</td>
</tr>
<tr>
<td>Hair Sample Collection Report Form for relevant study (IMPAACT 2016 Pharmacokinetics Specimen Collection-Single [PKW10063])</td>
</tr>
</tbody>
</table>

Suggest making these “hair kits” ahead of time.
### Step 1
Before each sample is taken, clean the blades of a pair of scissors with an alcohol pad and allow blades to completely dry.

*Clean off the blades of scissors between patients.*

### Step 2
Lift up the top layer of hair from the occipital region of the scalp. Isolate a small thatch of hair (~50-60 fibers of hair) from underneath this top layer.

*If helpful, a hair clip can be used to keep the top layer of hair away.*

### Step 3
Cut the small hair sample as close to the scalp as possible.

*STRAIGHT HAIR*
CURLY HAIR

SHORT HAIR

Can let hair fall directly into piece of tin foil when very short/cropped (no need to label end since it is very short)
BRAIDED HAIR

Cut hair thatch from in-between braids or dread locks

Step 4

Keep your fingers on the part of the hair that is FURTHEST away from the scalp and put the hair sample down on an unfolded piece of tin foil.

Cut hair thatch from in-between braids or dread locks

Step 5

Put a thin label over the end of the hair sample that was FURTHEST away from the scalp.

If hair is very short just let it fall into the piece of tin foil and no need to label the distal end.
**Step 6**

Refold the foil over to completely enclose the hair and place a study ID label on the folded piece of foil.

**Step 7**

Place the folded piece of foil inside the plastic zipper bag with the desiccant packet inside and seal the bag.

**Step 8**

Complete/enter IMPAACT 2016 Pharmacokinetics Specimen Collection-Single (PKW10063)

**Storage of Hair**

Hair samples should be logged into the LDMS and the zipper bags should be labeled with LDMS-generated labels. Hair samples should be kept at room temperature and in a dark place at each site until a request is received to ship the samples for testing.
Correct methods for hair labeling

The collector should ensure that the label is not placed centrally on the piece of hair, but distally to allow the laboratory to distinguish between the root (proximal, closest to the scalp, where the hair is cut) and distal (farthest from the scalp) end. The sticker should be narrow enough when placed on a short section of hair to be able to distinguish the two ends.

Drawing an arrow to the root end via marker on the piece of tin foil can help distinguish the two sides if there is any confusion.

Good collection: Distal end (side farthest from scalp) labeled

Bad collection: Distal end should have been labeled (long enough) but not

Okay not to label because too short

8.0 Data Management Considerations

Refer to protocol Section 10. Further information on data collection expectations is available in the eCRF completion guide developed by the DMC for this study, which is available on the DMC portal. eLearning modules and other operational guidance on use of Medidata Rave are also available on the DMC portal.
## Appendix I: Session-specific supplies for TI-CBT Intervention Group Sessions

(Notes: All sites are to acquire the supplies in the tables below for use in both the Pilot Test and Randomized Trial. Some supplies can be reused in subsequent group sessions. Focus Group host sites which previously acquired specific supplies for the identified session(s) delivered in the Focus Groups do not need to re-acquire such supplies unless there are insufficient quantities.)

