



## 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 Clinical Site Selection Committee (CSSC)

The IDCRC CSSC will be composed of six voting members, with appropriate supporting personnel as noted. The Vaccine and Treatment Evaluation Unit (VTEU) Principal Investigators (PI, Co-PIs) are invited to self-nominate for the Vice Chair positions. The Chair will typically have served as a vice chair, but an open selection may be necessary if the person serving as the vice-chair is unable or unwilling to assume the duties of the chair. Nominees are considered by the Clinical Operations Unit (COU) and selected based on appropriate and relevant experience. The term for the CSSC Chair will be for one year while the Vice Chair will serve one year as Vice-Chair and then the 2<sup>nd</sup> year as Chair as noted below in Table 1. The term for the Chair may be extended for an additional year based on IDCRC needs at the direction of the IDCRC co-PI's and with the concurrence of the Chair. A Leadership Operations Center (LOC) Co-Director will also participate in the CSSC as a voting member to provide oversight and continuity across CSSC terms. The DMID / OCRR representative will be determined by DMID and does not have a specified term limit.

**Table 1. CSSC Membership**

<b>CSSC – Voting Members</b>	<b>Term</b>
Chair or designee (PI of an IDCRC VTEU)	1 year
Vice Chair or designee (PI of an IDCRC VTEU)	2 years (1 full year as Vice-Chair, and 2 <sup>nd</sup> year as Chair)
COU Co-Director	No term limit (rotate as needed)
LOC Co-Director	No term limit (rotate as needed)
Subcontractor (FHI 360) Representative	No term limit (rotate as needed)
Laboratory Operations Unit (LOU) representative	No term limit (rotate as needed)
<b>CSSC – Non-Voting Members</b>	<b>Term</b>
EWG representative to ensure subject matter expertise	per EWG
OCRR/Program Officers as appropriate	No term limit
PI from Concept	per protocol

#### 10.1.1 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 have completed a standardized Confidentiality Disclosure Agreement (CDA) form that is on file with 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 caveat that the declaration of conflict of interest may require individual members to recuse themselves from the discussion, all members of the CSSC (to include PIs of a VTEU under consideration) will be permitted to participate in full discussion and voting processes.

## **10.2 Initial Site Selection for New Studies**

For each new IDCRC study, a site selection process will be carried out by the IDCRC COU CSSC in consultation with NIAID. Objectives of the process are 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 participant 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 VTEUs, and for certain studies to VTEU expansion and protocol-specific 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 may include follow-up studies proceeding directly from a prior study (at the same sites), studies conducted in collaboration with investigators outside the IDCRC, or studies where designated sites have unique relevant capacities or access to participant populations.

### **10.2.1 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.

### **10.2.2 Step 1 of the Site Selection Process: Review of Site Selection Parameters**

The site selection process is initiated after a study concept (Extended Concept Proposal (ECP)) has been approved by the IDCRC leadership for protocol development. (See IDCRC MOP Section 9 for details about protocol development process). At this stage, the Protocol Co-Chairs will be designated by the LOC and the COU.

To initiate the site selection process, the Protocol Co-Chair(s), ECP submitter(s), LOC Co Director(s), Co Director(s) of the COU and LOU, SDSU Director, and CSSC Chair and Vice Chair will meet to discuss the approved concept proposal, preliminary budget, sample size calculations, eligibility criteria, proposed # of sites, target populations, 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) and assess if any adjustments to site selection parameters (e.g., # sites) are needed. Additionally, the group will specify any critical issues that should be considered by the CSSC during site selection.

### **10.2.3 Step 2 of the Site Selection Process: Notice to Sites**

Once this input is compiled and site selection parameters are confirmed, the COU will then draft a Site Interest Form (SIF) and circulate to the Protocol Co-Chairs, COU Co Directors and the Chair and CSSC Vice Chair for final review and approval.

The SIF will be modeled on a rapid response Request for Application (RFA) in which sites are invited to apply for participation in a specific study (submission of a SIF). The SIF should include as much detail as is known at the time of the request, which may differ for Fast Track protocols. An SIF template will be generated and modified per protocol. In general, information will be sought on ability to conduct protocol specific requirements, plans for inclusion and mentoring of new / early career investigators, site capacity, access to appropriately diverse study participants, investigator and staff training, laboratory and pharmacy capacity, local IRB approvals. For international sites, requirements regarding importation of study product, importation of required equipment and export of participant samples will also be included. Additionally, for standard protocols, the SIF will include a preliminary estimate of the per participant budget (based on the concept proposal).

The deadline for receipt of the SIFs 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 COU for further evaluation. Alternatively, if it is known in advance that site selection will be limited geographically based on specific study objectives, or based on current standards of care or other considerations, the application distribution may be targeted accordingly.

Primary VTEU sites are prioritized in site selection for IDCRC protocols. However, when the target population or sample size for a particular protocol cannot be met by Primary VTEU sites, or if a Primary VTEU site does not have the research capacity, the CSSC will query Primary VTEUs about access to candidate study populations within their *sub sites / expansion sites*. See **Table 2** for Site Definitions. As needed to meet target population enrollment goals, *protocol-specific sites* may also be subcontracted to perform protocol-specific domestic or international clinical studies, as described below in Sections 10.5-10.6.

The sites defined in Table 2 are considered distinct, individual sites from the perspective of IDCRC and DMID support services and oversight. When completing an SIF, investigators should list any sites/locations that will be participating in study activities to facilitate planning and resource allocation at DMID, clearly describing whether they will include:

- Sites that operate under their Primary VTEU site as described in table below
- Satellite sites
- Sub sites / expansion sites

**Table 2. Site Definitions**

Primary VTEU Site	<ul style="list-style-type: none"> <li>• Main VTEU site for an institution whose application was funded directly from NIAID as part of the IDCRC network</li> <li>• Enrollment locations: no sub-award, same 1572, same clinical lab and pharmacy</li> <li>• Enrollment capabilities included in primary site commitments</li> <li>• All locations operate under single FWA and require only one local IRB review / approval</li> </ul>
Satellite Site	<ul style="list-style-type: none"> <li>• Site administered under the primary site VTEU Principal Investigator (PI)</li> <li>• Does not require a sub-award or separate 1572 or Investigator of Record (IoR) form</li> <li>• May have a separate clinical lab and/or pharmacy</li> <li>• Will be assessed for capability and capacity independently from the primary site</li> <li>• If not used previously in IDCRC or DMID-supported studies, will require approval from the IDCRC and DMID prior to selection as a site</li> </ul>
Sub-sites/Expansion Site	<ul style="list-style-type: none"> <li>• Site named in a funded VTEU application</li> <li>• Has a certified clinical laboratory, a pharmacy that has been inspected and approved by NIH/DMID and a sample processing laboratory that meets NHSTP shipping standards</li> <li>• Requires a sub-award and/or a separate Form FDA 1572 from the primary site</li> </ul>

	<ul style="list-style-type: none"> <li>• Will be assessed for capacity and capability independently from the primary site</li> <li>• May require DMID approval prior to selection as a site</li> </ul>
Protocol-Specific Site	<ul style="list-style-type: none"> <li>• Site that is not affiliated with a VTEU network or part of a funded VTEU application</li> <li>• Has an existing clinical research infrastructure to conduct IDCRC protocol(s) and experience conducting protocols under an IND</li> <li>• Will require sub-award and separate Form FDA 1572</li> <li>• Will require approval by DMID</li> </ul>

### 10.2.4 Step 3: Receipt and Review of Site Applications

The SIF applications will be received by the COU. In advance of the CSSC meeting, the COU will compile all completed SIF applications into a summary table of major SIF components (e.g., interest, expertise, anticipated barriers to enrollment, subsites) and distribute the table along with completed SIFs to the CSSC members.

When selecting clinical sites for study performance, the CSSC will consider the information provided in the submitted SIFs and the factors below. The criterion listed do not carry equal weight.

1. Site expertise – **expertise or 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 may include ability to conduct the study in 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) with IDCRC 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 SIFs and known IDCRC portfolio;
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 SIF) as to their interest in participating in a proposed study;
9. **Opportunity to train new / early career investigator(s)** – a key goal of the IDCRC is to develop new clinical investigators; opportunities to mentor new / early career investigators will be a consideration in site selection and protocol development. Guidance for proposing an early career investigator on an IDCRC protocol is as follows:
  - An early career investigator who has served as co-investigator on an NIH funded trial in the past is eligible to be proposed as Site PI;

- An early career investigator with no prior co-investigator experience may be proposed as a co-investigator on an IDCRC protocol.

Sites should have a defined mentoring/supervisory plan with a senior investigator in place for any early career investigators proposed on the SIF. For fast track protocols, it is generally not recommended to have an early career investigator as the site PI given the speed of development/implementation.

- 10. Costs** – recognizing the merits of cost-efficiency, the costs of conducting a study will be a consideration, with sites that have higher costs at a disadvantage relative to those that are more cost efficient. However, cost will only be one of the considerations as detailed above. The COU, LOC and NIAID may consider and approve the selection of a higher cost site as an investment in that site or if the site can make a unique contribution to the study conduct, for example, to develop an investigator or enroll a particularly desirable study population.

#### **10.2.5 Step 4: Clinical Site Selection Committee (CSSC) Meeting**

The committee will meet via virtual meeting format to discuss the merits of each SIF. At the conclusion of the meeting, the CSSC should reach consensus on next steps for site selection – either to seek additional information or to proceed to submitting a recommendation to the EMT. In addition to site selection, the CSSC may also include a recommendation for the enrollment plan based on SIF responses.

For more details about the conduct of the CSSC meeting, please see the **IDCRC CSSC Meeting SOP**.

#### **10.2.6 Step 5: CSSC Recommendation and EMT Approval**

After the CSSC committee meeting and any additional information has been provided, the CSSC will make a recommendation to the EMT on which sites are best suited for inclusion for each protocol. Additionally, the CSSC may also include a recommendation for the enrollment plan for sites. Recommendations will include a clear justification for the decision of the committee. If the recommendations are approved by the EMT, the LG will collaborate with NIAID for final approval and assignment of resources.

#### **10.2.7 Step 6: Site Selection Notification**

On completion of the selection process, the COU will notify sites via email that have been successfully selected as well as those who have not. Sites not selected will be provided an explanation as to their unsuccessful bid. Additionally, the COU will notify the protocol chair(s), LOU, SDSU, FHI 360 Protocol Specialist (PS), DMID Clinical Project Manager (CPM), DMID Medical Officer (MO), and/or DMID Scientific Lead (SL) and other protocol team members as appropriate. Shortly after site selection notification, the FHI 360 PS will invite site investigators to join protocol team meetings for protocol development.

Additionally, the COU will provide DMID with a list of the selected sites, all study locations and contacts including the correct MI Codes<sup>1</sup> to facilitate setup of DMID support services such as clinical monitoring, and others as applicable.

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<sup>1</sup> An MI code is a unique identifier for sites (issued by DMID) which DMID references for a variety of internal resources such as clinical monitoring, pharmacy/product shipments, regulatory document submission, etc. It is critical that sites have a valid MI code associated with their facility address to ensure proper identification across various DMID resources.

### 10.3 Reviews of Fast-Track Concepts/SIFs

While the process outlined in this MOP will be required for all proposed research, circumstances such as public health emergencies may dictate a need for expediting or streamlining the formal process as described. For concepts approved for protocol development that are considered “fast track”, the timeframes for solicitation and return of SIFs will be truncated. The CSSC will meet to discuss as soon as all SIFs are returned. The review process as outlined will be followed to maintain the rigor and quality required. Recommendations may bypass the typical review process and go only to the IDCRC co-PIs in an expedited fashion; responses by email will be requested to ensure appropriate documentation trail maintained. When time permits, recommendations will go to the EMT; however, this step may be abbreviated due to urgency of implementation.

### 10.4 Protocol Development and Impact on Site Selection

Since site selection is based on preliminary parameters gleaned from an approved concept proposal, it is possible that protocol requirements may change, and these parameters shift during protocol development. If, during protocol development, it is determined that a selected site is no longer able to meet protocol requirements or that additional sites may be needed, the protocol team will make a recommendation to the COU about the need for an alternate or additional site(s) so that any impact on budget and/or support services can be assessed.

### 10.5 Changes in Site Locations

During pre-implementation as sites solidify plans for recruitment and protocol implementation, the protocol specialists will circulate a **site update form** to all selected sites requesting information about recruitment locations, satellite and/or sub sites that the site plans to involve in study activities. If a site includes new locations, satellite and/or sub sites from what was proposed during site selection, the FHI 360 PS will forward this information to the COU to explore impact on site activation requirements as well as IDCRC and DMID resources.

### 10.6 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. 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 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 infrastructure to conduct IDCRC protocol(s) for which they are selected since funding is provided to such sites for protocol implementation, not infrastructure development.

### 10.7 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 the IDCRC has with experienced clinical 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 a protocol must be implemented at sites other than existing VTEUs, the COU will prioritize sites that meet the criteria as outlined below in **Table 3**. Sites that express an interest after being contacted by the COU will be sent an SIF.

**Table 3. Site Selection Prioritization Criteria (for expansion beyond Primary VTEUs)**

Priority	IDCRC VTEU Affiliation	Lab, Pharmacy Status	NIAID / IND Experience
1 <sup>st</sup> Priority	A VTEU satellite site or sub-site / expansion site <b>(named in a funded VTEU application)</b>	Site has a CAP or similarly certified clinical laboratory, an NIH DMID inspected / approved pharmacy, a sample processing laboratory that meets NHSTP shipping standards	N/A
2 <sup>nd</sup> Priority	Sites <b>not</b> named in a funded VTEU application	Sites with a CAP or similarly certified clinical laboratory, an NIH DMID inspected / approved pharmacy, and a sample processing laboratory that meets NHSTP shipping standards	<b>Currently</b> performing interventional clinical trials for <b>another NIAID funded network</b> that requires ICP/GCP level expertise and processes
3 <sup>rd</sup> Priority	Sites <b>not</b> named in a funded VTEU application	Sites with a CAP or similarly certified clinical laboratory, an NIH DMID inspected / approved pharmacy, and a sample processing laboratory that meets NHSTP shipping standards	Sites that have conducted a NIH-funded interventional clinical trial <b>within the last three years</b>
4 <sup>th</sup> Priority	Sites <b>not</b> named in a funded VTEU application	Lab or pharmacy not currently accredited	Sites that have conducted a NIH-funded interventional clinical trial <b>within the last three years</b>
5 <sup>th</sup> Priority	Sites <b>not</b> named in a funded VTEU application	Lab or pharmacy not currently accredited	Sites that have performed a <b>clinical trial under an IND within the last 3 years</b> and can provide monitoring reports detailing site quality