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4 PROTOCOL TEAMS

Protocol teams assume primary responsibility for scientific and operational leadership in the development, implementation, and oversight of IMPAACT studies and dissemination of study results. This section outlines the selection process of protocol chair, the selection and assignment of other team members, the responsibilities of protocol team members, and the protocol team’s relationship with IMPAACT oversight and scientific committees. IMPAACT scientific and oversight committees and groups are outlined in Section 2 and Section 13, respectively; the protocol development process is further detailed in Section 9.

4.1 Protocol Chair and Vice Chair

Key protocol team members are proposed in study concept sheets, and proposed protocol chairs and vice chairs are reviewed by the IMPAACT Scientific Leadership Group (SLG) at the time of concept review.

4.1.1 Protocol Chair and Vice Chair Selection

One protocol chair and one vice chair are typically proposed in the concept sheet. Exceptions are assessed by the SLG on a case-by-case basis (e.g., co-chairs or multiple vice chairs). As noted in Section 9, the SLG reviews the proposed protocol chair and vice chair based upon past leadership performance, current commitments, and relevant expertise and experience. The SLG also considers whether proposed chairs have the capacity to serve concurrently as chair or vice chair of multiple IMPAACT studies and/or network committees. Protocol chairs need not be affiliated with an IMPAACT study site or other IMPAACT organization. Network resources are allocated to support these critical positions.

Members of the IMPAACT Management Oversight Group (MOG) and SLG are not eligible to serve as protocol chair or vice chair due to potential conflict with their oversight responsibilities. Selection as protocol chair or vice chair does not imply that a site with which a chair is affiliated will be selected for study participation (see Section 10).

4.1.2 Protocol Chair and Vice Chair Responsibilities

The protocol chair provides scientific leadership during the development, implementation, and reporting of the study. They assume responsibility for completion of protocol team responsibilities and other study activities within the approved budget and timeline. Protocol chairs may often delegate specific areas of responsibility to the vice chair, but decision-making authority and ultimate responsibility for the execution of the study rests with the protocol chair.

Protocol chairs must familiarize themselves with IMPAACT processes as outlined in the IMPAACT Network Manual of Procedures (MOP) and adhere to them. A list of study responsibilities is included in the scope of work, which is part of the contractual agreement that provides network resources to support each protocol chair and vice chair.

Protocol team business is planned and managed by the protocol chair and the clinical trials specialist (CTS), in consultation and with the support of other protocol team members. Specifics of protocol team management vary according to the needs and type of study, the number and location of sites involved, and individual leadership and management approaches.

General Responsibilities (throughout the lifecycle of the study):

- Ensuring study compliance with ICH/GCP and IMPAACT policies and procedures in the Network MOP
- Leading protocol team meetings and calls
- Coordinating the establishment and dissolution of study-specific groups as necessary to achieve efficiency in the development, implementation, and reporting of the study
- Coordinating protocol team member activities to meet study targets and timelines
- Collaborating with protocol team members on the development and execution of study activities and materials, as outlined in Table 4-1 below
- Monitoring progress in relation to established timelines and working with protocol team members as needed to address delays that may be encountered
- Monitoring the quality and progress of study conduct and working with protocol team members and study sites as needed to address study implementation issues
- Providing status updates to IMPAACT leadership, as needed
- Acting as a liaison between the protocol team, the study sponsor, and network leadership and oversight groups
- Provide active and timely scientific and operational guidance to support participating study sites

Pre-Implementation:

- Leading protocol development in coordination with the CTS
- Working with the CTS to complete the study site selection process
- Working with Operations Center staff to develop the study budget
- Working with the CTS to determine the training plan, develop the training materials, and participate in training sites on protocol requirements
- Ensuring timely development and sign-off of required key study implementation plans and materials
- Providing scientific expertise and facilitating final decision making within the protocol team to achieve agreement on scientific or operational issues brought before it; if agreement cannot be reached, referring the issue to the MOG/SLG

Study Implementation:

- Participating in study data reviews consistent with the study monitoring plan
- Together with the protocol statistician(s), reporting on the status of the study to the Study Monitoring Committee (SMC) and/or Data and Safety Monitoring Board (DSMB)
- Ensuring timely development of study closure plans and materials

Publications:

- Overseeing analysis and writing teams (designating writing team members, reviewing schedules, monitoring progress, prioritizing analyses, communicating publication plans, responding to IMPAACT Publications Committee review, advocating for additional resources as required), as further described in Section 19
- Ensuring review and approval of all study-related manuscripts, abstracts, and presentations

4.2 Protocol Team

Protocol teams assume primary responsibility for scientific and operational leadership in the development, implementation, and oversight of IMPAACT studies and dissemination of their results.

4.2.1 Protocol Team Membership

The protocol chair identifies investigators with expertise relevant to the study. Investigators involved with the development of the concept sheet may not necessarily be invited to be a member of the protocol team. Additional team members are assigned by the Operations Center, Statistical and Data Management Center (SDMC), Laboratory Center (LC), NIH, and DAIDS Pharmaceutical Affairs Branch (PAB), as applicable. The Operations Center coordinates and communicates the protocol team formation. Team members need not be affiliated with an IMPAACT study site or other IMPAACT organization. Membership of each protocol team will vary according to the protocol, but membership should generally include:

- Protocol chair (and/or co-chair, vice chair)
- DAIDS medical officer (MO)
- NICHD MO
- NIMH MO (if applicable)
- CTS(s)
- Statistician(s)
- Protocol data manager(s)
- Laboratory data manager(s)
- DAIDS protocol pharmacist(s) (if applicable)
- Community representative(s)
- LC representative
- Pharmaceutical or industry representative(s) (if applicable)
- Laboratory technologist
- Westat representative (if applicable)
- Investigator(s)
- Site investigator from each participating CRS

Additional members, as required for a specific protocol, may include a pharmacologist, virologist, behavioral scientist, immunologist, etc.

4.2.2 Protocol Team Responsibilities

Although individual protocol team members have different roles in fulfilling specific protocol team responsibilities (see Table 4-1), all members are expected to provide scientific, operational, or site-specific input, as appropriate, to protocol team activities.

Table 4-1. Roles of Key Protocol Team Members

Team Member	Primary Roles and Responsibilities
Protocol chair	<ul style="list-style-type: none"> • Ultimate responsibility for execution of the study and final decision-making authority • See Section 4.1.2 for further details of chair responsibilities
Vice chair	<ul style="list-style-type: none"> • Collaborate with the protocol chair for execution of the study • See Section 4.1.2 for further details of chair responsibilities
Medical Officer (DAIDS, NICHD, or NIMH)	<ul style="list-style-type: none"> • Participate fully in protocol team discussions and decisions • Facilitate communication between protocol team and relevant NIH groups and staff • Provide timely MO review of study documents and response to queries • Provide oversight of safety monitoring during study implementation • DAIDS MO to review and sign-off on each MOP version
Clinical Trials Specialist (CTS)	<ul style="list-style-type: none"> • With protocol chair, provide scientific and operational input to the protocol and coordinate and lead protocol development and any subsequent protocol modifications, as applicable • Organize and document protocol team conference calls and meetings • Prepare study budget with Operations Center financial staff, in collaboration with the protocol chair and, as applicable, with input from site representatives • Submit protocol for required IMPAACT and DAIDS reviews (MPRG, applicable Sciences Review Committee, Regulatory, MO) and manage response/revision process as needed (see Section 9) • Coordinate the site selection process (see Section 10) • Develop and produce the study-specific manual of procedures (MOP) with input from DMC, LC, and other protocol team members, as applicable (see Section 11) • Collaborate with protocol team members to coordinate the completion of study opening requirements (see Section 11) • Coordinate and develop the training plan and materials and provide study-specific training with DMC, LC, and other protocol team members, as applicable (see Sections 11 and 16) • Coordinate the site activation process (see Section 11) • Assess the performance of and provide operational guidance to sites during study conduct, enabling the sites to respond to problems and issues that arise during implementation of studies and dissemination of findings • Provide information on study progress to the sites, protocol teams, Network leadership, pharmaceutical representatives (if applicable), and/or DAIDS • With the SMC or DSMB coordinator, collaborate with SDMC on SMC and/or DSMB reviews and reports • Contribute to study close-out procedures (see Section 14) • Participate in publication activities and facilitate as needed (see Section 19) • See Section 2 for further details of Operations Center responsibilities

Table 4-1. Roles of Key Protocol Team Members

Team Member	Primary Roles and Responsibilities
Statistician	<ul style="list-style-type: none"> • Provide design, statistical, and scientific input during protocol development and throughout the conduct of the study • Lead development of statistical components of the protocol • Collaborate in protocol development and protocol related materials • Develop randomization and enrollment plan, as needed • Lead development and implementation of the Study Progress, Data, and Safety Monitoring Plan (SPDSMP), including routine reports (see Sections 11 and 13), in collaboration with the protocol data manager (PDM) and laboratory data manager (LDM) • Lead development and implementation of the Statistical Analysis Plan (SAP), in collaboration with the protocol chairs, MOs, and other protocol team members • Conduct data analyses and generate interim analysis reports for the SMC or DSMB, in collaboration with the PDM and other protocol team members • Conduct data analyses and generate final analysis reports, in collaboration with the PDM and other protocol team members • Contribute to study close-out procedures (see Section 14) • Collaborate on publication activities and lead analyses, as needed • Submit study results to ClinicalTrials.gov • See Section 2 for further details of SDMC responsibilities
DAIDS Protocol Pharmacist (if applicable)	<ul style="list-style-type: none"> • Lead development of pharmacy and study drug/product components of the protocol • Collaborate with the CTS to develop and produce the MOP, with primary responsibility for pharmacy sections (see Section 11) • Advise protocol team on all study product-related issues, including study drug/products and associated materials for administration • Collaborate with CTS on review of site-specific study activation requirements related to pharmacy requirements prior to study activation • Interact with pharmaceutical companies to ensure study product supply and materials as needed • Provide and monitor timely study product shipment to study sites • Monitor drug supply, expiration dates, and budgets for drug, where necessary
Investigators	<ul style="list-style-type: none"> • Provide scientific input into protocol development • Provide input and review clinical related sections of study implementation documents as applicable • Provide investigator-specific expertise, as applicable • Participate in publication activities as applicable
Pharmaceutical or industry representative	<ul style="list-style-type: none"> • Provide input in protocol development and implementation as applicable and as outlined in network and/or sponsor agreements

Table 4-1. Roles of Key Protocol Team Members

Team Member	Primary Roles and Responsibilities
Protocol Data Manager (PDM)	<ul style="list-style-type: none"> • Collaborate in development of protocol • Collaborate with the CTS to develop and produce the MOP, with primary responsibility for data management, reporting, and randomization sections • Lead the development of Clinical Data Interchange Standards Consortium (CDISC)-compliant data collection instruments (e.g., case report forms [CRFs], computer-based questionnaires) and instructions, in collaboration with LDM and statistician, as needed • Collaborate with CTS on review of site activation requirements related to data management prior to activation • Conduct training on data management and data collection instrument completion • Collaborate with statistician and LDM to develop and implement the SPDSMP (including development and distribution of routine reports) • Collaborate with LDM, pharmacologist, and statistician in the development and implementation of the PK management plan, when applicable • Collaborate with statistician to generate interim analysis reports for the SMC or DSMB and final analysis reports • Provide support for data collection and management • Collaborate with CTS to provide support for operational matters that may influence study data • Assess the data management quality of sites and report results to protocol team • Conduct data management site visits as needed • Contribute to study close-out procedures, including data collection and cleaning (see Section 14) • Participate in publication activities and facilitate as needed • See Section 2 for further details of SDMC responsibilities
Laboratory Data Manager (LDM)	<ul style="list-style-type: none"> • Collaborate in development of protocol • Collaborate with PDM to develop data collection instruments and instructions • Collaborate with the LC representative and LT on development of the Laboratory Processing Chart (LPC; see Section 11) • Lead the development and implementation of the LDMS preloads (Windows) and Quick Add Templates (Web) • Collaborate with the statistician and PDM to develop and implement the SPDSMP • Lead development and implementation of the PK data management plan with the protocol pharmacologist, statistician, and PDM, when applicable • Assess the quality of laboratory data for the study, including but not limited to, specimen completeness, in collaboration with the PDM, and report results to protocol team as needed • Coordinate specimen shipping requests and data transfer agreements for receipt of resulting assay data as needed • Contribute to study close-out procedures (see Section 14) • Participate in publication activities and facilitate as needed • See Section 2 for further details of SDMC responsibilities

Table 4-1. Roles of Key Protocol Team Members

Team Member	Primary Roles and Responsibilities
Community representative(s)	<ul style="list-style-type: none"> • Provide perspective of community and potential participants during protocol development, study implementation, and publications and results dissemination • Facilitate communication with the ICAB, throughout the life of the study • Work with protocol team and CABs to develop and implement plans for dissemination of study results to the community, as needed
LC Representative	<ul style="list-style-type: none"> • Collaborate in development of protocol • Collaborate with the LT and LDM to develop and produce the LPC, with input from other protocol team members, as applicable (see Section 11) • Collaborate with LT to provide laboratory expertise in development of data collection instruments • Collaborate with CTS on review of site-specific study activation requirements related to laboratory requirements prior to study activation; for NIAID sites, confirm laboratory readiness (for NICHD sites, laboratory readiness is confirmed by Westat) • Collaborate with LT to conduct training on study-specific laboratory procedures and processes • Collaborate with CTS and LT to provide support for operational matters that may influence laboratory procedures or results • Participate in publication activities and facilitate as needed • See Section 17 for further details of LC responsibilities
Laboratory Technologist (LT)	<ul style="list-style-type: none"> • Collaborate in development of protocol • In collaboration with LC representative and LDM, lead and coordinate the development of the LPC (see Section 11) • In collaboration with LC representative, provide laboratory expertise in development of data collection instruments • In collaboration with LC representative and other protocol team members, identify study-specific laboratory requirements and materials • In collaboration with LC representative, conduct training on study-specific laboratory procedures and processes • Collaborate with CTS and LC representative to provide support for operational matters that may influence laboratory procedures or results • In collaboration with LC representative and CTS, develop and review laboratory related sections of the MOP • Participate in publication activities as needed
Westat Representative(s) (if applicable)	<ul style="list-style-type: none"> • For studies with NICHD site participation, facilitate communication between protocol team, Westat colleagues, and NICHD sites • Westat laboratory colleagues, collaborate with CTS on review of site-specific study activation requirements related to laboratory requirements prior to study activation; for NICHD sites, laboratory readiness is confirmed by Westat

Table 4-1. Roles of Key Protocol Team Members

Team Member	Primary Roles and Responsibilities
Site investigator from each participating CRS	<ul style="list-style-type: none">• Provide site-informed input into protocol development and implementation• Review and comment on study implementation materials and data collection instruments• Participate in publication activities as needed

4.2.3 Study-Specific Groups

The protocol chair may identify study-specific groups to address specific needs/activities during protocol development and study conduct and appoint protocol team members or external investigators to these study-specific groups. Examples might include study-specific groups to address:

- Development and/or oversight of specialized behavioral procedures for a study
- Development and/or oversight of specialized clinical procedures for a study
- Development of specialized data collection modules (in collaboration with SDMC)
- Ongoing support of site clinicians regarding toxicity management and study drug dosing, such as a Clinical Monitoring Committee (or Core Team)
- Review of safety assessments and reports or determination of outcome measures (e.g., external safety review groups or outcome review groups)
- Drafting and submission of manuscripts and presentations (see Section 19)

The CTS facilitates and generally participates in the conference calls and meetings of these study-specific groups. Where applicable, the CTS provides summaries to the protocol team for the study-specific group meetings and conference calls. Delegation of responsibilities for ongoing, study-specific groups is outlined in the protocol during development; membership and roles and responsibilities of these groups is generally described in the SPDSMP. Network leadership review of membership on atypical study-specific groups may be required.

When protocol chairs are not included in the group membership, a group chair is typically identified to assume leadership responsibilities and decision-making authority. When the CTSs are not included in the group membership, a group member is designated to assume group management and documentation responsibilities and key decisions; see Section 12 for details on quorum and documentation requirements.

4.3 Relationship of Protocol Team to IMPAACT Management Oversight Group (MOG)

The MOG monitors each IMPAACT protocol team with regard to protocol development, implementation, analysis, and reporting. This oversight is accomplished through the SMC, Operations Center, LC, and SDMC by a mixture of formal reviews of key documents produced by the protocol teams (study protocol, protocol summaries, open reports to the SMC or DSMB, and primary and secondary manuscripts) as well as review of prepared reports.

In addition to oversight provided by the SMC or DSMB, as detailed in Section 13, routine MOG oversight includes:

- Evaluation of study progress in relation to key implementation benchmarks established by the MOG and information from the protocol teams (e.g., timeliness of enrollment and follow-up targets, routine reports to the SMC or DSMB, and progress in data analysis and reporting). The MOG identifies and

communicates recommended actions on delayed protocols and unexpected problems during protocol implementation.

- Assistance to DAIDS in determining the need for additional resources, for example, because of unexpected costs associated with planned study procedures.
- Adjudication of conflicts that cannot be resolved within the protocol teams. If all reasonable attempts to adjudicate conflicts or address problems with the protocol team do not result in resolution of the conflict, the MOG may direct that the protocol team membership or its leadership be modified.

The SLG may also provide scientific guidance, as needed. In particular, protocol changes including significant changes to the scientific goals, study objectives, or design must be approved by the relevant SC and SLG, as described further in Section 9.

4.4 Conflict Resolution within Protocol Teams

Conflicts within IMPAACT are handled by referring the issue in dispute to the next level of the IMPAACT organizational structure.

If a conflict arises within a protocol team and cannot be resolved between the members involved, the issue is referred to the protocol chair. If the protocol chair cannot resolve the issue with the protocol team, the issue is referred to the MOG.