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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 evaluates and confirms the proposed protocol chair and vice chair based upon past leadership performance, current commitments, and relevant expertise and experience. 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).

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.

#### **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 rest 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 activities are planned and managed by the protocol chair and the clinical research manager (CRM), 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 life cycle of the study):

- Ensuring study compliance with Good Clinical Practice (GCP) guidelines (International Council on Harmonisation Good Clinical Practices, ICH E6(R2)) and IMPAACT policies and procedures in the Network MOP
- Managing the study's overall operations in coordination with the CRM
- Developing meeting agendas and 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
- Working with the CRM to identify study targets, milestones, and timelines
- 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
- 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
- Providing active and timely scientific and operational guidance to support participating study sites

Pre-Implementation:

- Leading protocol development in coordination with the CRM
- Working with the CRM to complete the study site selection process
- Working with Operations Center staff to develop the study budget
- Working with the CRM 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 (e.g., designating writing team members, reviewing schedules, monitoring progress, prioritizing analyses, communicating publication plans, responding to IMPAACT Publications Committee reviewer comments, 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 team will be established following study approval by the SLG and the selection of a protocol chair. Investigators involved with the development of the concept sheet may not necessarily be invited to be a member of the protocol team. The protocol chair identifies investigators with expertise relevant to the study. The Operations Center coordinates and communicates the protocol team formation to protocol team members. 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/ vice chair)
- DAIDS medical officer (MO)
- NICHD MO
- NIMH MO (if applicable)
- CRM(s)
- Statistician(s) (and/or epidemiologist(s))
- Protocol data manager(s) (PDM)
- Laboratory data manager(s) (LDM)
- DAIDS protocol pharmacist(s) (if applicable)
- Community representative(s)
- Laboratory Center (LC) representative(s)
- Pharmaceutical or industry representative(s) (if applicable)
- Laboratory technologist (LT)
- Westat representative (if applicable)
- Investigator(s)
- Site investigator from each participating Clinical Research Site (CRS)

Additional members, as required for a specific protocol, may include a pharmacologist (or pharmacometrician), 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
<b>Protocol chair</b>	<ul style="list-style-type: none"> <li>• Hold ultimate responsibility for execution of the study and final decision-making authority</li> <li>• See Section 4.1.2 for further details of chair responsibilities</li> </ul>
<b>Vice chair</b>	<ul style="list-style-type: none"> <li>• Collaborate with the protocol chair for execution of the study</li> <li>• See Section 4.1.2 for further details of vice chair responsibilities</li> </ul>
<b>Medical Officer (DAIDS, NICHD, or NIMH)</b>	<ul style="list-style-type: none"> <li>• Participate fully in protocol team discussions and decisions</li> <li>• Facilitate communication between protocol team and relevant NIH groups and staff</li> <li>• Provide timely review of study documents and response to queries</li> <li>• Provide oversight of safety monitoring during study implementation</li> <li>• DAIDS MO to review and sign-off on each study-specific MOP version</li> </ul>
<b>Clinical Research Manager (CRM)</b>	<ul style="list-style-type: none"> <li>• With protocol chair, provide scientific and operational input to the protocol and coordinate and lead protocol development and any subsequent protocol modifications, as applicable</li> <li>• Organize and document protocol team conference calls and meetings</li> <li>• Prepare study budget with Operations Center financial staff, in collaboration with the protocol chair and, as applicable, with input from other protocol team members and site representatives</li> <li>• Submit protocol for required IMPAACT and DAIDS reviews (Multidisciplinary Protocol Review Group (MPRG), applicable Scientific Review Committee, Regulatory, MO, Regulatory Affairs Branch) and manage the response/revision process, as needed (see Section 9)</li> <li>• Coordinate the site selection process (see Section 10)</li> <li>• Develop and produce the study-specific MOP with input from the Data Management Center (DMC), LC, and other protocol team members, as applicable (see Section 11)</li> <li>• Collaborate with protocol team members to coordinate the completion of study open to accrual requirements (see Section 11)</li> <li>• 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)</li> <li>• Coordinate the site activation process (see Section 11)</li> <li>• 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</li> <li>• Provide information on study progress to the sites, protocol teams, Network leadership, pharmaceutical representatives (if applicable), and/or DAIDS</li> <li>• With the SMC or DSMB coordinator, collaborate with Statistical and Data Management Center (SDMC) on SMC and/or DSMB reviews and reports</li> <li>• Contribute to study close-out procedures (see Section 14)</li> <li>• Participate in publication activities and facilitate, as needed (see Section 19)</li> <li>• See Section 2 for further details of Operations Center responsibilities</li> </ul>

**Table 4-1. Roles of Key Protocol Team Members**

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

**Table 4-1. Roles of Key Protocol Team Members**

Team Member	Primary Roles and Responsibilities
<p><b>Protocol Data Manager (PDM)</b></p>	<ul style="list-style-type: none"> <li>• Collaborate in the development of the protocol</li> <li>• Collaborate with the CRM to develop and produce the MOP, with primary responsibility for data management, reporting, and randomization sections</li> <li>• 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</li> <li>• Collaborate with CRM on review of site activation requirements related to data management prior to activation</li> <li>• Conduct training on data management and data collection instrument completion</li> <li>• Collaborate with statistician and LDM to develop and implement the SPDSMP (including development and distribution of routine reports)</li> <li>• Collaborate with LDM, pharmacologist, and statistician in the development and implementation of the PK data management plan, when applicable</li> <li>• Collaborate with statistician to generate interim analysis reports for the SMC or DSMB and final analysis reports</li> <li>• Provide support for data collection and management</li> <li>• Monitor study data in accordance with the protocol requirements and issue site queries as needed for quality assurance</li> <li>• Collaborate with CRM to provide support for operational matters that may influence study data</li> <li>• Assess site data quality and report results to protocol team, as needed</li> <li>• Conduct data management site visits, as needed</li> <li>• Contribute to study close-out procedures, including data collection and cleaning (see Section 14)</li> <li>• Participate in publication activities and facilitate, as needed</li> <li>• See Section 2 for further details of SDMC responsibilities</li> </ul>
<p><b>Laboratory Data Manager (LDM)</b></p>	<ul style="list-style-type: none"> <li>• Collaborate in the development of the protocol</li> <li>• Collaborate with PDM to develop data collection instruments and instructions</li> <li>• Collaborate with the LC representative and LT on development of the Laboratory Processing Chart (LPC; see Section 11)</li> <li>• Lead development and implementation of the LDMS Quick Add Templates</li> <li>• Collaborate with the statistician and PDM to develop and implement the SPDSMP</li> <li>• Lead development and implementation of the PK data management plan with the pharmacologist, statistician, and PDM, when applicable</li> <li>• Monitor laboratory data for the study in accordance with the protocol requirements and issue lab queries as needed for quality assurance</li> <li>• 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</li> <li>• Coordinate specimen shipping requests and data transfer agreements for receipt of resulting assay data, as needed</li> <li>• Contribute to study close-out procedures (see Section 14)</li> <li>• Participate in publication activities and facilitate, as needed</li> <li>• See Section 2 for further details of SDMC responsibilities</li> </ul>

**Table 4-1. Roles of Key Protocol Team Members**

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

**Table 4-1. Roles of Key Protocol Team Members**

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

### 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 Management 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 CRM facilitates and generally participates in the conference calls and meetings of these study-specific groups. Where applicable, the CRM 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 CRMs are not included in the group membership, a group member is designated to assume group management and documentation responsibilities of 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 (e.g., 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 (see Section 4.4).

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. 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.