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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 for more information on the protocol development process). The process will result in the development of a Site Selection and Accrual Plan for review and approval by the MOG. Objectives of the process include:

- Identifying the appropriate priority populations for enrollment into studies (e.g., pregnant people, people living with human immunodeficiency virus (HIV) and tuberculosis (TB))
- Distinguishing if sites have the resources to enroll the study population(s) and perform procedures as necessary; if not, the Network may be able to provide needed resources
- Involving site investigators and other key site staff early in protocol development and preparation for study implementation
- Enhancing 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
- Fostering site staff investment in and accountability for meeting study accrual targets and successful study implementation
- Optimizing allocation of Network resources
- Targeting study-related communications, training, and materials to participating sites

For most studies, a one-step site selection process utilizing a **study site application** will be undertaken by the protocol team. If the protocol team determines that additional implementation details are needed after reviewing the study site applications, then solicitation, review, and approval of a more extensive **site implementation plan (SIP)** may be appropriate, as described below. In some cases, a modified process may be utilized, such as 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). In the event that a modified process is utilized, deviations from the standard IMPAACT site selection processes described below should be documented in the Site Selection and Accrual Plan (See Section 10.1.4).

10.1.1 Study Site Application

To maximize site input and protocol team representation during protocol development, development and distribution of the study site application 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). Site selection should generally be completed prior to submission of the protocol for review by the IMPAACT Multidisciplinary Protocol Review Group.

The purpose of the site application is to identify interested sites that meet minimum requirements to conduct a study (and to rule out those that do not) and to 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. For most studies, the site 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 site application and return it to the protocol team for further evaluation. This is the preferred option. However, in some cases, site selection will be limited geographically, based on current standards of care, anticipated post-study access to the product or intervention, study design specifications, or other reasons. When limited based on one of these considerations, the site application distribution may be distributed only to representatives from sites in the specific countries and/or with the specific qualifications. The rationale for limitations should be clearly described in the Site Selection and Accrual Plan; if limited for scientific reasons or based on the study design, the rationale should also be included in the protocol.

Protocol team members will review all applications received. For NICHD sites, this includes representatives from NICHD coordinating center. Depending on the needs of the study and the number of applications received, teams may delegate this responsibility to a subset of team members, minimally including the protocol chair, vice chair(s), clinical research manager(s) (CRM), and NICHD coordinating center representative as needed. During the review, designated team members will determine which sites meet minimum requirements to conduct the study and how many total sites are required to ensure both high quality and timely conduct of the study. If more sites meet the minimum requirements than are needed for study implementation, the protocol team may consider other factors such as:

- 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 and Network resources
- 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)

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 CRM. It is generally expected that site

selection will be limited to the number of sites needed to meet accrual targets and fulfill the study objectives.

10.1.2 Site Implementation Plan

As noted above, if the protocol team (or designated subset) determines that additional implementation details are needed after reviewing the study site applications, the CRM(s) will ask sites to complete a SIP. 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.

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

Protocol team members will review all SIPs. 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 CRM(s). 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 CRM. 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.

10.1.3 Site Selection and Accrual Plan

Based on their study site application and SIP review (when utilized), the CRMs, with input from the protocol team, will develop a Site Selection and Accrual Plan for review by the MOG. In general, this plan should present an overview of the study and population of interest as well as the overall process of site selection, the criteria used to evaluate the applications received. The protocol team should specify which sites they propose for inclusion in the study and the total time expected to enroll all participants at the recommended sites. The MOG will determine whether to approve the plan as proposed or to recommend or require modifications. Once the plan is approved, the CRM will inform each site that submitted a study site application, and SIP if applicable, of the final review outcome.

10.1.4 Designation of Sites for Protocol Registration

Once final site selection decisions are made, and sites are informed of these decisions (as described above). The CRM will then 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, an alternative approach may be proposed to the MOG. For example, a site that previously submitted a site application and SIP that met the requirements, but was not previously selected, 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 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.