10. SITE SELECTION FOR IDCRC STUDIES

This section describes the initial site selection process for IDCRC studies in development, for adding new sites for ongoing IDCRC studies, and for protocol-specific sites.

10.1 Initial Site Selection for New Studies

For each new IDCRC study, a site selection process will be carried out by IDCRC[LG] Clinical Operations Unit (COU) Clinical Site Selection Committee (CSSC), with input from the Leadership Operations Center (LOC) and NIAID, to determine which clinical research sites will conduct the study. Objectives of the process include to:

- Achieve the optimal balance of sites for implementation of the clinical research, based on the diverse nature of IDCRC clinical research needs and required patient populations
- Involve site investigators and others who have been invested in concept and protocol development in preparation for study implementation
- Be fair, equitable and transparent

For most studies, the site selection process is open to all Vaccine and Treatment Evaluation Units (VTEUs), and for certain studies to VTEU expansion and protocol specific sites (i.e., IDCRC-affiliated sites). This process involves initial solicitation, review, and approval of a study site application (Site Interest Form). In some cases, however, a modified process may be utilized. Examples of this would be follow-up studies proceeding directly from a prior study (at the same sites), studies conducted in collaboration with investigators outside the Network, or studies where designated sites have unique relevant capacities or patient populations.

10.1.1 Preliminary Assessment of Site Capacity

A Database will be created and maintained to catalog the research capacity of VTEUs. Aspects of site capacity maintained in the database include VTEU site populations, clinical capacities, affiliates, proposed expansion including international sites, and specialized expertise. This information will be updated annually.

10.1.2 Step 1 of the Site Selection Process: Notice to Sites

The site selection process is initiated after a study concept (Extended Concept Proposal (ECP)) has been approved for protocol development (see Section 9 of this manual for more information on the protocol development process). However, initiation of the process will require, at a minimum, a clear understanding of the study objectives, eligibility criteria, and any operational requirements that may impact site selection (e.g., access to a 24-hour pharmacokinetic processing facility, laboratory

certification to perform certain assays, ability to ship specimens outside of the study site location, if central testing is required for a specific study).

The LOC Executive Management Team (EMT) and COU Co-Directors will notify the COU Program Manager (PM) that clinical research sites are necessary, and the number and name of the protocol that has been approved for development. The Protocol Co-Leads will be designated by the LOC and the COU PM. LOC Administrative Core (AC) will set up a conference call between the protocol Co-Leads, the Expert Working Group (EWG) Co-Chairs that reviewed the approved ECP, the Chair of the CSSC, the COU Co-Directors and a DMID representative. This group will construct the notice and customize the Site Interest Form (SIF) to be sent to site VTEU sites contacts.

The notice will be structured on a rapid response Request for Application (RFA) model where sites are invited to apply for participation in a specific study (submission of a SIF). A series of detailed requirements specific to the protocol, including plans for inclusion and mentoring of new/young investigators, will be outlined in the SIF. For expansion sites (see below) additional information will be collected, including site capacity, investigator and staff training, laboratory capacity, pharmacy capacity, local IRB approvals; and for international sites national requirements regarding importation of study product, importation of required equipment and export of patient samples. The deadline for receipt of applications will be set by the CSSC but will usually be within a week of release. For most studies, the form is distributed to all VTEUs with an invitation to interested sites to complete the application and return it to the team for further evaluation. Alternatively, if it is known in advance – based on specific study objectives – that site selection will be limited geographically, or based on current standards of care or other considerations, the application distribution may be targeted accordingly.

If a review of the database and information collected from the Site Interest Forms does not identify a needed population, or if new populations are needed, the COU will reach out to the VTEUs to query them about access to candidate study populations within their expansion sites (i.e., a site named in the application by a funded VTEU). If needed, protocol-specific sites (i.e., sites not affiliated with the VTEU network that have an existing clinical research foundation to conduct IDCRC protocol(s)) may be subcontracted to perform protocol-specific domestic or international clinical studies, as described below.