### Youth Group Sessions

*(IYL should bring their Youth Intervention Manual to all youth group sessions)*

<table>
<thead>
<tr>
<th>Session Part</th>
<th>Item (handouts, worksheets, diagrams, certificate template provided by the Adaptation Team)</th>
<th>Quantity</th>
<th>Check box if on site for session</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Session 1 Supplies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A – Ice breaker</td>
<td>Ball with questions (IYL write questions on ball prior to session)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>B – Group Rules, D – Introduce Stress</td>
<td>Flip chart (with markers)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>D – Introduce Stress</td>
<td>Stress Reaction Cycle Diagram Handout (print copies for participants and IYL)</td>
<td>1 handout per participant and IYL</td>
<td></td>
</tr>
<tr>
<td>E – Body Mapping</td>
<td>Large piece of paper (large enough to draw an outline of each participant’s body)</td>
<td>1 piece per participant</td>
<td></td>
</tr>
<tr>
<td>E – Trace Stress, F – Express Feelings</td>
<td>Box of assorted colored markers (for participants to share)</td>
<td>Multiple boxes at site discretion</td>
<td></td>
</tr>
<tr>
<td><strong>Session 2 Supplies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C – Review Stress</td>
<td>Stress Reaction Cycle Diagram Handout (print copy or use from previous session)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>D – Small groups for Stressors and Responses</td>
<td>Group Worksheet: Stress Response (print copies)</td>
<td>2 (1 per small group)</td>
<td></td>
</tr>
<tr>
<td>E – Stressors and Responses, H – Health Response</td>
<td>Flip chart (with markers)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>I – Homework</td>
<td>Homework: Stress and Happiness Worksheet (print copies)</td>
<td>1 per participant</td>
<td></td>
</tr>
<tr>
<td><strong>Session 3 Supplies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B – Review homework, D – Stressful/Pleasant Events</td>
<td>Flipchart (with markers)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>C – Thoughts-Feelings-Behaviors (T-F-B)</td>
<td>T-F-B Cognitive Triangle Diagram (print copy)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>E – Small groups for T-F-B</td>
<td>Plain white piece of paper and markers</td>
<td>1 set per participant</td>
<td></td>
</tr>
<tr>
<td>I – Homework</td>
<td>Homework: T-F-B Blank Cognitive Triangle Worksheet (print copies)</td>
<td>1 per participant</td>
<td></td>
</tr>
</tbody>
</table>
### Session 4 Supplies

<table>
<thead>
<tr>
<th>Supplies</th>
<th>Description</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>C and D – Small groups for Gender Roles/Expectations</td>
<td>Large piece of paper and markers</td>
<td>2 sets per small group</td>
</tr>
<tr>
<td>F – Family and Community Roles</td>
<td>Basket</td>
<td>1</td>
</tr>
<tr>
<td>F – Family and Community Roles</td>
<td>Small pieces of paper (write each of the following roles on a piece: parent, grandparent, teacher, church leader, community authority, male friend, female friend, neighbor, female elder, male elder, doctor, nurse, counselor)</td>
<td>13 (At site discretion if more roles)</td>
</tr>
<tr>
<td>G – Large Group Discussion</td>
<td>Country-specific data on GBV</td>
<td>Verbalize or print handout</td>
</tr>
<tr>
<td>H – Homework</td>
<td>Homework: Gender-based Messages Worksheet (print copies)</td>
<td>1 per participant</td>
</tr>
</tbody>
</table>

### Session 5 Supplies

<table>
<thead>
<tr>
<th>Supplies</th>
<th>Description</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>C – Interpersonal Interactions</td>
<td>Plain white piece of paper and pens or markers</td>
<td>2 sets</td>
</tr>
<tr>
<td>D – Role Play for Interactions</td>
<td>T-F-B Cognitive Triangle Diagram (use copy from Session 3)</td>
<td>1</td>
</tr>
<tr>
<td>D – Role Play for Interactions</td>
<td>Flipchart (with markers)</td>
<td>1</td>
</tr>
<tr>
<td>E – Small Group Safe Sex Demonstration</td>
<td>Condoms</td>
<td>1 per participant</td>
</tr>
<tr>
<td>E – Small Group Safe Sex Demonstration</td>
<td>Plain white piece of paper and pens or markers</td>
<td>1 set per small group</td>
</tr>
<tr>
<td>H – Homework</td>
<td>Homework: T-F-B Unhealthy Interactions Worksheet (print copies)</td>
<td>1 set participant</td>
</tr>
</tbody>
</table>

