1 OVERVIEW OF THE IMPAACT NETWORK

1.1 Background of the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network

The International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network is a global collaboration of investigators, institutions, community representatives, and other partners organized for the purpose of evaluating prevention and treatment interventions for HIV and HIV-associated complications and co-infections, including tuberculosis (TB), in infants, children, adolescents, and pregnant and postpartum women through the conduct of high quality clinical trials. IMPAACT's vision and overall goal is to end the worldwide HIV epidemic among these vulnerable populations. To achieve this goal, the IMPAACT Network evaluates novel and durable treatments for both HIV and TB, strategies for antiretroviral treatment (ART)-free remission, and strategies to address the complications, co-morbidities, and co-infections affecting these populations of interest with or at risk of HIV.

IMPAACT was formed in 2006 through a merger of investigators from the Pediatric AIDS Clinical Trials Group (PACTG) and the Perinatal Scientific Working Group of the HIV Prevention Trials Network (HPTN). Following re-competition of leadership grants in 2013–2014, a new seven-year funding cycle began in December 2014. The Network was successfully re-competed in 2020, with a new seven-year funding cycle beginning in December 2020.

Overall support and funding for IMPAACT is provided by the National Institute of Allergy and Infectious Diseases (NIAID), with support and co-funding from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), and the National Institute of Mental Health (NIMH), all components of the United States National Institutes of Health (NIH). See Section 1.5, below, for additional details related to NIH support of IMPAACT.

In this Manual of Procedures (MOP), "HIV" refers to HIV-1 unless otherwise stated, as HIV-1 is the most widespread type of HIV worldwide and is the most common circulating type of HIV among in locations where IMPAACT studies are conducted.

See the IMPAACT Network website for additional details: http://impaactnetwork.org.

1.2 IMPAACT Mission and Scientific Agenda

IMPAACT's mission is to significantly decrease incident HIV and HIV-associated infections and to decrease mortality and morbidity due to HIV and HIV-associated infections and co-morbidities among infants, children, adolescents, and pregnant and postpartum women. IMPAACT's research agenda aims to:

- Advance ART of pregnant and postpartum women with HIV, aiming to optimize maternal and child health outcomes, and accelerate the evaluation (pharmacokinetics [PK], safety, antiviral efficacy), licensure, and optimal use of potent and durable ARVs for pregnant women and infants, children, and adolescents with HIV.
- Evaluate the potential for ART-free remission through therapeutic interventions aimed at prevention, clearance and post-treatment control of HIV reservoirs in infants, children, and adolescents with HIV.
- Evaluate novel approaches for TB prevention, diagnosis and treatment in pregnant and postpartum women and infants, children, and adolescents with and without HIV that will lead to optimal dosing and regimens, licensing and improved treatment outcomes.
- Determine optimal and feasible methods for the prevention and management of complications and co-infections of HIV and its treatment in infants, children, adolescents, and pregnant and postpartum women.

IMPAACT's mission and research agenda are organized into four research areas: novel and durable interventions for treatment of HIV (treatment), tuberculosis, ART-free remission, and complications and co-infections. These research areas are described in detail below.

1.2.1 Novel and Durable Interventions for Treatment of HIV (Treatment)

Despite rapid advances in ARV development, the mean delay from approval of HIV drugs in adults to the availability of data in children is 3.8 years (range 1–9 years), with most drugs still lacking dosing data in neonates. The knowledge gap in pregnant women is worse, with a median of six years from time of drug approval to the first-published PK data in pregnancy. As a result, pregnant and breastfeeding women inevitably use ARVs in the absence of any pregnancy-specific safety or dosing data, potentially putting both the mother and infant at risk. Additionally, ART virologic suppression rates in infants, children, and adolescents lag behind those observed in adults. To address these gaps, the IMPAACT Network's treatment aims are to advance the development and approval of novel and durable interventions for the treatment of HIV in pregnant women and infants, children, and adolescents. Priorities include:

