**DAIDS REQUIRED SITE SOPS FOR THE REPRIEVE STUDY**

The following Standard Operating Procedures (SOPs) are the minimum required prior to the initiation of the REPRIEVE study. Please note that it is acceptable to combine multiple procedures in a single document. Sites are expected to be compliant with GCP, HSP, NIAID policies and 45 CFR 46.

This document contains sample SOPs that are utilized by other clinical research site, they are provided as samples for your site to adapt and use to submit to DAIDS as part of the Site Approval process. If you are going to use one of these sample templates please be sure that the language is accurate according to the policies at your clinical research site and adapt the sample language as necessary.

REGULATORY

* Essential Documents: see *sample SOP for Maintaining Essential Documents*, **pg. 2**
* Source Documents: *see sample SOP for Source Documents*, **pgs. 3-4**

SAFETY ASSESSMENT AND REPORTING

* Reporting Adverse Events: *see sample SOP for Documenting and Reporting Adverse Events AND SOP for Internal Adverse Event Reporting,* ***pgs. 5-8.***

PROTOCOL IMPLEMENTATION

* Unblinding for Safety: see *SOP for Unblinding Procedure.* **pg. 9**

PHARMACY

* Pharmacy Establishment Plan (PEP): *see sample of completed PEP* **(listed as a separate document on this webpage)**

(Refer to the Pharmacy section of the Manual of Operations for any additional requirements)

DATA MANAGEMENT

* Clinical Site Data Collection: *see sample SOP Data Collection,* **pgs. 10-11**
* Management: *see sample SOP Management of Records,* **pg. 12**
* Security: *see sample SOP Computer Room, Hardware and Data Securit,* **pg. 13**
* Reporting: *see sample SOP for Documenting and Reporting Adverse Events AND SOP for Internal Adverse Event Reporting,* ***pgs. 5-8.***

ADMINISTRATIVE

Sites should review the DAIDS policies identified for REPRIEVE sites (as noted in the addendum of REPRIEVE site policies) and attest to the presence of adequate policies and procedures for the following:

* Training staff: *see sample SOP Staff Education and Training,* **pg. 14.**
* Presence of a Quality Management Plan that meets the requirements outlined in the DAIDS Policy titled: Requirements for Clinical Quality Management Plans. *see sample Quality Management Plan* **pg. 15-16.**

SOP Name: Maintaining Essential Documents

Standard Operating Procedure

[insert site name]

Version [insert version and date]

**Responsible Person(s):** Principal Investigator (PI)

Regulatory Operations Manager (ROM)

Clinical Trials Manager (CTM) Executive Staff Assistant (ESA)

**Policy:** Essential documents are the documents that permit evaluation of both the conduct of a clinical trial and the quality of the data produced. The [insert site name] CTU/CRS MOP contains standard operating procedures relating to the regulatory activities of the CTU. They are in compliance with the Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS funded/sponsored clinical trials. (DWD-POL-RA-03.00)

**Procedure:**

1. The CTU/CRS MOP contains a section for Regulatory Standard Operating Procedures.

These SOPs pertain to Essential Documents.

1. The PI or designee will refer to DAIDS DWD-POL-RA-03.00 [https://www.niaid.nih.gov/LabsAndResources/resources/DAIDSClinRsrch/Documents/essentialdocpolicy.pdf](https://www.niaid.nih.gov/LabsAndResources/resources/DAIDSClinRsrch/Documents/essentialdocpolicy.pdf%20) to ensure that the MOP contains all necessary SOPs for regulatory operations and documents.

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PRINCIPAL INVESTIGATOR DATE

SOP Number (insert SOP number if applicable)

SOP Name Use of Source Document Templates (templates) and Study Specific Tools (tools)

Effective Date (insert date)

1.0 **SCOPE**

1.1 Entire Research Team

2.0 **PURPOSE**

2.1 In order to collect quality study documentation, templates and tools are available on the Share Drive to all research staff.

3.0 **DEFINITIONS**

3.1 PRN – Primary Research Nurse

3.2 CTM – Clinical Trials Manager

3.3 DM – Data and QA Manager

4.0 **PROCEDURES**

4.1 All research team members have access to electronic versions of the templates and study specific tools.

4.2 The templates are originated and updated centrally by the DM or designee.

4.3 The following templates are available: *(insert list of applicable templates, the following are examples)*

• Informed Consent/Screening Log

• Informed Consent Progress Note

• Inclusion and Exclusion

• Required Demographics

• Screening History and Physical

• Screening Lab Evaluations

• Day of Entry History and Physical

• Day of Entry Lab Evaluations

• On Study Interval History and Physical

• Lab Evaluation on Study

• Record of Other Contact

• Dear Doctor

• CRF as Source Documentation

• Vital signs

4.4 The PRN or designee uses templates to create tools at the time of protocol submission to the IRB

4.5 The PRN or designee refers to the protocol to customize the tools.

4.6 The PRN identifies a person (i.e. back-up nurse, CTM or DM for independent review of the tool. She provides the first draft of tools to the independent reviewer.

4.7 The reviewer will check the tools against the protocol. Independent reviewer assesses accuracy of existing information and makes sure that there are not items in the protocol that are not captured on the drafts. The reviewer will return the reviewed tools to the RN with any suggested changes.

4.8 The PRN will make any changes, if necessary, and send the set of tools out to the research team one week before the local start-up meeting for a final review.

4.9 Final draft of the tools will occur prior to the local Study Start-up Meeting.

4.10 Source document tools are reviewed during a portion of the start-up meeting and given to the DM or designee to load into the research database.

4.11 Enrollment into the study may only commence after the study specific source document tools are loaded onto the database, unless otherwise approved by the CTM or designee.

**Updates, revisions, new versions or amendments:**

4.12 RN or designee updates existing tools at the time of amendment or new version submission to the IRB. The original date is left on with a new date and the word ‘revised’ added.

4.13 RN identifies a person (i.e. back-up nurse, CTM or DM) for independent review of the tools. She provides the updated version of the tools to the independent reviewer.

4.14 The reviewer will check the tools against the protocol. The independent reviewer assesses accuracy of existing information and makes sure that there are not items in the protocol that are not captured on the drafts. The reviewer will return the reviewed tools to the RN with any suggested changes.

4.15 The RN will update the tools and email them to the DM or designee.

4.16 The DM or designee will load the updated tools in the Research Database.

**5.0 APPROVAL**

PRINCIPAL INVESTIGATOR DATE

*SOP Number [insert SOP number]*

*SOP Name* ***Documentation of Serious Adverse Experiences (SAE) and Expedited Adverse Experiences (EAE)***

*Effective Date [insert version and date]*

## SCOPE

* 1. Principal Investigator (PI)
  2. Sub-Investigator (Sub-I)
  3. Clinical Trials Manager (CTM)
  4. Research Nurse (RN)
  5. Data and Quality Assurance Manager (DM)
  6. Regulatory Operations Manager (ROM)

## PURPOSE

* 1. Complete documentation of all Serious Adverse Experiences (SAE) or Expedited Adverse Experiences (EAE) will take priority above all other case report forms and other documentation.

## REFERENCES

3.1 For important and comprehensible guidance on internal AE reporting please see SOP on Internal Adverse Event Reporting to Local Institutional Review Board.

## PROCEDURES

* 1. Adverse experiences will be graded according to protocol immediately upon site awareness.
  2. The RN refers to protocol and local IRB guidelines to determine where to record the AE and whether or not it is reportable to the sponsor and the IRB.
  3. If the SAE or EAE is reportable to the sponsor (DAIDS) or IRB or both, the RN completes the required SAE/EAE form(s). This includes the sponsor’s form (see URL listed in 4.4) and the local IRB form.
  4. Please refer to DAIDS EAE Manual, version 2.0 dated January 2010 <http://rsc.tech-res.com/document/safetyandpharmacovigilance/manual_for_expedited_reporting_aes_to_daids_v2.pdf>.
  5. When completing the SAE/EAE form(s) the RN must fill in all fields on the form with any available information related to the SAE-EAE. If there is only partial information available at the time of site awareness, the RN will document that in the report.
  6. The RN will obtain consultation, any further written information and inform all PIs/Sub-Is of need for signature. To ensure meeting the standard of submission to the sponsor and the EAE office within the required time frame, the RN must refer to the DAIDS EAE manual and/or protocol immediately upon review of the adverse event.
  7. Please note the following:

**Reporting Days:** “Reporting days” are those that count toward the 72 hour timeline provided for reporting of EAEs to DAIDS. The criteria used to determine reporting days are as follows:

* A reporting day starts at 12:00 AM (midnight) and ends at 11:59 PM local time.
* Any holiday (U.S. or in-country/local) that occurs on a Monday through Friday counts as a reporting day.
  1. In the event that the report is faxed, the person who faxes the report is to wait for the fax confirmation receipt to print.
  2. Upon receipt of the fax transmission receipt, the SAE/EAE and fax transmission receipt will be photo copied and stapled together.
  3. The original will be placed in the research source document binder and the copy will go to the ROM for IRB submission if it meets the IRB submission criteria.

## APPROVAL

PRINCIPAL INVESTIGATOR DATE

*SOP Number [insert SOP number if applicable]*

*SOP Name* ***Internal Adverse Event Reporting to Local Institutional Review Board (IRB)***

*Effective Date [insert version and date]*

## SCOPE

* 1. Principal Investigator (PI)
  2. Sub-Investigator (Sub-I)
  3. Regulatory Operations Manager (ROM)
  4. Research Nurse (RN)
  5. Data and Quality Assurance Manager (DM)

## PURPOSE

* 1. Internal Adverse Events will be reported to the local IRB according to the policies and procedures set forth by the [insert IRB’s name here]. Current adverse event reporting policy and appropriate forms can be found on-line at [insert URL for IRB’s AE reporting policy here].

## BACKGROUND

* 1. Adverse Event Reports (AERs) are summaries about side effects experienced by any subject on a particular study, and are submitted to the sponsor as they occur. These AERs must also be submitted to the local IRB on the IRB AER reporting form if it meets the following criteria: EXAMPLE LANGUAGE TO USE, PLEASE USE YOUR IRB’s POLICY HERE*: The standard reporting to the IRB includes an adverse event or injury that was serious and unexpected, and definitely, probably, or possibly related to the study. However, if there is any doubt about whether or not to report an adverse event, the CTU staff shall always refer to the IRB web site listed above.*

## PROCEDURES

* 1. Upon awareness of an adverse event, the *(example: RN)* must consult the PI or Sub-I to determine and substantiate seriousness and relatedness of an adverse event for all study subjects.
  2. The *(example: RN)* completes an IRB AER form at the time he/she becomes aware of the event.
  3. The *(example: RN)* forwards the IRB AER to the study PI for review and signature.
  4. The *(example: RN)* copies the IRB AER for study case report form and forwards original to the ROM with any necessary accompanying information.
  5. The ROM copies the IRB AER for regulatory study file then scans the copy and submits through *(insert mechanism for submission to IRB)* for submission to the IRB. *EXAMPLE LANGUAGE PLEASE USE YOUR IRB’S POLICY HERE:* Note*: the IRB must be notified of event within 10 working days of the site becoming aware of the event. (In order to expedite the process, the completed IRB AER form may be faxed. However, the document is still required to be sent to the IRB). If the AER is faxed, the RN or designee must wait until the receipt of fax notifications prints.*
  6. A copy of the fax notification shall be stapled and filed with the AER form and placed in the SAE section of the Research Source Document Binder.
  7. The *(example: RN)* is responsible for clarifying any information for the IRB as requested. *(insert any specific language on how clarification will be performed).*
  8. The reporting *(example: RN)* will copy any email correspondence with the IRB regarding AERs to the PI, CTM, DM and ROM.

## APPROVAL

PRINCIPAL INVESTIGATOR DATE

*SOP Number [insert SOP number if applicable]*

*SOP Name* ***Unblinding Procedure***

*Effective Date [insert version and date]*

**1.0 SCOPE**

* 1. Principal Investigator (PI)
  2. Pharmacist of Record
  3. Research Nurse (RN)

## PURPOSE

* 1. Some studies are designed so that knowledge of individual treatment assignments of subjects enrolled in studies is withheld from certain individuals. This is to limit the potential for introducing bias into the study. Subjects may be unblinded during a trial for an acute reaction (for safety issues) or once a study is completed and the sponsor unblinds the study. Ideally and conventionally, unblinding takes place when all data forms have been keyed into the database for all subjects and the team has declared the study data set to be complete.

## PROCEDURES

* 1. For any study, ACTG or industry, the RN shall contact the PI or Sub-PI about any adverse events that may lead to the need for unblinding.
  2. The PI and RN will review the protocol and the subject’s clinical and/or laboratory information. The PI will determine if unblinding the patient is deemed necessary.
  3. The local PI and research team will seek guidance and permission from the sponsor/protocol team prior to unblinding the study subject.
  4. For any ACTG study, refer to ACTG-SOP no.123 regarding unblinding patients, along with the protocol specific unblinding information to determine what the proper course of action will be.
  5. All information relating to this event shall be documented thoroughly in the source document and recorded onto any additional forms as needed.
  6. If permission is received to unblind the subject, the documentation stating this is kept in the subject’s source document binder.
  7. Unblinding information should be shared with as few individuals as possible and can only be shared by the designated individual (based on the ACTG SOP or Industry Study) on a ‘need to know’ basis.
  8. At the end of a study, participants will be unblinded per study specific procedures or ACTG policy.
  9. The RN/Pharmacist of Record will contact patient and primary care physician to inform them of unblinding information. Note: EMR and research database should reflect actual drug/placebo used in study once subject is unblinded.

## APPROVAL

PRINCIPAL INVESTIGATOR DATE

*SOP Name* ***Use of Source Document Templates (templates) and Study Specific Tools (tools)***

*Effective Date [insert version and date]*

## SCOPE

* 1. Entire Research Team

## PURPOSE

* 1. In order to collect quality study documentation, templates are available OpenClinica (electronic data capture) and tools are available on the ACTG Protocol Specific Web Page to all research staff.

1. **DEFINITIONS**
   1. PRN – Primary Research Nurse
   2. CTM – Clinical Trials Manager
   3. DM – Data and QA Manager

## PROCEDURES

* 1. All research team members have access to electronic versions of the templates in OpenClinica and study specific tools.
  2. The templates are originated and updated centrally by the DM or designee.
  3. For the necessary templates the PRN or designee uses templates to create tools at the time of protocol submission to the IRB.
  4. The PRN or designee refers to the protocol to customize the tools.
  5. The PRN identifies a person (i.e. back-up nurse, CTM or DM for independent review of the tool. She provides the first draft of tools to the independent reviewer.
  6. The reviewer will check the tools against the protocol. Independent reviewer assesses accuracy of existing information and makes sure that there are not items in the protocol that are not captured on the drafts. The reviewer will return the reviewed tools to the RN with any suggested changes.
  7. The PRN will make any changes, if necessary, and send the set of tools out to the research team one week before the local start-up meeting for a final review.
  8. Final draft of the tools will occur prior to the local Study Start-up Meeting.
  9. Source document tools are reviewed during a portion of the start-up meeting and given to the DM or designee to load into the research database.
  10. Enrollment into the study may only commence after the study specific source document tools are loaded onto the database, unless otherwise approved by the CTM or designee.

**Updates, revisions, new versions or amendments:**

4.11 RN or designee updates existing tools at the time of amendment or new version submission to the IRB. The original date is left on with a new date and the word ‘revised’ added.

4.12 RN identifies a person (i.e. back-up nurse, CTM or DM) for independent review of the tools. She provides the updated version of the tools to the independent reviewer.

4.13 The reviewer will check the tools against the protocol. The independent reviewer assesses accuracy of existing information and makes sure that there are not items in the protocol that are not captured on the drafts. The reviewer will return the reviewed tools to the RN with any suggested changes.