### Session 6 Supplies

<table>
<thead>
<tr>
<th>Supplies</th>
<th>Description</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>B – Review Homework, C/G – Small Groups, H – T-F-B</td>
<td>Flipchart (with markers)</td>
<td>1 set per small group</td>
</tr>
<tr>
<td>C – Small Groups for lessons learned</td>
<td>Plain white piece of paper and pens or markers</td>
<td>1 set per small group</td>
</tr>
<tr>
<td>F – Body Drawings</td>
<td>Box of assorted colored markers (for participants to share)</td>
<td>Multiple boxes at site discretion</td>
</tr>
<tr>
<td>G – Small Groups for Reflecting on Sessions</td>
<td>T-F-B Cognitive Triangle Diagram (use copy from Session 3)</td>
<td>1</td>
</tr>
<tr>
<td>Celebration</td>
<td>Celebration Supplies</td>
<td>Site discretion</td>
</tr>
<tr>
<td>Celebration</td>
<td>Certificate of Completion (site to customize with names and print)</td>
<td>1 per participant</td>
</tr>
<tr>
<td>Booster Session Supplies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>-------------------------------------------------------------</td>
<td>---</td>
</tr>
<tr>
<td><strong>A – Welcome</strong></td>
<td>Rules (use rules written on flipchart paper from Session 1)</td>
<td>1</td>
</tr>
<tr>
<td><strong>B – Deep Breathing,</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E – Capacitor</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td><strong>C – TFB, D – Gender-Violence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flipchart (with markers)</td>
<td>1</td>
</tr>
<tr>
<td><strong>C – TFB</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Claude's vignette (print copies)</td>
<td>1 per youth</td>
</tr>
<tr>
<td><strong>C – TFB</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Claudette's vignette (print copies)</td>
<td>1 per youth</td>
</tr>
<tr>
<td><strong>D – Gender-Violence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Definition of Sex and Gender Handout (print copy)</td>
<td>1</td>
</tr>
<tr>
<td><strong>D – Gender-Violence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>T-F-B that Promotes Gender Equality Worksheet (print copies)</td>
<td>1 per youth</td>
</tr>
<tr>
<td><strong>D – Gender-Violence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>T-F-B Cognitive Triangle Diagram (use copy from Session 3)</td>
<td>1</td>
</tr>
</tbody>
</table>
### Caregiver Group Sessions
(Adult study staff should bring their Caregiver Intervention Manual to all caregiver group sessions.)

<table>
<thead>
<tr>
<th>Session Part</th>
<th>Item</th>
<th>Quantity</th>
<th>Check box if on site for session</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Session A Supplies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B – Group Rules,</td>
<td>Flip chart (with markers)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>C – HIV Knowledge,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D – Stigma,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E – Adherence Obstacles</td>
<td>Plain white piece of paper (or notepad) and pens or markers</td>
<td>3 set per small group</td>
<td></td>
</tr>
<tr>
<td>E – Adherence Obstacles</td>
<td>Adherence Meaning Handout (print copy)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>G – Homework</td>
<td>Homework: Adherence Support Basket Worksheet (print copies)</td>
<td>1 per participant</td>
<td></td>
</tr>
<tr>
<td><strong>Session B Supplies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D – Adherence Importance</td>
<td>Adherence Meaning Handout</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>D – Adherence Importance</td>
<td>Flip chart (with markers)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>E – Role Plays</td>
<td>Adherence Plan Handout/Poster (print copy)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Celebration</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Celebration</td>
<td>Celebration Supplies</td>
<td>Site discretion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Certificate of Completion (site to customize with names and print)</td>
<td>1 per participant</td>
<td></td>
</tr>
<tr>
<td><strong>Booster Session Supplies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C – HIV Knowledge,</td>
<td>Flip chart (with markers)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>E – Adherence Obstacles,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F – Stigma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D – Adherence Importance</td>
<td>Adherence Meaning Handout/Poster (print copy)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>G – Adherence Plan</td>
<td>Adherence Plan Handout/Poster (print copy)</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
Appendix II: Evaluating participants for imminent risk of suicide and abuse

A. Example questions for evaluating youth participants for imminent risk of suicide

The following questions may be used by the on-site study clinician when evaluating a youth participant who discloses suicidal ideation or attempt: plan to hurt or kill self, attempt to hurt or kill self, or cutting.

On-site study clinician should remind the youth of the following: “At the beginning of this study you signed a consent (or assent) form indicating that your responses to questionnaires and study participation will be kept confidential except in cases where you may be at risk of harm. The questionnaire you took today (or during the group session/follow-up visit, you/your caregiver/your peer) suggested you have had thoughts of ending your life or hurting yourself. I am worried about your safety, and I would like to ask you some questions about it. If you remember, I am required to report any situations in which you may be in danger. I know that this might be difficult for you. I would appreciate your honesty in helping me understand what you are feeling or thinking or what has happened to you.”

1. I know this might be uncomfortable for you, but can you tell me a little more about these thoughts?

2. Are you currently having thoughts of hurting yourself? (If yes → Imminent risk)
   On-site study clinician: currently means having thoughts right now

3. Do you have a plan for hurting yourself? (If yes → Imminent risk)

   IF YES TO #3, GO TO QUESTION 4. IF NO TO #3, GO TO QUESTION 5.

