18   NETWORK EVALUATION

The IMPAACT Network is committed to excellence in all aspects of its research. The Management Oversight Group (MOG) is responsible for overseeing a comprehensive process for evaluation of the Network with both ongoing and periodic components. The purpose of the evaluation process is to ensure that IMPAACT-affiliated National Institute of Allergy and Infectious Diseases (NIAID)-funded and *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD)-funded clinical research sites and other Network entities are functioning appropriately, and contributing to the successful development, execution, oversight, completion, and publication of studies and other activities that advance the IMPAACT research agenda. A robust system of ongoing and periodic performance evaluation through the procedures outlined in this section serves to document the success of Network entities in meeting evaluation standards and identify areas for improvement. It informs leadership decisions about changes that may be necessary to improve functioning and performance while ensuring participant safety and data integrity. It also provides information needed to facilitate appropriate allocation of Network resources.

Evaluations are performed on an ongoing basis by the MOG; comprehensive periodic reviews are conducted by the Network Evaluation Group (NEG), on behalf of the MOG. The Laboratory Center (LC) closely monitors the ongoing performance of specialty and site laboratories on behalf of the MOG. In addition to the ongoing and periodic evaluation activities of the MOG, LC, and NEG, the overall scientific direction and leadership of the Network, including the work of the scientific committees (SCs), will be evaluated every three years by an external scientific advisory group, on behalf of the Scientific Leadership Group (SLG). The group is directly advisory to the SLG and consists of experts in the Network's research areas who are free from conflicts of interest. Details related to the external scientific advisory group are provided in Section 2; the remainder of this section focuses on the ongoing and periodic evaluations by the MOG and NEG.

Ongoing Evaluation

The MOG routinely monitors the status of IMPAACT studies, which reflect the collective efforts of Network entities, and performance of clinical research sites (CRSs) through review of reports generated by the Operations Center and Statistical and Data Management Center (SDMC). The Operations Center generates a monthly Study Operations Report that provides updates on the status of studies in development and ongoing, participating CRSs, participant accrual, and study implementation issues. The SDMC generates monthly participant accrual and retention reports, by study and by CRS, as well as monthly site data management reports that provide information on data timeliness, data completeness, error responsiveness, and query responsiveness.

The LC closely monitors the ongoing performance of specialty and site laboratories. The SDMC provides laboratory data management reports to the LC with information on query responsiveness, quality of shipments to the Biomedical Research Institute (BRI), and data timeliness.

Additionally, the IMPAACT Study Monitoring Committee (SMC) provides the MOG with updates on study reviews. As described in detail in Section 13, the SMC routinely monitors participant safety, study progress, and the quality of study conduct for designated IMPAACT studies. SMC review findings and

recommendations are summarized for the MOG monthly; the MOG is also notified immediately of any SMC findings or recommendations that may have a significant impact on study implementation. Problems and performance deficiencies may also be reported to the MOG by the SCs and Network central resources (Operations Center, SDMC, LC). Similarly, for studies overseen by a Data and Safety Monitoring Board, any urgent findings or recommendations are shared with Network leadership as outlined in Section 13.

Ongoing evaluation of CRS performance is also performed by protocol teams through review of the same participant accrual and retention reports provided to the MOG, as well as review of study-specific monitoring reports provided by the SDMC, consistent with specifications of each study protocol and study progress data and safety monitoring plan (SPDSMP). Protocol team members from the Operations Center, SDMC, and LC also continually monitor all available information on CRS performance and notify teams and the MOG of any issues or concerns.

Through all of these mechanisms, the MOG continuously evaluates Network activities, sites, and studies so that performance problems are identified as soon as possible and can be addressed in a timely manner. Findings and recommendations identified during ongoing MOG evaluations are communicated to sites, study teams, and other Network entities as needed to ensure resolution and corrective action.

Periodic Evaluation

On behalf of the MOG, the NEG develops and carries out the Network evaluation program. The NEG is chaired by a non-voting *ex officio* member of the SLG; membership includes:

- IMPAACT Operations Center representative
- IMPAACT SDMC representative
- IMPAACT LC representative
- IMPAACT Community Advisory Board (ICAB) representative
- CRS representative
- Division of AIDS (DAIDS) representative
- NICHD Coordinating Contractor representative

The NEG oversees periodic evaluations of all IMPAACT-affiliated sites, as described in the remainder of this section. Performance is generally evaluated annually and, as each evaluation is completed, an evaluation report is generated and submitted to the MOG for review and action. This report focuses on critical aspects of study implementation at the site level, such as participant accrual and retention, data quality, laboratory performance, and regulatory issues. Evaluation reports are shared with the entities whose work was evaluated and with Network sponsors, as appropriate. Site community engagement programs are evaluated separately as determined by the ICAB in consultation with the MOG. At the request of the MOG, the NEG may evaluate and report on other Network entities in a similar manner.

18.1   Network Evaluation Plan and Performance Measures

The NEG develops performance metrics and an evaluation plan, utilizing the approach described below:

- Objectives, and the activities necessary to achieve them, are identified, reviewed, and adjusted as needed prior to each periodic evaluation by the NEG to determine their appropriateness and relevance to the performance of the Network at the time of the review.
- For each activity, the NEG identifies indicator(s) of whether objectives are being satisfactorily met; see Table 18-1. These are reviewed and adjusted as needed prior to each periodic evaluation to

determine their appropriateness and relevance to the performance of the Network at the time of the review.

- Indicator data are compiled to determine the extent to which objectives are being met; see Table 18-1.
- Based on the compiled data, the NEG submits an evaluation report to the MOG, highlighting successes and making recommendations for improvement.
- Evaluation reports are also sent to NIAID clinical trials unit (CTU) principal investigators (PIs) and CRS leaders (for their site), NICHD site PIs (for their site), Laboratory PIs and Directors, the Network sponsors, Operations Center, SDMC, and LC.
- Sites are provided the opportunity to confirm the accuracy of their evaluation results and are requested to respond to the NEG's findings and recommendations, as needed. Responses are reviewed by the NEG and recommendations for any follow-up actions are provided to the MOG. See Section 18.4 for a description of follow-up actions and possible outcomes.

18.2   Performance Criteria for IMPAACT-affiliated NIAID-funded Clinical Research Sites

Site performance within each study and across studies is reviewed for the period of evaluation (a 12-month time period, generally), with consideration of the number and stage of studies in which each is participating, recency of site engagement, and external factors that may impact site readiness and accumulation of sufficient data for meaningful evaluation.

Site performance measures and standards, as determined by the NEG, are specified in Table 18-1 below.

Table 18-1. Performance Measures and Standards for NIAID Clinical Research Sites

Criterion	Measure(s)	Standard/Satisfactory	Source
Protocol Implementation Timeline	Time to enrollment once site receives the final protocol for submission to the institutional review board/ethics committee (IRB/EC) and other regulatory entities: • Date protocol distributed to site • Date of protocol registration approval • Date of study-specific activation • Date of first enrollment at site Note: Includes protocols finalized for implementation during the evaluation period	Informational only	Operations Center, NIAID Clinical Research Management System (CRMS), SDMC
Participant Accrual	• Number of participants enrolled across the life of the study and within past 12 months compared to site-specific accrual target for study Note: Includes studies currently enrolling (or open to accrual) and studies closed to accrual during the evaluation period	Projected number versus actual number (projected number is based on site-provided goals); goal is >90% over the study accrual period for studies that have closed to accrual in the evaluation period Note: For NIAID-funded sites: DAIDS may consider discontinuing core funding for sites with <5 new enrollments or <3 in complex or high-priority studies	SDMC (with projections provided by the sites through the Operations Center)
Participant Retention	• Number of participants on study for the past 12 months • Number of participants reported to the data management center (DMC) as lost to follow-up for any reason (e.g., participant withdrawal, participant did not return/could not be located by the site) in past 12 months and over life of the study Note: Includes studies currently enrolling (or open to accrual) and studies closed to accrual during the evaluation period	>90% overall retention or as per protocol	SDMC