- Characterizing the PK properties and dosing of ARVs and relevant drug-drug interactions (DDIs) among women during pregnancy and lactation, and their infants
- Evaluating novel prophylaxis regimens for infants born to women with HIV
- Identifing and rapidly evaluating the PK, safety, and antiviral efficacy of the most promising ARVs for first-line treatment, accelerating licensure for pediatric populations living with HIV
- Optimizing the use of currently available ARVs in achieving virologic suppression among pediatric populations with ARV experience
- Evaluating ARVs and regimens that address the specific needs of adolescents with HIV

1.2.2 Tuberculosis

Globally, 10 million cases of active TB disease and 1.6 million TB-related deaths occurred in 2017; TB is both the most common cause of death by a single infectious agent overall and the leading cause of death in people living with HIV. Pregnant and postpartum women, children ages <15 years, and persons with

HIV constitute at least 20% of the global TB burden, and TB is one of the top three causes of mortality among women of childbearing age. Multidrug-resistant TB (MDR-TB), with its increasing prevalence and high mortality – especially among persons with HIV – threatens global progress towards the World Health Organization (WHO) "End TB Strategy" targets. With the co-occurrence of the TB and HIV epidemics, understanding the drug interactions between treatments for these two infectious diseases is critical. Of additional concern is the lack of drug dosing and safety data in pregnant women, neonates and infants, for existing and novel anti-TB therapies and especially for MDR-TB, due to the historic exclusion of these populations from interventional TB trials. Priorities include:

- Evaluating the efficacy, PK, and safety of new and shorter drug regimens to prevent DS-TB and DR-TB in infants, children, adolescents, and pregnant and postpartum women with and without HIV
- Evaluating the efficacy, PK, safety, and acceptability of new drug regimens, optimize existing drug dosing and evaluating novel drugs for the treatment of DS-TB and DR-TB disease in infants, children, adolescents, and pregnant and postpartum women with and without HIV
- Evaluating novel tools for the diagnosis of active TB, correlates of TB treatment response and markers of disease progression in infants, children, and adolescents with and without HIV
- Evaluating novel TB vaccines for prevention of TB disease in infants, children, adolescents, and pregnant women

1.2.3 ART-Free Remission

The scientific premise of the Network's ART-free remission research agenda is that infants, children, and adolescents with perinatally-acquired HIV have distinct biological features that will enable favorable responses to very early (within the first 48 hours of life) and early ART, combined with immune-based therapeutic interventions or other novel interventions resulting in reservoir restriction or eradication with a goal of long-term control of HIV off ART. A major barrier to ART-free remission is the latent HIV reservoir that resides predominantly in resting memory CD4+ T cells. Perinatal infection, which includes a known time-frame of HIV exposure, is a unique opportunity to facilitate very early treatment with novel ART strategies, including immune-based therapies that can control HIV latency. The Network continues to build on a successful foundation to investigate strategies to achieve ART-free remission. Priorities include:

- Evaluating whether very early (within the first 48 hours of life) therapy with more potent ART that blocks virus entry and/or integration, in combination with broadly neutralizing antibodies (bNAbs), sufficiently limits HIV reservoir establishment in infants and leads to ART-free remission
- Evaluating immune-based therapies, including therapeutic HIV vaccines and bNAbs, in children and adolescents with HIV who have displayed long-term suppression on ART and therefore have small, low-diversity HIV reservoirs, with the goal of achieving ART-free remission
- Examining the potential for ART-free remission following combined initial therapy with ARVs plus immunotherapies, with and without latency reversal agents, in adolescents and young adults with horizontally-acquired HIV to rapidly induce virologic control and potentiate elicitation of a "vaccinal effect" mediated through antigen-antibody immune complexes
- Examining the role of the central nervous system and T follicular helper CD4+ T cells as sanctuary sites following perinatal HIV infection and developing studies to explore the elimination of HIV reservoirs within these anatomic locations
- Identifying, within the context of IMPAACT ART-free remission and other clinical trials, optimal virologic and immunological biomarkers to detect and quantify HIV reservoirs, and predictors of reservoir size and time to viremic rebound

