DAIDS PROTOCOL REGISTRATION MANUAL

Office for Policy in Clinical Research Operations Division of AIDS

DAIDS PROTOCOL REGISTRATION MANUAL

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I. Introduction

The Division of AIDS (DAIDS) Office for Policy in Clinical Research Operations (OPCRO) has established a protocol registration manual that details, in a step-wise manner, the protocol registration process to ensure that all clinical research sites (CRSs) conducting National Institute of Allergy and Infectious Disease (NIAID)DAIDS-supported and/or -sponsored clinical research do so in accordance with DAIDS Clinical Research Policies and Standard Procedures in addition to all applicable regulations for human subjects protection and the use of investigational drugs, biologics and/or devices. Each CRS will complete the protocol registration process for all clinical research supported and/or sponsored by NIAID (DAIDS) that is reviewed by CSRC or PSRC. Submission of an incomplete package by failing to include all required documents for protocol registration at the time of submission to the DAIDS PRO will result in processing delays until all the required documents are received.

The DAIDS Protocol Registration Manual is a reference tool to help CRSs successfully complete the DAIDS protocol registration process. This manual explains the different types of protocol registration submissions as well as a list of the required documents for each type of submission. Critical pointers are provided in the NOTES throughout the DAIDS Protocol Registration Manual. Failure to include any required documents for protocol registration at the time of submission to the DAIDS PRO will result in processing delays until all the required documents are received.

The protocol registration process begins once a protocol has completed the DAIDS protocol development requirements. All protocols must receive final DAIDS approval either after DAIDS Clinical Sciences Review Committee (CSRC) or Prevention Sciences Review Committee (PSRC) and after regulatory review and DAIDS Medical Officer sign-off. For protocols conducted under a DAIDS-held Investigational New Drug (IND) Application, the final DAIDS approved version of the protocol must be submitted to the U.S. Food and Drug Administration (FDA).

The DAIDS protocol registration process verifies that CRSs have received the necessary Institutional Review Board (IRB)/Ethics Committee (EC) and other applicable Regulatory Entity (RE)/Regulatory Authority approvals and have provided to DAIDS all documentation pertaining to investigator qualifications and responsibilities that are required by The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), the U.S. federal regulations and the National Institutes of Health (NIH). The DAIDS protocol registration process also verifies that site-specific informed consent forms contain the necessary information to comply with ICH, and the U.S. federal regulations. This includes the basic and additional informed consent form elements as required by U.S. federal regulations at 45 CFR 46.116 and 21 CFR 50.25.

II. Summary of Changes

This manual has been reviewed for accuracy and updated to meet 508 compliance guidelines. Several sections have been updated to be consistent with current NIAID (DAIDS) requirements. Key changes to note in this version of the Manual include:

1. DAIDS requirement of Protocol Signature Page (PSP) to document the commitment of the Investigator of Record (IOR) to conduct the trial in compliance with regulations/Laws and ensure compliance with ICH E6 GCP 4.5.1 and 5.6.3.

2. The requirement to submit the Clinical Trial Application (CTA) Form/documentation that identifies the study sponsor.

3. The requirement to submit translation certificate (or translation documentation) confirming a true and accurate translation of documents from local language into English language.

4. Clarification regarding staff that must be listed on the Form FDA 1572 an/or DAIDS IOR Forms in compliance with U.S. regulations and ICH E6 standards.

5. Adjusted the timeline to submit updated DAIDS IOR Forms and Form FDA 1572s from 30 days to 15 days.

6. Formatting changes and hyperlinks added to improve navigation of the manual.

7. Clarified requirements regarding documents required to be submitted to DAIDS from IRBs, ECs, REs, and Regulatory Authorities.

8. Provide guidance on the use of electronic signatures.

9. Change to requirements regarding justifications for non-submission of Regulatory Authority approvals of full version protocol Amendments and Letter of Amendments (LOA).

10. Clarification of Continuing Review requirements based on the October 2018 FDA guidance, 21 CFR 56.109 and 45 CFR 46.109.

This Manual supersedes the version 3.0 dated April 2015.

III. Protocol Registration Required Documents by Submission Type

DAIDS reviews and approves the latest version of each protocol and Sample Informed Consent Form (ICF) before distribution to the CRSs. CRSs are required to submit the initial version and all subsequent versions of a NIAID (DAIDS) -supported and/or -sponsored protocol, including the DAIDS-approved Sample ICF and site-specific ICFs, to their reviewing IRB/EC and other applicable RE/Regulatory Authority(ies) for review and approval.

Prior to implementing the protocol and enrolling participants, a CRS must receive approval from their IRB/EC and other applicable RE/ Regulatory Authorities. In addition, the CRS must successfully complete the DAIDS protocol registration process. When cleared to open to enrollment, a CRS will be notified by the appropriate DAIDS scientific program (e.g., Program/Contracting Officer Representative), Operations Center or Data Management Center when enrollment may begin.

Detailed information on specific requirements for each required document for protocol registration is included in sub-sections A-H of Document Requirements (Concise) of the manual.

A. Submission Requirements by Submission Type

Submission Type	Submission Requirements	Document Requirement	Page
Initial Registration	Form FDA 1572 for IND studies and DAIDS IOR Form for Non-IND studies	Form FDA 1572/DAIDS IOR Form	10
	IOR CV	Curriculum Vitae	11
	IOR Medical License (License equivalent)	Medical License	12
	IRB/EC Approval Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	IRB/EC Submissions Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	All IRB/EC Correspondence	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	Documentation of Pediatric risk/benefit category per 45 CFR 46 and 21 CFR 50 (if applicable)	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	Clinical Trial Application Form/document	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	Regulatory Entity (RE)/Regulatory Authority Approval Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	RE/Regulatory Authority Submission Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	RE/Regulatory Authority/Acknowledgement Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	All RE/Regulatory Authority Correspondence	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	IBC Approval Letter and applicable correspondence (when applicable)	Institutional Biosafety Committee (IBC)	13
	Protocol Signature Page	Protocol Signature Page (PSP)	14

Submission Type	Submission Requirements	Document Requirement	Page
	Site Specific Informed Consent(s) - all applicable languages. All ICFs required by the protocol are required to be submitted or justification for the omission is required.	Site Specific Informed Consents	15
	Site Specific Informed Assent(s) - all applicable languages	Site Specific Informed Consents	15
	Translation Certificate (if applicable)	Translation requirements	36
	Translation Confirmation Documentation (if applicable)	Translation requirements	36
Amendment	IRB/EC Approval Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	IRB/EC Submission Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	All IRB/EC Correspondence	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	Documentation of Pediatric risk/benefit category per 45 CFR 46 and 21 CFR 50 (if applicable)	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	RE/Regulatory Authority Approval/Acknowledgement Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	RE/Regulatory Authority Submission Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	All RE/Regulatory Authority Correspondence	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	Protocol Signature Page	Protocol Signature Page (PSP)	14
	Site Specific ICF - all applicable languages. All previously approved ICFs must be submitted or justification provided for their omission must be provided. Any new ICFs added within the protocol ICFs must be submitted as an Additional ICF type or justification provided for their omission must be provided.	Site Specific Informed Consents	15

Submission Type	Submission Requirements	Document Requirement	Page
	Site Specific Informed Assent(s) - all applicable languages. All previously approved Assents must be submitted, or justification provided for their omission must be provided. Any new Assents required must be submitted as Additional ICF types or justification provided for their omission must be provided.	Site Specific Informed Consents	15
	Translation Certificate (if applicable)	Translation requirements	36
	Translation Confirmation Documentation (if applicable)	Translation requirements	36
Letter of Amendment (LOA)	IRB/EC Approval Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	IRB/EC Submissions Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	All IRB/EC Correspondence	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	Documentation of Pediatric risk/benefit category per 45 CFR 46 and 21 CFR 50 (if applicable)	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	RE/Regulatory Authority Approval/Acknowledgement Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	RE/Regulatory Authority Submission Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	RE/Regulatory Authority Correspondence	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	Site Specific ICFs - all applicable languages. Any revised ICFs should be submitted as a Site Revised ICF submission along with the LOA. Any new ICFs added within the protocol ICFs must be submitted as an Additional ICF type or justification provided for their omission must be provided.	Site Specific Informed Consents	15

Submission Type	Submission Requirements	Document Requirement	Page
	Site Specific Informed Assent(s) - all applicable languages. Any revised Assent forms should be submitted as a Site Revised ICF submission along with the LOA. Any new Assents required must be submitted as Additional ICF types or justification provided for their omission must be provided.	Site Specific Informed Consents	15
	Protocol Signature Page	Protocol Signature Page (PSP)	14
	Translation Certificate (if applicable)	Translation requirements	36
	Translation Confirmation Documentation (if applicable)	Translation requirements	36
Administrative Registration	Form FDA 1572 for IND studies and Form FDA 1572 or IOR Form for Non-IND studies	Form FDA 1572/DAIDS IOR Form	10
	IOR CV	Curriculum Vitae	11
	IOR Medical License (License equivalent)	Medical License	12
	IRB/EC Approval Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	IRB/EC Submissions Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	All IRB/EC Correspondence	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	RE/Regulatory Authority Approval/Acknowledgement Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	RE/Regulatory Authority Submission Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	All RE/Regulatory Authority Correspondence	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	IBC Approval Letter and applicable correspondence (when applicable)	Institutional Biosafety Committee (IBC)	13
	Protocol Signature Page	Protocol Signature Page (PSP)	14
	Translation Certificate (if applicable)	Translation requirements	36

Submission Type	Submission Requirements	Document Requirement	Page
	Translation Confirmation Documentation (if applicable)	Translation requirements	36
Change of Investigator	Form FDA 1572 for IND studies and Form FDA 1572 or IOR Form for Non-IND studies	Form FDA 1572/DAIDS IOR Form	10
	IOR CV	Curriculum Vitae	11
	IOR Medical License (License equivalent)	Medical License	12
	Protocol Signature Page	Protocol Signature Page (PSP)	14
Continuing Review	IRB/EC Approval Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	IRB/EC Submission Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	All IRB/EC Correspondence	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
Site Initiated Revised ICFs	IRB/EC Approval Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	IRB/EC Submission Letters	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	All IRB/EC Correspondence	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	RE/Regulatory Authority/ Acknowledgement Letters (if applicable)	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	RE/Regulatory Authority Submission Letters (if applicable)	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	RE/Regulatory Authority Approval/Acknowledgement Letters (if applicable)	IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation	12
	Site Specific ICFs - all applicable languages	Site Specific Informed Consents	15
	Site Specific Informed Assent(s) - all applicable languages	Site Specific Informed Consents	15
	Translation Certificate (if applicable)	Translation requirements	36

Submission Type	Submission Requirements	Document Requirement	Page
	Translation Confirmation Documentation (if applicable)	Translation requirements	36
Updated Form FDA 1572 or DAIDS IOR Form	Form FDA 1572 for IND studies and Form FDA 1572 or IOR Form for Non-IND studies	Form FDA 1572/DAIDS IOR Form	10
Deregistration	Request stating that the CRS no longer intends to participate in the protocol(s) and/or A Copy of the IRB/EC closure/termination letter for the protocol if the protocol has been closed with the IRB/EC at the time of deregistration	Deregistration	57
Suspension or Termination of IRB/EC Approval	Documentation from the IRB/EC that identifies the reason for suspension or termination	Suspension or Termination of IRB/EC Approval	31

IV. Document Requirements (Concise)

A. Form FDA 1572/DAIDS IOR Form

Section	General Requirement	Detailed Requirement
Section 1 - Name and Address of Investigator of Record (IOR)	Complete legal name (first and last name) and address of the IOR at the CRS that is responsible for the conduct of the clinical trial. The complete legal name of the IOR and the IOR's complete office address (complete physical location/street address/country)	Section 1 - Name and Address of Investigator of Record (IOR)
Section 2 - Education, Training, and Experience	Requires the IOR to check the appropriate box on how they plan to verify their education, training and experience that qualifies them as an expert in the clinical investigation of the study product (drug or biologic) being tested	Section 2 - Education, Training, and Experience
Section 3 - Name and Address of Location(s) Where the Study Will be conducted	Complete name and address of all locations where the clinical trial will be conducted and where clinical data will be generated or collected. The complete name and physical address of all the locations (medical school, hospital, clinics, additional locations, or research facility)	Section 3 - Name and Address of Location(s) where the Study will be conducted
Section 4 - Name and Address of Clinical Laboratory	Complete name(s) and complete physical address (including country) of ALL clinical laboratories or testing facilities which will be used for the clinical trial to process study related and/or study defined samples that will directly contribute to or support the clinical trial	Section 4 - Name and Address of Clinical Laboratory
Section 5 - Institutional Review Board (IRB)/Ethics Committee (EC) and All Other Regulatory Entity(ies) (RE)/ Regulatory Authority(ies)) and Institutional Biosafety Committees (IBCs)	Complete name and address of all IRBs, ECs and other applicable Regulatory Authority(ies) and IBCs which are responsible for the review and approval for the conduct of clinical trials at a CRS	Section 5 - Institutional Review Board (IRB)/Ethics Committee (EC) and All Other Regulatory Entity(ies) (RE)/Regulatory Authority(ies) and Institutional Biosafety Committees (IBCs)
Section 6 - Names of Sub-Investigators	Complete legal name (first and last name) of study staff at a CRS responsible for making a "direct and significant contribution to data"	Section 6 - Names of Sub-Investigators
Section 7 - Protocol Name and Protocol Number	DAIDS ES/Network protocol ID number and the complete protocol title	Section 7 - Protocol Name and Protocol Number
Section 8 - Clinical Protocol Information	Leave blank	Section 8 - Clinical Protocol Information
Sections 9 - Commitments	Read and understand	Sections 9, 10 and 11

Section	General Requirement	Detailed Requirement
Section 10 - Date	Handwritten or electronic date is acceptable. If utilizing electronic date, an electronic signature must be utilized, and the electronic date and the date identified in the electronic signature must correspond. See Signature Requirement Guidance regarding electronic signature requirements.	Sections 9, 10 and 11
Section 11 - Signature of Investigator	Handwritten or electronic signature is acceptable. If utilizing electronic signature, an electronic date must be utilized and the electronic date and the date identified in the electronic signature must correspond See Signature Requirement Guidance regarding electronic signature requirements.	Sections 9, 10 and 11

B. Curriculum Vitae

	General Requirement	Detailed Requirement
Curriculum Vitae (CV)	Submitted (or on file and less than two years old)	Curriculum Vitae (CV)
	Name on the CV matches IOR identified on current Form FDA 1572 or DAIDS IOR Form	
	Complete (all pages submitted, and the document is legible)	
	Dated: Handwritten or electronic date is acceptable. If utilizing electronic date, an electronic signature must be utilized, and the electronic date and the date identified in the electronic signature must correspond. See Signature Requirement Guidance regarding electronic signature requirements.	
	Signed: Handwritten or electronic signature is acceptable. If utilizing electronic signature, an electronic date must be utilized and the electronic date and the date identified in the electronic signature must correspond See Signature Requirement Guidance regarding electronic signature requirements.	

C. Medical License

	Review Requirement	Detailed Requirements
Medical License (ML)	Name on the ML or equivalent document matches IOR identified on current Form FDA 1572 or IOR Form	Curriculum Vitae (CV) and Medical License
	The ML or equivalent document is current (not expired). Note that if the ML does not designate an expiration date, it can be accepted.	

D. IRB/EC/Regulatory Entity(ies)/Regulatory Authority(ies) documentation

	Review Requirement	Detailed Requirements
IRB/EC/RE/Regulatory Authority(ies)	Complete protocol title or short title for the current DAIDS approved version of the protocol.	IRB/EC Approvals
	DAIDS-ES and/or Network Protocol ID	
	DAIDS Protocol Version Number from the final version of the protocol approved by DAIDS and/or the final version date of the protocol document	Regulatory Entity (RE)/Regulatory Authority Approvals
	Final approval letter (conditional approvals not accepted)	
	Pediatric Risk Assessment included in the IRB approval Letter, if applicable	Documentation of Pediatric Risk/Benefit Category
	For LOAs and full version protocol amendments - The date that the amended protocol documents were submitted to the reviewing IRB/EC must be identifiable or provided on the IRB/EC approval letter or on the memo/CRS note, and the date must predate the final IRB/EC approval	Amendment Registrations
		Letter of Amendment (LOA) Registration
	Approval letters from all applicable IRB/EC/ RE/Regulatory Authority(ies) as listed on the Form FDA 1572 or DAIDS IOR Form or justification for their omission	Amendment Registrations
		Letter of Amendment (LOA) Registration

E. Institutional Biosafety Committee (IBC)

	Review Requirement	Detailed Requirements
Institutional Biosafety Committee (IBC)	Complete protocol title or short title for the current DAIDS approved version of the protocol	Institutional Biosafety Committee (IBC) Approval
	DAIDS-ES and/or Network Protocol ID	
	DAIDS Protocol Version Number from the final version of the protocol as approved by DAIDS and/or the final version date of the protocol document	
	Final approval letter (conditional approvals not accepted)	

F. Protocol Signature Page (PSP)

	Review Requirement	Detailed Requirements
Protocol Signature Page (PSP)	Submitted for Initial, Amendment or LOA and Change of IOR submissions Contains the following statement verbatim, "I will conduct the study in accordance with the provisions of this protocol and all applicable protocol-related documents. I agree to conduct this study in compliance with United States (US) Health and Human Service regulations (45 CFR 46); applicable U.S. Food and Drug Administration regulations; standards of the International Conference on Harmonization Guideline for Good Clinical Practice (E6); Institutional Review Board/Ethics Committee determinations; all applicable in-country, state, and local laws and regulations; and other applicable requirements (e.g., US National Institutes of Health, Division of AIDS) and institutional policies."	Protocol Signature Page (PSP)
	Signed by the IOR (s) that is listed on item #1 on the site's current Form FDA 1572/DAIDS IOR Form on file at DAIDS. Handwritten or electronic signature is acceptable. If utilizing electronic signature, an electronic date must be utilized, and the electronic date and the date identified in the electronic signature must correspond. See Signature Requirement Guidance regarding electronic signature requirements.	
	Dated: Handwritten or electronic date is acceptable. If utilizing electronic date, an electronic signature must be utilized, and the electronic date and the date identified in the electronic signature must correspond. See Signature Requirement Guidance regarding electronic signature requirements.	
	Lists the complete DAIDS Protocol Title	
	Lists the DAIDS Protocol Number	
	Lists the correct DAIDS Protocol Version (include the protocol and LOA version when applicable)	
	Lists the correct DAIDS Protocol Version Date	

G. Site Specific Informed Consents

	Review Requirement	Detailed Requirements
Site Specific Informed Consent/ Assent Forms	Lists the complete DAIDS Protocol Title	Site-Specific Informed Consent Forms (ICFs)
	Lists the DAIDS Protocol Number	
	Lists the correct DAIDS Protocol Version	
	All ICFs included in the DAIDS approved protocol are submitted or justification for their omission is provided	
	All ICFs are submitted in all applicable languages or justification for their omission is provided	
	All ICFs should meet all requirements as specified in CFR 46.116, 21 CFR 50.25 DAIDS Policy DWD-POL-CL-02.00 and local laws and regulations	
	Full version protocol Amendments only - All ICFs Types previously registered as part of initial registration are submitted or justification for their omission is provided	

H. Clinical Trial Applications Form/Document

	Review Requirement	Detailed Requirements
Clinical Trial Application Form/Document	Lists the complete DAIDS Protocol Title	Clinical Trial Applications (CTA) for In-country Regulatory Entity (RE)/Regulatory Authority(ies)
	Lists the DAIDS Protocol Number	
	Lists the correct DAIDS Protocol Version	
	Lists the correct DAIDS Protocol Version dated	
	Documentation to confirm that the correct sponsor is identified	
	Complete (all pages) and legible	

V. Protocol Registration Required Documents (Detailed)

A. Form FDA 1572/DAIDS IOR Form

REQUIRED FOR:

- INITIAL REGISTRATION
- WHEN THERE IS ANY MAJOR CHANGE TO THE INFORMATION ON THE CURRENT FORM FDA 1572/DAIDS IOR FORM.

Form FDA 1572 must be submitted for studies being conducted under an IND application. The DAIDS IOR Form or Form FDA 1572 can be submitted for an initial registration for studies not conducted under an IND application.

A signed Form FDA 1572/DAIDS IOR Form is required for each investigator that participates in any clinical trial (drug or biologic). By signing the Form FDA 1572/DAIDS IOR Form, the Investigator of Record (IOR) affirms that he/she will conduct the clinical trial according to the research protocol and all applicable U.S. federal regulations and the ICH E6 GCP guidelines. By signing the Form FDA 1572/DAIDS IOR Form, investigators at non-U.S. sites affirm to DAIDS their commitment to comply with local laws and regulations throughout the course of the clinical trial.

All CRSs participating in a NIAID (DAIDS)-supported and/or -sponsored clinical trials conducted under an IND must submit a copy of the signed and dated Form FDA 1572 to the DAIDS PRO as part of the protocol registration submission for review and for submission to the U.S. FDA.

NOTE: *CRSs are required to retain the original signed Form FDA 1572/DAIDS IOR Form in their regulatory files at the site. Original Forms should not be sent to the DAIDS PRO.*

CRSs requiring more space than what is provided on the Form FDA 1572/DAIDS IOR Form can use a supplemental page. The supplemental page provides additional space to document: additional research locations and addresses; laboratory facilities and addresses; and the names of additional sub-investigators. The supplemental page should identify the CRS and protocol number. If used, a copy of the supplemental page must also be sent to the DAIDS PRO as part of the protocol registration submission.

A CRS must update and submit within 15 calendar days a revised copy of the Form FDA 1572/DAIDS IOR Form when there is ANY major change to the information on the current Form FDA1572/DAIDS IOR Form submitted to the DAIDS PRO. Any correction or revision requires the IOR to sign and date the newly revised form. CRSs must submit BOTH pages of the revised Form FDA 1572/DAIDS IOR Form to the DAIDS PRO even if the changes only affect one page of the form. An updated Form FDA 1572/DAIDS IOR Form that has the same date as the original or previous version will not be accepted.

NOTE: *Examples of major changes to the Form FDA 1572/DAIDS IOR Form include but are not limited to:*

- *Change in IOR*
- *Change in Sub-IOR*
- *Addition of a new or additional DAIDS approved location where the research will be conducted*
- *Addition of a laboratory*
- *Addition or change in an IRB/EC/ RE/Regulatory Authority(ies) that is responsible for review and approval of the clinical research protocol*

The most current version of the Form FDA 1572/DAIDS IOR Form is available for download on the DAIDS RSC Website under the "Protocol Registration" section or from the U.S. FDA website.

B. How to complete the Form FDA 1572/DAIDS IOR Form

Below is detailed information to assist a CRS when completing these Forms.

1. Section 1 - Name and Address of Investigator of Record (IOR)

This section must contain the complete legal name (first and last name) and complete office address (complete physical location/street address) address of the IOR at the CRS that is responsible for the conduct of the clinical trial. Non-U.S. CRSs should include the complete physical address, including
the country.

If a CRS has more than one IOR sharing responsibilities for a clinical trial, the CRS has the following options:

- The CRS can submit a separate Form FDA 1572/DAIDS IOR Form for each IOR that is responsible for the study at that CRS(s) and other DAIDS approved location(s). The CRS must provide documentation explaining that the investigators listed on the two Form FDA 1572s/DAIDS IOR Forms are sharing responsibilities for the conduct of the study at the CRS and DAIDS approved additional location(s).
- The CRS can submit one Form FDA 1572/DAIDS IOR Form that lists both investigators in Section 1 of the Form FDA 1572. This indicates that both

investigators are sharing equal responsibilities for the conduct of the study at the CRS(s) and other DAIDS approved location(s). Each investigator must date sections 10 and sign Section 11 of the Form FDA 1572/DAIDS IOR Form.
The CRS must provide documentation stating that the two investigators listed on the Form FDA 1572 are sharing responsibilities for the conduct of the study at the CRS(s) and other DAIDS approved location(s).

NOTE: *Requirements for the documentation regarding shared responsibilities can be fulfilled in one of the following ways:*

- *Provide a written document that specifies how responsibilities will be shared and the role of each IOR at their respective location(s).*

- *Provide a copy of the study specific Delegation of Duties/Delegation of Responsibility log that indicates how responsibilities will be shared and the roles of each IOR at their respective location(s).*

- *Provide a statement in item 1 of the Form FDA 1572/DAIDS IOR Form that specifies that the two IORs are Co-Investigators and how responsibilities will be shared and the role of each IOR at their respective location(s).*

2. Section 2 - Education, Training, and Experience

This section requires the IOR to check the appropriate box on how they plan to document their education, training and experience that qualifies them as an expert in the clinical investigation of the study product (drug or biologic) being tested. The box marked "Curriculum Vitae" should be checked and a copy of the IOR's CV must be included in the registration packet that is submitted to the DAIDS PRO. DAIDS does not require the submission of CVs for sub-investigators. However, sites should keep a copy of all sub-investigator CVs in the regulatory files at the site. DAIDS requires that all CVs be submitted in English and must be signed and dated.

3. Section 3 - Name and Address of Location(s) where the Study will be conducted

This section must list the complete name and physical address of all locations (medical school, hospital, clinics, satellite sites, or research facility) where the clinical trial will be conducted and where clinical data will be generated or collected. This includes facilities where participants will be seen and study procedures performed. Non-U.S. CRSs should include the country in addition to the complete physical address.

If a CRS utilizes a DAIDS-approved pharmacy, it is not necessary to list the pharmacy on the Form FDA 1572/DAIDS IOR Form. If a CRS out-sources the pharmacy responsibilities

for a clinical trial the CRS must list the name and complete physical address of the contracted pharmacy in Section 3.

If an IOR is conducting the same research protocol at more than one CRS overseen by the same IRB/EC, then it is acceptable to submit one Form FDA 1572/DAIDS IOR Form which lists all locations where the clinical trial will be conducted. If more than one CRS is included in Item 3, include the DAIDS site ID (if available) for each CRS.

4. Section 4 - Name and Address of Clinical Laboratory

This section must list the complete name(s) and complete physical address of ALL clinical laboratories or testing facilities which will be used for the clinical trial to process study related and/or study defined samples that will directly contribute to or support the clinical trial (e.g., diagnostic labs performing blood work, imaging centers, cardiology labs, non-local labs). This may include analytical labs that provide pharmacokinetic analysis, and laboratories supplying efficacy data. The official name of the laboratory (e.g., Department of Pathology) should be included. If multiple CRSs and/or locations are listed on the Form FDA 1572/DAIDS IOR Form, the corresponding clinical laboratories must be listed for each CRS and/or location.

Exceptions for not including ALL clinical laboratories or testing facilities include:

- If a primary laboratory is sending samples to a satellite or other contract labs for additional testing, or
- If a laboratory is being used only to store study samples.

The additional labs do not need to be listed as long as the primary laboratory can trace, through written records, the shipment of samples to the additional labs where the tests were performed.

5. Section 5 - Institutional Review Board (IRB)/Ethics Committee (EC) and All Other Regulatory Entity(ies) (RE)/Regulatory Authority(ies) and Institutional Biosafety Committees (IBCs)

This section must list the complete name and address of all IRBs, ECs REs, IBCs and all other Approving Entities including all National Regulatory Authorities which are responsible for the review and approval of clinical trials at a CRS prior to the CRS's initiation of the protocol and during the implementation of the study (if applicable).

NOTE: *In addition to U.S. FDA requirements, DAIDS requires that all sites participating in NIAID (DAIDS)-supported and/or -sponsored clinical trials list all authorities that must review /approve/acknowledge the clinical trial prior to implementation at a CRS.*

These regulatory entities may include any authorities that regulate, provide permits and/or provide authorization before commencing any clinical trial at a CRS.

The official name (refer to the title provided on the IRB/EC and all other RE/Regulatory Authority(ies) approval letter(s)) and complete physical address of the IRBs/ECs and other REs/Regulatory Authority(ies) which reviewed the protocol should be included in Section 5. IRBs/ECs reviewing and approving the clinical trial do not have to be at the same location as the research being conducted.

NOTE: *The DAIDS PRO must receive an approval letter for each entity listed in Section 5 of the Form FDA 1572/DAIDS IOR Form. The RE/* Regulatory Authority *should not be removed/omitted from FORM FDA 1572/DAIDS IOR Form if they are not responsible for/or do not require the review and approval of full version protocol amendments, LOAs or changes to the CRS's site-specific ICF(s). The CRS Leader or IOR must document in writing to the DAIDS PRO and must also provide documentation (letter from the entity or SOP/guidance/regulation/procedure document of the entity) that shows that the entity doesn't review/approve full version protocol amendments/LOAs/Site specific ICs, when submitting registration materials.*

6. Section 6 - Names of Sub-Investigators

This section must list the complete legal name (first and last name) of all study staff at a CRS that are responsible for making a "direct and significant contribution to the data". A direct and significant contribution includes any persons directly responsible for the treatment or evaluation of research participants. This includes site personnel who have more than minimal involvement with the conduct of the research (performing study evaluations or procedures, conducting Informed Consent or providing intervention) or more than minimal study conduct-related contact with study participants or confidential study data, records, or specimens. A study specific Delegation of Duties/Delegation of Responsibilities log must be maintained at the site and should include all persons identified as providing a direct and significant contribution to the data.

Hospital staff, including nurses, residents, fellows, and office staff who provide ancillary or intermittent care and who do not make a direct and significant contribution to the data do not need to be listed. It is not necessary to include in Section 6 a person with only an occasional role in the conduct of the research (i.e., an on-call physician who temporarily dealt with a possible adverse event or a temporary substitute for any research staff). If a number of residents on rotation will participate in the clinical trial, a general statement regarding their planned participation may be included in Section 6.

The decision about whether to list a pharmacist or research coordinator on the Form FDA 1572/DAIDS IOR Form is the responsibility of the IOR at the CRS and should be based on the contribution that the individual makes to the study.

For example, a research pharmacist may prepare test articles and maintain drug accountability for many clinical trials that are ongoing concurrently at an institution. Because the pharmacist is not making a direct and significant contribution to the data for a particular study, it would not be necessary to list the pharmacist as a sub- investigator in Section 6, but he/she should be listed in the investigator's study records.

CRSs are required to list, at a minimum, a qualified sub-investigator (who will be responsible for fulfilling the requirements of the IOR should the IOR not be able to meet his/her requirement for any given reason). The complete legal name(s) of the sub-investigators who will assist the IOR in the conduct of the protocol should be listed in Section 6.

The IOR is responsible for determining the sub-investigators to be included on the Form FDA 1572/DAIDS IOR Form. Individuals who will sign study medication prescriptions and physicians who submit SAE/EAEs to DAIDS must be listed on the Form FDA 1572/DAIDS IOR Form. The IOR must designate a physician as a sub-investigator who will be responsible to serve as the IOR's backup.

NOTE: *Any physician who is responsible for the review and submission of SAE/EAEs to DAIDS must be listed in Section 6 of the Form FDA 1572/DAIDS IOR Form. Safety reports cannot be submitted by a physician who is not listed in Section 6 of the Form FDA 1572/DAIDS IOR Form.*

NOTE: *CRSs must list the CRS Leader as a Sub-investigator in Section 6 on all Form FDA 1572s /DAIDS IOR Forms if the IOR for the protocol, listed in Section 1, is not the CRS Leader. If the CRS Leader is the same person listed in Section 1 on the Form FDA 1572/DAIDS IOR Form, then the CRS Leader does NOT need to be listed again as a sub-investigator.*

NOTE: *Personnel at facilities where the study uses certain tests (e.g. cardiologist reading ECG or personnel at ECG facilities) do not have to be listed if they are not considered to be engaged in research activities. Per B1 of* OHRP's guidance document on engagement*; not all personnel are considered engaged in research activities unless they have other activities, such as administering study interventions being tested or evaluated or being a collaborator on the publication.*

7. Section 7 - Protocol Name and Protocol Number

The DAIDS ES/Network protocol ID number and the complete protocol title must be included in Section 7. CRSs should not include the DAIDS protocol version number, and/or protocol date in Section 7.

NOTE: *Short titles cannot be accepted and will result in the CRS having to submit a revised Form FDA 1572/ DAIDS IOR Form which will delay protocol registration.*

8. Section 8 - Clinical Protocol Information

NOTE: *The DAIDS IOR Form does not include a Clinical Protocol Information Section*

As the IND sponsor, DAIDS submits the protocol and all relevant information to the FDA on behalf of the investigator. This section should be left blank for both boxes. If DAIDS is not the IND sponsor for a trial, the IND sponsor is responsible for submitting the protocol and all relevant information including the Form FDA 1572 to the FDA and can determine the appropriate information for this section.

9. Sections 9, 10 and 11

NOTE: *These sections are numbered 8, 9, and 10 on the DAIDS IOR Form.*

The IOR must read Section 9, date Section 10 and sign Section 11. The complete legal handwritten or electronic signature of the IOR should be included in Section 11 and should correspond with the name in Section 1 of the Form FDA 1572/DAIDS IOR Form.

NOTE: *If more than one IOR is listed in Section 1 of the Form FDA 1572/ DAIDS IOR Form, both IOR's must sign and date this section.*

NOTE: *Electronic Signature are permissible using the Adobe Acrobat Self-Sign plug-in to insert your signature on fillable FDA forms. Security certificates associated with your digital signatures should be maintained at the site in compliance with 21 CFR 11.1(a). See Signature Requirement Guidance for additional information regarding electronic signatures. If utilizing electronic signatures, the date listed in the date field should be the same date identified on the electronic signature. If signed using hand written signature, the date must also be handwritten.*

NOTE: *If a CRS updates their Form FDA 1572/DAIDS IOR Form, the IOR(s) is responsible for signing and dating the new document even if the change(s) only affect page 1.*

NOTE: *An updated Form FDA 1572/ DAIDS IOR Form that is dated the same as the original or previous version will not be accepted.*

C. Financial Disclosure (FD) by Clinical Investigators

Effective July 1, 2014, any investigator (including sub-investigators) listed on the Form FDA 1572 must complete a financial disclosure (FD) form/statement for all DAIDS sponsored and/or supported studies where DAIDS holds the IND.

Per the regulatory requirements of 21 CFR 54, a person listed as an investigator or sub-investigator on the Form FDA 1572 must complete and submit financial disclosure information for all DAIDS sponsored and/or supported studies where DAIDS holds the IND. Each clinical trial Leadership and Operations Center has developed a generic financial disclosure form/statement for all network studies that are conducted under DAIDS held IND. These forms should be used unless DAIDS or the protocol team provides sites with a different FD Form/statement.

For all Non-Network studies that are conducted under a DAIDS held IND, DAIDS has developed a financial disclosure form/statement and this form is available on the DAIDS RSC website Financial Disclosure Form for Non-Network under Clinical Research Sites.

All original, completed and signed DAIDS approved network financial disclosure Forms/statements or the drug company-specific financial disclosure forms/statements must be filed and retained in a CRS's regulatory binder along with the original and/or updated, signed Form FDA 1572 for that study. These forms need not be submitted to DAIDS or the Network Operations Centers unless requested. For Non-DAIDS held INDs, investigators should follow the IND sponsor's instructions for the collection of financial disclosure form/statement (which may be a company or institution).

If FD forms/statements are required for a regulatory submission, CRS Leaders are responsible for making sure that a financial disclosure form is completed and submitted to their appropriate Network Operations Center per affiliated network requirements for each individual listed in Sections 1 and 6 of the Form FDA 1572.

This process is not required for Non-IND/IDE studies. Refer to the Protocol Registration Frequently Asked Questions on the DAIDS RSC website for additional information on the completion, implementation and collection of FD forms/statements.

D. Curriculum Vitae (CV) and Medical License (ML)

REQUIRED FOR:

- INITIAL REGISTRATION
- WHEN THERE IS ANY MAKOR CHANGE TO THE CURRENT CV ON FILE WITH THE DAIDS PRO.

OR

- UPDATED EVERY TWO YEARS

The IOR overseeing DAIDS-supported and/or sponsored clinical research must provide evidence of qualifications (experience, training and education) to assume responsibility for the conduct of a clinical trial. All CVs must provide sufficient documentation for DAIDS to verify the IOR's qualification to conduct a clinical trial.

IORs must sign and date their CV prior to submission to the DAIDS PRO. All IORs are required to submit an updated, newly signed and dated CV when there is ANY major change to the current CV on file with the DAIDS PRO or at a minimum of every 2 years.

If the IOR is a physician, a copy of the IOR's current medical license documentation or equivalent (i.e., documentation of good standing in the country where they are practicing) must be submitted with all CVs.

NOTE: *Examples of major changes to the IOR CV include but are not limited to:*

- *Change in contact information*
- *Change in education, Change in experience, New trainings*
- *New publications*

U.S. federal regulations require that the IOR's CV be submitted to the U.S. FDA for all studies being conducted under an IND. DAIDS, as the IND sponsor, submits the IOR CV to the U.S. FDA. Sub-investigators are not required to submit CVs to the DAIDS PRO. However, sites should keep a copy of all sub- investigator CVs in the regulatory files at the site.

DAIDS accepts a NIH Bio-Sketch formatted CV that includes education/training, current employment, past relevant employment, licensures/memberships, and any relevant publications.

The NIH Bio-Sketch formatted CV template is available at NIH Grant Application Guide.

NOTE: *Electronic Signature are permissible using the Adobe Acrobat Self-Sign plug-in to insert your signature on fillable FDA forms. Security certificates associated with your digital signatures should be maintained at the site in compliance with 21 CFR 11.1 (See Signature Requirement Guidance for additional information regarding electronic signatures.*

NOTE: *If handwritten signatures are used, the date must also be handwritten.*

E. Documentation of Institutional Review Board/ Ethics Committee (IRB/EC) and Other Regulatory Entity (RE)/Regulatory Authority(ies) Approvals

REQUIRED FOR:

- ALL INITIAL, AMENDMENT and LOA REGISTRATIONS, ADMINSTRATIVE REGISTRATIONS
- CONTINUING/ ANNUAL REVIEW SUBMISSIONS
- SITE INITIATED REVISIONS TO SITE- SPECIFIC ICFs and SUBMISSION OF REVISED SITE ICF(s) IN RESPONSE TO A DISAPPROVAL NOTIFICATION.

1. IRB/EC Approvals

CRSs are required to submit to their IRB/EC, the initial version and all subsequent full version amendment and LOA versions of NIAID (DAIDS)-supported and/or sponsored clinical trials and observational studies for review and approval, including the DAIDS-approved sample ICF and site- specific ICFs to the DAIDS PRO. The site's submission to the IRB/EC should include DAIDS approved sample protocol and Site ICF, all site specific ICFs, and any material/information that the site plans to provide to participants. CRSs must submit to the DAIDS PRO a copy of ALL documentation to and from the IRB/EC along with a copy of all the final approval letter(s). Original documents should be kept in the regulatory files at the CRS. The IRB/EC approval letter(s) for all initial, full version protocol amendment, and LOA registrations must be a final approval not noting any required modifications or stipulations.

NOTE: *Documentation to and from IRB/EC includes but is not limited to:*

- *the submission letter from the site to the IRB/EC*
- *the letter(s) from the IRB/EC documenting queries and changes required to the site-specific ICFs*
- *site response to the queries*
- *final approval letter(s)*

All IRB/EC approval letter(s) must be able to be linked to the DAIDS-approved version of the protocol. If an IRB/EC approval letter(s) does not include the DAIDS required identifying information in their approval letters, CRSs can submit a memo with their IRB/EC submission that includes: identifying information corresponding to the protocol, lists all the documents submitted for IRB/EC review, as well as the date of submission to the IRB/EC. The required identifying information are:

- Complete Protocol Title as listed on the current DAIDS-approved version of the protocol. The DAIDS PRO will accept a long or short title for those protocols which include both in the DAIDS SAMPLE ICF.

- DAIDS ES and/or Network Protocol ID Number.

- DAIDS Protocol Version Number from the final version of the protocol approved by DAIDS and/or the final version date of the protocol document approved by DAIDS.

The CRS's memo/submission letter can be used to document that the IRB/EC/RE/Regulatory Authority received the correct version of the protocol and may be included with the IRB/EC/RE/Regulatory Authority approval letters that are submitted to the DAIDS PRO.

NOTE: *The CRS's memo to the IRB/EC/RE/Regulatory Authority requesting review must pre-date the date on the final IRB/EC/RE/Regulatory Authority approval letter(s).*

NOTE: *Sites are strongly advised to document the date the CRS receives each final IRB/EC/RE/Regulatory Authority approval letter to ensure compliance with the DAIDS protocol registration policy regarding submission of amendment and LOA registration materials to the DAIDS PRO within 14 calendar days of receipt of all final IRB/EC/RE approval letters. This documentation should be kept in the site's regulatory files for verification by monitors.*

NOTE: *If the reviewing IRB transferred the responsibility to another IRB, a site needs to provide documentation of the delegation of authority to the other IRB to the DAIDS PRO*

NOTE: *If any of the IRB/EC/RE/Regulatory Authority approval letter(s) or CRS's memo do not contain enough information to be linked to the most current DAIDS- approved version of the protocol, designated site personnel (i.e., CRS coordinator, IOR) and/or additional personnel listed in the DPRS will be sent a Requested Materials notice that details the missing and/or corrected information/materials that must be submitted to the DAIDS PRO for registration processing to continue. The review process will not continue until the requested materials are received at the DAIDS PRO. For information on how to submit requested materials refer to Requested Materials" of this manual.*

2. Regulatory Entity (RE)/Regulatory Authority Approvals

When other approvals are required in addition to the reviewing IRB/EC at a CRS prior to implementation of a protocol at a CRS, copies of those approval letters and any other appropriate correspondence (as noted in Section 1 above) must be submitted to the DAIDS PRO with registration materials.

NOTE: *If a given RE/Regulatory Authority requires review/approval of initial versions of protocols but does not review and approve full version amendments and LOAs, the CRS Leader or IOR should provide letter/documentation from the Regulatory Authority or by submission of the applicable regulation that defines the specific requirement when submitting registration materials. The CRS Leader or IOR must document in writing to the DAIDS PRO and also provide documentation (letter from the entity or SOP/guidance/regulation/procedure document of the entity) that shows that the entity doesn't review/approve full version protocol amendments/LOAs/Site specific ICs, when submitting registration materials*

NOTE: *In addition to U.S. FDA requirements, DAIDS requires that all sites participating in NIAID (DAIDS)-supported and/or -sponsored clinical trials list all authorities that must review/approve/acknowledge the clinical trial prior to implementation at a CRS. These regulatory entities may include any authorities that regulate, provide permits and/or provide authorization before commencing any clinical trial at a CRS. For information on completing the Form FDA 1572 and/or DAIDS IOR Form, refer to Section V, Sub Sections A and B -* *"Section 5 - Institutional Review Board (IRB)/Ethics Committee (EC) and All Other Regulatory Entity(ies) (RE)/Regulatory Authority(ies) and Institutional Biosafety Committees (IBCs)"*

3. Clinical Trial Applications (CTA) for In-country Regulatory Entity (RE)/Regulatory Authority(ies)

DAIDS requires the submission of Clinical Trials Applications (CTAs) to DAIDS to ensure compliance with ICH E6. DAIDS requires that a copy of the CTA submitted to the competent National Regulatory Authority(ies) be submitted to the DAIDS RSC to verify the accuracy of the application/submission prior to sites being allowed to complete the initial protocol registration process for a protocol. Refer to the Clinical Trial Application Submission Guidance on how to submit CTA documents to the DAIDS RSC.

Per the DAIDS Policy for Protocol Registration (DWD-POL-RA-011), the in-country Clinical Trial Application Form/Document submitted to National Regulatory Authorities must be submitted to the DAIDS RSC prior to a CRS's being able to participate in the trial. The Clinical Trial Application Form/Document is required for National Regulatory Authorities identified on the Form FDA 1572 or DAIDS IOR Form.

Attachments included with the applications are not required unless required to identify the sponsor and applicable protocol information. See specific document requirements and follow submission instructions as stated in the Clinical Trial Application Submission Guidance.

4. Documentation of Pediatric Risk/Benefit Category

Per the DAIDS Policy for Enrolling Children (including Adolescents) in NIAID (DAIDS)-supported and/or sponsored Human Subject Clinical Research, for research studies including children or adolescents, DAIDS requires documentation of the IRB/EC designation of the pediatric risk/benefit category per the U. S. Federal regulations, 45 CFR 46, 404-407 and 21 CFR 50.51-54 and IRB /EC approval for involvement of children based on the determination specified by that category. This requirement applies to the initial and continuing/annual reviews of research protocols and to any subsequent reviews of full version protocol amendments and LOAs involving potential study risks or benefits. The documentation may be in the IRB/EC approval letter(s) or in other official correspondence from the IRB/EC to the site Investigator.

NOTE: *Failure to submit documentation of the IRB/EC designation of the pediatric risk/benefit category or documentation that the CRS will not enroll children or adolescents at the time of registration submission to the DAIDS PRO will result in delays in protocol registration.*

F. Institutional Biosafety Committee (IBC) Approval

REQUIRED FOR ALL INITIAL REGISTRATIONS FOR RESEARCH THAT INVOLVES RECOMBINANT DNA.

Research supported by NIH funding that involves recombinant DNA is subject to special regulatory oversight by an IBC. In addition, clinical trials testing products containing recombinant DNA must be submitted to the NIH Office for Biotechnology Activities (OBA) for review by the NIH Recombinant DNA Advisory Committee (RAC). Detailed information regarding the requirements for NIAID (DAIDS) -sponsored and/or -supported research involving recombinant DNA is available on the DAIDS RSC website under the “Protocol Registration” section.

Once IBC approval is received, a copy of the final approval letter and any other appropriate correspondence (as noted in Section 1 above) must be submitted to the DAIDS PRO with the initial registration submission. Failure to submit documentation of IBC approval at the time of initial registration submission to the DAIDS PRO will result in delays in protocol registration.

If an IBC must review and approve all full version protocol amendments and LOAs prior to the implementation at a CRS, documentation of the IBC approval should be submitted to the DAIDS PRO at the time of amendment or LOA registration.

All IBC approval letter(s) must be able to be linked to the current DAIDS- approved version of the protocol at the time of initial protocol registration. Since not all IBCs include the DAIDS-required identifying information in their approval letters, a CRS can submit a memo with their IBC submission which lists identifying information corresponding to the protocol, all the documents submitted for review as well as the date of submission to the IBC. The required identifying information are:

- Complete Protocol Title for the current DAIDS-approved version of the protocol. The DAIDS PRO will accept a long or short title for those protocols which include both on the DAIDS sample informed consent forms.

- DAIDS ES and/or Network Protocol ID Number.

- DAIDS Protocol Version Number from the final version of the protocol approved by DAIDS AND/OR the final version date of the protocol document approved by DAIDS.

The CRS's memo can be used to document that the IBC received the correct version of the protocol and may be included with the IBC approval letter that is submitted to DAIDS PRO.

NOTE: *The CRS's memo to the IBC requesting review must pre-date the date on the final IRB/EC approval letter(s).*

NOTE: *If the IBC approval letter or CRS's memo does not contain enough information to be linked to the most current DAIDS-approved version of the protocol, designated site personnel (i.e., CRS coordinator, IOR) and/or additional personnel listed in the DPRS will be sent a Materials Request notice that details the missing and/or corrected information/materials that must be submitted to the DAIDS PRO for registration processing to continue. The review process will not continue until the requested materials are received at the DAIDS PRO. For information on how to submit requested materials refer to Requested Materials" of this manual.*

G. Protocol Signature Page (PSP)

REQUIRED FOR ALL INITIAL, AMENDMENT, LOA, AND CHANGE OF IOR SUBMISSIONS

DAIDS has implemented a new regulatory requirement effective May 07, 2017 a Protocol Signature Page (PSP) to document the commitment of the IOR to conduct the trial in compliance with the protocol as agreed to by the sponsor and in compliance with United States (US) Health and Human Service regulations (45 CFR 46); applicable U.S. Food and Drug Administration regulations; standards of the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (E6); Institutional Review Board/Ethics Committee determinations; all applicable in-country, state, and local laws and regulations; and other applicable requirements and institutional policies.

NOTE: *DAIDS does not require submission of the PSP to an IRB/IEC or regulatory authority, unless required by the IRB/EC/RE.*

The following language must be included in all PSPs:

"I will conduct the study in accordance with the provisions of this protocol and all applicable protocol-related documents. I agree to conduct this study in compliance with United States (US) Health and Human Service regulations (45 CFR 46); applicable U.S. Food and Drug Administration regulations; standards of the International Conference on Harmonization Guideline for Good Clinical Practice (E6); Institutional Review Board/Ethics Committee determinations; all applicable in-country, state, and local laws and regulations; and other applicable requirements (e.g., US National Institutes of Health, Division of AIDS) and institutional policies."

A site should not alter the above template language but may add required language (e.g., institutional requirement) for the IORs commitment to conduct the trial in accordance with all applicable regulations.

All PSPs must be able to be linked to the current DAIDS- approved version of the protocol at the time of protocol registration. The required identifying information are:

- Complete Protocol Title for the current DAIDS-approved version of the protocol. The DAIDS PRO will accept a long or short title for those protocols which include both on the DAIDS sample.
- DAIDS ES and/or Network Protocol ID Number.
- DAIDS Protocol Version Number (including LOA version when applicable) for the version being registered.
- DAIDS Protocol Version Date for the version being registered.

All PSPs must be signed by the DAIDS approved IOR listed on the Form FDA 1572/DAIDS IOR Form. The PSP is protocol-specific and must be signed by the IOR at each participating site. This responsibility may not be delegated. If there are more than one IOR, a PSP is required for each IOR or a Single PSP can be submitted that is independently signed and dated by each IOR. If there is changes of IOR, an updated PSP is required as part of the Change of IOR submission. All original PSPs must be maintained in the regulatory binder at the site.

NOTE: *Failure to include s signed PSP at the time of submission to the DAIDS PRO will result in processing delays until the required document is received.*

NOTE: *Electronic Signature are permissible using 21 CFR 11.1compliant signatures. Security certificates associated with your digital signatures should be maintained at the site in compliance with 21 CFR 11.1(a). If utilizing electronic signatures, the date listed in the date filed should be the same date identified on the electronic signature. For additional information regarding electronic signatures, please see the Signature Requirement Guidance.*

NOTE: *If handwritten signatures are used, the date must also be handwritten.*

H. Suspension or Termination of IRB/EC Approval

Per U.S. federal regulations, 45 CFR 46.113 the IRB/EC has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's/EC's requirements or that has been associated with unexpected serious harms to participants. The regulations mandate that when the reviewing IRB/EC suspends or terminates its approval of research, this information be reported to, among others, the investigator and sponsor.

Per the DAIDS Critical Events Manual, for any studies that are protocol registered through the DAIDS PRO, the CRS must submit documentation of the suspension or termination of IRB/EC approval to DAIDS as soon as possible, but not later than 3 reporting days through the DPRS. If a study is not registered through the DAIDS PRO, the CRS must notify the appropriate DAIDS Program Officer (PO) or Contracting Officer Representative (COR) of the IRB/EC actions to suspend or terminate IRB/EC approval.

I. Site-Specific Informed Consent Forms (ICFs)

REQUIRED FOR:

- ALL INITIAL, FULL VERSION PROTOCOL AMENDMENT and LOA REGISTRATIONS
- CONTINUING /ANNUAL REVIEW SUBMISSIONS
- SITE-INITIATED REVISIONS TO SITE-SPECIFIC ICFs, and IF THERE WAS A CHANGE TO THE SITE-SPECIFIC ICFs
- SUBMISSION OF REVISED SITE ICFs IN RESPONSE TO A DISAPPROVAL NOTIFICATION.

Site-specific ICF(s) must contain all information necessary to comply with U.S. federal regulations, local laws and regulations, ICH and DAIDS policies. This includes all the basic and additional elements, as outlined in U.S. federal regulations, 45 CFR 46.116 and 21 CFR 50.25. To assist sites with developing their site-specific ICF(s), DAIDS works with the Protocol Teams to create sample ICFs that contain all the specific elements required by the U.S. federal regulations, 45 CFR 46.116 and 21 CFR 50.25.

A CRS must submit to the DAIDS PRO a copy of all site-specific ICF(s) that will be used during the informed consent process at the site after review and approval by the IRB/EC and other applicable Regulatory Entity (RE)/Regulatory Authority(ies). and retain the original(s) on file at the site.

All materials that are used in the informed consent process (e.g., ICFs, questionnaires, etc.) that are given to participants should be submitted to DAIDS for sponsor files along with any approvals (if any) IRB/EC/ RE of these documents.

If there any Sample ICFs provided with the final DAIDS approved version of the protocol that will *not* be needed at a CRS, (i.e., if a pregnancy ICF is not needed because pregnant women will not be enrolled), the CRS must document this either in the comments section of the ICF field of the DPRS or with a memo to the DAIDS PRO with the registration submission.

If a Sample ICF is removed as part of an amended protocol and the site will no longer be using the consent form, a memo or note must be included with the Amendment registration submission declaring that the specific consent form will no longer be utilized at the site.

When an IRB/EC/ RE/Regulatory Authority(ies). approves a site-specific ICF and the site contact information is left blank, the CRS must include a memo with their registration submission explaining that the CRS will insert the site-specific contact information prior to consenting participants.

If an IRB/EC/RE/Regulatory Authority(ies) requires language in a site-specific ICF specific to the institution or based on local regulations/requirements, the site should include that information in the site-specific ICF and must provide documentation from IRB/EC/RE regarding the required language in the site-specific ICF. However, even though an IRB/EC/RE requires language in site-specific ICF, none of the basic and additional elements found in the DAIDS approved Sample ICF or required by DAIDS policy should be removed. Refer to the Frequently Asked Questions and the Informed Consent Process Information on the DAIDS RSC website for additional information regarding the development of site-specific ICFs.

If a CRS deletes or makes any substantive change to basic and/or additional elements as presented in the DAIDS-approved Sample ICF, the IOR or designee for the clinical trial must provide written documentation to explain the deletions/change(s) at the time of registration submission to the DAIDS PRO.

All site-specific ICF(s) must be able to be linked to the current DAIDS approved version of the protocol. The DAIDS-required identifying information are:

- Complete Protocol Title for the current DAIDS-approved version of the protocol. The DAIDS PRO will accept a long or short title for those protocols which include both on the DAIDS-approved Sample ICF forms.

- DAIDS ES and/or Network Protocol ID Number.

- DAIDS Protocol Version Number from the final version of the protocol approved by DAIDS and/or the final version date of the protocol document approved by DAIDS.

NOTE: *For version tracking purposes at the CRS (i.e., at the request of an IRB/EC and other applicable REs/Regulatory Authority(ies)), CRSs can specify the site (local) version number or version date of the site-specific ICF(s) in the header or footer of their site-specific ICF(s). However, the DAIDS protocol version number and/or the final version date of the DAIDS-approved protocol must remain on all site-specific ICFs as well.*

NOTE: *If any of the site-specific ICF(s) do not contain enough information to be linked to the most current DAIDS-approved version of the protocol, designated site personnel (i.e., CRS coordinator, IOR) and/or additional personnel listed in the DPRS will be sent a Materials Request notice that details the missing and/or corrected information/materials that must be submitted to the DAIDS PRO for registration processing to continue. The review process will not continue until the requested materials are received at the DAIDS PRO. For information on how to submit requested materials refer to Requested Materials" of this manual.*

J. Types of ICFs and Protocol Registration Requirements

Main ICF - The Main ICF issued for enrollment of participants into the protocol. The Main ICF should include all of the basic and appropriate additional elements as outlined in U.S. federal regulations, 45 CFR 46.116 and 21 CFR 50.25. The link to OHRP's guidance on informed consent form required elements can be found here.

Screening and Stored Specimen ICFs - The following are DAIDS requirements regarding generic screening and stored specimen consent forms and protocol- specific screening consent forms.

Generic screening and stored specimen ICF - A generic screening and/or stored specimen ICF is an ICF that is developed by a CRS for its own purposes and not related to any DAIDS requirement and should NOT be submitted to the DAIDS PRO. The DAIDS PRO will NOT review or approve any such generic screening and/or stored specimen ICFs if they are submitted with registration materials.

Protocol-specific screening and stored specimen ICF - A protocol-specific screening and/or stored specimen ICF is an ICF developed for a specific protocol that is approved by DAIDS and is included as part of the final protocol and DAIDS-approved Sample ICFs. If the DAIDS-approved Main ICF includes screening procedures and stored specimen information and a CRS chooses to develop a separate protocol-specific screening and/or stored specimen ICF to be used at the site, then the screening and eligibility and/or stored specimen information can be removed from the site-specific main ICF. In this instance, the CRS must submit BOTH the protocol-specific screening and/or stored specimen ICF and the site-specific main ICF to the DAIDS PRO for review and approval.

Short ICFs - If a CRS elects to use a short ICF in addition to the main ICF, the CRS must have a main ICF OR written summary that includes all the required basic and appropriate additional elements which have been approved by the IRB/EC and has been submitted to the DAIDS PRO for registration. A CRS must receive a Registration Notification from the DAIDS PRO for all short form ICFs prior to implementation.

Sub-study ICFs - If a NIAID (DAIDS)-supported and/or-sponsored protocol includes a separate DAIDS-approved Sample ICF for a sub-study that is part of the main protocol and the CRS anticipates participating in the sub-study, the CRS must include the sub-study site-specific ICF in their protocol registration submission. A CRS must receive a Registration Notification from the DAIDS PRO for all sub- study ICFs prior to implementation.

Pregnancy ICF - If a DAIDS-supported and/or sponsored protocol includes a DAIDS-approved Sample ICF for women who become pregnant while on study and the CRS anticipates that some pregnant women may be included or followed on the study, the CRS must submit the site-specific pregnancy ICF to the DAIDS PRO.

Sites have the flexibility to combine the pregnancy ICF and the main ICF into one ICF, as long as the required information is still present, and this approach is approved by the IRB/EC. If one or more ICFs are combined, there should be a note to the DAIDS PRO documenting why one of the original consents is not included in the registration submission.

If the site will not follow or enroll pregnant women, the pregnancy ICF does not need to be submitted, and the site should document the plan not to include pregnant women with a note to the DAIDS PRO. A CRS must receive a Registration Notification from the DAIDS PRO for any pregnancy ICF prior to implementation.

Assents - The IRB/EC must determine that adequate provisions are made for soliciting the assent of children and/or adolescents when in the judgment of the IRB/EC the children and/or adolescents are capable of providing it, 45 CFR 46.408. The IRB/EC is responsible for determining the age of assent and for determining whether the use of an assent form is appropriate. A CRS must receive a Registration Notification from the DAIDS PRO for all assents prior to implementation.

1. Health Insurance Portability and Accountability Act (HIPAA) - Privacy Rule

The Privacy Rule is a U.S. federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information.

The DAIDS PRO does not review site-specific ICFs for information related to HIPAA. If the site-specific ICF(s) contains language pertaining to HIPAA authorization, the DAIDS PRO will NOT assess this language for Privacy Rule compliance.

In addition, it is very important that confidentiality language included in the DAIDS-approved sample informed consent remain in the site-specific ICF even if this information is included in a separate HIPAA authorization form.

NOTE: *The HIPAA regulations do not apply to non-U.S. CRSs.*

Information related to the Privacy Rule can be found at the following HHS website.

2. ClinicalTrials.gov Informed Consent Requirements

ClinicalTrials.gov is the clinical trial registry databank maintained by the NIH National Library of Medicine (NLM) which was created by statute outlined in the Food and Drug Administration Amendments Act of 2007 (FDAAA). Through FDAAA, the U.S. Food and Drug Administration (FDA) amended current informed consent regulations (21 CFR 50.25) to now require that all informed consent documents for applicable drug (including biological products) and device clinical trials include a specific statement that clinical trial information will be entered into ClinicalTrials.gov. As of December 1, 2011, for new protocols, the following language **MUST** be included in the DAIDS-approved sample ICF for applicable trials:

"A description of this clinical trial will be available on ClinicalTrials.gov, as required by U.S. law. This Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search this Website at any time."

The DAIDS PRO will review site-specific ICFs for information related to clinicaltrials.gov. If the DAIDS-approved Sample ICF contains the clinicaltrials.gov language, then the language MUST be in all site-specific informed consents for that study. Failure to include this language exactly as stated above in all applicable Site ICFs will result in an Approval with Required Corrections notification.

NOTE: *Per U.S. federal regulations, this language cannot be modified.*

NOTE: *Participants do not need to be re-consented for existing or ongoing studies unless the IRB/EC determines otherwise.*

NOTE: *The required language can be translated into local language.*

NOTE: *If the inclusion of the ClinicalTrials.gov language is mandated by the IRB/EC/RE (for non-applicable trial), documentation from the IRB/EC/Regulatory Authority mandating the statement inclusion must be provided to the DAIDS PRO.*

Information related to the informed consent requirement for clinicaltrials.gov can be found on the following HHS website.

K. Translation requirements

For all documents that require translation to a language other than Spanish, a CRS must submit to the DAIDS PRO a copy of the DAIDS Protocol Registration Translation Confirmation Document, attesting that the translation is a true and accurate reflection of the local language documents that have been reviewed and approved by the IRB/EC and other REs/Regulatory Authority.

In addition, sites must submit a translation certificate or its equivalent (i.e., a signed and dated documentation by the translator/translators attesting that the translation is a true and accurate interpretation of the local language document).

NOTE: CRSs are not required to complete the DAIDS Protocol Registration Translation Confirmation Document for any protocol registration documents in Spanish.

An electronic copy of the DAIDS Translation Confirmation Document can be found on the DAIDS RSC Website under the "Protocol Registration" section.

1. Form FDA 1572, IOR Form, CVs, and Medical Licenses

All Form FDA 1572s, DAIDS IOR Forms, CVs and Medical Licenses must be prepared in English. Non-English versions of these documents will not be accepted by the DAIDS PRO.

2. IRB/EC, other RE/Regulatory Authority, and IBC approval letters

All non-English IRB/EC, other applicable RE/Regulatory Authority, and IBC approval letter(s) must be translated into English, except for Spanish. CRSs must submit copies of both the local language and translated English approval letter(s) to the DAIDS PRO.

NOTE: *CRSs should provide an English translation of any other appropriate IRB/EC/RE/IBC documentation that explains changes/deletions in the site specific ICFs or that could assist the DAIDS PRO when reviewing registration materials.*

3. Site-specific ICFs

CRSs must prepare site-specific ICFs in all languages in which they will conduct informed consent discussions for each study. If CRSs elect to use short ICFs in addition to the Main ICF, the short ICF must also be prepared in all languages in which the informed consent discussions will be conducted. After approval by all applicable IRBs/ECs and REs, copies of the approved site-specific ICFs must be submitted to the DAIDS PRO.

If informed consent discussions will be conducted in English and another local language, including Spanish, the site-specific English and local language ICFs must be submitted to the DAIDS PRO. No back-translations are required by DAIDS.

If informed consent discussions will be conducted in a local language other than English or Spanish, site-specific local language ICFs must be submitted to the DAIDS PRO. Back-translations (into English) of the site-specific local language ICFs for which discussion will be conducted also must be submitted to the DAIDS PRO.

NOTE: *If a DAIDS Clinical Trials Network has specific requirements regarding translation of site-specific ICFs, the CRS should follow those requirements as well as any applicable translation and back-translation requirements specified in institutional policies, the study protocol, and/or the network Manual of Operations.*

NOTE: *Site specific ICFs in languages that were not submitted with the original initial registration should be submitted as additional ICF language type within DPRS and will be considered initial registration in the newly submitted language type.*

4. Clinical Trial Application (CTA) Form/Document

All non-English Clinical Trial Application Form/Documentation must be translated into English, except for Spanish. Copies of both the local language and translated English applications must be submitted to the DAIDS RSC along with the translation certificate and the Translation Confirmation Document (TCD).

VI. Protocol Registration Submissions

Prior to implementing a protocol and enrolling participants, a CRS must receive final approval for the site-specific ICFs from the IRB/EC and other applicable REs/Regulatory Authority(ies). In addition, the CRS must successfully complete the DAIDS initial protocol registration process. However, successfully completing the DAIDS initial protocol registration process does not authorize a CRS to begin enrollment of participants. CRSs will be notified by the appropriate DAIDS scientific program (i.e., Program Officer), Operations Center or Data Management Center when enrollment may begin for a protocol.

Each CRS will complete the protocol registration process for all clinical research supported and/or sponsored by DAIDS that is reviewed by DAIDS Scientific Review Committees, namely the Prevention Sciences Review Committee (PSRC) and the Clinical Sciences Review Committee (CSRC) and if it is determined protocol Registration is required. Upon receiving final IRB/EC and other applicable RE/Regulatory Authority approval(s), the CRS will submit all required registration documents to the DAIDS PRO via the DAIDS DPRS.

Upon making ANY submission to the DAIDS PRO, a CRS will receive a Confirmation of Submission notice that indicates successful submission of materials to the DAIDS PRO. If a CRS does not receive a Confirmation of Submission notice within 24 - 48 hours of submitting materials, the CRS should contact the DAIDS PRO.

The CRS must place a copy of all final Protocol Registration notifications from the DAIDS PRO in the site's regulatory files. Refer to Definitions of this manual for a list of final registration notifications.

A. Initial Registration

A CRS that has **not previously** received a Registration Notification from the DAIDS PRO for any version of the protocol must complete the initial protocol registration process.

If a CRS has previously received a DAIDS PRO Registration Notification for one language (i.e., English) and later submits registration documents for a new language (i.e., Spanish), the new language should be submitted as an Additional ICF Language submission type but will be considered an initial registration as this is the first time the specific language has been submitted to the DAIDS PRO for review.

If a CRS has previously received a Registration Notification from the DAIDS PRO for one informed consent type (e.g., main, pregnancy) and later submits registration documents for a new informed consent type (e.g., stored specimen, short form), the new informed consent type should be submitted as an Additional ICF Type but is considered an initial registration as this is the first time the informed consent form has been submitted to the DAIDS PRO for review.

NOTE: *If a CRS has previously received a Registration Notification from the DAIDS PRO and is only submitting an additional language or informed consent type, the site is NOT required to resubmit the Form FDA 1572/DAIDS IOR Form and the IOR CV with the protocol registration submission.*

The following documents **must** be submitted to the DAIDS PRO for all initial registration submissions:

- A copy of the Form FDA 1572 signed and dated by the IOR (for studies conducted under an IND) OR a copy of the DAIDS IOR Form signed and dated by the IOR (for non-IND studies).
- Investigator of Record CV and other required documentation (current medical license or equivalent).
- Protocol Signature Page (PSP).
- A copy of the CRS's IRB/EC and other applicable RE/Regulatory Authority approval letter(s) (see IRB/EC Approvals" of this manual)
- A copy of the IRB/EC and other applicable RE/Regulatory Authority approved site-specific ICFs (all languages including English translations, if applicable). Refer to Translation requirements" of this manual.
- A copy of the CRS's IBC approval letter, if applicable.
- Clinical Trial Application Form/Document for the site and study
- A copy of the CRS's IRB/EC/Regulatory Authority submission letter(s).
- A copy of all correspondence between the CRS and IRB/EC/Regulatory Authority
- Translation Certificate (if applicable).
- Translation Confirmation Document (if applicable).

NOTE: *If an initial registration submission is missing any required documents or is incomplete, designated site personnel (i.e., CRS coordinator, IOR) and/or additional personnel listed in the DPRS will be sent a Requested Materials notice that details the missing and/or corrected information/materials that must be submitted to the DAIDS PRO for registration processing to continue. The review process will not continue until the requested materials are received at the DAIDS PRO. For information on how to submit requested materials refer to Requested Materials" of this manual. Not submitting all documentation may delay registration.*

When all required documents have been received and reviewed, a CRS will receive a Registration Notification from the DAIDS PRO that will include all languages and informed consent types that have been submitted. The Registration Notification from the DAIDS PRO indicates successful completion of the initial protocol registration process.

If a CRS receives a Registration with Required Corrections Notification, a CRS must make the required corrections and submit them to their IRB/EC for review and approval OR must submit justification for why the required correction(s) will not be made to the DAIDS PRO within 120 calendar days of the date the Required Corrections Notification was issued. For information on how to submit required corrections refer to Registrations with Required Corrections" of this manual.

NOTE: *The 120 calendar days is for submission of IRB/EC approved corrections OR justifications for why the corrections will not be made to the DAIDS PRO.*

Upon successful completion of the DAIDS PRO initial registration process, indicated when a CRS receives a Registration Notification or a Registration with Required Corrections Notification, a CRS will begin receiving safety information for the protocol (i.e., safety reports, safety memos, investigator's brochures, etc.) from the DAIDS RSC Safety Information Center.

If a site-specific ICF(s) does not include all the required basic and appropriate additional elements to comply with U.S. Federal Regulations and DAIDS policies, designated CRS personnel (i.e., CRS Coordinator, IOR) will be notified via a Disapproval Notification from the DAIDS PRO regarding the deficiencies. The Disapproval Notification will outline the deficiencies in the site-specific ICF(s) that must be revised/corrected before a final Registration Notification can be issued.

NOTE: *A Disapproval Notification is not a final notification and DOES NOT indicate successful completion of the protocol registration process.*

For information on the options a CRS has upon receipt of a Disapproval Notification from the DAIDS PRO, refer to VI of this manual.

B. Amendment Registrations

1. Full Version Protocol Amendment Registration

A full version "Protocol Amendment" is a revision to a protocol made by the Protocol Team/Chair/Awardee that requires DAIDS review and final approval/sign-off before implementation. The changes to the protocol are incorporated into the protocol document and will result in a change to the DAIDS protocol version number (e.g., 2.0, 3.0). Sites should refer to the protocol document for information on the protocol registration process for full version protocol amendments.

CRSs should submit the amended protocol, DAIDS-approved Sample ICF(s), and the amended site-specific ICF(s) to their IRBs/ECs/REs and other applicable Regulatory Authority(ies) for review and approval as soon as possible. Per the DAIDS Protocol Registration policy, submission to the reviewing IRB/EC must take place within 45 calendar days for U.S. sites and 75 calendar days for non-U.S. sites of the date the amendment was approved by DAIDS and distributed to the sites.

NOTE: *The 45 or 75 calendar day requirement for submission of full version protocol amendment registration materials is for reviewing IRB/EC only.*

Amendments including any revised site-specific ICF(s) must be implemented immediately (i.e., without delay no later than 5 business days, usually at the participant's next scheduled study visit) upon CRS receipt of all required IRB/EC/ RE/Regulatory Authority(ies)approvals unless the amendment specifies otherwise. DAIDS PRO approval notification is not required for amendments unless specified in the protocol.

The CRS may delay implementing an amendment when the IRB/EC/ RE/Regulatory Authority(ies) approved amendment states the protocol changes will be implemented once specific operational issues (i.e., training on new procedures added in the amendment) are addressed. The IRB/EC/ RE/Regulatory Authority(ies) documentation must be kept in the site's regulatory files for verification by monitors.

When the IRB/EC/ RE/Regulatory Authority(ies) approved amendment and revised site-specific ICFs are not implemented immediately after final IRB/EC/ RE/Regulatory Authority(ies) approval, sites may continue conducting protocol related interactions and interventions with already enrolled study participants under the previously approved version as long as the IOR has determined that this is in the participant's best interest. After receiving final IRB/EC/ RE/Regulatory Authority(ies) approval and while operational issues are being addressed, new participants may only be enrolled under the previously approved version of the site-specific ICFs when the IRB/EC/RE/Regulatory Authority(ies). has determined this is acceptable. The IRB/EC/ RE/Regulatory Authority(ies) determination should be documented in writing and filed in the site's regulatory files.

A CRS must submit full version protocol amendment registration documents to the DAIDS PRO within 14 calendar days of the CRS's receipt of all the required final written IRB/EC approval documentation for the amendment. The submitted documents must include documentation of the date the amended protocol and any revised site-specific.

NOTE: *Sites are strongly advised to document the date the CRS receives each final* IRB/EC/ RE/Regulatory Authority(ies) *approval letter. Documenting this information supports the CRS's action to comply with the DAIDS protocol registration policy regarding submission of amendment and LOA registration materials to the DAIDS PRO within 14 calendar days of receipt of all final* the IRB/EC/RE/Regulatory Authority(ies) *approval letters. This documentation should be kept in the site's regulatory files for verification by monitors.*

If a CRS has received a Registration Notification from the DAIDS PRO for an earlier version of the protocol including all informed consent types and specific language(s), then the registration to a new version of the protocol would be a full version protocol amendment. A CRS that has never received a Registration Notification from the DAIDS PRO for any version of the protocol, language or informed consent type must follow the instructions for Initial Registration of this manual.

NOTE: *If a CRS has submitted a registration packet for a previous version of a protocol prior to a new version being approved by DAIDS and distribution to the sites, the DAIDS PRO will continue to process the registration for the earlier version.*

The following documentation must be submitted to the DAIDS PRO for all full version protocol amendment registration submissions:

- A copy of the site's IRB/EC and other applicable RE/Regulatory Authority approval letter(s)

Refer to Documentation of Institutional Review Board/ Ethics Committee (IRB/EC) and Other Regulatory Entity (RE)/Regulatory Authority(ies) Approvals" of this manual for detailed information.

- Documentation of the date the amended protocol and any revised site- specific ICF(s) were submitted to the reviewing IRB/EC.
- Protocol Signature Page (PSP) to document the commitment of the IOR(s) to conduct the trial in compliance with regulations/laws.
- A copy of the IRB/EC/RE and other applicable Regulatory Authority (ies) approved site ICF(s) (all languages including English translations, if applicable). Refer to section V, "Translation Requirements" of this manual.
- A copy of the CRS's IBC approval letter, if applicable
- Any amended (if applicable) in-country Clinical Trial Application Form/Document for all applicable entities. See the Clinical Trial Application Submission Guidance on DAIDS RSC website for additional information.
- A copy of the CRS's IRB/EC and other applicable /Regulatory Authority(ies) submission letter(s).
- A copy of all correspondence between the CRS and IRB/EC and other applicable RE/Regulatory Authority(ies).
- Translation Certificate (if applicable).

- Translation Confirmation Document (if applicable).

NOTE: *If any Site Specific ICFs registered in the previous version will no longer be utilized at the site, documentation must be submitted that states that the Site Specific ICFs will no longer be utilized at the site.*

NOTE: *Examples of appropriate documentation of the date the amended protocol and any revised site-specific ICF(s) were submitted to the reviewing IRB/EC includes but is not limited to the submission letter from the site to the IRB/EC, a memo from the IOR or designee specifying the date of submission to the IRB/EC.*

NOTE: *If the IRB/EC determines that a full version protocol amendment does not require changes to the site-specific ICF(s), the CRS should document this either in the comments section of the ICF field of the DPRS or with a memo to the DAIDS PRO with the full version protocol amendment registration submission. Otherwise, all previously registered Site Specific ICF types must be submitted with the amended version or Justification for the omission of Site Specific ICF type must be provided. Documentation of approval of the amended protocol is still required from of the site's IRB/EC and other applicable RE/Regulatory Authority(ies) approval letter(s) and any other appropriate documentation from the IRB/EC and other applicable RE/Regulatory Authority(ies) regardless of whether the site specific ICFs were revised.*

NOTE: *Re-consenting participants as a result of amendment (Change or new information that may affect subject participation) is the decision of the CRS's IRB/EC. CRSs should follow their IRB/EC/RE/ Regulatory Authority instructions for re- consenting participants as a result of a full version protocol amendment. For additional information regarding re-consenting see the DAIDS Memo Regarding Timing of Consent and Re-Consent with Updated IRB/EC/RE-Approved Consent Forms on the DAIDS RSC website Site Informed Consent Process Information.*

NOTE: *If a full version protocol amendment registration submission is missing any required documents or is incomplete, designated site personnel (i.e., CRS coordinator, IOR) and/or additional personnel listed in the DPRS will be sent a Requested Materials notice that details the missing and/or corrected information/materials that must be submitted to the DAIDS PRO. For information on how to submit requested materials refer to "Requested Materials" of this manual.*

When all required documents have been received and approved, a CRS will receive a Registration Notification from the DAIDS PRO that will include all languages and informed consent types that have been submitted. The Registration Notification from the DAIDS PRO indicates successful completion of the full version protocol amendment registration process.

NOTE: *A Registration Notification from the DAIDS PRO is NOT required prior to implementing a full version protocol amendment at a CRS.*

NOTE: *Once a new version of a protocol is approved by DAIDS and has been distributed to the sites, a CRS will no longer be able to register for a previous version.*

2. Letter of Amendment (LOA) Registration

CRSs should submit the LOA and any amended site-specific ICF(s) to their IRBs/ECs and other applicable REs/ Regulatory Authority (ies) for review and approval as soon as possible. Per the DAIDS Protocol Registration policy, submission to the reviewing IRB/EC must take place within 45 calendar days for U.S. sites and 75 calendar days for non-U.S. sites of the date the LOA was approved by DAIDS and distributed to the sites.

NOTE: *The 45 or 75 calendar day requirement for submission of LOA materials is for reviewing*
IRB/EC only.

NOTE: *Protocol revisions resulting from LOAs DO NOT affect the DAIDS protocol version. For version tracking purposes at the CRS (i.e., at the request of an IRB/EC and other applicable Regulatory Authority(ies)/Regulatory Authority(ies), CRSs can specify the site (local version number or version date of the site-specific ICF(s) in the header or footer of their site-specific ICF(s). However, the DAIDS protocol version number and/or the final version date of the DAIDS-approved protocol should remain on all site-specific ICFs.*

LOAs including any revised site-specific ICF(s) must be implemented immediately (i.e. without delay no later than 5 business days, usually at the participant's next scheduled study visit) upon a CRS' receipt of all required IRB/EC and RE/ Regulatory Authority approvals DAIDS PRO approval notification is not required for LOA unless specified in the LOA.

The CRS may delay implementing a LOA when the IRB/EC/ Regulatory Authority (ies)/Regulatory Authority(ies) approved LOA states the protocol changes will be implemented once specific operational issues (i.e., training on new procedures added in the LOA) are addressed. The IRB/EC/RE/Regulatory Authority(ies) documentation must be kept in the site's regulatory files for verification by monitors.

When the IRB/EC/ RE/Regulatory Authority(ies) approved LOA and revised site-specific ICFs are not implemented immediately after final IRB/EC/RE approval, sites may continue conducting protocol related interactions and interventions with already enrolled study participants under the previously approved version as long as the IOR has determined that this is in the participant's best interest. After receiving final IRB/EC/ RE/Regulatory Authority(ies) approval and while operational issues are being addressed, new participants may only be enrolled under the previously approved version of the site-specific ICFs when the

IRB/EC/RE has determined this is acceptable. The IRB/EC/ RE/Regulatory Authority(ies) determination should be documented in writing and filed in the site's regulatory files.

A CRS must submit LOA registration documents to the DAIDS PRO within 14 calendar days of the CRS's receipt of all the required final written IRB/EC approval documentation for the LOA. The submitted documents must include documentation of the date the LOA and any revised site-specific ICF(s) were submitted to the reviewing IRB/EC. The DAIDS PRO will not review any revised site-specific ICF(s) unless otherwise noted in the LOA.

NOTE: *Sites are strongly advised to document the date the CRS receives each final IRB/EC/ RE/Regulatory Authority(ies) approval letter. Documenting this information supports the CRS's action to comply with the DAIDS protocol registration policy regarding submission of amendment and LOA registration materials to the DAIDS PRO within 14 calendar days of receipt of all final IRB/EC/ RE/Regulatory Authority(ies) approval letters. This documentation should be kept in the site's regulatory files for verification by monitors.*

The following documentation must be submitted to the DAIDS PRO for all LOA registration submissions:

- A copy of the site's IRB/EC and other applicable RE/Regulatory Authority(ies) approval letter(s)for all Entity(ies) listed on the FDA Form 1572/DAIDs IOR Form (refer to Documentation of Institutional Review Board/ Ethics Committee (IRB/EC) and Other Regulatory Entity (RE)/Regulatory Authority(ies) Approvals" of this manual for detailed information on IRB/ RE/Regulatory Authority(ies))

- Documentation of the date the LOA and any revised site-specific ICF(s) were submitted to the reviewing IRB/EC.

- Protocol Signature Page (PSP) to document the commitment of the IOR(s) to conduct the trial in compliance with regulations/Laws

- A copy of the IRB/EC and other applicable RE/Regulatory Authority(ies) approved site ICF(s) (all languages including English translations, if applicable). Refer to Translation requirements" of this manual.

- A copy of the CRS's IBC approval letter, if applicable.

- A copy of the CRS's IRB/EC and other applicable RE/ Regulatory Authority submission letter(s).

- A copy of all correspondence between the CRS and IRB/EC and other applicable RE/Regulatory authorities.

- Translation Certificate (if applicable).

- Translation Confirmation Document (if applicable).

NOTE: *Examples of appropriate documentation of the date the LOA and any revised site-specific ICF(s) were submitted to the reviewing IRB/EC includes but is not limited to -*

- *the submission letter from the site to the IRB/EC.*
- *a memo from the IOR or designee specifying the date of submission to the IRB/EC.*

NOTE: *Re-consenting participants as a result of LOA (Change or new information that may affect subject participation) is the decision of the CRS's IRB/EC. CRSs should follow their IRB/EC/ RE/Regulatory Authority(ies)instructions for re- consenting participants as a result of the LOA.*

NOTE: *If a LOA registration submission is missing any required documents or is incomplete, designated site personnel (i.e., CRS coordinator, IOR) and/or additional personnel listed in the DPRS will be sent a Requested Materials notice that details the missing and/or corrected information/materials that must be submitted to the DAIDS PRO. For information on how to submit requested materials refer to Requested Materials" of this manual.*

When all required documents have been received, a CRS will receive a Registration Notification from the DAIDS PRO for each LOA registration submission. The Registration Notification from the DAIDS PRO indicates successful completion of the LOA registration process.

NOTE: *LOAs are considered individual amendments to a protocol. Thus, sites must protocol register to all LOAs independent of initial and full version amendment registrations. If a site elects to include a LOA as part of another submission to the IRB/EC/ RE/ Regulatory Authority(ies) (i.e., continuing review, amendment review, and initial review) the site must clearly document all the materials that are being submitted to the IRB/EC/ RE/Regulatory Authority(ies) for review and approval. It is a CRS's responsibility to inform the DAIDS PRO regarding all registrations (i.e., LOA, full version amendment, initial, continuing review) the site is requesting at the time of submission. Failure to register to a LOA may result in a CRS being out of compliance with DAIDS policies and may result in delays in implementing operational changes triggered by LOA registrations.*

NOTE: *All submission types (Initial, Full Version Amendment, LOA) must be submitted independently.*

NOTE: *A Registration Notification from the DAIDS PRO is NOT required prior to implementing a LOA at a CRS.*

C. Sub-Study Registration

A CRS must protocol register to all sub-studies that have a protocol number and/or DAIDS protocol identification number if a site anticipates enrolling participants. A CRS will receive a registration notification for each sub-study that is submitted for protocol registration. CRSs must register to embedded sub-studies as part of the main study registrations. Registration for embedded sub-studies is required for all versions of the main study unless the site informs the DAIDS PRO that they are no longer participating in the embedded sub-study and request deregistration. CRSs should register to stand alone sub-studies as separate registrations and can be done independently from the main study registration. A CRS registering to a stand-alone sub-study is required to submit all required documents (i.e., IRB/EC approval letter(s), site-specific consent(s), Form FDA 1572 and/or DAIDS IOR Form, and IOR CV) when registering to a stand- alone sub-study.

NOTE: *For an explanation of embedded and stand-alone sub-studies refer Definitions of this manual.*

D. Other Submissions

Other submissions are ANY submissions made to the DAIDS PRO that are not Initial, Full Version Amendment or LOA registrations. Below is detailed information on requirements related to "other submissions" a CRS may submit to the DAIDS PRO.

1. Requested Materials

Requested materials are additional and/or corrected materials requested by the DAIDS PRO as a result of an incomplete submission to the DAIDS PRO. If any required documents are missing, incomplete, or are inaccurate, the DAIDS PRO will issue a Requested Materials notice to designated CRS personnel (i.e. CRS Coordinator, IOR). ***This request will stop the registration review process.***

NOTE: *The Protocol Registration review process will not continue until all Requested Materials have been received by the DAIDS PRO.*

A copy of the requested materials must be submitted to the DAIDS PRO in response to a Materials Request Notification as a "materials Request" type submission.

A CRS will receive a Confirmation of Submission notice once the requested materials have been received by the DAIDS PRO.

2. Disapprovals

If it is determined during the DAIDS PRO review process that a site-specific ICF(s) does not include all the required basic and appropriate additional elements to comply with Federal Regulations and DAIDS policies, designated CRS personnel (e.g., CRS Coordinator, IOR)

will be notified via a Disapproval Notification from the DAIDS PRO regarding the deficiencies. The disapproval notification will outline the deficiencies in the site-specific ICF(s) that must be revised or corrected before a final Registration Notification can be issued.

Upon receipt of a Disapproval Notification from the DAIDS PRO a CRS has two options:

1. Make the necessary revisions/corrections and submit the revised document(s) to their IRB/EC and other applicable RE/Regulatory Authority(ies) approval(s) for review and approval. Upon receiving final IRB/EC/ RE/Regulatory Authority(ies) approval for the revised document(s) the CRS must make a "Corrected Materials" submission to the DAIDS PRO, or

2. Submit justification for the omission/changes to the DAIDS PRO via a request for Disapproval Reversal.

Under Option 1 - The following documentation must be submitted to the DAIDS PRO as “Corrected Materials” once a CRS receives final IRB/EC and other applicable RE/ Regulatory Authority approval for the revised document(s) -

- A copy of the site’s IRB/EC and other applicable RE/Regulatory Authority(ies) approval letter(s) and any other appropriate documentation from the IRB/EC other applicable REs/ Regulatory Authority (ies).

  NOTE: *For examples of other appropriate IRB/EC/RE/Regulatory Authority(ies) documentation refer to Documentation of Institutional Review Board/ Ethics Committee (IRB/EC) and Other Regulatory Entity (RE)/Regulatory Authority(ies) Approvals” of this manual.*

- A copy of the IRB/EC and other applicable RE/Regulatory Authority(ies) approved revised site-specific ICF(s).

When ALL required documents have been received and it is confirmed that the required corrections have been made, the DAIDS PRO will issue a Registration Notification.

Under Option 2 - If a CRS believes that a Disapproval Notification has been issued in error, the CRS can submit a request for Disapproval Reversal. A CRS must provide justification and/or documentation explaining why the disapproval should be reversed.

The following documentation must be submitted to the DAIDS PRO to request a disapproval reversal:

- Written justification and/or a copy of any documentation supporting the CRS’s request for the disapproval reversal

A CRS will be notified within 4 business working days as to whether or not the disapproval will be reversed via e-mail from the DAIDS PRO.

3. Registrations with Required Corrections

If a CRS receives a Registration with Required Corrections Notification, a CRS must make the required corrections and submit them to their IRB/EC/ RE/Regulatory Authority(ies) for review and approval OR must submit justification for why the required corrections will not be made within 120 calendar days of the date the Registration with Required Corrections Notification was issued.

A Registration with Required Corrections Notification indicates that a CRS may begin using the site-specific ICFs after protocol activation by the appropriate Operations Center, Data Management/Statistical Center or DAIDS Program.

Upon receipt of a Registration with Required Correction Notification from the DAIDS PRO a CRS has two options:

1. Make the necessary required corrections and submit them to their IRB/EC for review and approval. Upon receiving final IRB/EC and other applicable RE/Regulatory Authority(ies) approval for the corrected document(s) the CRS must make a "Corrected Materials" submission to the DAIDS PRO, or

2. Submit justification for the omission/changes via a "Corrected Materials" submission to the DAIDS PRO.

Under Option 1 - The following documentation must be submitted to the DAIDS PRO as “Corrected Materials”, once a CRS receives final IRB/EC and other applicable RE/Regulatory Authority(ies) approval for the corrected document(s):

- A copy of the site’s IRB/EC and other applicable RE/Regulatory Authority(ies) approval letter(s) and any other appropriate documentation from the IRB/EC other applicable RE/Regulatory Authority(ies).

- A copy of the IRB/EC and other applicable RE/Regulatory Authority(ies) approved revised/corrected site-specific ICF(s).

NOTE: *For examples of other appropriate IRB/EC/ RE/Regulatory Authority(ies) documentation refer to IRB/EC Approvals” of this manual.*

Under Option 2 - If a CRS has believed that a Registration with Required Corrections Notification has been issued in error, the CRS can submit justification and /or documentation explaining why the Registration with Required Corrections Notification should be reversed.

The following documentation must be submitted to the DAIDS PRO as “Corrected Materials”:

- Written justification and/or a copy of any documentation supporting the CRS’s request for the Registration with Required Corrections reversal.

For Option 1 and 2, a CRS will receive an Approval of Required Corrections Notification from the DAIDS PRO when all the required corrections have been reviewed and approved. The official registration date will remain the date the Registration with Required Correction Notification was issued.

4. Administrative Registration

Administrative registrations should occur when a site is not recruiting participants in a NIAID (DAIDS)-supported and/or -sponsored clinical trial but has administrative functions only. Protocol/Grant PI/Protocol Chair/Co-Chair’s routinely make substantial study interventions (decisions and interpretations) that affect study participants even though participants may not be enrolled or seen at the Protocol/Grant PI/Protocol Chair/Co-Chair’s CRS. As a result, the Protocol/Grant PI/ Protocol Chair/Co-Chair’s institutions are considered engaged with the research and must assure compliance with applicable Department of Health and Human Services (DHHS) regulations. For more information on engagement refer to the OHRP guidance document.

Based on U.S. federal regulation 45 CFR 46.103(a), “each institution engaged" in human subject research that is supported and/or sponsored by the DHHS must provide the OHRP with a satisfactory Assurance of Compliance with the regulations, unless the research is exempt under U.S. federal regulation 45 CFR 46.101(b).

For all administrative registrations, DAIDS requires that that the Protocol/Grant PI/Protocol Chair/Co-Chair consults with their IRB/EC and receive documentation in writing of the IRB/EC's decision concerning their protocol review and approval. At least two different kinds of decisions can be made:

1. IRB/EC wants to be involved in reviewing and approving the protocol.

2. IRB/EC does not want to be involved in reviewing and approving the protocol and will rely on another IRB/EC, designated on the Federal Wide Assurance (FWA), for review and approval.

DAIDS will honor the decision of the IRB/EC. The Protocol/Grant PI/ Protocol Chair/Co-Chair (s) need to consult with their IRB/EC and obtain written documentation of the IRB/EC's decision regarding their review and approval of the protocol in order to comply with U.S. federal regulations.

Upon receipt of final approval and/or documentation from the IRB/EC, an administrative registration submission should be made to the DAIDS PRO.

The following documentation must be submitted to the DAIDS PRO for all Administrative Registrations:

- A copy of the IRB/EC approval letter *AND* any other appropriate documentation from the IRB/EC including the IRB/EC decision regarding protocol review and approval.

  NOTE: *For examples of other appropriate IRB/EC/ RE/Regulatory Authority(ies) documentation refer to Documentation of Institutional Review Board/ Ethics Committee (IRB/EC) and Other Regulatory Entity (RE)/Regulatory Authority(ies) Approvals" of this manual.*

- A copy of the Form FDA 1572 signed and dated by the Protocol/Grant PI/Protocol Chair/Co-Chair (for studies conducted under an IND) OR a copy of the DAIDS IOR Form signed and dated by the Protocol Protocol/Grant PI/ Protocol Chair/Co-Chair (for non-IND studies)

- A copy of the Protocol/Grant PI/Protocol Chair/Co-Chair CV and corresponding Medical license/equivalent

A CRS will receive a Registration Notification from the DAIDS PRO for each administrative registration submission when all required documents have been received. The Registration Notification from the DAIDS PRO indicates successful completion of the administrative registration process.

5. Change of Investigator of Record (IOR)

When there is a change in the IOR listed in Section 1 on the Form FDA 1572 or DAIDS IOR Form, a CRS should submit a copy of the revised Form FDA 1572 or the revised DAIDS IOR Form to the DAIDS PRO. To officially change the IOR for a protocol(s), the CRS must submit the documentation within 15 calendar days of the CRS's notification that the current IOR will no longer serve as the IOR for the study. CRS must notify DAIDS when there is a change of IOR in a timely manner.

The following documentation should be submitted to the DAIDS PRO for all Change of IOR requests:

- Memo requesting a change of IOR.
- A copy of the new Form FDA 1572 signed and dated by the new IOR (for studies conducted under an IND) OR a copy of the new DAIDS IOR Form signed and dated by the new IOR (for non-IND studies).
- CV for the new IOR and other required documentation (current medical license or equivalent).
- A Protocol Signature Page for the new Investigator of Record.
- If IRB/EC or RE/Regulatory Authority(ies) approval is required to change the investigator at the CRS, the submission and approval letters from the entity(ies) is required.

A CRS will receive a Change of IOR Approval Notification from the DAIDS PRO when the change of IOR has been reviewed and approved by the DAIDS PRT.

NOTE: *The Change of IOR is NOT official until the CRS receives a Change of IOR Approval Notification from the DAIDS PRO.*

NOTE: *A CRS must notify their DAIDS Office for Clinical Site Oversight (OCSO) representative and/or DAIDS Program Officer when there is a change in CRS Leader or other key CRS site personnel and/or contact information.*

6. Continuing/Annual Review

Per the October 2018 FDA Guidance on FDA-Regulated Clinical Investigations (studies under an IND), IRB/ECs must continue to comply with current FDA requirements for IRB/ECs continuing review at 21 CFR 56.109(f), including for clinical investigations that are subject to both HHS and FDA jurisdiction. IRB/ECs are required to conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year (21 CFR 56.109(f)).

For studies that are NOT conducted under an IND, DHHS regulations, 45 CFR 46.109(e) require that all DHHS supported research undergo continuing IRB/EC review at intervals appropriate to the degree of risk, but NOT LESS than once per year.

As described in §46.109(f)(1)

Unless an IRB determines otherwise, continuing review of research is not required in the following circumstances:

(i) Research eligible for expedited review in accordance with §46.110;

(ii) Research reviewed by the IRB in accordance with the limited IRB review described in §46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8);

(iii) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

(A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

(B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

NOTE: *For the continuing review implementation delay period from July 19,2018 through January 20, 2019, institutions may elect to implement certain "burden-reducing" provisions if they plan to transition their research to comply with the 2018 HHS requirements ("Revised Common Rule"). One of these provisions is the allowance for no annual continuing review of certain categories of research.*

NOTE: *Per §46.115, the IRB/EC or CRS must document the IRB/EC's transition decision (including the date of the decision). CRSs must keep this documentation in their regulatory binder at the site.*

In the above instance, if the site's reviewing IRB/EC elects to implement the burden-reducing provision and determines that a study does not require continuing review under the 2018 HHS continuing review requirements at §46.109(f))(1) and will not conduct continuing reviews annually during the delay period, sites must submit to the DAIDS PRO documentation from the IRB/EC that documents this IRB/EC determination, including reference to the applicable CFR that states the reason an annual continuing review is not required.

If an individual IRB/EC determines that a protocol meets the requirements within §46.109(f) and will not conduct continuing reviews annually, sites must submit documentation from the IRB/EC that documents the determination including reference to the applicable CFR that states the reason an annual review is not required.

For protocols that must undergo continuing review on an annual or more frequent basis, continuing review must be performed prior to the expiration date specified on the IRB/EC approval letter(s) and/or site-specific ICFs. The frequency of ongoing reviews should be documented in IRB/EC policies and procedures and may be protocol/study specific. CRSs can visit the OHRP website for additional guidance related to continuing review.

CRSs participating in NIAID (DAIDS)-supported and/or -sponsored clinical trials, reviewed by the DAIDS Scientific Review Committees and are protocol registered are required to submit documentation of IRB/EC Continuing/Annual review approval to the DAIDS PRO. Continuing/Annual review documentation must be submitted to the DAIDS PRO within 14 days of the CRS receiving final written documentation of IRB/EC Continuing/Annual review approval. The IRB/EC approval of continuing review must be a final approval and not require any modifications or further input by the CRS.

The following documents must be submitted to the DAIDS PRO for all continuing/annual review submissions:

- A copy of the IRB/EC Continuing/Annual review approval/determination letter AND any other appropriate documentation from the IRB/EC. *(Refer to Documentation of Institutional Review Board/ Ethics Committee (IRB/EC) and Other Regulatory Entity (RE)/Regulatory Authority(ies) Approvals" of this manual.)*

- A copy of the IRB/EC approved site-specific ICF(s) if revised at the time of Continuing/Annual review.

- A copy of the CRS's IRB/EC and other applicable RE/Regulatory Authority(ies) submission letter(s).

- A copy of all correspondence between the CRS and IRB/EC and other applicable RE/Regulatory Authority(ies).

NOTE: *All IRB/EC approval letters for Continuing/Annual review must state that the approval is for continuing review (i.e., similar terminology is acceptable: yearly review, annual review)*

NOTE: *Documentation of IRB/EC receipt of continuing review request alone does not satisfy the DHHS requirement regarding documentation of Continuing/Annual review and approval by the IRB/EC.*

NOTE: *The DAIDS PRO will not review any revised site-specific ICF(s) submitted with the continuing/annual review registration submission.*

CRSs will only be sent a Confirmation of Submission notice that indicates continuing/annual review materials have been received by the DAIDS PRO. CRSs will *NOT* receive any additional notifications from the DAIDS PRO for Continuing/Annual review documentation unless there is a problem with the documentation submitted (i.e., incomplete packet or inappropriate review by the IRB/EC). If problems are noted, the DAIDs PRO will follow-up via e-mail to inform the CRS about the deficiencies and to request corrected continuing/annual review documentation.

If a CRS's IRB/EC procedures for expedited review deviate from those as specified in OHRP guidance (i.e., specific pre-approved country procedures), then the CRS must provide documentation of the IRB/EC procedures to the DAIDS PRO at the same time the CRS submits their IRB/EC Continuing/Annual review approval documents. In addition, documentation of any change in timing of the IRB/EC review procedure for Continuing/Annual reviews for the CRS must be submitted to the DAIDS PRO along with the final IRB/EC Continuing/Annual review approval letter(s).

Lapses in Continuing Review

Per the DHHS regulations 45 CFR 46.103(b) and 46.109(e) and OHRP guidance on continuing review, if there is a lapse in continuing review (i.e., If an investigator has failed to provide continuing review information to their IRB/EC or the IRB/EC has not reviewed and approved a research study by the Continuing/Annual review date specified by the IRB/EC), the research at the CRS must stop, unless the IRB/EC finds that it is in the best interest of individual participants to continue participating in the research interventions or interaction. Enrollment of new participants cannot occur after the expiration of IRB/EC approval(s).

CRSs should contact their DAIDS Office for Clinical Site Oversite (OCSO) representative and/or DAIDS Program Officer when there is any lapse and for additional guidance and information.

CRSs should submit IRB/EC lapse documentation (i.e., the site's documentation of the lapse to the IRB/EC and the IRB/EC's response) to the DAIDS PRO.

7. Site Initiated Revisions to Site Informed Consent Forms (ICFs)

Modifications to a CRS's site-specific ICFs are considered site initiated when the changes are made as a result of new information or at the request of the IRB/EC and other applicable REs/ Regulatory Authority(ies).

Revisions to a CRS's site-specific ICFs are only considered site-initiated when revisions have been made after the CRS has received a Registration Notification from the DAIDS PRO for the most current DAIDS-approved protocol version. Any changes made to a CRS's ICF(s) prior to receiving a Registration Notification from the DAIDS will be considered part of the CRS's initial or amendment registration. For additional information on initial and amendment registration submissions refer to Initial Registration and Amendment Registrations of this manual.

Site-initiated revisions DO NOT affect the final DAIDS protocol version number and CRSs must be sure that the correct DAIDS protocol version number, remains on all site ICF(s). For version tracking purposes at the CRS, CRSs can specify the site (local) version number or version date of the site-specific ICF(s) in the header or footer of their site-specific ICF(s). However, the final DAIDS protocol version number and/or final version date of the protocol document approved by DAIDS should remain on all site- specific ICFs as well.

The following documentation must be submitted to the DAIDS PRO for all site-initiated revised ICFs:

- A copy of the site-initiated revised ICF(s).
- A copy of the site's IRB/EC and other applicable RE/Regulatory Authority(ies) approval letter(s) and any other appropriate documentation from the IRB/EC other RE/Regulatory Authority(ies). *Refer to Documentation of Institutional Review Board/ Ethics Committee (IRB/EC) and Other Regulatory Entity (RE)/Regulatory Authority(ies) Approvals" of this manual for detailed information)*

NOTE: *If a site initiated revised ICF submission is missing any required documents or is incomplete, designated site personnel (i.e., CRS coordinator, IOR) and/or additional personnel listed in the DPRS will be sent a Requested Materials notice that details the missing and/or corrected information/materials that must be submitted to the DAIDS PRO. For information on how to submit requested materials refer to Requested Materials" of this manual.*

Once the CRS receives approval from their IRB/EC and other applicable RE/ Regulatory Authority(ies), the CRS may implement the revised site-specific ICFs immediately (i.e. without delay, usually at the participant's next scheduled study visit). The DAIDS PRO will not review the site-initiated revisions to CRS's ICFs.

CRSs will be sent a Confirmation of Submission notice that indicates materials have been received by the DAIDS PRO. CRSs will NOT receive any additional notifications from the DAIDS PRO for site-initiated revisions to site-specific ICFs.

8. Updated Form FDA 1572 or DAIDS IOR Form

When there is **any** major change to the information listed on the Form FDA 1572/DAIDS IOR Form submitted to the DAIDS PRO, a CRS should submit an updated Form FDA 1572 (IND studies) or DAIDS IOR Form (Non-IND studies) to the DAIDS PRO within 15 calendar days.

The following documentation should be submitted to the DAIDS PRO for all Updated Form FDA 1572s/DAIDS IOR Forms -

- A copy of the updated Form FDA 1572 signed and dated by the IOR (for studies conducted under an IND), or
- A copy of the updated DAIDS IOR Form signed and dated by the IOR (for non- IND studies).

NOTE: *If there is a Change of IOR (listed in Section 1 of either form), refer to Change of Investigator of Record (IOR)" of this manual.*

NOTE: *CRSs should submit a copy of the signed and dated Form FDA 1572/DAIDS IOR Form to the DAIDS PRO and retain the original version in their regulatory files at the site.*

CRSs will be sent a Confirmation of Submission notice that indicates materials have been received by the DAIDS PRO. CRSs will NOT receive any additional notifications from the DAIDS PRO for updated Form FDA 1572s or DAIDS IOR Form unless the updated document(s) results in a Change of IOR at the CRS.

9. Deregistration

Any CRS that has completed the DAIDS protocol registration process for a protocol (main or sub-study), must complete the DAIDS deregistration process for each protocol to which it is registered.

NOTE: *Deregistration is NOT automatic when a study is completed.*

Deregistration can occur when:

- The CRS no longer has participants on study (all follow-up has been completed) and does not plan to enroll additional subjects.
- If no participants were ever enrolled at the CRS and the study has closed to accrual.

In addition, a CRS should check with their DAIDS Clinical Trials Network or DAIDS Program Officer to confirm if there are any protocol, network and/or DAIDS specific requirements prior to deregistering with the DAIDS PRO and/or closing/terminating the study with the IRB/EC.

The DAIDS deregistration process is independent of a CRS's closure/termination of a study at their IRB/EC. The IRB/EC's determination to close or terminate a study is *NOT* required for a CRS to deregister with DAIDS. Completion of the DAIDS deregistration process indicates that a CRS's participation in a study is complete but does not reflect the closure of a multi-center study at all CRSs participating in the study.

If a CRS plans to complete the DAIDS deregistration process for a study but will not be closing/terminating the study at their IRB/EC, the CRS should consult its IRB/EC to confirm any requirements and/or standard operating procedures that must be met prior to deregistration. A CRS's IRB/EC may require the continued submission of safety information and/or other data for the study. In this case, deregistration with DAIDS PRO should *NOT* be done until the study has been completed at all participating sites.

The following documentation must be submitted to the DAIDS PRO for all deregistration requests:

- Request stating that the CRS no longer intends to participate in the protocol(s), and/or
- A Copy of the IRB/EC closure/termination letter for the protocol if the protocol has been closed with the IRB/EC at the time of deregistration

A CRS will receive a Deregistration Notification from the DAIDS PRO when deregistration has been reviewed and approved by the DAIDS PRO.

NOTE: *A CRS is not considered deregistered until a Deregistration Notification has been issued by the DAIDS PRO.*

Once a CRS receives a Deregistration Notification for a protocol, the CRS is no longer required to submit any additional protocol registration documents to the DAIDS PRO if the protocol amends. A CRS must continue to follow their IRB/EC requirements for submission of documents if the protocol has not been closed/terminated with the IRB/EC.

Upon completion of the DAIDS deregistration process, a CRS will no longer receive safety information (i.e., safety reports, safety memos, investigator's brochures) from the DAIDS RSC Safety Information Center.

Additional guidance is available regarding the DAIDS registration process along with a summary of site responsibilities once deregistration is complete. This information is located on the DAIDS Deregistration Process Guidance under the "Protocol Registration" section.

VII. Definitions

Clinical Research - Research conducted on participants, material, or data of human origin with an identifiable person as the source. Clinical research includes exploratory, behavioral and observational studies. All clinical trials are a subset of clinical research. (DAIDS)

Clinical Research Site (CRS) - Distinct locations (i.e., hospitals, outpatient clinics, health maintenance organizations, community health centers, private practices, clinics) supported and/or sponsored by NIAID (DAIDS) where qualified professionals conduct clinical research in accordance with good clinical practice (GCP) and applicable regulations. (DAIDS)

Clinical Research Site (CRS) Leader - The onsite senior research scientist responsible for the administrative and scientific components of the CRS. The CRS leader is responsible for overall site activities, including day-to-day operations, performance, and compliance at the site level. (DAIDS)

Clinical Sciences Review Committee (CSRC) - The Division of AIDS internal scientific review committee responsible for the programmatic review of therapeutic protocols sponsored by DAIDS. The review will include careful assessment of the scientific objectives, design, safety, ethics, and feasibility of proposed research protocols. Scientific representatives from collaborating NIH Institutes and Centers participate as appropriate. (DAIDS)

Clinical Trial - A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. (NIAID).

Clinical Trial Applications (CTA): An Investigational New Drug Application for any Product filed with the FDA pursuant to Title 21 of the Code of Federal Regulations, Part 312 ("IND") or the submission to a competent Regulatory Authority within the EU of a request for an authorization concerning a clinical trial, as envisaged in Article 9, paragraph 2, of Directive 2001/20/EC, or any comparable filing made with a Regulatory Authority in another country or territory other than the U.S. or the EU.

Code of Federal Regulations (CFR) - Published by the U.S. Office of the Federal Register National Archives and Records Administration, these are detailed procedures for meeting requirements authorized by law:

> ***Title 21*** - Food and Drugs (covers regulations administered by FDA as authorized by the Food, Drug and Cosmetic Act).
>
> ***Title 45*** - Public Welfare (includes regulations administered by Office for Human Research Protections (OHRP) relating to the protection of human subjects). (DAIDS)

Curriculum Vitae (CV) - A statement of investigator's qualifications including professional experience accomplishments, educational background, and any publications. This document is required for all initial protocol registrations. (DAIDS)

Division of AIDS (DAIDS) - One of six divisions within the National Institute of Allergy and Infectious Diseases. DAIDS is responsible for the initiation, management, and oversight for the clinical trials and research that is sponsored and/or supported by NIAID (DAIDS). (DAIDS)

DAIDS Protocol Registration Office (PRO) - An office within the DAIDS Regulatory Support Contract (RSC) that receives and processes all protocol registration materials for DAIDS. (DAIDS)

DAIDS Protocol Registration System (DPRS) -An internet-based system that allows DAIDS Clinical Research Sites (CRS) to submit and track all documents submitted to the DAIDS Protocol Registration Office (PRO). (DAIDS)

DAIDS Regulatory Support Contract (RSC) - A contract that provides clinical, regulatory and technical support services for NIAID (DAIDS)-supported and/or - sponsored clinical trials. (DAIDS)

DAIDS-sponsored - DAIDS is responsible for the management (including submission of the Investigational New Drug Application (IND) and Investigational Device Exemption (IDE) Application to FDA, and initiation of the study) and oversight for the trial. (DAIDS)

DAIDS-supported - Clinical research activities would be considered to be supported by NIAID (DAIDS) under one or more of the following circumstances:

1. DAIDS provides direct funding to an institution via a grant, contract or cooperative agreement for the clinical research activities; or indirect funding via a subcontract executed under a DAIDS-supported award to another institution.

2. DAIDS provides other tangible support for the clinical research activities which includes, but is not limited to, regulatory support, site monitoring services, study product supply, management and distribution services.

3. DAIDS-supported central laboratory or data management center receives from other organizations specimens or data for processing or analysis and the results or analyses, will be used to direct involvement of participants in clinical research activities. (DAIDS)

Electronic Protocol Registration (EPR) - An alternate way CRSs can submit registration materials via e-mail to the DAIDS PRO if they encounter problems when trying to submit registration materials through the DPRS. (DAIDS)

European Medicines Agency (EMA) - A decentralized agency of the European Union (EU) responsible for the scientific evaluation, supervision and safety monitoring of medicines in the EU.

Food and Drug Administration (FDA) - A public health agency within the United States (U.S.) Department of Health and Human Services. FDA's mission is to promote and protect public health by helping safe and effective products reach the market in a timely way and monitoring products for continued safety after they are in use as authorized by The Federal Food, Drug and Cosmetic Act. (DAIDS)

Form FDA 1572 - FDA required document in which clinical investigators agree to conduct the clinical trials according to U.S. federal regulations. The Form FDA 1572 is signed, and a copy submitted to the IND sponsor. (DAIDS)

Full Version Protocol Amendment - Protocol modifications that result in a change in protocol version number. This new protocol version incorporates any currently proposed changes in addition to those made in all Clarification Memos (CMs) and Letter of Amendments (LOAs) that have been approved since the finalization of the previous protocol version. (DAIDS)

International Conference on Harmonisation (ICH) Guidelines
Developed, through a collaboration between the FDA and regulatory agencies in Japan and the European Union, to "harmonize" regulatory requirements to produce marketing applications acceptable to the United States, Japan, and the countries of the European Union. (DAIDS)

Institutional Biosafety Committee (IBC) - Committee set up by an institution under NIH guidelines to review recombinant DNA research and ensure its appropriate use. IBCs may also review other bio hazardous research, including select agents. (NIAID)

Institutional Review Board/Ethics Committee (IRB/EC) - Committee used by an institution to ensure the protection of human subjects by independently approving, modifying, or disapproving research protocols. (NIAID)

Investigational New Drug (IND) Application - A request for authorization from the FDA to administer an investigational drug or biological product to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biological product that is not the subject of an approved New Drug Application or Biologics/Product License Application. (FDA) An IND application is required by the FDA before clinical trials of an investigational drug or biological agent may be initiated. An IND is also generally required if the U.S. FDA has not approved the route of administration, dosage level, or patient population for the drug or biological agent. (DAIDS)

Investigator of Record (IOR) - The individual at the CRS responsible for ensuring that a clinical trial is conducted in accordance with the protocol, applicable U.S. federal regulations, in-country regulations and any provisions imposed by the reviewing IRB/EC/other regulatory entity. This person is the signatory for the Form FDA 1572 for studies conducted under an IND or the DAIDS Investigator of Record Form for non-IND studies.

Investigator of Record (IOR) Form - A document required by DAIDS for non-IND studies. By signing the document, the IOR accepts full responsibility for conduct of the trial at their CRS. (DAIDS)

Letter of Amendment (LOA) - A revision to a protocol made by the Protocol Team/Chair/Awardee through a letter that requires DAIDS final approval/sign-off before implementation. Changes described in a LOA are listed in a document that is separate from the protocol document itself and will NOT result in the change to the DAIDS protocol version number. (DAIDS)

National Institute of Allergy and Infectious Diseases (NIAID) - NIH institute that conducts and supports research to understand, treat, and prevent infectious, immunologic, and allergic diseases. (NIAID)

National Institutes of Health (NIH) - A Federal agency whose mission is to improve the health of the people of the United States. NIH is a part of the Public Health Service, which is part of the U.S. Department of Health and Human Services. (NIH)

Observational Study - A type of study in which individuals are observed or certain outcomes are measured, but no treatments or interventions are assigned by the study. (DAIDS)

Office for Human Research Protections (OHRP) - U.S. Department of Health and Human Services (DHHS) office overseeing human subject protection regulations for HHS-supported research. (NIH)

Office for Policy in Clinical Research Operations (OPCRO) - An office in DAIDS that provides a variety of clinical research management resources and oversight to the DAIDS clinical research portfolio. This includes overseeing the development, standardization, implementation and execution of policies, procedures and standards of conduct for all DAIDS domestic and international clinical research. (DAIDS)

Prevention Sciences Review Committee (PSRC) - The Division of AIDS internal scientific review committee responsible for the programmatic review of vaccine and prevention protocols sponsored by DAIDS. The review will include careful assessment of the scientific objectives, design, safety, ethics, and feasibility of proposed research protocols. Scientific representatives from collaborating NIH Institutes and Centers participate as appropriate. (DAIDS)

Protocol Registration Notifications - The following are notifications that a CRS may receive from the DAIDS PRO:

1. ***Confirmation of Submission*** - A notification sent out to the CRS Coordinator and IOR confirming that registration materials have been successfully submitted to the DAIDS PRO. If a CRS does not receive a Confirmation of Submission Notification within 24-48 hours of submitting registration documents to the DAIDS PRO, the CRS should contact the DAIDSPRO to find out how to proceed.

2. ***Registration Notification*** - A final notification from the DAIDS PRO indicating that a CRS has successfully completed the protocol registration process.

3. ***Registration with Required Corrections Notification*** -A notification from the DAIDS PRO indicating that a CRS must make required corrections and submit them to their IRB/EC for review and approval OR must submit justification for why the required correction will not be made within 120 calendar days of the date the Registration with Required Corrections Notification was issued. A Registration with Required Corrections Notification indicates that a CRS may begin using the site- specific informed consent forms (ICFs) after protocol activation by the appropriate Operations Center, Data Management/Statistical Center or DAIDS Program.

4. ***Disapproval Notification*** - A notification from the DAIDS PRO indicating that the site-specific informed consent forms (ICFs) do not include all the required basic and additional elements to comply with U.S. federal regulations and DAIDS policy. The Disapproval Notification will outline the deficiencies that must be revised/corrected before a final Registration Notification can be issued. All revised site-specific ICFs must be approved by the IRB/EC prior to submission to the DAIDS PRO. A disapproval notification is NOT a final notification since corrective materials must be resubmitted.

5. ***Deregistration Notification*** - A final notification from the DAIDS PRO indicating that a CRS is no longer registered to a study and all associated sub-studies.

6. ***Change of IOR Approval Notification*** - A final notification from the DAIDS PRO indicating that DAIDS has approved the change of IOR for a protocol at a CRS.

7. ***Requested Materials Notice*** - A message from the DAIDS PRO indicating that additional/corrected materials are required as a result of an incomplete or inaccurate submission to the DAIDS PRO.

A Materials Request Notification stops the registration review process until the requested materials have been received at the DAIDS PRO. (DAIDS)

Protocol Registration Team (PRT) - A team within OPCRO responsible for managing the Protocol Registration (PR) process, which includes oversight of the DAIDS PRO. (DAIDS)

Regulatory Entity (RE)/Regulatory Authority - Any entity/body that has the power to regulate which includes authorities that review submitted clinical data and those that conduct inspections. These are sometimes referred to as competent authorities. These are entities/bodies whose approval/authorization/acknowledgment of a clinical trial is required for conducting a clinical trial. Any organization whose approval is required prior to a CRS's participation in DAIDS funded and/or Sponsored Clinical Trial. Includes but not limited to approvals from state/national health systems and administrative bodies, drug agencies etc. (DAIDS adopted from ICH E6)

Sub-Investigator - Any member of the clinical research team designated and supervised by the CRS Leader/IOR of a protocol at a CRS to perform critical trial related procedures and/or to make important clinical trial-related decisions. (DAIDS)

Sub-Study - A sub-study asks a separate research question from the parent protocol and may or may not contribute to the parent protocol's objectives but uses all or a subset of study participants or specimens. A sub-study can be included as part of the main/parent protocol document or may not be included in the main protocol but requires current or previous participation in the main protocol. (NIAID)

The following are different types of sub-studies that a site may protocol register:

1. ***Embedded Sub-study*** - A sub-study that is part of a main protocol that may or may not have a separate ICF. Embedded sub-studies have the same protocol version number as the main study and have a separate protocol number and/or DAIDS protocol ID number. If there is a full version Amendment to the main study, when protocol registering to the amendment, sites are required to protocol register to all embedded sub-studies. A CRS will receive a registration notification for each embedded sub-study that is submitted for protocol registration. LOA registrations are only completed under the Main study however if the LOA requires revision to the sub-study IC, then the site IC should be submitted under the sub-study as a Site Revised IC.

2. ***Stand Alone Sub-study*** - A sub-study that is not part of the main protocol but requires participants to be enrolled in the main study or have previously participated in the main study. A stand-alone sub-study is an independent protocol that may or may not have the same protocol version number/date as the main study and will always have a separate protocol number and/or DAIDS protocol ID number. A CRS should submit all required documents (i.e. IRB/EC approval letter[s], site-specific informed consent form[s], Form FDA 1572 and/or DAIDS IOR Form, and IOR CV) when registering to a stand- alone sub-study. A CRS will receive a registration notification for each stand-alone sub-study that is submitted for protocol registration. (DAIDS). Amendment and LOA registrations should be submitted independently from the main study.

VIII. DAIDS Protocol Registration Office Contact Information and DPRS Access

The DAIDS Protocol Registration Office (PRO) has two different e-mail addresses - one for submission of protocol registration documents and a second for questions and general correspondence.

A. Contact Information for Questions and General Correspondence

E-mail: protocol@tech-res.com
Phone: 301-897-1707
Office Hours: Monday through Friday 8:30 AM to 5:00 PM (U.S. Eastern Standard Time)

Effective January 2012, all sites participating in NIAID (DAIDS)-supported and/or - sponsored clinical research that requires protocol registration, are required to submit protocol registration materials to the DAIDS PRO through the DAIDS Protocol Registration System (DPRS). Information on the DPRS and how to access the system is available on the DPRS website or information on how to submit protocol registration materials through the DPRS once a CRS has received a user name and password, refer to Appendix A of this manual.

In order to gain access to the DPRS, site personnel must complete the DPRS training that's available online at DAIDS Learning Portal.

First, log in to the DAIDS Learning Management System (LMS) with your user name and password. Then enter DPRS into the search field and select the DPRS training course. If you do not have a DAIDS LMS account, click to request account access.

At the time of completion of the DPRS training, a username and password will be provided to the person who completed the training. If DPRS login details have not been received, contact DAIDS-ES Support at CRMSSupport@niaid.nih.gov.

If a CRS encounters problem when submitting protocol registration materials through the DPRS, a CRS can submit protocol registration materials via e-mail to the DAIDS Electronic Protocol Registration (EPR) mailbox. If a CRS submits materials through the EPR mailbox, the e-mail message must outline the details of what is being submitted, and the kind of registration that is being submitted.

Information on protocol registration timelines is available on the DAIDS RSC Website under the "Protocol Registration" section.

B. Appendix A - Instructions on How to Access and Submit Protocol Registration Materials through the DAIDS Protocol Registration System (DPRS)

How do I gain access to DPRS?

1. DPRS Access

DPRS can be accessed via the DAIDS Learning Portal. DPRS Training completion is required to gain DPRS access. Log into the DAIDS Learning Management System (LMS) with your user name and password. Then enter DPRS into the search field and select the DPRS training course. If you do not have a DAIDS LMS account, click here to request account access.

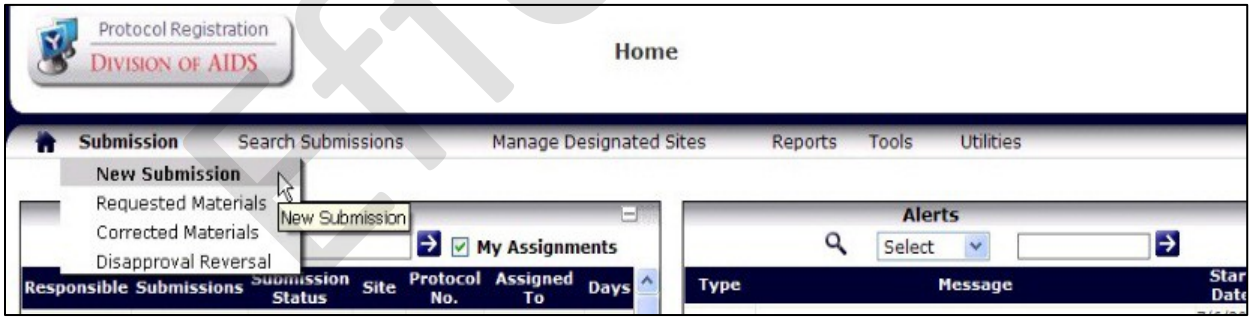
Once the DPRS training has been completed, DPRS user log-in and password will be sent to the trainee. If the training has been completed, but have not received DPRS login details yet, contact DAIDS-ES Support at CRMSSupport@niaid.nih.gov.

2. How do I access the New Submission screen?

Go to the DAIDS Protocol Registration Page. Enter your user name and password and click **Login**.

From the Home Page, click Submission on the main navigation bar and then click New Submission from the drop-down menu, which takes you to the New Submission page.

Figure 1: New Submission Option



3. How do I complete the Site Submission process?

Enter the Submission Details - Enter the appropriate information under the **Site and Protocol details** heading. Click the LOV icon to select the Site, IOR and Protocol No. Click the list of values to select the version/LOA.

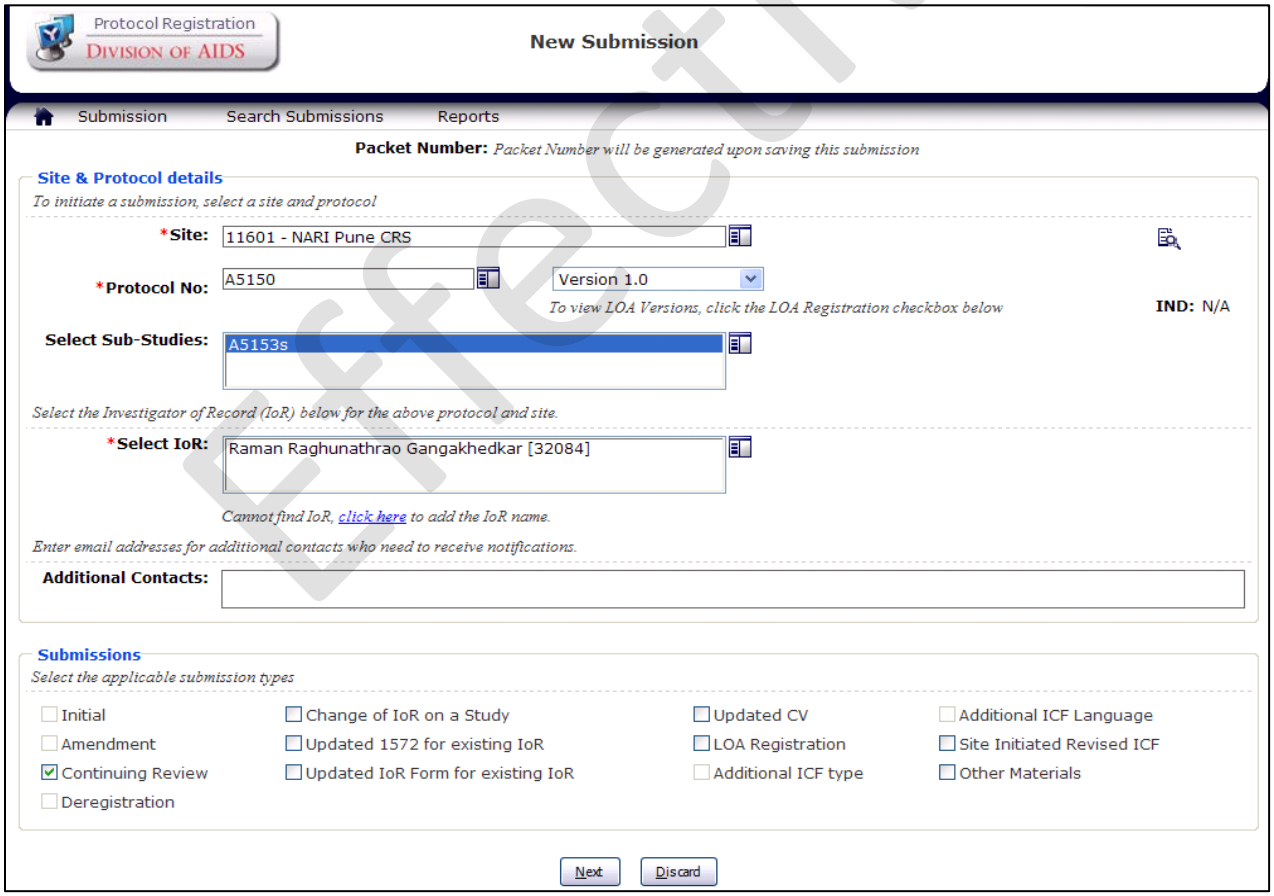
Select Sub-Studies - This list of values displays all embedded sub-studies associated with the study. Select a sub-study displayed to submit materials for the sub-study along with the study. The packet will be created when the main study is submitted.

Submissions - Select the appropriate checkboxes under the Submissions heading.

***NOTE:** The system selects the same submission type for the sub-study as on the main study.*

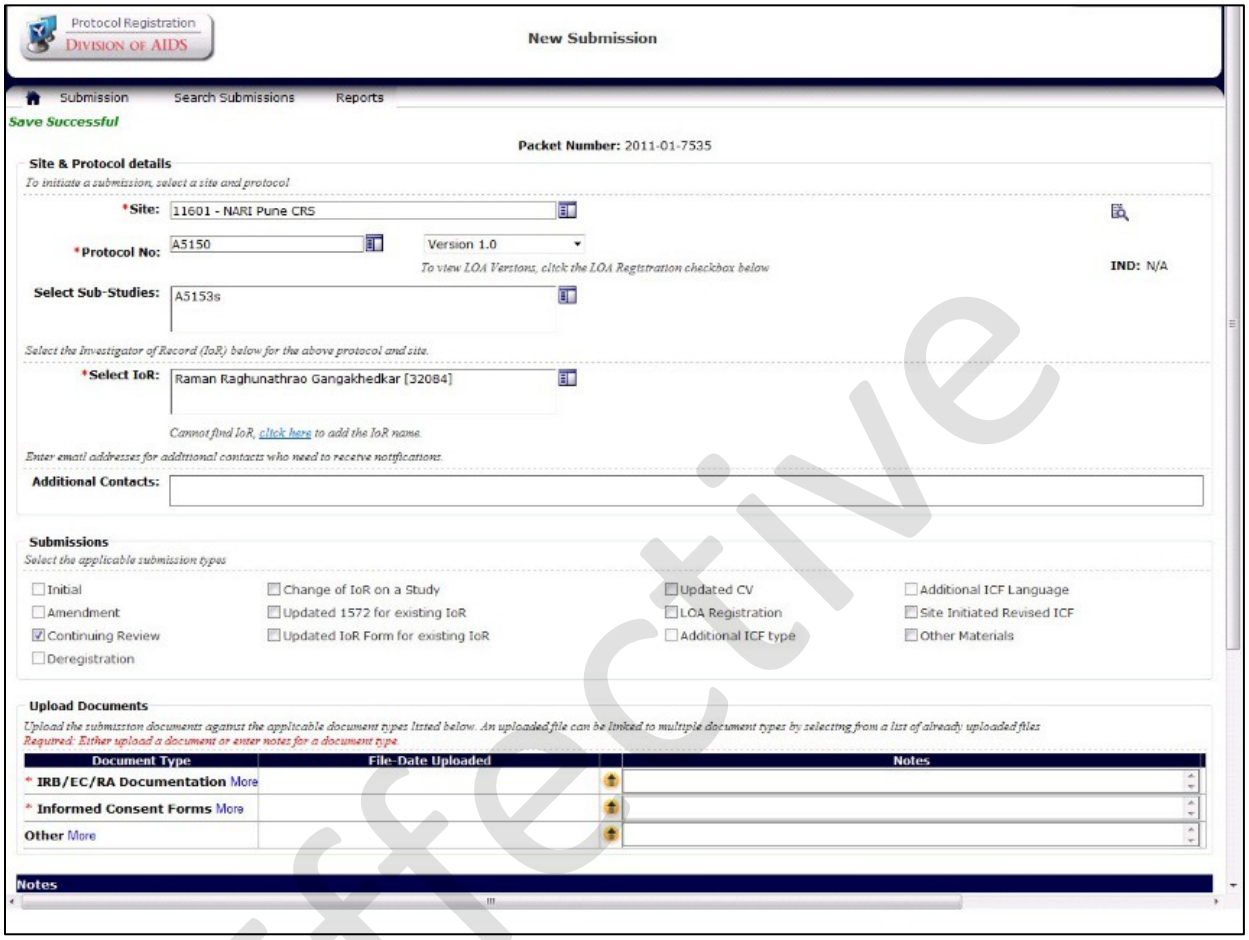
Next - Click **Next**. If the save is successful, the Upload Documents heading appears in the lower half of the screen.

Figure 2: Enter details in the New Submission screen.



Upload Documents - Click the upload icon to upload the appropriate documents. Enter notes to provide additional clarification. Click **Save**.

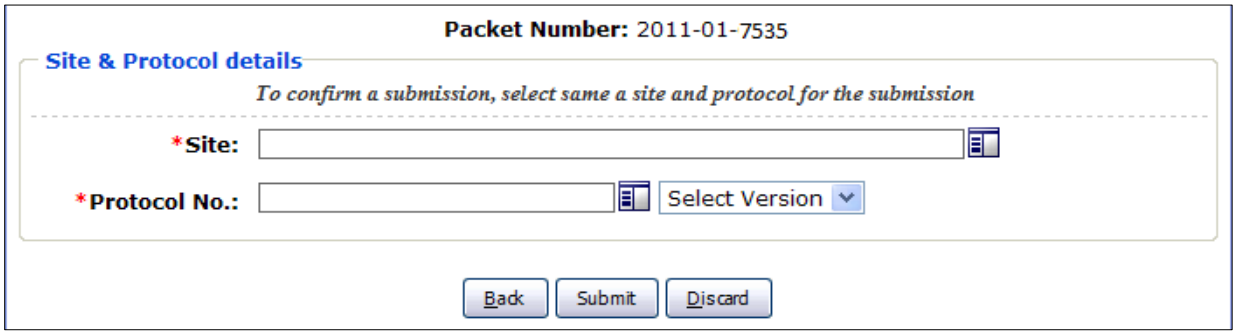
Figure 3: Upload documents in the New Submission screen and add notes.



Confirm Submission Details - When finished, click **Submit**. At the pop-up confirmation window, confirm the Site, IOR Name and Protocol No. Select the version and again click **Submit**.

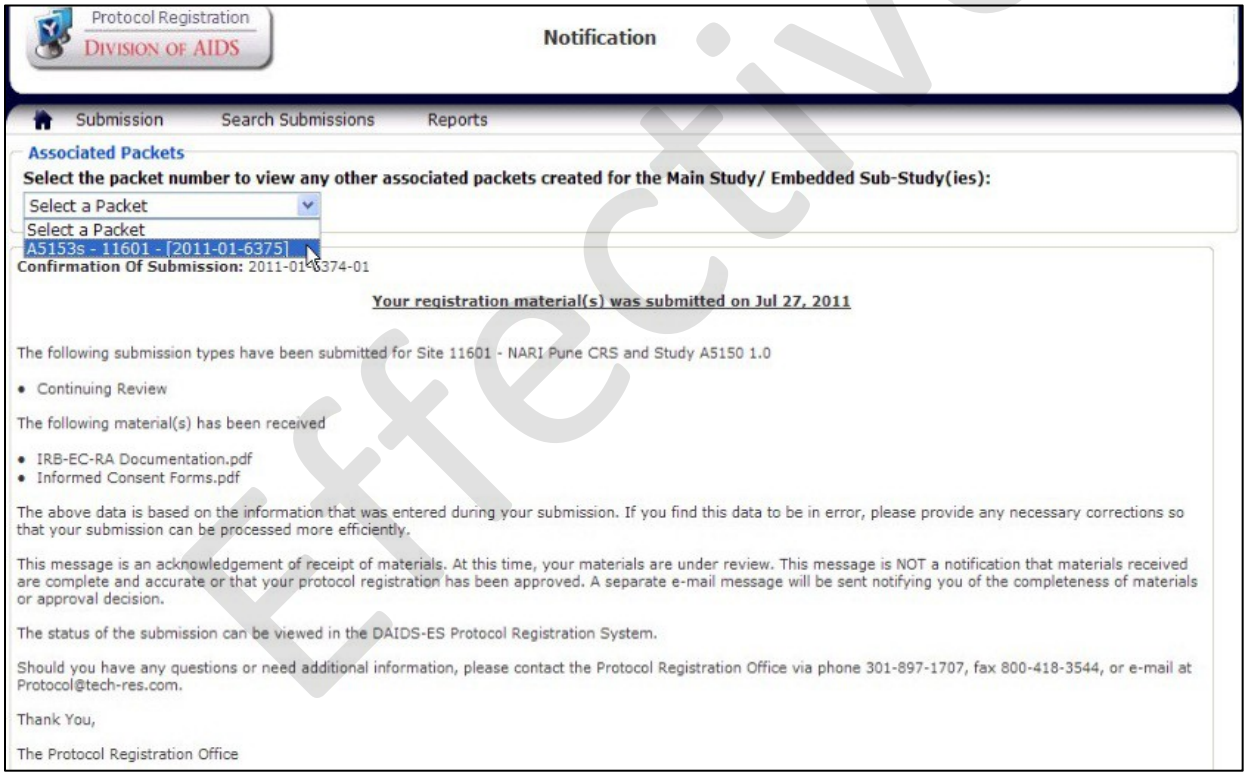
The system confirms whether the submission was successful.

Figure 4: Confirm Submission Details.



Optional - System will provide option to submit sub-study packets that have not yet been submitted by selecting a packet number at the top of the Notification screen.

Figure 5: Navigate to associated packets yet to be submitted.



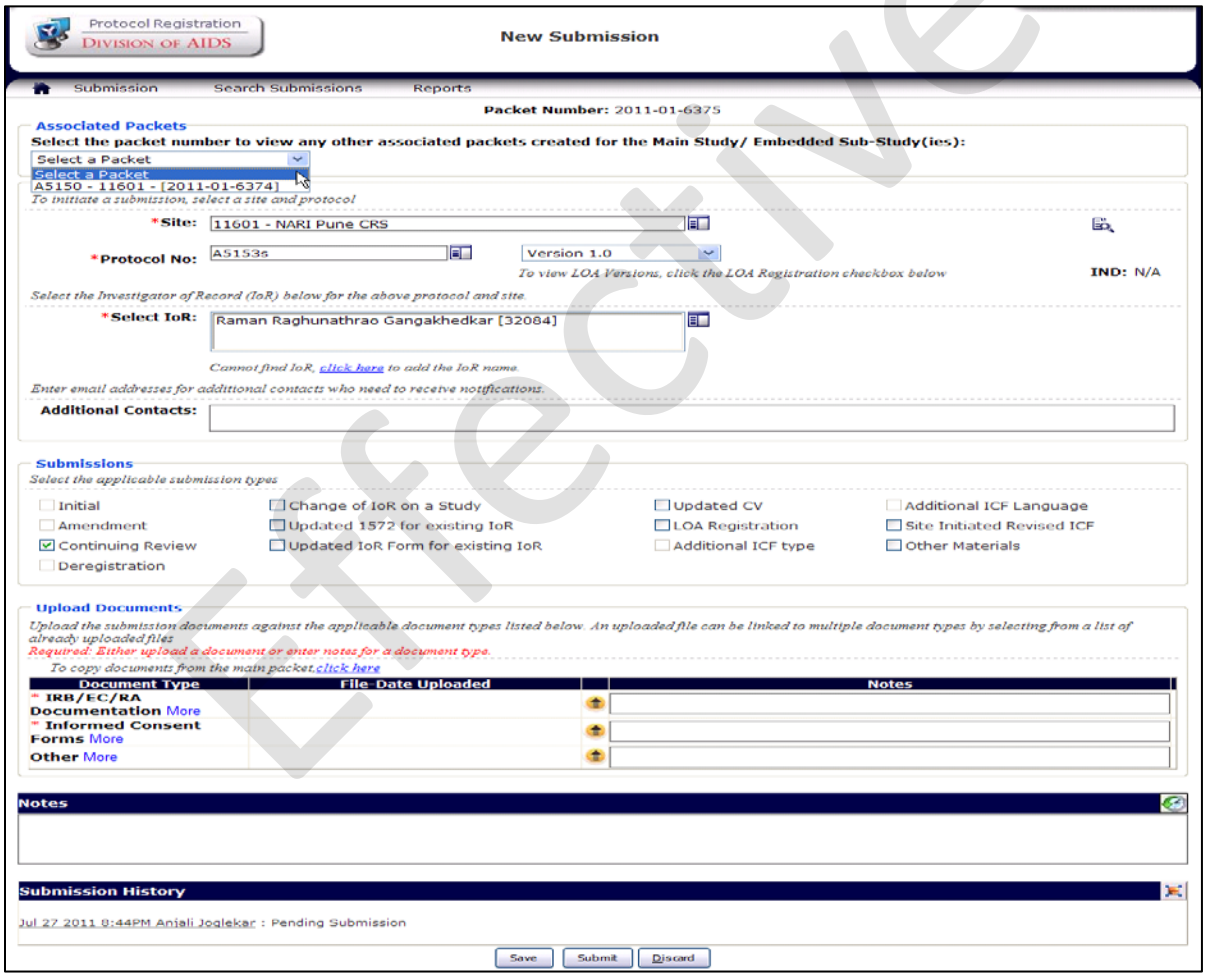
4. How do I view the sub-study packet?

Select a packet number at the top of the screen to view any other associated packets for this study. The Sub-Study screen appears similar to the main submission except the Protocol Number is changed to the sub-study number. The submission type remains the same.

NOTE: *You can use this feature to toggle between the sub-study packets. You also can copy person information to sub- study packets.*

Click the Upload Documents hyperlink in the associated packets to copy documents from the main packet.

Figure 6: Viewing the sub-study packet.



5. Still Have Questions?

E-mail: CRMSSupport@niaid.nih.gov

Phone: 1-240-778-2517

IX. DAIDS Protocol Registration Revision History and Approval

MAN-A15-OPC-001.00 is the initial version of the DAIDS Protocol Registration manual submitted to the DAIDS Quality Management System (QMS) as version 00. Refer to section II. for a detailed list of updates for this version.

There were four previous versions of the DAIDS Protocol Registration Manual, August 2004, March 2010, May 2012, and April 2015 published on the DAIDS Clinical Research Policies webpage prior to the implementation of the DAIDS QMS in 2018

Printed Name/Title	Signature	Date