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Division of AIDS (DAIDS) Site Clinical Operations and Research Essentials (SCORE) Manual: Informed Consent of Participants

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Informed Consent of Participants

Clinical Research Sites (CRSs) are required to develop CRS-specific informed consent forms (ICFs) from the DAIDS-provided protocol/sample ICFs, and to get these ICFs approved from the required entities before administering them to clinical research participants.

The United States (U.S.) Health and Human Services (HHS) 45 Code of Federal Regulations (CFR) part 46 which includes the revised Common Rule, International Council for Harmonisation (ICH) Good Clinical Practices (GCP), also referred to as ICH E6, U.S. Food and Drug Administration (FDA) 21 CFR part 50, other applicable health authorities, and local laws and regulations mandate certain protections for clinical research participants, depending on the risk level they may encounter when participating in clinical research.

Note: All clinical research conducted or supported by National Institute of Allergy and Infectious Diseases (NIAID) must comply with 45 CFR part 46.

For each study, the Protocol team works with DAIDS Clinical Trials Networks to create protocol/sample ICF templates that accurately reflect the content of the protocol document, and meets all applicable regulations, laws, institutional policies and procedures including:

- U.S. CFR requirements from 45 CFR part 46.116.
- National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID), DAIDS policies and any other applicable requirements.
- ICH E6 section 2.8, “Informed Consent of Trial Participants.”
- Other applicable health authorities (such as FDA, European Medicines Agency (EMA), South African Health Products Regulatory Authority (SAPHRA), etc.).
- U.S. FDA-mandated ClinicalTrials.gov language for applicable clinical trials (21 CFR part 50.25[c]).

The Principal Investigator (PI)/Investigator of Record (IoR) must use the DAIDS-provided protocol/sample ICF to create the CRS-specific ICF.

CRS-specific Informed Consent Form Development

When customizing a DAIDS-provided protocol/sample ICF to create a CRS-specific ICF, the PI/IoR must ensure that the CRS follows any Institutional Review Board (IRB)/Ethics Committee (EC) and/or local requirements (e.g., local laws and regulations and institutional policies and procedures). In the absence of specific local requirements for consent, CRSs must follow ICH E6 and U.S. CFR requirements when participating in DAIDS clinical research, if reviewed and approved by their local IRB/EC and/or Regulatory Entity (RE)/Regulatory Authority (RA). Refer to the [DAIDS Protocol Registration Manual](#) for additional guidance on developing CRS-specific ICFs.

CRS-specific ICFs will contain information unique to the CRS (e.g., CRS address, contact information, PI/IoR, clinical research staff, etc.).

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If required by country regulations, CRSs must add applicable insurance information to the CRS-specific ICFs and adopt/revise the following language, as appropriate:

“Consistent with in-country guidelines (add as appropriate: regulations, laws, institutional policies, etc.), our clinic has purchased insurance to cover your medical treatment for trial-related physical injuries that you are experiencing from participating in this clinical trial. We can also provide compensation for (add/clarify as appropriate: type of non-physical research-related injury compensation coverage provided by the site’s policy, e.g., psychological such as emotional distress, social such as family discrimination, financial such as lost wages, etc.).”

Approval of CRS-specific Informed Consent Forms

CRSs must submit their initial, CRS-specific ICFs for clinical research to their applicable local IRB/EC and/or RE/RA for review and approval (herein after referred to as approved ICF). CRSs must then submit the approved initial ICFs to the Protocol Registration Office (PRO) for review and approval.

If the IRB/EC and/or RE/RA requires substantial changes to the content related to the DAIDS-provided protocol/sample ICF, CRS staff must consult with PRO to document these changes.

The CRS must also submit all subsequent, revised, CRS-specific ICFs to the applicable IRB/EC and/or RE/RA for approval. For additional guidance on required approvals from PRO please refer to the DAIDS Protocol Registration Manual.

Implementation of Approved Informed Consent Forms

CRS can only implement initial ICFs after all the required approvals are in place. For the initial ICF, PRO approval is required before consenting potential participants. Once the CRS receives all required approvals, they can consent participants with these approved ICFs.

Note: CRSs **MUST** submit all approved, revised ICFs to PRO; however, CRSs do not have to wait for PRO to approve the revised ICFs to administer them to participants.

Process for Obtaining Informed Consent from Participants

The Informed Consent is a process by which a potential participant or their legally acceptable representative voluntarily confirms their willingness to participate in a trial, after having been informed and been provided with the opportunity to discuss all aspects of the clinical research that are relevant to the participant’s decision to participate (ICH E6 Glossary).

Varied approaches to the provision of information and discussion about the trial can be used. This may include, for example, providing text in different formats, images and videos and using telephone or video conferencing with investigator site staff. Informed consent is documented by means of a written (paper or electronic), signed and dated informed consent form. Obtaining consent remotely may be considered when appropriate. (ICH E6 Glossary).

The consent process starts with participant recruitment, when potential participants are first contacted with the clinical research information. Any clinical research–specific materials used to recruit participants, such as social media platforms, digital advertising, or posters/brochures/flyers, must be reviewed and approved by the IRB/EC and/or RE/RA as applicable prior to use.

All CRSs conducting DAIDS clinical research must develop and implement an Informed Consent Process Standard Operating Procedure (SOP) that describes the CRS’s consenting process and includes references to applicable ICH E6 requirements, local laws, regulations, guidelines, and DAIDS policies. This SOP must describe how CRSs are to document the consent process. The SOP must be submitted to the site’s Office of Clinical Site Oversight (OCSO) Program Officer (PO) for review and approval per the SCORE Manual’s [Quality Management](#) section.

Please see this section’s appendix [CRS Requirements for the CRS-specific Informed Consent Process Standard Operating Procedure](#) for additional requirements of this SOP.

Screening and Enrollment Informed Consent Forms

CRSs will screen potential participants for protocol eligibility criteria before enrolling them in clinical research.

If a protocol/CRS uses a screening-specific ICF, participants are asked to provide personally identifiable information and consent to a limited number of tests/procedures to determine if they meet the inclusion/exclusion criteria and are eligible to enroll. If they are found to be eligible for the clinical research, CRS staff must then obtain additional consent using a separate enrollment ICF before enrolling the participant in the clinical research.

Requirements for the Person Obtaining Informed Consent

PIs/IoRs can delegate the responsibility of conducting the consent process to qualified CRS staff, if permissible by applicable local laws, regulations, and institutional policies. Before delegating such responsibilities, PIs/IoRs must ensure that these CRS staff are qualified by education, experience, documented training, and knowledge of the clinical research.

CRS staff who have a significant role in conducting the consent discussion and obtaining consent must be listed on the Form FDA 1572 or DAIDS IoR Form and the Delegation of Duties (DoD) Log.

In cases where the person obtaining informed consent is not the PI/IoR, the PI/IoR should be available to answer any additional questions posed by the participants, this requirement should be addressed in the site’s consent process SOP.

Parameters and Considerations for Consenting Participants

CRSs must use a private setting to consent potential participants to ensure their comfort and maintain confidentiality of the participant’s personally identifiable information.

To ensure a thorough and compliant consenting process, the person(s) obtaining informed consent adheres to the following practices:

- Introduce themselves and provide information about the CRS.

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- Speak plainly in a language understood by participants that facilitates their understanding of the clinical research and allows them to make an informed decision on whether to participate in the clinical research.
- Consider using an approved script to explain the clinical research for consistency.
- Provide information about the clinical research, pathology, and any general information that may help participants understand why they were invited to participate in the clinical research.
- ** Consider using an approved script to explain the clinical research for consistency.

Present the ICF and/or recruitment materials and ensure that participants understand the form contents by:

- Reviewing all ICF elements in detail with potential participants.
- Allowing participants ample time to read the ICF and other recruitment materials on their own and ask questions about any information in the ICF.

**To facilitate this process, consider providing potential participants with an unsigned, approved copy of ICF and/or recruitment materials before the consenting visit so they have time to read the form and consult with others as needed, before deciding to participate in the clinical research.

Never coerce or attempt to improperly influence a potential participant to enroll in the clinical research.

Before any study-specific procedures (including screening) are conducted:

- Assess whether participants understood the ICF information presented to them, document this assessment of understanding in the source records (e.g., participant research record, study-provided assessment of understanding form/questionnaire, etc.) and answer any questions, address any concerns, and clarify any misunderstandings before all applicable parties sign the ICF.
- The participant and the person obtaining consent must sign and date the consent forms.
- Witnesses and/or Legally Authorized Representatives (LARs), if required by ICH E6, HHS, local laws and regulations, or IRB/EC requirements, must participate in the entire consent process and sign/date the ICF.
- Complete any other local requirements for the ICF signature, such as initialing all ICF pages.
- Provide a copy of the signed ICF as per local requirements/SOP to participants and document in the source records that the ICF (original or copy) was offered to the participants. The person obtaining consent must also note (in the source records) cases where participants refuse to take the signed ICF copy.
- Review the signed ICF and its documentation in the source records to ensure the person obtaining informed consent administered a proper consent process to the participant.

Consenting Language

ICH E6 (section 2.8.1) and HHS/FDA regulations require Informed Consent information be presented to participants using layperson terms to describe scientific and medical terms, in participants' native language or a language they understand.

If potential participants do not speak/understand the ICF language, CRSs should present them with a consent document written in a language and at a language level they understand. CRSs should not exclude potential participants from participating in a clinical research due to language issues and barriers.

When PIs/IoRs can reasonably anticipate potential participants that may not speak/understand the language used in the CRS-specific ICFs, they should submit appropriately translated consent documents in these anticipated languages to the IRB/EC and/or applicable RE/RA for approval. CRS-specific ICFs must meet the following language requirements:

- All translated versions of the ICFs must include the same content as the CRS-specific ICF, regardless of the language used.
- Translated ICFs do not have to use the same phrasing, language, and organization (e.g., section numbering) as the CRS-specific ICFs; however, they must include all concepts included in the CRS-specific ICFs.
- Translations must be either certified or documented appropriately (per a CRS SOP) or according to the DAIDS Protocol Registration Manual).

Please refer to the Translation Requirements section of the DAIDS Protocol Registration Manual for additional guidance.

Use of Short-Form Informed Consent Forms

When permitted by the IRB/EC and local laws/regulations, CRSs may use an alternate method to consent participants such as the use of a short-form ICF.

In this scenario, the person obtaining informed consent would present complete consent information to the participant orally, in a language they understand. The CRS must arrange for an impartial witness (defined below) and/or an interpreter to attend the entire oral presentation. This individual must be fluent in the language used in the CRS-specific ICF and the language understood by the participant.

Per ICH E6 (Glossary), an impartial witness is "a person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the participant or the participant's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject or read to the participant and/or their legally acceptable representative."

An interpreter is an individual who provides an oral translation between speakers who speak different languages.

Impartial witnesses and/or interpreters:

- Must be impartial third parties who are not connected with the clinical research (i.e., not involved in the design, conduct, or reporting) and allowed per the CRS Consent SOPs and Institutional Policies.
- May be a family member or friend, participant advocate, institution member not involved in the clinical research or who does not work directly for the PI/IoR, or anyone who can act in the participant's best interest.

In addition to the detailed oral presentation, person obtaining consent must:

- Provide participants with a signed and dated short-form ICF, in a language understood by the participant, that states the person obtaining consent presented HHS and FDA required elements of consent orally. This short-form ICF must state that the person obtaining consent presented participants with concise, focused, key information most likely to assist potential participants in understanding why they may want to participate in the clinical research (45 CFR part 46.116[a][5][i]) before discussing other information about the study (45 CFR part 46.117[b][2]).
- Provide participants with an approved written summary of their oral presentation or approved ICF.

In this scenario, the impartial witness and/or an interpreter is needed to:

- Corroborate that the participant's consent was voluntary, and the consent process was adequate.
- Ensure the informed consent information was accurately explained, and the person obtaining informed consent/PI/IoR addressed the participant's questions satisfactorily.

While applicable rules may permit CRSs to use the procedures described above to recruit and consent participants who do not speak any of the languages spoken by the site staff, CRSs should consider how they will communicate with these participants throughout the clinical research. Particularly for studies that carry more than minimal risk, CRSs should plan how they will address future communications, e.g.: when adverse events (AEs) require oral or written communication and an interpreter is not available (occurs over the weekend).

Consenting Illiterate Individuals

CRSs may consent and enroll individuals who speak and understand the language used for the consenting process (including ICFs) but do not read and write this language. These individuals may participate in clinical research by consenting orally and either "making a mark" or by adding a fingerprint/thumbprint on the ICF, as long as these methods of consent meet applicable local laws and regulations, CRS Consent SOPs, and institutional policies and procedures. In the participant's research record, CRSs must indicate why there is no participant signature, how they communicated with the potential participant, and how the potential participant communicated agreement to participate in the clinical research (e.g., participant used a thumbprint on the ICF). An impartial witness must participate in the entire consent process, sign/date the consent document, and add the participant's name and date in the ICF's "participant" fields.

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To ensure a complete understanding, CRSs may implement a process to assess participant literacy, as needed. CRS must obtain required approvals before using specific tools to assess participant literacy.

Consenting Populations Requiring Additional Protections

CRSs with adequate, established provisions (45 CFR part 46 subparts B, C, and D as well as 21 CFR part 50 subpart D) may consider consenting potential participants that require additional protections during the consent process, such as pregnant women, fetuses and neonates, or participants that are vulnerable to coercion or undue influence. Vulnerable populations may include minors; prisoners; wards; individuals with impaired decision-making capacity; members of a group with a hierarchical structure; individuals with incurable diseases; individuals in nursing homes; refugees; individuals in emergency situations; lesbian, gay, and bisexual populations; women in some global cultures such as with limited rights; and economically or educationally disadvantaged individuals. CRSs must communicate with the Protocol Team before enrolling any participants that require additional protections to seek approval unless a specific protected population is pre-approved to be enrolled in the clinical research by the Protocol Team, e.g. minors in pediatric clinical research.

All CRSs need to provide the additional protections mandated for pregnant women, fetuses and neonates, and vulnerable populations by 45 CFR part 46 subparts B, C, and D as well as 21 CFR part 50 subpart D for FDA regulated research.

MINORS IN CLINICAL RESEARCH

Children and adolescents (Minors) are individuals younger than the legal age required to consent to treatments or procedures involved in clinical research. Legal requirements for classifying an individual as a minor may vary in different locations. CRSs must define consenting age using applicable laws of the jurisdiction where the study will be conducted.

Where applicable, the PI/IoR in conjunction with the IRB/EC may determine that minors can give assent to participate in the clinical research. As such, CRSs should engage the minor in the clinical research discussion using age-appropriate information. The IRB/EC must determine whether adequate provisions exist for obtaining minor's assent and parent/legal guardian permission. The IRB/EC may also decide that the assent is not needed.

It is important to note that in some cases, an assent is available/approved by the IRB/EC, but the minor has intellectual disparity/delay and cannot read/understand the assent. In those cases, CRSs must include adequate documentation to support the lack of assent in the source records and inform the IRB/EC, if applicable.

In cases where minor participants are unaware of their disease/diagnosis due to parental/legal guardian's decision and for that reason, the approved assent cannot be obtained, CRSs must discuss the case with the parent(s)/legal guardian and consult with the IRB/EC. If local laws and regulations allow, PI/IoR in conjunction with the IRB/EC may generate and approve a generic assent without disclosing the minor's disease/diagnosis. Minor participants must be consented using the CRS-specific ICF if they reach the locally defined age of majority during the course of the study, in order to continue participating in the clinical research.

CRS-specific Responsibilities for Enrolling Minors (including Adolescents) in Clinical Research

DAIDS requires CRSs to develop and implement a CRS-specific SOP for enrolling minors in DAIDS clinical research that aligns with local laws, regulations, institutional policies and procedures, and DAIDS requirements. CRSs must submit this SOP to the OCSO PO for review and approval per the SCORE Manual's [Quality Management](#) section.

CRSs should ensure that all CRS staff involved in consenting minors have documented training on this SOP. Refer to the [Clinical Research Site Requirements for Enrolling Minors into DAIDS Clinical Research](#) appendix to this section for additional guidance on DAIDS requirements for enrolling minors in DAIDS clinical research.

PIs/IoRs must ensure they inform Protocol Registration Office (PRO) of the IRB/EC determinations on enrolling minors, including risk/benefit analysis, IRB/EC approval of studies and amendments, and decisions regarding the need for waiver of an assent from a minor. Please refer to the DAIDS Protocol Registration Manual for specific submission requirements.

Obtaining Parental/Legal Guardian Permission and Legally Authorized Representative Permission

For studies that will involve minors, PI/IoR must ask the IRB/EC to determine what criteria CRSs need to meet so that they may solicit each minor's parent/legal guardian permission for the minor to participate in the clinical research; this is required by 45 CFR 46 Subpart D, ICH E6, and 21 CFR Subpart D for FDA-regulated research.

For non-FDA regulated, U.S.-based clinical research, IRBs/ECs may determine that parental/legal guardian permission is not a reasonable requirement or effective means to protect minor participants (e.g., neglected or abused minors). Therefore, IRB/EC may waive the permission requirements and substitute this permission with an appropriate mechanism to protect participants. The IRBs/ECs would choose the most appropriate mechanism by evaluating the nature and purpose of the protocol's procedures; the risk and anticipated benefit to participants; and participants' age, maturity, status, and condition.

Parental/Legal Guardian Permission

Where CRSs need to obtain parental permission to conduct clinical research involving minors, the IRB/EC may determine that CRSs only need permission from one parent, unless local laws and regulations require both parents' consent.

Where a clinical research is approved under 45 CFR part 46.406 and 46.407 (or 21 CFR part 50.53 or 50.54 for FDA-regulated research) and any other local regulation that requires CRSs to obtain permission from both parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the minor's care and custody. CRSs must document parental permission as required by 45 CFR part 46.117 (and 21 CFR part 50.27 for FDA-regulated research) and applicable local requirements.

Legal guardian permission may replace parental permission in cases where both parents are deceased, unknown, incompetent, or not reasonably available. Guardian is defined as an individual who is authorized

under applicable State or local law to consent on behalf of a minor to general medical care (45 CFR part 46.402(e)).

Legally Authorized/Acceptable Representative Permission

The laws of the jurisdiction where the clinical research is being conducted (e.g., local laws, institutional policies, etc.) determine who can act as a LAR. As per ICH E6 and 45 CFR 46, a participant's LAR is:

"An individual or judicial or other body authorized under applicable law to consent, on behalf of a prospective participant, to the participant's participation in the clinical trial. When a legally acceptable representative provides consent on behalf of a prospective participant, activities related to the consenting process (and re-consent, if applicable) and, where relevant, activities associated with the withdrawal of consent described in this guideline are applicable to the participant's legally acceptable representative." (ICH E6 Glossary).

"An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to the participant's participation in the procedure(s) involved in the research. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective participant to the participant's participation in the procedure(s) involved in the research." (45 CFR part 46.102[i]).

LARs should consider whether clinical research participation is in the potential participant's best clinical interest and base their decision on the participant's preferences and values when applicable.

For participants whom a LAR provided informed consent, if the participant subsequently regains the ability to provide independent informed consent, the participant must be consented again to continue participating in the clinical research.

Ongoing Consent Process

The consent process does not end when a CRS obtains a signature on an ICF. Rather, the process is ongoing through the entire clinical research until the participant decides to end participation or until the clinical research closes. CRSs must maintain informed consent by promptly providing participants with any new information and/or substantive changes in conditions or procedures that arise during the clinical research (e.g., changes in risk, benefit, etc.) that may affect the participants' decision to continue participating. The method used to inform already enrolled participants is determined by the IRB/EC and/or applicable RE/RA.

If determined by the IRB/EC and/or applicable RE/RA, CRSs will revise ICFs to include important new information and/or changes to the clinical research that are relevant for potential and enrolled participants. CRSs will use the revised, approved ICFs to consent new participants to join the clinical research and will provide the new information to already enrolled participants via the revised approved ICF or other applicable approved method. Already-enrolled participants must be consented to the most current version of the approved ICF(s) during their participation in the study. IRBs/ECs will determine if it is necessary for CRSs to obtain the participant's consent to the changes or new information based on the nature of the change in the clinical research and the new information that warranted the change. This process is referred to as re-consenting the participant.

The path for CRSs to notify participants of such new findings or changes may depend on the impact to participants of the clinical research, risk and the urgency of communicating such information. Final determination for the appropriate method for informing participants of any important new information and/or changes to the clinical research is usually decided by the IRB/EC.

CRSs must document participant receipt of this new information.

When CRSs re-consent participants, they need to provide participants a signed and dated copy of the most recent, approved ICF (ICH E6 2.8.11).

ICH E6 section 2.8.2(p) states:

“... that the participant or the participant’s legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject’s willingness to continue trial participation. The communication of this information and confirmation of the willingness to continue trial participation should be documented.”

HHS regulations at 45 CFR part 46.116(c)(5) and FDA regulations at 21 CFR part 50.25(b)(5) state:

“A statement that significant new findings developed during the course of the research which may relate to the participant’s willingness to continue participation will be provided to the participant.”

ICH E6 (section 2.8.2) uses the phrase “timely manner” but does not quantify this term; U.S. regulations and applicable guidance’s do not mandate a timeframe for CRSs to provide participants with the new information. To ensure alignment on timing, DAIDS expects that when ICFs used in DAIDS clinical research change, that CRSs revise and submit these updated CRS-specific ICFs to the IRB/EC and/or applicable RE/RA for review and approval and implement updated ICFs “immediately” upon receipt of the approved ICF. In this context, DAIDS defines “immediately” and the ICH E6 language use of “timely manner” as “without delay”. Based on this, participants should be re-consented using the most recent approved CRS-specific ICF(s) without delay, usually by or at the participant’s next study visit if the IRB/EC and/or applicable RE/RA determines that re-consent is required.

Note: Participants do not need to attend a visit outside the protocol schedule to re-consent unless the IRB/EC and/or applicable RE/RA stipulates (e.g., participants may be asked to come to the clinic if the revisions are due to a safety issue, etc.).

Addenda

An addendum is a supplement to the ICF or another way of conveying new information to already enrolled participants; therefore, it does not need to contain all of the regulatory required elements of informed consent. The PI/IoR must also be aware about local regulations and IRB/EC requirements before implementing this type of document.

Some countries do not permit addenda to the ICF and in those cases a new revised ICF must be generated.

Each addendum must be approved by the IRB/EC and/or applicable RE/RA before it is provided to participants, and its use must be documented in the participant's research record to provide written documentation of the participant's receipt of the new information and willingness to continue clinical research participation. An addendum may include PI/IoR/designee and participant signature blocks as directed by the IRB/EC IRB/EC and/or applicable RE/RA.

CRS Considerations to Prevent Delays in Implementing Revised Informed Consent Forms

To prevent delays in implementing updated, CRS-specific, approved ICFs ("approved, updated ICFs" in this subsection), CRSs should consider the following actions:

Administrative Steps: CRSs should anticipate and prepare for any administrative steps they will need to take to implement approved, updated ICFs at the same time they submit the updated ICFs for review/approval.

Consider the following:

- Checking participant visit schedules to be aware of upcoming visits that may occur when the approved, updated ICFs are available for use
- Copying the updated ICFs (once approved) for distribution to participants using a different color paper to differentiate from previous ICF version.
- Removing old ICFs from use once the IRB/EC and/or applicable RE/RA communicates that it has approved the updated ICF
- Performing quality control activities on approved ICFs.
- Familiarizing staff with protocol and ICF changes that do not require additional training
- Ensuring all relevant clinical research staff are aware of the forthcoming, updated ICF.

Training: To ensure a prompt, efficient consent/re-consent process, CRSs should define any CRS staff training (and accompanying documentation) necessitated by the revised ICF and protocol.

Staffing Issues: CRSs should ensure coverage/back-up staff to prevent delays in implementing the most recent approved ICFs.

Closing Clinical Research

Once the study has concluded, as part of the ongoing consent process, participants should be notified of aggregated findings that may or may not impact each individual participant. Furthermore, if these findings result in changes to standard of care for the condition under study, alternative treatments and/or post-trial access information should be provided to all participants.

Documenting Informed Consent

To ensure an ICF is completed appropriately and the consent process is adequately documented, CRS staff need to review applicable law(s), IRB/EC requirements, institutional policies, internal site SOPs (i.e., their Consent Process SOP), and the approved protocol.

When a participant signs an ICF and/or assent documents (initially and for any re-consent), their signature denotes that the participant (or the LAR on behalf of a participant) is willing to participate in the clinical research. The person obtaining informed consent must ensure they document the consenting process completely in participants' research records, detailing:

- The participant signed/dated (including time stamp, if required) the ICF before being subjected to any clinical research procedures.
- The CRS supplied the participant with a copy of the signed ICF and whether the participant accepted or refused the document.
- The participant had time to read and understand the ICF's content.
- The participant had questions related to the ICF or the clinical research.
- Who participated in the consenting process (e.g., witness, PI/IoR, participant/LAR, or person obtaining informed consent).
- The participant understood the ICF presented and how CRS staff assessed their understanding.
- The CRS staff clarified any misunderstanding after assessing a participant's understanding of the ICF.
- ICF version and date.

Considerations for Signatures on Informed Consent Forms

In general, individuals must sign ICFs using their legal names, but participants may adopt any designation (e.g., traditional signature, a mark, thumb print, or other method of "making their mark") as a signature for the duration of the clinical research, as permitted by local law or institutional standards.

Please note:

- Participants must use their complete first and last names; they are not allowed to use initials.
- Participants providing consent should date the ICF, not CRS staff.

- CRSs should verify participants' legal name, where possible.
- Person obtaining informed consent must review the consent forms for completion before signing and dating the consent forms.

Person(s) obtaining informed consent may obtain an electronic signature (e-signature) to document informed consent, if e-signatures are legally valid within the local jurisdiction where the study is being conducted and the IRB/EC and/or applicable RE/RA has approved e-signatures to document informed consent. The person obtaining informed consent should be able to verify that the e-signature is legitimate. The CRS's informed consent process SOP should include relevant information about this alternative process, as applicable. As per FDA guidance, an e-signature is considered to be the "legally binding equivalent of the individual's handwritten signature" (21 CFR part 11.3[b][7]). Refer to the [Electronic Systems](#) section of the manual for additional information on e-signatures.

Waiving the Requirement for Signed Informed Consent Forms

HHS and FDA regulations allow an IRB/EC to waive the requirement for U.S.-based CRSs to obtain a signed ICF for some or all participants.

If the IRB/EC waives this consent requirement, the IRB/EC may:

- Require person(s) obtaining informed consent to provide participants with a written ICF or summary research statement (e.g., information sheet).
- Determine that person(s) obtaining informed consent may accept the participant's oral consent, or in the case of online survey research, that the participant's consent is implied by their completing the survey instrument.

When an IRB/EC waives the requirement to obtain a signed ICF and approves obtaining the participants' verbal consent, the person obtaining informed consent must:

- Provide participants with all relevant clinical research information (e.g., review the basic elements of Informed Consent 45 CFR part 46.116 and 21 CFR part 50.25, if applicable).
- Answer participant questions.
- Confirm that participants understand the information provided.
- Document the date (and time, when required) they obtained verbal consent in participant research records.
- Document what information they provided to participants (e.g., information sheet) in participant research records.

Electronic Informed Consent Guidance

Electronic Informed Consent (eIC) refers to using electronic systems and processes to convey clinical research-related information and to obtain and document informed consent. CRSs must use electronic systems and processes that comply with: FDA regulations in 21 CFR part 11, similar electronic signature/record rules in the CRS's jurisdiction, and the [Electronic Information Systems Policy](#). CRSs may include text, graphics, audios, podcasts, and interactive case report forms (CRFs) in their eICs.

Approval for Electronic Informed Consent

The IRB/EC and/or applicable RE/RA must review and approve eICs and any amendments to the eIC.

Electronic Informed Consent Process

The eIC must contain the same required elements of written informed consent unless the IRB/EC approves a process that alters or waives some or all elements.

CRSs must present information in eICs clearly and in a format and language that potential participants understand. This includes spelling out abbreviations on first use.

CRSs should take steps to accommodate individuals who have impairments such as poor vision or limited motor skills or who are unfamiliar with electronic devices.

The eIC process must allow potential participants to ask questions and receive answers by any means or combination of methods, such as messaging, telephone calls, or videoconferencing before signing the eIC.

If the eIC is interactive, it must be easy to use and allow potential participants to go back and review information.

Electronic Informed Consent Confidentiality

CRSs may transmit a printed or electronic copy of the eIC to participants. If the eIC is transmitted using an individual's electronic device such as a smartphone, CRSs should advise participants of the risk of loss of confidentiality.

Electronic Informed Consent Assent

CRSs may also use the eIC process to obtain assent from minors. The language and presentation of the information must be understandable to minors. The requirements for documenting assent are the same as that used for adult participants.

Documenting Electronic Informed Consent

As required for any type of consent, all details about the consenting process must be documented in the participant's research records. If CRSs conduct the consent process remotely, they must use software that documents interactive responses and signatures by participants and/or other parties electronically. The system must capture the date that participants give consent. CRSs must provide a copy of the eIC to the individual signing the form.

Appendices

1. [Clinical Research Site Requirements for the CRS-specific Informed Consent Process Standard Operating Procedure](#)
2. [Clinical Research Site Requirements for Enrolling Minors into DAIDS Clinical Research](#)

References

1. [U.S. Code of Federal Regulations, Title 21, Parts 11, 50, 54, 56, 312 and 812](#)
2. [U.S. Code of Federal Regulations, Title 45, Part 46 and Subparts](#)
3. [International Council for Harmonisation Good Clinical Practice \(ICH E6\)](#)
4. [FDA Guidance: Investigator Responsibilities - Protecting the Rights, Safety, and Welfare of Study Subjects \[Oct 2009\]](#)
5. [Office for Human Research Protections \(OHRP\)](#)
6. [HHS -Revised Common Rule](#)
7. [Impact of Certain Provisions of the Revised Common Rule on FDA-Regulated Clinical Investigations](#)
8. [DAIDS Protocol Registration Manual](#)
9. [National Institute of Health \(NIH\) Central Resource for Grants and Funding Information](#)
10. [Genetic Information Nondiscrimination Act Guidance \(2009\)](#)
11. [NIH Genomic Data Sharing Policy](#)
12. [OHRP Informed Consent Frequently Asked Questions;](#)
13. [FDA Draft Guidance 7/2014: Informed Consent Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors;](#)
14. [FDA Draft Guidance 6/2017: Use of Electronic Records and Electronic Signatures in Clinical Investigations Under 21 CFR Part 11 – Questions and Answers Guidance for Industry](#)
15. [OHRP Guidance: Informed Consent of Subjects Who Do Not Speak English](#)
16. [OHRP and FDA Use of Electronic Informed Consent: Questions and Answers. Guidance for IRBs, Investigators, and Sponsors, December 2016;](#)
17. [OHRP Use of Electronic Informed Consent: Questions and Answers](#)
18. [E11\(R1\) Clinical Investigation of Medicinal Products in the Pediatric Population](#)

Revision Summary

Version/ Revision	Summary of Changes
1.0	Original Version and became effective on 1/19/2021.
2.0	Corrected typos on pg. 3 and 12.; version became effective on 6/30/2021
3.0	Pgs. 6-7 - Clarified the sequence/timing to assess participant comprehension of study requirements as part of the ICF process. Updates hyperlinks to Reference #s: 4, 14. Corrected version number. Version became effective on 6/10/2024.
01	DAIDS-OCS-A28-MAN-00019 rev 01 is the first revision of this manual in MasterControl and became effective 8/16/2025. The document number and format were updated to meet current requirements of new document management system. Removed language to align language as required by current Executive Orders. Aligned with International Council for Harmonisation Good Clinical Practice (ICH E6(R3))
02	DAIDS-OCS-A28-MAN-00019 rev 02 is a revision to align terminology with ICH GCP E6(R3).