1.2.4 Complications and Co-Infections

People with HIV are living longer, with emerging complications and co-infections increasingly affecting the management of their HIV. Growing evidence indicates that infants, children, and adolescents (with both perinatally- or horizontally-acquired infection) with HIV experience substantial neurodevelopmental, neuropsychological, and mental health complications. Infants and children with HIV have significant neurodevelopmental delays including deficiencies in learning and executive function that persist despite early ART initiation. Adolescents with HIV often face substantial mental health co-morbidities, including depression, and overall poorer quality of life – both affecting ART adherence. A number of studies have found higher rates of depression among pregnant and postpartum women living with HIV than women without HIV; the challenging management of the dual epidemics of HIV and depression form a vicious cycle, with each disease worsening the status of the other and potentially contributing to inadequate ART adherence and a resulting lack of viral suppression, putting the woman, child and partners at risk. Priorities include:

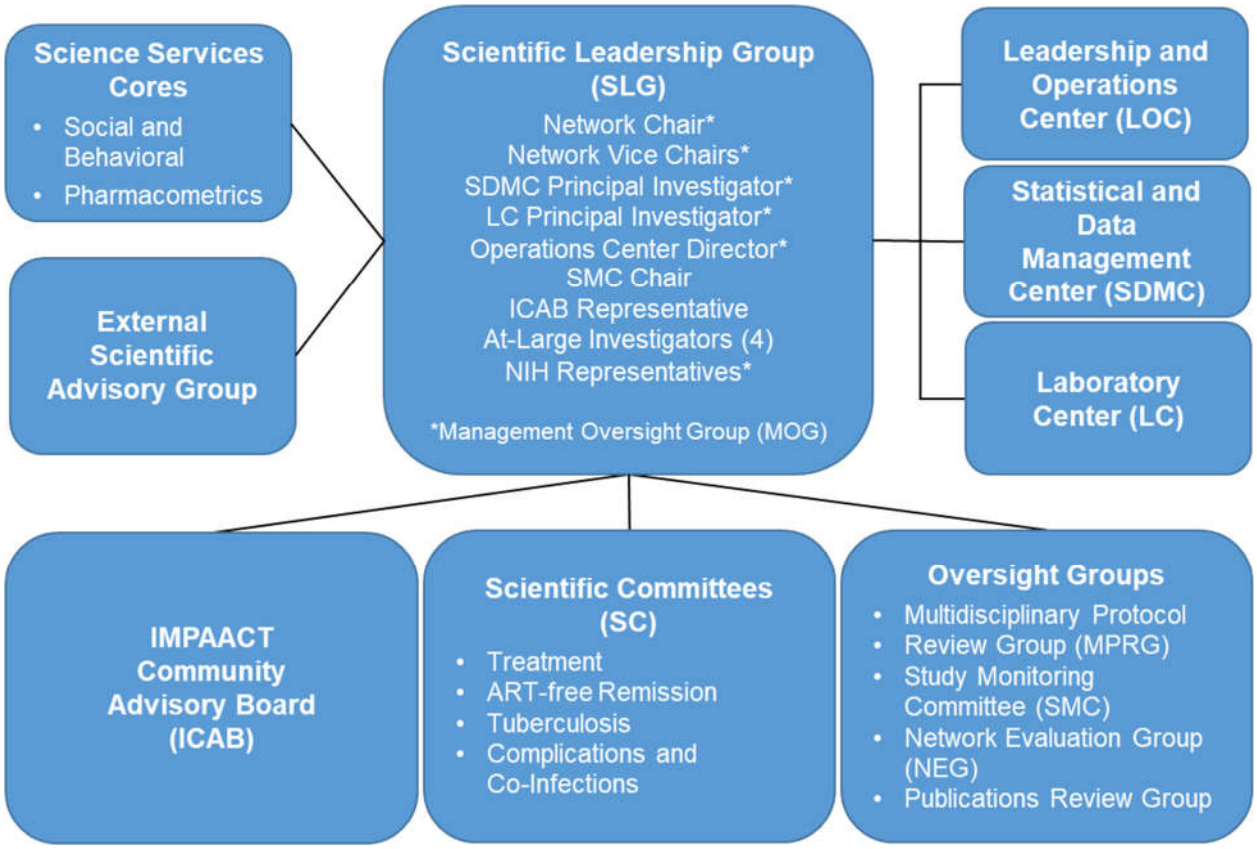
- Investigating potential neuroprotective and neurotoxic effects of ART to preserve neurocognitive development and mental health in infants, children, and adolescents
- Refining and optimizing the evaluation and treatment of neurocognitive and mental health disorders, particularly executive dysfunction, depression and PTSD
- Evaluating novel preventive and/or therapeutic approaches to high-priority diseases among pediatric populations with or affected by HIV, including respiratory syncytial virus (RSV), working with NIAID and other partners
- Evaluating other co-morbidities and complications of importance for pediatric, adolescent and pregnant populations with HIV, with other partners and NIH institutes.