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Table 18-1. Performance Measures and Standards for NIAID Clinical Research Sites

Criterion	Measure(s)	Standard/Satisfactory	Source
Clinical Data Management	• Data timeliness: Percent of visit tracking and study event tracking electronic case report forms (eCRFs) keyed within 14 days. Assesses the amount of time to key visit tracking and study event tracking eCRFs based on the participant's visit date.	≥ 90%	SDMC
	• Data completeness: Percent of eCRFs entered. Assesses the current form status of Rave eCRFs that are not marked as overdue.	≥ 95%	SDMC
	• Error responsiveness: Percent of errors answered within 3 days. Assesses site responsiveness to Site from System queries (errors). These are queries automatically triggered on the eCRF, immediately after saving the record.	≥ 95%	SDMC
	• Query responsiveness: Percent of queries answered within 14 days. Assesses site responsiveness to Site from DM and Site from Coder queries.	≥ 90%	SDMC
	• Regulatory: Percent of serious adverse events (SAEs) reported within 3 days to DAIDS Adverse Experience Reporting System (DAERS), including SAEs for studies in eData	100%	SDMC
Laboratory Data and Specimen Management	• Lab Query Responsiveness: Respond to queries within 2 weeks	≥ 90%	SDMC
	• BRI Repository Shipment Evaluations: Overall resolution and responsiveness to shipment problems based on the total number of shipments. See Shipment Evaluation SOP.	≥ 90 composite score	SDMC
Laboratory Quality Assurance	• Safety Testing (50% of score) • DAIDS Virology Quality Assurance (VQA) Test Performance (25% of score) • Immunology Quality Assessment (IQA) Test Performance (12.5% of score) • Peripheral blood mononuclear cell (PBMC) Cryopreservation (12.5% of score)	≥ 90% composite score	LC
Outstanding Laboratory Critical Action Items	• Resolution of critical action items within 90 days of notification	≤ 90-day resolution	LC
Protocol Deviations	• Listing of reportable protocol deviations per site (see Section 12)	No protocol deviations	SDMC

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18.3   Overall Network Productivity

Overall Network function and productivity are evidenced in a number of ways, including but not limited to, development, review, and approval of new study proposals (concept sheets, data analysis concept sheets [DACS], new works concept sheets [NWCS]) and protocols; initiation of new studies and completion of ongoing studies; results reporting, presentation, and publication; and evidence of impact on public health policy and/or product licensure or labeling changes. The NEG will report on these outcomes periodically as requested by the MOG and as part of the overall Network evaluation.

18.4   Outcomes and Actions

As noted above, each Network entity evaluated will be provided an opportunity to review evaluation findings and confirm their accuracy.

Sites with below-standard performance measures will generally have 30 days to provide the NEG with a written plan for corrective action in the relevant performance areas. The NEG may offer technical assistance and guidance and may recommend actions to facilitate improvement. Improvement must be demonstrated within six months or reasons provided for why this cannot be achieved. In such cases, an alternate time period must be agreed to by the NEG.

If a site fails to meet the standard for a specific measure(s) in two or more consecutive periodic evaluation cycles, the NEG may recommend to the MOG specific actions such as temporary closure of enrollment screens, pending review of site or laboratory procedures in that area(s).

A site's failure to meet the Network's performance requirements in two consecutive evaluation cycles – or by an earlier timepoint as determined by the MOG – may result in the withdrawal of protocol funds and/or a recommendation that Network affiliation with the site be terminated, with appropriate close-out activities to be completed. A site that is not meeting performance standards and is at risk of losing Network affiliation is provided the opportunity to summarize any extenuating circumstances that they would like considered before a final decision is made. The final decision on the site status with the Network will be determined by the MOG in consultation with the sponsors after considering the recommendations made by the NEG.

Network sponsors' requirements and/or cross-network evaluation of site performance and contributions – including the determination of whether the site is needed to support the scientific agenda of one or more networks – may result in a change in funding status, irrespective of the Network's evaluation.