4. Can you tell me more about what you were thinking of doing to hurt yourself?
   a. Do you have these things (insert: gun, knife, pills, etc.) you would need to do it? (i.e. If participant says they would use a gun, does she have access to a gun, etc.) (If yes → Imminent risk)

5. Have you tried to hurt yourself before?
   a. If yes, would you feel comfortable sharing what happened with me?
      On-site study clinician: note the incident if youth is comfortable sharing with you

6. Does anyone know that you’ve been having these thoughts? If so, who?

7. Do you currently have a therapist? If yes, does your therapist know?

8. Have you ever been hospitalized for trying to hurt yourself?

9. How upset are you now that we’ve talked about this?

10. Do you feel like you can stay safe tonight? (If no → Imminent risk)

Following the evaluation, the on-site study clinician will notify the site IoR or designee of information collected, per Step 2 in Section 6.1 of this MOP, and complete the remaining steps. As described in Section 6.1.3 of this MOP, if a participant is determined to be at imminent risk, the on-site study clinician should follow the standard of care at the site.
B. Example questions for evaluating youth participants for imminent risk of abuse

The following questions may be used by the on-site study clinician when evaluating a youth participant who discloses abuse: sexual or physical.

On-site clinician should remind the youth of the following: “At the beginning of this study you signed a consent (or assent) form indicating that your responses to questionnaires and study participation will be kept confidential except in cases where you may be at harm. The questionnaire you took today (or during the group session/follow-up visit, you/your caregiver/your peer) suggested we should discuss some of your experiences further to better understand. I am worried about your safety, and I would like to ask you some questions about it. If you remember, I am required to report any situations in which you may be in danger.

I know that this might be difficult for you. I would appreciate your honesty in helping me understand what you are feeling or thinking or what has happened to you. I’m not sure which items were true for you, but these might be things like: (a) Someone tried to make you do sexual things, (b) Someone tried to touch you, (c) You felt forced to have sex, (d) An older person had sex with you, or (e) Someone tried to physically hurt you such as hit you.”

1. I know this might be uncomfortable for you, but can you tell me more about what happened?
2. When did this happen?
3. Where did this happen?
4. How old were you when it happened?
5. What is/was this person’s relationship to you?
   (On-site study clinician: If the perpetrator is in a position of authority or guardianship, immediate action should be taken per local standard of care.)
6. How old is (was) he/she?)
7. Do you live with this person or do you see them on a regular basis? (If yes → Imminent risk)
8. When was the last time you saw this person?
9. How much time does this person spend around you now?
10. Is it still going on right now? (If yes → Imminent risk)
11. Does anyone know about this? If so, who?
12. Do you currently have a therapist? If yes, does your therapist know?
13. Are Department of Child and Family Services (DCFS) or the police currently involved?
14. Is there another incident that you experienced? If no, skip to question 15. If yes, repeat questions above.
May ask these questions for ALL SITUATIONS even if no abuse occurred

15. Do you feel safe? (If no → Imminent risk)
   (On-site study clinician: If no, PROBE further: “Why don’t you feel safe?” “Do you think you can stay safe tonight?” etc.)

16. Do you think this person might hurt you again now or in the future? (If yes → Imminent risk)

17. How upset are you now that we have talked about this?

18. [If very upset] Do you think you might hurt yourself? (If yes → Imminent risk)
   a. [If yes] Do you have a plan?
   b. [If yes] Have you tried to hurt yourself in the past?

Following the evaluation, the on-site study clinician will notify the site IoR or designee of information collected per Step 2 in Section 6.1 of this MOP, and complete the remaining steps.
Appendix III: Standard of Care Resources

A. The African Network for the Care of Children Affected by AIDS (ANECCA)

The African Network for the Care of Children Affected by AIDS (ANECCA) with support from AIDSFree developed and published the *Handbook on Counselling and Psychosocial Care for Children and Adolescents Living with and Affected by HIV in Africa* and a *Pocket Guide*, a condensed version of handbook designed for on-the-job use. Sites are encouraged to use this handbook and pocket guide for standard of care information on HIV clinical care; growth and development; mental health; child protection; counseling and communication; disclosure; loss, grief, and bereavement; adherence; sexual and reproductive health; transition of care; support systems; and monitoring and evaluation of psychosocial services.

A PDF of the Handbook is available at:


A PDF of the Pocket Guide is available at: