DAIDS Collaborator's Guide

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DAIDS COLLABORATORS

Who Are They?

Networks – Each Division of AIDS (DAIDS) network is comprised of A) a Leadership and Operations Center (LOC), B) a Statistical and Data Analysis Center/Data Management Center (SDAC/DMC), and C) a Laboratory Center (LC). Multiple clinical trials units (CTUs) and clinical research sites (CRSs) affiliated with the Network to support a common research agenda.

1. **Operations Center (Ops)** – As part of the LOC, develops and implements protocols, conducts site training, and updates protocol milestones within the database of record. (See Study Statuses and Milestones Definitions for a list of applicable milestones.) Also, provides scientific leadership and fiscal/organizational management.
2. **Statistical and Data Analysis Center/ Data Management Centers (SDAC/DMC)** – Provides statistical support throughout the protocol lifecycle, generates protocol-specific case report forms, conducts protocol- and site-specific trainings, and prepares standard reports as needed (e.g., annual FDA progress reports).
3. **Laboratory Center** – The DAIDS Clinical Laboratory Team (DCLOT), made up of DAIDS laboratory staff from the therapeutic and prevention Programs at DAIDS, is responsible for lab establishment, oversight and implementation of laboratory policies, evaluation of lab performance and follow-up on lab-related issues. Working closely with their respective DCLOT POC, each Network has a laboratory management and oversight team that also supports site laboratories, focusing on protocol-related laboratory issues. The Network has the final word on a laboratory's readiness to participate in a study.

There are 5 DAIDS Networks:

1. **AIDS Clinical Trials Group (ACTG)** – Conducts translational and therapeutic clinical research on HIV/AIDS at U.S. and international sites.
   a) Operations Center run by Social and Scientific Systems(SSS)
   b) SDAC run by the Harvard School of Public Health, Statistical and Data Analysis Center (HSPH-SDAC)
   c) DMC run by Frontier Science and Technology Research Foundation (FSTRF)
   d) ACTG Laboratory Information

2. **International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT)** – Aims to significantly decrease the mortality and morbidity associated with HIV disease in children, adolescents, and pregnant women.
   a) Operations Center run by Social and Scientific Systems (SSS)
   b) SDAC run by the Harvard School of Public Health, Statistical and Data Analysis Center (HSPH-SDAC)
   c) DMC run by Frontier Science and Technology Research Foundation (FSTRF)
   d) IMPAACT Laboratory Information

3. **HIV Prevention Trials Network (HPTN)** - Develops and tests the safety and efficacy of primarily non-vaccine interventions designed to prevent the acquisition and transmission of HIV worldwide.
   a) Operations Center run by Family Health International 360 (FHI360)
   b) SDAC/DMC run by the Statistical Center for HIV/AIDS Research and Prevention (SCHARP)
   c) HPTN Laboratory Information

4. **HIV Vaccine Trials Network (HVTN)** - Facilitates the process of testing preventive vaccines against HIV/AIDS, and conducts all phases of clinical trials, from evaluating experimental vaccines for safety and the ability to stimulate immune responses, to testing vaccine efficacy via an international collaboration of scientists searching for an effective and safe HIV vaccine.
   a) Operations Center run by the Fred Hutchinson Cancer Research Center (FHCRC)
   b) SDAC run by the Statistical Center for HIV/AIDS Research and Prevention (SCHARP)
   c) HVTN Laboratory Information

5. **Microbicide Trials Network (MTN) –** Aims to reduce the sexual transmission of HIV through the development and evaluation of microbicide products via a strong network of expert scientists and investigators from domestic and international sites.
   a) Operations Center run by Family Health International360 (FHI360) and University of Pittsburgh
   b) SDAC run by the Statistical Center for HIV/AIDS Research and Prevention (SCHARP)
   c) MTN Laboratory Information

DAIDS Regulatory Support Center (DAIDS RSC) - Provides comprehensive clinical regulatory support services for all NIAID/DAIDS-supported network and non-network clinical trials. (run by Technical Resources International, Inc.)

Clinical Research Products Management Center (CRPMC) - Provides comprehensive pharmacy services for DAIDS studies through pharmacy audits and study product distribution activities. (run by Fisher BioServices)

Clinical Research Support Services (CRSS) - Provides flexible and comprehensive site-specific, protocol-specific, and logistical services to the DAIDS clinical research community. (run by WESTAT and FHI 360)

Clinical Site Study Monitoring - Provides monitoring services from site initiation through site close-out per DAIDS-approved procedures. (run by Pharmaceutical Product Development)

DAIDS Enterprise System (DAIDS-ES) Support Team - Ensures the proper functioning of the DAIDS clinical trial management system (the DAIDS-ES) to facilitate clinical research implementation. (run by Digital Infuzion)

HIV/AIDS Network Coordination (HANC) – Works with DAIDS Networks to provide leadership and logistical support for cross-network coordination efforts. HANC's mission is to support the science and operations of the DAIDS networks by increasing efficiency and resource-sharing through coordination of critical activities across networks and with other research and advocacy partners.

How Are DAIDS Collaborators Involved In the Protocol Development Lifecycle?

Clinical Trial Steps for DAIDS Protocols

A. Concept Development - During Concept Development, protocol ideas are generated and network approvals are obtained. (DAIDS-ES study status of "Proposed")

1. **Network Action:** The protocol team develops a concept sheet/proposal and presents the study for necessary approvals within the network.

2. **HANC Action:** Works with network personnel to ensure coordination with other networks, if applicable.

B. Regulatory Clearance - During Regulatory Clearance, protocols are reviewed to ensure compliance with local, federal, and sponsor requirements. (DAIDS-ES study status of "In Development".)

1. **Network Action:** The protocol team submits draft versions of the protocol to the DAIDS RSC CSIO (CSIO@tech-res.com) to upload and abstract (if applicable) it in the DAIDS-ES. Milestone protocol versions are submitted per approved processes at the following stages for applicable reviews and approvals:

    a) Science Review Committee (SRC)
    b) Regulatory (Reg)
    c) Medical Officer (MO)
    d) DAIDS Regulatory Affairs Branch (RAB)

    The protocol team also updates protocol status/milestones via web-services or by notifying the DAIDS RSC CSIO (CSIO@tech-res.com) of the status change. (See Study Statuses and Milestones Definitions for a full list of protocol statuses and milestones)

    i. **Data Management Center Action:** Develops Case Report Forms to ensure data measured by the study is properly captured.

2. **HANC Action:** Supports the operations of the networks by increasing efficiency and resource-sharing through coordination of critical activities across networks and with other research and advocacy partners. This includes the harmonization of data management as well as the development and application of consistent standards of performance evaluation.

3. **DAIDS RSC Action:**

i. **Clinical Study Information Office (CSIO):** Receives and abstracts protocols and/or contact information into the DAIDS Enterprise System (DAIDS-ES) for use by DAIDS and their collaborators. This includes:

a) Uploading protocols to the DAIDS-ES Document Library
b) Abstracting key data points into the DAIDS-ES
c) Abstracting personnel and their associations within the DAIDS-ES
d) Abstracting submitted status and milestones (Study Statuses and Milestones Definitions) into the DAIDS-ES

ii. **Protocol Registration Office (PRO):** Receives and processes protocol registration materials submitted by sites participating in DAIDS-supported and/or sponsored clinical trials. This includes review of the following essential documents:

a) Form FDA 1572/DAIDS IoR Form
b) Curriculum Vitae
c) IRB Approval Letters
d) Site-Specific Informed Consent

Also responds to queries from study sites related to protocol registration.

iii. **Human Subjects Protection Team (HSP):** Reviews protocol sample informed consent(s) (SIC) at the DAIDS Scientific Review Committee (SRC) and Regulatory Review stages for compliance with federally mandated and DAIDS requirements.

iv. **Regulatory Team:** Reviews protocol documents to ensure compliance with all applicable federally mandated and DAIDS requirements, and prepares and submits Investigational New Drug Applications (IND) and subsequent amendments to the FDA.

4. **DAIDS Enterprise System Support Team Action:** Works with networks and the protocol team to ensure that DAIDS-ES requirements are properly addressed.

C. Trial Conduct

- During Trial Conduct, site registration occurs, and protocols open to enrollment and are conducted. (DAIDS-ES study statuses of "Pending", "Open to Accrual", "Enrolling", "Closed to Accrual", and "Closed to Follow-up")

1. **Network Action:** The protocol team may amend the protocol by three methods:

a) Clarification Memo
b) Letter of Amendment
c) Full Protocol Amendment

The protocol team also updates protocol status/milestones via web-services or by notifying the DAIDS RSC CSIO (CSIO@tech-res.com) of the status change. (See Study Statuses and Milestones Definitions for a full list of protocol statuses and milestones)

i. **Data Management Center Action:** Manages clinical trial data collection, prepares reports, stores data, and ensures that data can be properly recalled and shared as appropriate.

2. **HANC Action:** Supports the operations of the networks by increasing efficiency and resource-sharing through coordination of critical activities across networks and with other research and advocacy partners. This includes support for clinical trial logistics, laboratory support, and facilitating effective community engagement in the research process.

3. **Clinical Research Products Management Center Action:** Provides comprehensive pharmacy services to DAIDS studies through study product distribution activities and pharmacy audits.

4. **Clinical Site Study Monitoring Action:** Provides clinical site monitoring services to clinical research sites conducting DAIDS sponsored research.

5. **Clinical Research Support Services Action:** Provides site-specific, protocol-specific and logistical clinical research services, such as: site assessments, site support, clinical site auditing, GCLP auditing, and training.

6. **DAIDS RSC Action:**

   i. **Clinical Study Information Office (CSIO):** Receives and abstracts protocols and/or contact information into the DAIDS Enterprise System (DAIDS-ES) for use by DAIDS and their collaborators. This includes:
      a) Uploading protocols to the DAIDS-ES Document Library
      b) Abstracting key data points into the DAIDS-ES
      c) Abstracting personnel and their associations within the DAIDS-ES
      d) Abstracting submitted protocol status and milestones (Study Statuses and Milestones Definitions) into the DAIDS-ES

   ii. **Protocol Registration Office (PRO):** Responsible for registering and maintaining registrations for sites approved to perform DAIDS-sponsored clinical research studies. This involves review of the following:

      a) Updated Form FDA 1572/DAIDS IoR Form
      b) Current Curriculum Vitae
      c) Registration to Letters of Amendment
      d) Registration to Full Protocol Amendments
      e) New/Updated Protocol Registration Materials (IRB Approval Letters, etc...)
      f) Updated site-Specific Informed Consent documents (if applicable)

      Also responds to queries from study sites related to protocol registration.

   iii. **Human Subjects Protection (HSP) Team:** Reviews protocol sample informed consent(s) (SICs) at the DAIDS Scientific Review Committee (SRC) and Regulatory Review stages for compliance with federally mandated and DAIDS requirements.

iv. **Regulatory Team:** Submits all required documents to the FDA for IND studies, including but not limited to Protocol Amendments, Safety Reports, Responses to FDA, Requests for Information, Annual Reports, Investigator's Brochures, Form FDA 1572 and Investigator's CVs. Also reviews Letters of Amendment and Full Protocol Amendments to ensure compliance with regulatory requirements.

v. **Safety Office:** Processes expedited adverse events (EAEs) from DAIDS-supported studies for review by the DAIDS Medical Officer (MO), and prepares the safety reports for submission to the Food and Drug Administration (FDA). Also responds to queries from study sites related to expedited adverse event reporting, and from DAIDS pharmaceutical collaborators in accordance to study clinical trial agreements.

vi. **DAIDS RSC Safety Information Center (RIC):** Distributes safety information (e.g. IBs, Safety Memos, DSMB Reports, etc.) and responds to queries from sites.

7. **DAIDS Enterprise System Support Team Action:** Works with networks and the protocol team to ensure that DAIDS-ES requirements are properly addressed.

D. Trial Completion - During Trial Completion, data is analyzed and the primary manuscript is submitted for publishing if applicable. (DAIDS-ES study status of "Participants Off Study/Primary Analysis Completed [POS/PAC]" and "Concluded")

1. **Network Action:** The protocol team updates protocol status/milestones via web-services or by notifying the DAIDS RSC CSIO (CSIO@tech-res.com) of the status change. (See Study Statuses and Milestones Definitions for a full list of protocol statuses and milestones)

    i. **Data Management Center Action:** Continues to store data and to ensure that data can be properly recalled and shared as appropriate.

2. **HANC Action:** Provides guidance and recommendations regarding community engagement for trial and site closure.

3. **Clinical Research Products Management Center Action:** If applicable, ensures the proper disposal of unused study interventions as described in the protocol.

4. **DAIDS RSC Action:**
    i. **Clinical Study Information Office (CSIO):** Updates protocol status information (Study Statuses and Milestones Definitions) in the DAIDS Enterprise System (DAIDS-ES) and ensures that personnel and their associations are properly maintained.

    ii. **Protocol Registration Office (PRO):** De-registers approved sites from DAIDS-sponsored research studies and responds to any site queries regarding protocol registration.

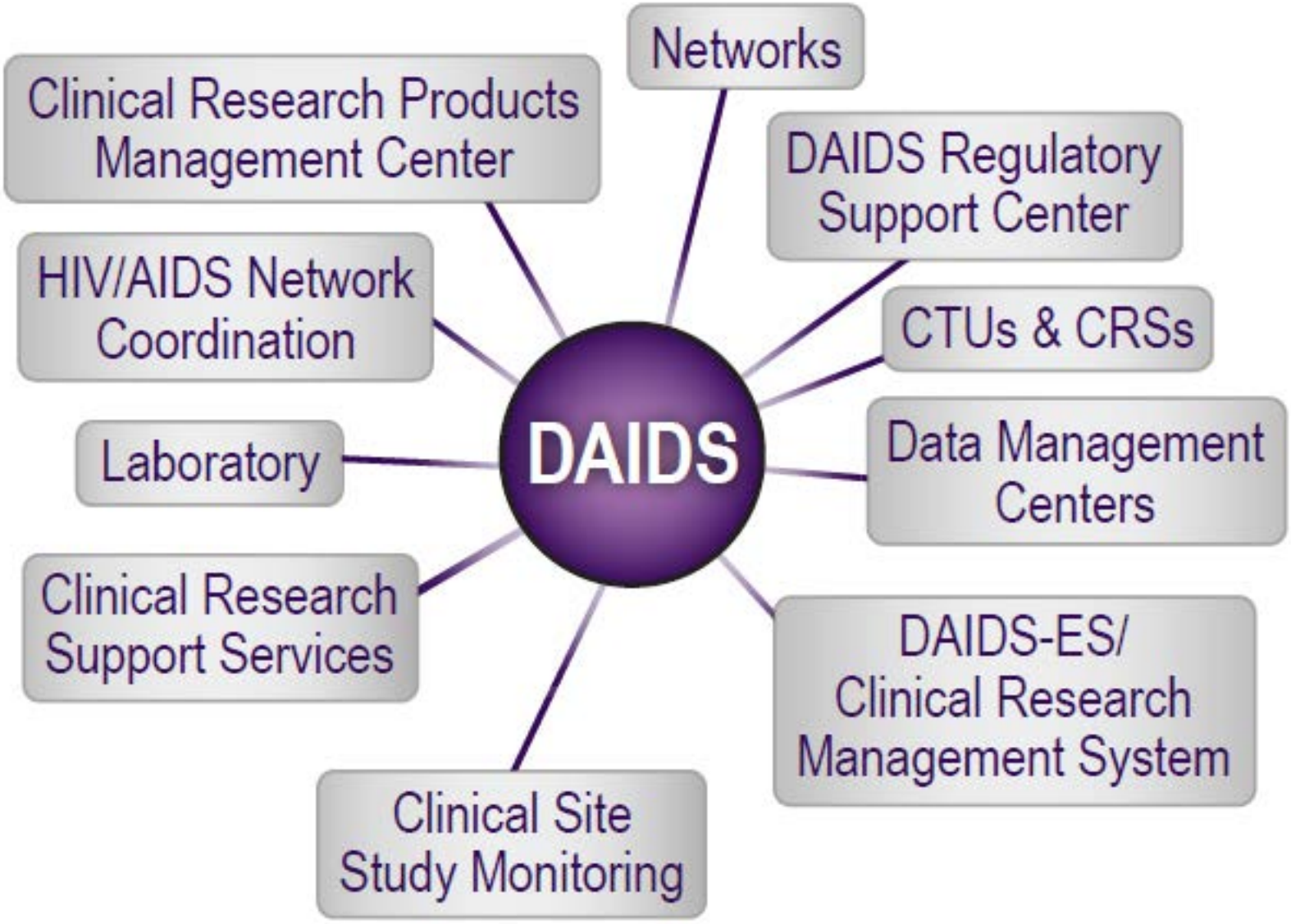
    iii. **Safety Information Office:** Distributes safety information (e.g. IBs, Safety Memos, DSMB Reports, etc...) and responds to queries.

iv. **Regulatory:** Submits IND study results (publications, final study reports, etc...) to the FDA and maintains a list of protocols having Case Report Form/Pharmacy Records that will not be stored by DAIDS on the DAIDS RSC website.

5. **DAIDS Enterprise System Support Team Action:** Ensures the DAIDS-ES maintains a historical record of trial conduct as applicable.

APPENDIX I: DOCUMENT SOURCE INFORMATION

Contract/Grant	Source
Clinical Research Products Management Center	RFP NIAID-DAIDS-NIH-AI-2011-444 (http://grants.nih.gov/grants/guide/notice-files/NOT-AI-12-032.html)
HIV/AIDS Network Coordination (HANC)	https://www.hanc.info/Pages/default.aspx
Network	http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-05-001.html
Laboratory Center	http://projectreporter.nih.gov/project_info_description.cfm?aid=8554494&icde=20601291&ddparam=&ddvalue=&ddsub=&cr=24&csb=default&cs=ASC
Statistical and Data Management Center	http://projectreporter.nih.gov/project_info_description.cfm?aid=8555001&icde=20601347&ddparam=&ddvalue=&ddsub=&cr=7&csb=default&cs=ASC
Clinical Research Support Services	https://www.daidscrss.com/About%20CRSS%20Contract/Pages/About.aspx https://www.daidscrss.com/About%20CRSS%20Contract/Pages/Scope%20of%20Services.aspx
Clinical Site Study Monitoring	https://www.fbo.gov/index?s=opportunity&mode=form&id=7ca7a7630f268010ecdc6bae31b426bf&tab=core&_cview=1
DAIDS-ES/Clinical Research Management System	http://www.ncbi.nlm.nih.gov/pubmed/21816958
DAIDS Regulatory Support Center	http://rsc.tech-res.com/
ACTG	https://www.hanc.info/about/Pages/networks.aspx
IMPAACT	https://www.hanc.info/about/Pages/networks.aspx
HPTN	https://www.hanc.info/about/Pages/networks.aspx
HVTN	https://www.hanc.info/about/Pages/networks.aspx
MTN	https://www.hanc.info/about/Pages/networks.aspx



APPENDIX II: DAIDS CLINICAL TRIAL COLLABORATORS

APPENDIX III: DAIDS CLINICAL TRIAL COLLABORATORS LIFECYCLE TABLE

	Concept Development	Regulatory Clearance	Trial Conduct	Trial Completion
Collaborators	Networks HIV/AIDS Network Coordination (HANC)	Networks HIV/AIDS Network Coordination (HANC) DAIDS Regulatory Support Center (DAIDS RSC) DAIDS Enterprise System Support Team (DAIDS-ES Support)	Networks HIV/AIDS Network Coordination (HANC) Clinical Research Products Management Center (CRPMC) Clinical Site Study Monitoring (CSSM) Clinical Research Support Services (CRSS) DAIDS Regulatory Support Center (DAIDS RSC) DAIDS Enterprise System Support Team (DAIDS-ES Support	Networks HIV/AIDS Network Coordination (HANC) Clinical Research Products Management Center (CRPMC) DAIDS Regulatory Support Center (DAIDS RSC) DAIDS Enterprise System Support Team (DAIDS-ES Support

APPENDIX IV: STUDY STATUSES AND MILESTONES

Study Status Name	Milestone Name	Status/Milestone Definition	Responsible Party for Status and Milestone	Additional Information
Proposed		The network leadership has decided to commit resources on the proposal. For non-network initiatives, DAIDS has decided to commit resources on the proposal.	DAIDS	The OPS Center/Site to send proposal document to DAIDS
	Proposal Approved for Protocol Development	Proposal is approved for protocol development	OPS Center/Site	
In Development		Protocol is being developed	DAIDS	
	Protocol received at DAIDS	The protocol has been received at DAIDS for the first time on this date. This is the initial draft of the protocol.		The OPS Center/Site to send protocol document to DAIDS
	Team Sign-off	The protocol team has signed off on the team sign-off version of the protocol before Full SRC Review on this date	OPS Center/Site	
	DAIDS SRC Full Review	CSRC or PSRC Full review has occurred on this date	RSC	
	Final Team Sign-off	The protocol team has signed off on the final team sign-off version of the protocol on this date.	OPS Center/Site	
	MO Sign-off	The MO has signed off on the MO Version of the protocol on this date.	RSC	

Study Status Name	Milestone Name	Status/Milestone Definition	Responsible Party for Status and Milestone	Additional Information
	RAB Sign-off	RAB has signed-off on the final version of the protocol on this date.	RSC	
In Development	Protocol Distributed to Field	The RAB sign-off final version of the protocol was distributed to sites on this date	OPS Center/Site	
Pending		Final protocol version has been approved by DAIDS and distributed to field, but has not yet met all conditions for opening to accrual.	DAIDS	
	Requirements Met to open to Accrual	The data management requirements, all the regulatory and any other requirements that need to be fulfilled are met prior to indicating that a study is allowed to open to accrual. 1. Study Agents/Products ready. 2. Regulatory requirements met. 3. All data management requirements met 4. Any protocol specific requirements.	OPS Center/Site	While each of the requirements may not be fulfilled by the Ops Center alone, the Ops Center will be responsible for updating the milestone in DAIDS-ES after all the requirements are met.
Open to Accrual		The study has met all conditions for opening and is awaiting the first enrollment.	DAIDS	
	First participant Enrolled	The first enrollment to the study has occurred on this date.	DMC/Site	

Study Status Name	Milestone Name	Status/Milestone Definition	Responsible Party for Status and Milestone	Additional Information
Enrolling		The study has enrolled the first participant	DAIDS	
	Temporarily Closed (Paused) to Study Agents/Products	Administration of Study Agents/Products is temporarily stopped (paused)on this date. This refers to the entire study and not to a pause on one arm or one product.	OPS Center/Site	
	Temporarily Closed (Paused) to Accrual and Study Agents/Products	The study has been temporarily closed to accrual and further administration of Study Agents/Products is stopped on this date. This refers to the entire study and not to a pause on one arm or one product.	OPS Center/Site	
	Temporarily Closed (Paused) to Accrual	The study has been temporarily closed to accrual on this date.	OPS Center/Site	
	Re-Opened	The study has been re-opened after a temporary closure on this date.	OPS Center/Site	
	Last Participant Enrolled	The last enrollment to the study has occurred on this date.	DMC/Site	
Closed to Accrual		The study is closed to accrual and no more participants are enrolled on the study.	DMC/Site	
	Closed to Study Agents/Products	The study has been permanently closed to accrual and all participants have completed study agents/products on this date.	DMC/Site	
	Last Participant Off Study	All participants have completed follow-up visits and are off study.	DMC/Site	

Study Status Name	Milestone Name	Status/Milestone Definition	Responsible Party for Status and Milestone	Additional Information
Closed to Follow-up		The study has been permanently closed to accrual and all participants have completed study agents/products and all follow-up visits have been completed.	DAIDS	
	Requirements Met for All Participants Off Study and Primary Analysis Completion (POS-PAC)	The study is "Closed to Follow-up" and the event "Primary Analysis is Completed" has occurred or it has been determined "No analysis can be done".	OPS Center/Site	
Participants Off Study and Primary Analysis Completed		All participants are off study and primary analysis is completed.	DAIDS	

Study Status Name	Milestone Name	Status/Milestone Definition	Responsible Party for Status and Milestone	Additional Information
Participants Off Study and Primary Analysis Completed	Requirements Met for Concluding	All requirements are met for concluding the study. 1. All protocol required data analyses are finished or it has been determined "No analysis can be done". 2. Primary manuscript has been accepted for publication or determined to be "not publishable" in any journal. 3. Primary manuscript is published if primary manuscript has been accepted for publication. 4. Other manuscripts from study's original plan have been accepted for publication or it has been determined that the analyses are "not publishable". 5. Final report or Executive Summary is submitted to DAIDS.	OPS Center/Site	
Concluded		The study is ended and no further activity or resource expenditure on the study is expected.	DAIDS	

Study Status Name	Milestone Name	Status/Milestone Definition	Responsible Party for Status and Milestone	Additional Information
Concluded	Requirements Met for Archival	All requirements are met for archiving the study. 1. SDMC dataset archived. 2. Site data/CRFs archived. 3. DMC raw data archived. 4. Dataset made public if available.	DMC/Site	
Archived		The study is archived.	DAIDS	
Withdrawn		The study is withdrawn prior to achieving "Enrolling" status.	DAIDS	