1.3 IMPAACT Network Organization

The IMPAACT Network is led by the Network chair and vice chairs. The Network chair serves as the chair of the Scientific Leadership Group (SLG), which sets the overall research priorities of the Network, in close consultation with five scientific committees (SCs) aligned with the four research areas described above. With input from the IMPAACT Community Advisory Board (ICAB) the SLG, along with the SCs, drives the scientific research agenda in alignment with the Network's mission and scientific agenda. To enable the SLG to focus on scientific priorities and leadership, most of the Network management functions are the responsibility of the Management Oversight Group (MOG), whose membership is a subset of the SLG. Through this structure, protocol teams are formed and studies are implemented at clinical research sites, which furthers the IMPAACT Network's mission. Additional details on the roles and responsibilities of each component included in Figure 1-1 are provided in Section 2.

In addition to the groups included in Figure 1-1, clinical research sites (CRSs) and protocol teams support the overall development and implementation of IMPAACT studies. IMPAACT research is conducted through the NIAID- and NICHD-supported sites throughout the world. Investigators and other representatives of these sites, including community representatives, participate in all levels of the IMPAACT Network structure. Further details on CRSs is included in Section 2. Protocol teams are created for each IMPAACT research study so that studies are designed and implemented with the highest scientific and ethical standards. Protocol teams assume primary responsibility for scientific leadership in the development, implementation, and day-to-day oversight of IMPAACT studies and the dissemination of their results. Further details on the composition and functions of protocol teams is included in Section 4.

Figure 1-1. Network Leadership Organizational Structure



1.4 IMPAACT Operational Policies

The organizations and individuals that comprise the IMPAACT Network adhere to relevant US Federal regulations, along with the NIH/NIAID/Division of AIDS (DAIDS) policies as a condition of receipt of Federal funding. Each clinical research site also adheres to relevant local regulations and policies. The work of the IMPAACT Network is performed in accordance with the standards of good documentation practices, as described further in Section 3.

In addition, IMPAACT-specific policies and procedures guide Network investigators, site staff, and other members in meeting relevant requirements and standardizing site operations for each IMPAACT study. These policies and procedures are contained in the following:

- ***IMPAACT Network MOP:*** This manual provides general guidelines for Network members and describes IMPAACT policies and procedures for all sites, protocol teams, and staff. The IMPAACT Operations Center coordinates the development and maintenance of the Network MOP in collaboration with representatives of the SDMC, LC, and Network leadership; representatives of the MOG are responsible for reviewing sections prior to their release.

- ***Study-specific Implementation Materials:*** In addition to study protocols, the conduct of each IMPAACT study may be guided by study-specific implementation materials, including a study-specific MOP, Laboratory Processing Chart (LPC), monitoring and analysis plans, and participant enrollment and data collection materials. The materials provide instructional and reference resources and are generally developed for each individual study. Note that study requirements and procedures

(including those described in site and study-specific standard operating procedures [SOPs]) must be conducted in accordance with the study protocol. In the event that study-specific implementation materials or tools are inconsistent with the protocol, the specifications of the protocol take precedence. See Section 11 for further details regarding study-specific implementation materials.

- ***Site and Study-specific SOPs:*** SOPs for site operations and study operations ensure standard, uniform performance of site and study-related tasks and compliance with IMPAACT procedures, International Council for Harmonisation Good Clinical Practices (ICH GCP) guidelines, and US Food and Drug Administration (FDA) regulations, where applicable.