10.1.3 Conflict of Interest

This policy is designed to ensure that no real or perceived conflict of interest on the part of CSSC members prejudices the objective review of site applications. All voting members of the IDCRC should complete a standardized COI form. Upon review and acceptance of the COI form by the LOC, members with potential conflicts of interest can participate in the discussion and may be asked to voluntarily recuse themselves from voting. However, with the declaration of conflict of interest, all members of the CSSC will be permitted to participate in full discussion and voting processes unless they themselves choose to recuse themselves or are asked to recuse themselves by the Chair.

10.1.4 Step 2 of the Site Selection Process: Receipt and Review of Site Applications

The applications will be received by the COU PM and assigned to reviewers from the CSSC without conflicts as discussed above. When selecting clinical sites for study performance, the CSSC will consider the information provided in the submitted Site Interest Forms and the factors below. Based on reviews

and discussions the CSSC makes recommendations to the LOC and NIAID on which sites might best be viewed for inclusion as clinical trial sites for each protocol. The criterion listed do not carry equal weight.

1. Site expertise – **past experience** in a specific disease or population can enhance the ability of a site to successfully conduct a planned study;
2. **Access to the appropriate study population** – this will be a critical requirement;
3. **Access to appropriate resources** – this can be inpatient or outpatient areas, needed equipment, storage and processing facilities, or other specialized research equipment or capabilities (e.g., ability to perform flow cytometry on freshly collected peripheral blood mononuclear cells);
4. **Past performance** – past performance issues (i.e. operations, enrollment and retention) may be an indicator of future performance concerns, and as the consortium progresses will be used as a factor in site selection. Sites will be informed of known deficiencies, as they are identified, and be given an opportunity to correct these – improvements may be tracked via monitoring reports, cQMPs, or site technical visits for example.
5. **Current workload and anticipated workload at the time of study implementation** – it is important to balance workload across VTEUs to enhance the ability of each VTEU to maintain infrastructure and operational efficiency; information in assessing workload will be taken from submitted Site Interest Forms;
6. **Concept development** – sites that have an investigator who develops a concept chosen for protocol development **will be selected to participate in study implementation**, if no significant barriers to their site participation are identified;
7. **Participation in protocol development** – sites that will conduct a study should participate in the protocol development process. If no site chosen to implement the study has an investigator on the protocol development team, then at least one will be added, if feasible;
8. **Site interest** – initially, only VTEU sites interested in conducting a study will be considered as potential study sites. VTEU PIs will be polled (asked to complete a Site Interest Form) as to their interest in participating in a proposed study;
9. **Opportunity to train new investigator(s)** – a key goal of the IDCRC^{LG} is to develop new clinical investigators, and opportunities to mentor new/young investigators will be a consideration in site selection and protocol development; and
10. **Costs** – the costs of conducting a study will be a consideration, with sites that have higher costs being at a disadvantage relative to those who are more cost-efficient. This will encourage efficiency; however, cost will only be one of the considerations as detailed above. The COU, LG and NIAID may consider and approve the selection of a higher cost site as an investment in that site, for example to develop an investigator or population.

10.2 The CSSC will be composed of five voting members, with appropriate supporting personnel as noted:

1. Committee Chair and Vice Chair – these will both be PIs of a network affiliated VTEU, with non-overlapping terms, and the Vice Chair will become the Chair when the Chair's term expires.
2. COU Co-Director (rotating annually)
3. Subcontractor (FHI 360) representative
4. Laboratory Operations Unit representative
5. EWG representative to ensure subject matter expertise (non-voting)
6. OCRR/Program Officers as appropriate (non-voting)
7. PI from Concept (non-voting)

The committee will meet via virtual meeting format. The chair and vice chair will review the applications and eliminate from consideration those that fail to follow the requirements outlined in the SIF. Two reviewers will be selected for each application and will prepare a summary of the strengths and weaknesses of the site. The committee will decide whether interviews of the Principal Investigators (PIs) or a site visit are needed to make a final decision. If a site visit is needed travel will typically be limited to the committee chair and/or the members listed in 2-4 above. In general, a preselection site visit is time-consuming, and instruction to the chair will be to avoid such unless necessary. The committee will make their recommendations to the LOC/EMT. Recommendations will include a clear justification for the decision of the committee. If the recommendations are approved the EMT will collaborate with NIAID for final approval and assignment of resources.

10.3 Addition of Sites during Accrual of Ongoing Studies

During the accrual phase of a study, the COU/EMT, in conversations with the protocol team, may determine that one or more additional sites are needed to enhance enrollment or otherwise meet the study objectives in a timely manner. However, the addition of sites is not the primary solution to resolving low accrual rates, but rather active management and involvement of the protocol team to facilitate participating sites in recruitment strategies should first be undertaken. Because of the potential implications for network resources, protocol teams must work with the COU/EMT to clarify the rationale for proposing additional sites and review the process that has been undertaken to address challenges in accrual. This communication should take the form of a short memorandum outlining the rationale, proposed approach, and implications for the study timeline (including an updated study accrual plan) and, if there are budget or cost implications, a relevant budget. The decision to add a new site to the study is at the discretion of the EMT in consultation with DMID/NIAID. If approved, the protocol team will proceed to contact potential additional sites per the approved plan. It is generally expected that the process described above in step 2 for the CSSC and the LOC/EMT will be followed to select additional sites; however, if a protocol team determines that a modified process would be more effective or efficient, the alternative approach may be proposed to the COU. For example, a site that previously submitted an application that met the requirements, but was not needed, may be approached first and asked to update their submission documents as needed. Protocol-specific sites must have an existing clinical research foundation to conduct IDCRC protocol(s) for which they are selected since funding is provided to such sites for protocol implementation, not infrastructure development.

10.4 Expansion Beyond VTEUs/Addition of Protocol-specific Sites

If there is a network need for protocol-specific or expansion sites to conduct a high-priority protocol, given the breadth of existing connections and collaborations our IDCRC[LG] with a large number of experienced, research sites, the COU will be well-positioned to facilitate identification of sites and to review sites proposed by the VTEUs.

Should the CSSC Chair and Vice-Chair anticipate that the study must be implemented at sites other than existing VTEUs the group will contact sites based on the prioritization in the table below.

Site Prioritization Criteria	
Domestic Sites	**International Sites**
1. A site named in a funded VTEU application. The sites will have a CAP or similarly certified clinical laboratory, a pharmacy that has been inspected and approved by the NIH PAB, and a sample processing laboratory that meets NHSTP shipping standards.	1. Sites with unique populations or disease exposures that are currently performing interventional clinical trials for another NIAID funded network. The sites will have a CAP or similarly certified clinical laboratory, a pharmacy that has been inspected and approved by the NIH PAB, and a sample processing laboratory that meets NHSTP shipping standards.
2. Sites not named in a VTEU application, but currently performing interventional clinical trials for another NIAID funded network that requires ICP or GRP level expertise and processes (otherwise meet all the criteria in #1)	2. Sites that meet all the criteria in #1, have conducted a NIH-funded interventional clinical trial within the last three years, but have no current studies
3. Sites that meet all the criteria in #2, have conducted a NIH-funded interventional clinical trial within the last three years, but have no current studies ongoing.	3. Sites that have previously performed a NIH-funded clinical trial within the previous three years, but whose clinical laboratory or pharmacy are not currently accredited.
4. Sites that have previously performed a NIH funded clinical trial within the previous three years, but whose clinical laboratory or pharmacy are not currently accredited.	4. Sites with no recent NIH-funded clinical trial, but have performed an Industry or equivalent clinical trial within the last 3 years and can provide monitoring reports detailing site quality
5. Sites with no recent NIH-funded clinical trial, but have performed a clinical trial under an IND within the last 3 years and can provide monitoring reports detailing site quality	5 Other international sites.

The COU will reach out to potential sites for preliminary interest. Sites that express an interest will be sent a SFI (as described above).