4.14 The RN will update the tools and email them to the DM or designee.

4.15 The DM or designee will load the updated tools in the Research Database.

## APPROVAL

PRINCIPAL INVESTIGATOR DATE

*SOP Number*

*SOP Name* ***Management of Records***

*Effective Date [insert version name and date]*

## SCOPE

* 1. Clinical Trials Manager (CTM)
  2. Regulatory Operations Manager (ROM)
  3. Data and QA Personnel

## PURPOSE

* 1. The Clinical Trials Unit/Clinical Research Site (CTU/CRS) has a systematic way to store documents from the beginning of a study through the end of the study. Once the study is closed, these documents are archived as addressed in SOP QA&QC. The [insert institution name] IRB policy is that clinical trial documents must be maintained at the study site for two years following market approval of the investigational drug or 2 years after the sponsor has formally discontinued development of the drug or up to 15 years after the end of the study, as dictated in the Clinical Study Agreement [insert IRB policy here, this language is provided as an example]. Records can be archived and stored at an off-site facility but must be accessible if needed. An accurate archival list is essential. The Sponsor must be notified prior to any action to destroy clinical trial documents.

## PROCEDURES

* 1. Active Case Report Forms (CRFs) are stored [if paper CRFs are used indicate where they are stored, alternatively OpenClinica will house electronic CRFs]. This CRF area is locked when the Research Clinic is closed or left unattended. The source documents (research medical records) are stored separately.
  2. CRFs for studies that have been recently closed my still be needed for queries and data resolution. They are stored in a room inside of the research nurses’ office or in the Resident’s Quarters. Once it is determined that access to these CRFs is no longer needed, they are removed from the binders, bagged and boxed and then stored in banker boxes which are kept in the Resident’s Quarters [provided as an example].
  3. Current volumes of research medical records are located in the Research Medical Record Room inside of the research nurses’ office and have a different lock than the research nursing office, therefore are behind double locks. Previous volumes are stored in the storage room located within the nurses’ office.
  4. Essential documents for sponsor supported studies are kept in binders that are located in the ROM’s office. ACTG essential documents are kept in a filing cabinet in the ROM’s office. Essential documents that are for pending studies are kept in the file cabinet in the ROM’s office for tracking.
  5. If it is determined that we do not need these records on-site, but due to regulations we need to maintain them, we will ship to the outside storage facility, [Example: Iron Mountain].

## REFERENCES

* 1. SOP Research Data Storage and Archiving
  2. SOP Storage of Regulatory Documents

## APPROVAL

PRINCIPAL INVESTIGATOR DATE

Quality Assurance and Quality Control Standard Operating Procedure

[insert site name]

Version [insert version]

**Subject:** Computer Room, Hardware and Data Security (including system user account maintenance)

**Responsible Person:** Principal Investigator

Data and QA Manager

Clinical Trials Manager

**Policy:** In order to ensure data security and authenticity, the [insert institution name and CRS] has standard operating procedures and measures in place regarding the computer room (data center), hardware and data security.

**Procedure:**

1. The Data Center of the [insert site name] is located [insert institution and location within institution]. It has a locked door and must be accessed with a key.
2. The main data entry computer and the unit-specific file server are in [insert location].
3. Confidential user names, passwords and other sensitive data that are kept in

the Data Center are kept locked [insert location]. This information is centrally located and accessible only to Data Staff and the Research Leadership Team so that information can be accessed in a timely manner in the event of an emergency.

1. Any individuals who are employees or volunteers of the [insert name of CRS] must sign the appropriate [insert institution name] form Notice of Data Security and Confidentiality. The signed copies of these forms are kept in the [insert name of CRS] administrative files.
2. All hardware and software applications are managed through [insert institution name]. This ensures minimal risk to personal computers and maximal protection of operating systems.

PRINCIPAL INVESTIGATOR DATE

*SOP Number Staff Education and Training*

*SOP Name* ***Continuing Staff Education, Required Training***

*Effective Date [insert version and date]*

## SCOPE

* 1. Clinical Trials Manager (CTM)
  2. Regulatory Operations Manager (ROM)
  3. Executive Staff Assistant (ESA)

## PURPOSE

* 1. The [insert name of CTS] recognized and is in compliance with the requirements set forth by the National Institute of Health and the [insert institution name]. The purpose of this SOP is to address required training for staff members. The required training includes collaborative Institutional Training Initiative (CITI) training modules for the ACTG, DAIDS and [insert other additional institutions that require training]. The staff members are also required to have Bloodborne Pathogen training, Basic Life Support (BLS) and other applicable training. Evidence of completion of these courses must be kept in the [example location: Administrative office on the third floor of the unit].

## DEFINITIONS

* 1. DAIDS – Division of AIDS

## PROCEDURES

* 1. The CTM and/or designee will maintain a record of all staff members and the dates they completed the required training. A copy of the training certificates will be kept in the Regulatory Department of the unit.
  2. CITI training is required every three years according to the Division of AIDS and the University Institutional Review Board (IRB). Employees must access these modules via the internet at the following address: [www.citiprogram.org](http://www.citiprogram.org). A certificate of completion must be on file for any individual who is directly related to the conduct of clinical trials. This includes: Investigators, Study Coordinators, Clinical and Virology Research Assistants, Screening Coordinators, Regulatory Operations Manager, Data and Quality Assurance Manager, Research Pharmacist and Research Coordinators. Other staff members are not required to complete the training, but are strongly encouraged to do so.
  3. Bloodborne Pathogens training is required annually for any staff member who comes in contact with patients or bodily fluids of the patients. This training is available on-line and in the classroom setting. A certificate of completion must be on file in the Regulatory Department and a copy must be provided to the Infectious Diseases Division file.
  4. BLS training is required every two years for clinicians.
  5. Certificates of completion shall serve as documentation of required training and will be made available to designated DAIDS staff and other monitors upon request.
  6. All other required training will be completed and tracked continuously throughout the year for all staff members.

## APPROVAL

PRINCIPAL INVESTIGATOR DATE

Sample Clinical Quality Management Plan (CQMP)

Approval Date:

Effective Date:

No.: DWD-POL-CL-009.03A1

**Sample Clinical Quality Management Plan (CQMP)**

(SAMPLE ONLY. The template below is provided for your convenience as an example of how this information may be provided. Frequency/percentage of reviews and types of tools/reports used should be selected to meet the specific needs of the clinical research site.)

**Site Number\_\_\_\_\_\_\_**

**Site Name\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Section I: Responsibility**

John Smith, MD, Principal Investigator, is responsible for the Clinical Quality Management Plan at \_\_\_\_\_\_\_\_\_\_.

Mary Brown, RN, Study Coordinator, has been designated by Dr. Smith to be responsible for the implementation of the Clinical Quality Management Plan.

**Section II: Key Quality Control (QC) Staff**

Bill Thomas, Data Manager, is responsible for the day-to-day QC activities, with support from other data personnel.

**Section III: Key Quality Assurance (QA) Staff**

Sara Johnson, RN, is responsible for QA activities at the site.

**Section IV: QM Activities and Tools**

**Quality Control (QC):**

The following activities and tools will be utilized in the QC process:

1. Error correction reports from the data management center will be reviewed by the Data Manager, who will immediately bring any errors identified to the attention of the appropriate site staff for correction. Errors will be corrected within 2 business days of identification.

2. Data entry and transmission reports will be reviewed by the Data Manager to assure that transmitted data was successfully entered into the database. Errors will be brought to the attention of the responsible person and corrected within one business day of identification.

3. Error tracking logs will be completed by the Data Manager. This log identifies and tracks categories of Case Report Form (CRF) errors. This information will be aggregated and reported to the site staff as a whole at weekly meetings.

4. Data staff will review 100% of CRFs prior to data entry for completeness, to ensure proper dating and signing, etc.

**Quality Assurance (QA):**

The following activities and tools will be utilized in the QA process:

1. The Chart Review Tool is utilized for participant specific chart review. It is inclusive of all key indicators for QA review as listed in Section V below.

2. The Regulatory Review Tool is used for quarterly review of regulatory documents, including Safety Report submission, Institutional Review Board (IRB)/Ethics Committee (EC) approvals and communications, Form FDA 1572, etc.

3. Monthly Activity Reports are protocol-specific summaries of QM activities that are shared with the site staff at monthly meetings.

4. Quarterly Site Monitoring Reports from the DAIDS Contract Monitor are utilized as a QA tool, checking for any adverse trends or problems. These reports will be shared quarterly during staff meetings.

**Section V: Key Indicators**

These indicators are part of the chart review:

1. Informed consent forms and processes

2. Eligibility criteria

3. Missed visits, tests, and procedures

4. Concomitant/prohibited medications

5. AE/SAE/EAE identification and reporting

6. Study Product administration

7. Protocol endpoint identification