1.5 Governmental Organizations Involved in IMPAACT Research

As described above, financial support for IMPAACT is provided by NIAID with co-funding from NICHD and NIMH. The Network works with governmental regulatory agencies including the US FDA, the US Office of Human Research Protection (OHRP), and similar agencies in other countries where IMPAACT research is conducted.

1.5.1 National Institute of Allergy and Infectious Diseases/Division of AIDS

NIAID and its co-funding Institutes have substantial scientific and programmatic involvement in the IMPAACT Network through technical assistance, advice, and coordination. The role of the NIH staff within IMPAACT is to assist and facilitate, not to direct, the research activities.

Within NIAID, DAIDS develops and implements the research agenda to address the HIV/AIDS epidemic, supporting a global research portfolio to advance biological knowledge of HIV/AIDS and its related co-infections and co-morbidities. DAIDS staff participate on IMPAACT protocol teams, as described in Section 4, and governing committees, as described throughout the Network MOP. They also facilitate communication among other partners, such as other funding agencies, pharmaceutical companies, the US FDA, and IMPAACT leadership. DAIDS also supports and funds clinical research sites that participate in the IMPAACT Network.

As shown in Figure 1-2, DAIDS is comprised of the Office of the Director and four scientific programs. The Prevention Sciences Program, which includes the Maternal, Adolescent, and Pediatric Research Branch, is the scientific program responsible for IMPAACT. In addition, several groups within the Office of the Director collaborate to support IMPAACT Network functions, including the Office of Clinical Site Oversight (OCSO), which includes the Pharmaceutical Affairs Branch (PAB) and Monitoring Operations Branch (MOB), and the Office for Policy in Clinical Research Operations (OPCRO), which includes the Regulatory Affairs Branch (RAB).

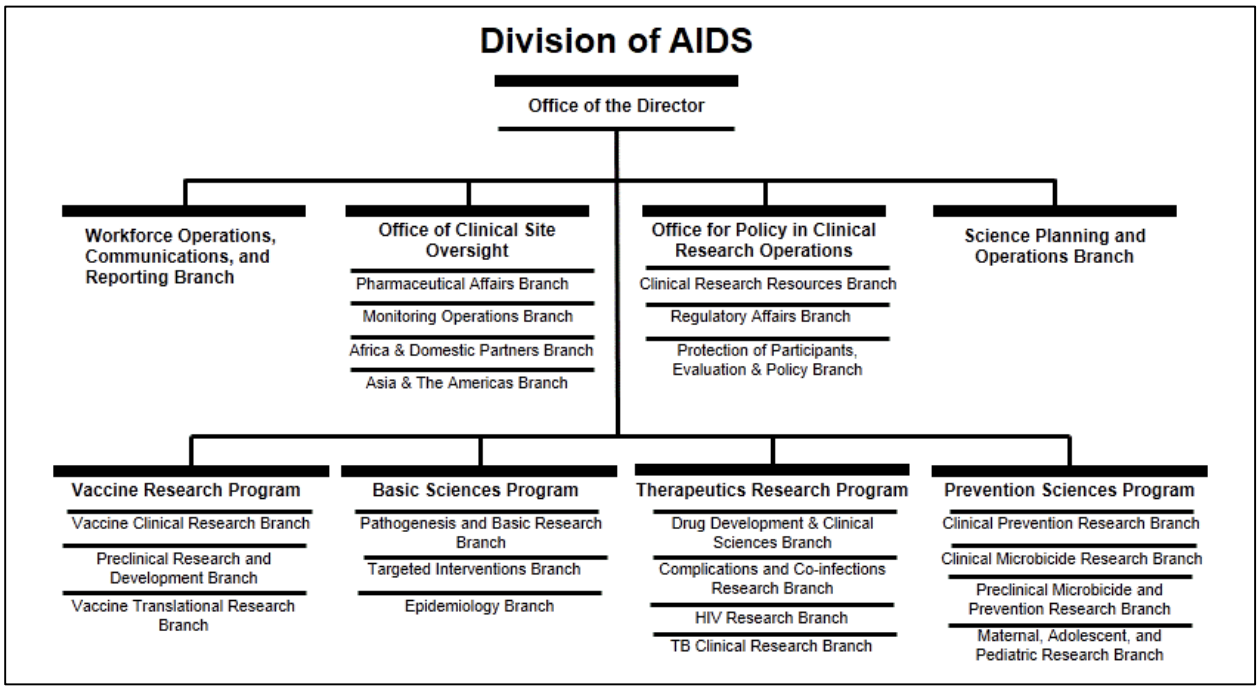
When an IMPAACT study is to be conducted under an Investigational New Drug (IND) application, DAIDS typically holds the IND and negotiates a clinical trial agreement (CTA) with the collaborating pharmaceutical company to document the responsibilities and rights of each party for the clinical trial. The agreement typically includes, but is not limited to, IND application sponsorship (if applicable), provision of study products, safety and data monitoring, confidentiality, and access to data. In general, terms in the CTA covering access to data conform to DAIDS and Network policies. See Section 11 for additional details related to the CTA process.

DAIDS typically has the option to file an IND application for investigational agents evaluated in IMPAACT studies. Appropriate DAIDS staff advise protocol teams on behalf of NIH on the specific regulatory requirements for IND sponsorship. In situations in which DAIDS is the IND sponsor, they also assemble, review, and submit the required regulatory documents to the US FDA, as described in Section 9.

Further detail on DAIDS's roles and responsibilities within the IMPAACT protocol development and modification process are described in Section 9.

General information on DAIDS may be found on the DAIDS website.

Figure 1-2. DAIDS Organizational Structure



Note: Accessed on 2 October 2018 from: https://www.niaid.nih.gov/about/division-aids-org-chart

1.5.1.1 Maternal, Adolescent, and Pediatric Research Branch of the Prevention Sciences Program

The Maternal, Adolescent, and Pediatric Research Branch of the Prevention Sciences Program within DAIDS is responsible for IMPAACT. As part of this responsibility, its representatives participate across all areas of the Network. DAIDS staff participate on IMPAACT protocol teams, as described in Section 4, and governing committees, as described through the Network MOP.

For all IMPAACT protocols, a DAIDS medical officer (MO) is assigned to the protocol team, as described in Section 4; of note, during study implementation, the DAIDS MO monitors the safety of the intervention(s) in ongoing studies and is provided with the interim and final analysis reports. When a protocol is sponsored or co-funded by a collaborating institution or research group (i.e., NICHD or NIMH), monitoring activities may also be conducted by their medical representative(s). As described further in Section 12, the NICHD MO may be designated by the DAIDS MO to serve as the DAIDS MO designee to meet quorum requirements.

1.5.1.2 Office for Policy in Clinical Research Operations

The Office for Policy in Clinical Research Operations (OPCRO) manages and supports DAIDS clinical research and helps ensure the following:

- Compliance with applicable regulations, standards, and good clinical practice guidelines
- Study participant safety and welfare
- Study quality and integrity

Regulatory Affairs Branch

The Regulatory Affairs Branch (RAB) is a branch within OPCRO. RAB is responsible for regulatory affairs across the DAIDS programs. RAB performs regulatory management and surveillance and is the liaison to the US FDA for clinical trials sponsored/funded by DAIDS. RAB members sign the Form FDA 1571 for DAIDS-sponsored INDs.

Protection of Participants, Evaluation, and Policy Branch

Protection of Participants, Evaluation, and Policy Branch (ProPEP) is a branch within OPCRO. ProPEP provides subject matter expertise on human subjects protections matters (i.e., 45 CFR 46, 21 CFR 50, and 21 CFR 56), Institutional Review Board/Ethics Committee (IRB/EC) requirements, and HSP/GCP compliance issues. ProPEP also develops and maintains DAIDS policy documents to promote harmonization and to ensure compliance with applicable laws, regulations, guidelines, and policies, and serves as the liaison to OHRP.

1.5.1.3 Office of Clinical Site Oversight

The Office of Clinical Site Oversight (OCSO) facilitates the clinical research of the DAIDS scientific programs by overseeing NIAID-supported clinical research sites associated with the NIAID-sponsored HIV/AIDS clinical trials networks. As such, it performs the following key functions:

- Manages the NIAID Clinical Trials Units and Clinical Research Sites associated with the HIV/AIDS Clinical Trials Networks
- Coordinates a range of clinical site management activities for the networks
- Serves as a resource on operational and regulatory issues and ensures that appropriate clinical research standards, policies, and procedures are used by clinical research sites
- Provides oversight and management of a contract to ensure that clinical site monitoring is conducted in accordance with applicable regulatory requirements
- Provides pharmaceutical expertise for protocol development and implementation, as well as oversight of a study product storage and distribution contract
- Verifies that optimal safeguards are employed for participant safety and ensures that high quality research practices are used
- Monitors clinical sites' progress enrolling underserved populations and ensuring community representation

Pharmaceutical Affairs Branch

The Pharmaceutical Affairs Branch (PAB) in OCSO assigns a DAIDS pharmacist to participate on each IMPAACT protocol team, as described in Section 4; the DAIDS pharmacists' roles include:

- Coordination and oversight of the supply, packaging, and distribution of study products
- Advisement to protocol teams on all pharmaceutical aspects of protocol development, including consultation on available dosage forms and placebos, product packaging, and supply to sites
- Coordination with pharmaceutical companies, as applicable, to ensure adequate and timely supply of study products
- Oversight and monitoring of quality assurance standards and SOPs for all pharmacy- and product-related issues at research sites participating in IMPAACT trials

PAB is responsible for the review and approval of each CRS Pharmacy Establishment Plan (PEP), which must be in place at each CRS prior to protocol registration. PAB assesses the pharmaceutical aspects of each protocol and communicates its assessment during Scientific Review Committee (SRC) reviews.

Monitoring Operations Branch

The Monitoring Operations Branch (MOB) in OCSO serves as a resource on operational and regulatory issues and ensures that appropriate clinical research standards, policies, and procedures are used by NIAID-funded clinical research sites and provides oversight and management of a contract to ensure that clinical site monitoring is conducted in accordance with applicable regulatory requirements. MOB staff coordinate with NICHD's clinical site monitoring contractor to ensure consistency in site monitoring plans and approaches across all sites (NIAID-funded and NICHD-funded) participating in IMPAACT studies.

1.5.1.4 DAIDS Contractors

Regulatory Support Center

The DAIDS Regulatory Support Center (RSC) is a contract-based organization that provides comprehensive clinical regulatory support for all IMPAACT studies. DAIDS RSC works closely with DAIDS OPCRO. This support consists of:

- Reviewing protocol documents for regulatory compliance
- Preparing and filing new IND Applications and amendments to existing INDs in compliance with the procedural and substantive requirements of 21 CFR 312 (examples of submissions to the FDA include original IND Applications, Annual Reports, Safety Reports, and Responses to FDA Requests for Information)
- Reviewing all informed consents (ICs) during review at the Clinical Sciences Review Committee (CSRC) and Prevention Sciences Review Committee (PSRC) and Regulatory Review stages.
- Translating sample ICs into Spanish
- Reviewing and tracking all required clinical site regulatory documents for all protocol versions at each CRS to ensure that all documents needed to fulfill the study sponsor's regulatory obligations relating to protocol registration are reviewed for completeness and accuracy within the specified timeline set up by the sponsor
- Planning and conducting trainings on protocol registration procedures as requested by DAIDS
- Collecting adverse events reported by sites participating in IMPAACT studies, processing the events for review by the DAIDS MO, and preparing the reports for transmittal to the FDA, if required

- Establishing internal procedures and developing safety training for the CRSs
- Supporting the DAIDS CSRC and PSRC by providing technical and administrative support to the SRC reviews of concept proposals and protocols
- Preparing CTAs
- Distributing and managing Investigator Brochures (IBs) and safety information

Clinical Research Products Management Center

The Clinical Research Products Management Center (CRPMC) is a contract-based organization that provides centralized ordering, storage, and distribution of study products evaluated in IMPAACT trials. The CRPMC works closely with PAB. CRPMC responsibilities include:

- Receiving shipments of study products from the manufacturer
- Storing products under appropriate and secure conditions
- Communicating with and distributing study products to authorized IMPAACT site pharmacists
- Monitoring study product inventories
- Monitoring study product expiry dates
- Recalling and processing study product returns
- Executing final dispositions of study products
- Maintaining records of study product management
- Repackaging or relabeling study products under Good Manufacturing Practices (GMP), as needed
- Preparing participant kits, if needed, for specific protocols

The CRPMC also provides the Clinical Site Monitor with reports of product shipments to the CRSs for protocol monitoring and study assessment visits.

Clinical Site Monitoring Contractor

The Clinical Site Monitoring Contractor (CSM) is a contract-based organization that evaluates the NIAID-funded CRSs for adherence to Good Clinical Practice (GCP), regulatory compliance, accurate protocol implementation, internal quality assurance, HIV testing and counseling, and test agent accountability. The CSM works closely with the MOB.

CSM staff visit CRSs periodically to review study documentation for selected protocols and participants, review regulatory documents, audit pharmacies, and document error resolution per assignments received from DAIDS. Further details on monitoring by the CSM are included in Section 13.

NICHD-funded CRSs are monitored by a separate contractor, which collaborates with the MOB to ensure a consistent monitoring approach for IMPAACT studies.

1.5.2 *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

NICHD is a co-funding Institute and has substantial scientific and programmatic involvement in the IMPAACT Network through technical assistance, advice, and coordination. NICHD staff participate on IMPAACT protocol teams, as described in Section 4, and governing committees, as described throughout the Network MOP. For all IMPAACT protocols, an NICHD MO is assigned to the protocol team, as described in Section 4.

NICHD also supports and funds CRSs that participate in the IMPAACT Network; these sites are overseen by a separate coordinating center that works collaboratively with DAIDS.

1.5.3 National Institute of Mental Health

NIMH is a co-funding Institute and has substantial scientific and programmatic involvement in the IMPAACT Network through technical assistance, advice, and coordination. NIMH staff participate on IMPAACT protocol teams, as described in Section 4, and governing committees, as described throughout the Network MOP. For select IMPAACT protocols, an NIMH MO is assigned to the protocol team, as described in Section 4.

1.5.4 US Food and Drug Administration

In its capacity as a regulatory agency of the US Federal government, the US FDA has responsibility for reviewing and approving protocols for IMPAACT studies conducted under an IND, regardless of whether the studies are conducted at US or non-US sites. For many IMPAACT studies, DAIDS holds the IND and thus is responsible for working directly with the US FDA. The US FDA receives and reviews copies of serious adverse event reports that meet the criteria of Title 21, Code of Federal Regulations (CFR) 312.56. The US FDA is responsible for review of study data that are submitted in support of licensure applications and may conduct audits of IMPAACT studies, including but not limited to conducting regulatory inspections at US and non-US sites.

Additionally, in-country agencies may also provide regulatory oversight of IMPAACT trials performed in non-US settings.

1.5.5 Department of Health and Human Services

1.5.5.1 Office for Human Research Protections

The US Office for Human Research Protections (OHRP) fulfills responsibilities set forth in the Public Health Service Act, including monitoring compliance relative to Department of Health and Human Services (DHHS) regulations for the protection of human subjects in research supported by any component of the DHHS. OHRP is also responsible for establishing criteria for and negotiating Assurances of Compliance with institutions engaged in research involving human subjects supported by the DHHS. The IMPAACT Network operates in full compliance with the regulations and guidelines of OHRP.

For IMPAACT, DAIDS is responsible for protocol review, including review and approval of sample IC language. The approved language is subsequently distributed with the protocol for relevant IRB/EC review and approval.

1.5.5.2 US Office for Civil Rights

For studies conducted in US settings in institutions that are covered entities, compliance with the Health Insurance Portability and Accountability Act (HIPAA) must be assured. Each institution is responsible for ensuring its own compliance. For non-US institutions, each institution is responsible for determining whether it is a covered entity under HIPAA and, if so, whether each covered entity is responsible for ensuring compliance with this requirement, as set forth in Title 45 CFR 160 and 164.