10 SITE SELECTION FOR IMPAACT STUDIES

This section describes the initial site selection process for IMPAACT studies in development, for adding new sites for ongoing IMPAACT studies, and for expansion to sites not affiliated with IMPAACT.

10.1 Initial Site Selection for New Studies

For each new IMPAACT study, a site selection process will be carried out by the protocol team, with oversight from the IMPAACT Management Oversight Group (MOG), to determine which clinical research sites (CRSs) will conduct the study. The site selection process is initiated after a study concept has been approved for protocol development and when the schema and eligibility criteria have been drafted (see Section 9 of this manual for more information on the protocol development process). The process will result in the development of a site selection and study accrual plan for review and approval by the MOG. Objectives of the process include to:

- Target the appropriate populations for enrollment into protocols (e.g., pregnant women, HIV/TB co-infection)
- Identify if sites have the resources to enroll the target populations and perform procedures as necessary; if not, the Network may be able to provide needed resources
- Involve site investigators and other key site staff early in protocol development and preparation for study implementation
- Enhance the ability to predict the timing of key study milestones (e.g., completion of enrollment) based on specific enrollment projections provided by each site and, together, for the study overall
- Foster site staff investment in and accountability for meeting study accrual targets and successful study implementation
- Optimize allocation of Network resources
- Target study-related communications, training, and materials to participating sites

For most studies, a two-step site selection process that is open to all IMPAACT-affiliated sites (see exceptions below) will be undertaken by the protocol team. This process involves initial solicitation, review, and approval of a brief **study site application** followed by solicitation, review, and approval of a more extensive **site implementation plan (SIP)**, as described below. In some cases, however, a modified process may be utilized; this is most likely in the context of follow-on studies proceeding directly from a prior study (at the same sites) and studies conducted in collaboration with sponsors other than Division of AIDS (DAIDS), *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), and National Institute of Mental Health (NIMH).

When reviewing applications and SIPs, protocol teams will aim to identify the optimal number of sites required to ensure both high quality and timely conduct of the study; the MOG will evaluate this as well when reviewing the team's site selection and accrual plan. Other factors that may be considered include:

- Site capacity, experience, and past performance in other studies
- Laboratory capabilities, including any study-specific assays or assessments
- Study-specific pharmacy requirements (e.g., freezers)
- Country-specific approval requirements and specimen shipment restrictions and approval requirements
- Concurrent participation in other studies that involve the same participant populations, staff, space/facilities, and/or other resources
- Optimal utilization of Network-affiliated sites
- Preferences to expand or limit locations driven by scientific gaps and/or requests from collaborators (e.g., National Institutes of Health Intramural Research Program, collaborating networks, or pharmaceutical co-sponsors)

10.1.1 Preliminary Assessment of Site Capacity

Site profile data will be maintained to catalog the research capacity of IMPAACT-affiliated sites. Aspects of site profile data include study site facilities and equipment as well as access to and size of populations of interest (e.g., number of pregnant women booked in antenatal care, number of antiretroviral naïve children entering care, number of antiretroviral experienced children and adolescents in care, and protocol approval timelines). Proposing investigators may request data from the Operations Center for planning purposes as study capsules, concepts, and protocols are developed, and this information may be reviewed and used to inform the site selection process described below.

10.1.2 Step 1 of the Site Selection Process: Site Application

To maximize site input and protocol team representation during protocol development, the first step of the selection process should begin as soon as possible after a study concept has been approved for protocol development. 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, and the ability to ship specimens outside of the study site location, if central testing is required for a specific study).

The purpose of this step is to rapidly identify interested sites that meet minimum requirements to conduct a study (and to rule out those that do not). To achieve this goal, the protocol team develops a brief application document that requests information on site capacity limited to the minimum requirements to conduct the study. For most studies, the application is distributed to **all** IMPAACT-affiliated DAIDS and NICHD sites (emailed by the Operations Center to CRS leaders/site principal investigators [PI], copied to clinical trials unit [CTU] PIs, and the NICHD coordinating center), with an invitation to interested sites to complete the application and return it to the protocol team for further evaluation. Alternatively, if it is known in advance – based on specific study objectives – that site selection will be limited geographically or limited based on current standards of care or other considerations, the application distribution may be targeted accordingly.

Protocol team members will review all applications received and determine which sites meet minimum requirements to conduct the study. Depending on the needs of the study and the number of applications expected, teams may delegate this responsibility to a subset of team members, minimally including the

protocol chair, vice chair(s), and clinical trial specialist (CTS). If a protocol team, or subset of team members, determines that additional information is needed to fully evaluate a site, the required information will be requested by the CTS. Each applicant site will be informed of the outcome of this review, and sites that meet the minimum requirements will proceed to Step 2 of the process. All communications to and from potential study sites will be coordinated by the CTS.

10.1.3 Step 2 of the Site Selection Process: Site Implementation Plan

Sites that are found to meet minimum requirements in Step 1 of the site selection process will be asked to complete an SIP in Step 2 of the process, coordinated by the CTS. The purpose of this step is to obtain sufficient operational detail from each potential site to optimize selection of sites with respect to overall capacity, quality of study implementation, efficiency, and budgetary considerations. To achieve this goal, the protocol team develops a SIP tailored to the operational needs of the study. Importantly, the SIP will also collect accrual projections that will be used by the protocol team to develop a site selection and accrual plan for review and approval by the MOG, as described below.

As with the application document in Step 1, all communications to and from potential study sites regarding SIPs will be coordinated by the CTS. However, NICHD-funded sites must submit their SIPs for review by the NICHD coordinating center prior to subsequent submission to the CTS.

Protocol team members will review all SIPs received to determine which sites to include in their study-specific **site selection and accrual plan**. Depending on the needs of the study and the number of SIPs expected, teams may delegate the review and approval responsibility to a subset of team members, including at minimum the protocol chair, vice chair(s), and CTS. Other team members may also review and approve selected portions of the SIP; for example, the Laboratory Center representative or laboratory technologist may review sections of the SIP related to specimen processing and other laboratory operations. Upon initial review of a SIP, if a protocol team determines that additional information is needed to fully evaluate a site, the required information will be requested by the CTS. Protocol teams may also utilize information from the site profile data to inform site selection decisions. When more sites meet the criteria for participation than are required to meet study objectives, the protocol team may rank the applicant sites based on available information and select the required number of sites based on this ranking.

10.1.4 Site Selection and Accrual Plan

Based on their SIP review, the CTSs with input from the protocol team will develop a **site selection and accrual plan** for review by the MOG. The MOG will determine whether to approve the plan as proposed or to recommend or require modifications. Once the plan is approved, the protocol team will inform each site that submitted a SIP of the final review outcome (including reasons for not being selected, when applicable).

10.1.5 Designation of Sites for Protocol Registration

Once final site selection decisions are made, and sites are informed of these decisions (as described above), the CTS will designate the selected sites as permitted to register for the study in the DAIDS Protocol Registration System.

10.2 Addition of Sites During Accrual of Ongoing Studies

During the accrual phase of a study, a protocol team or the MOG may determine that additional site(s) 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; 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 seek MOG approval before initiating a process to add sites to an ongoing study. A short memorandum outlining the rationale, proposed approach, and implications for the study timeline (including an updated study accrual plan) and a budget if there are budget or cost implications, is required. If approved, the team will proceed to contacting potential additional sites per the approved plan. It is generally expected that the two-step 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 MOG. For example, a site that previously submitted an application and SIP that met the requirements, but was not needed, may be approached first and asked to update their submission documents as needed.

10.3 Expansion Beyond the IMPAACT Network Affiliated Sites

In some cases, it may be necessary to engage sites that are not currently affiliated with IMPAACT to conduct a particular study. In such cases, additional capacity at sites affiliated with the other NIAID-funded networks would first be sought; this may be accomplished through a co-endorsement agreement with another network or through direct solicitation of sites affiliated with other networks (with permission of the leadership of those networks, as needed). If the required additional capacity cannot be identified among sites currently affiliated with other networks, engagement of sites that were proposed as part of a NIAID CTU application but not funded will be considered next, followed – if necessary – by soliciting sites that are not associated with a NIAID-funded network or with NICHD, following DAIDS protocol-specific site expansion procedures.

For some studies, IMPAACT research partners or sponsors may specifically request inclusion of sites beyond those currently funded for IMPAACT studies by NIAID or NICHD. In such cases, the MOG's approval must be obtained and the DAIDS protocol-specific site expansion procedures must be followed, regardless of funding source.