CIBMTR®
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Manual of Operations

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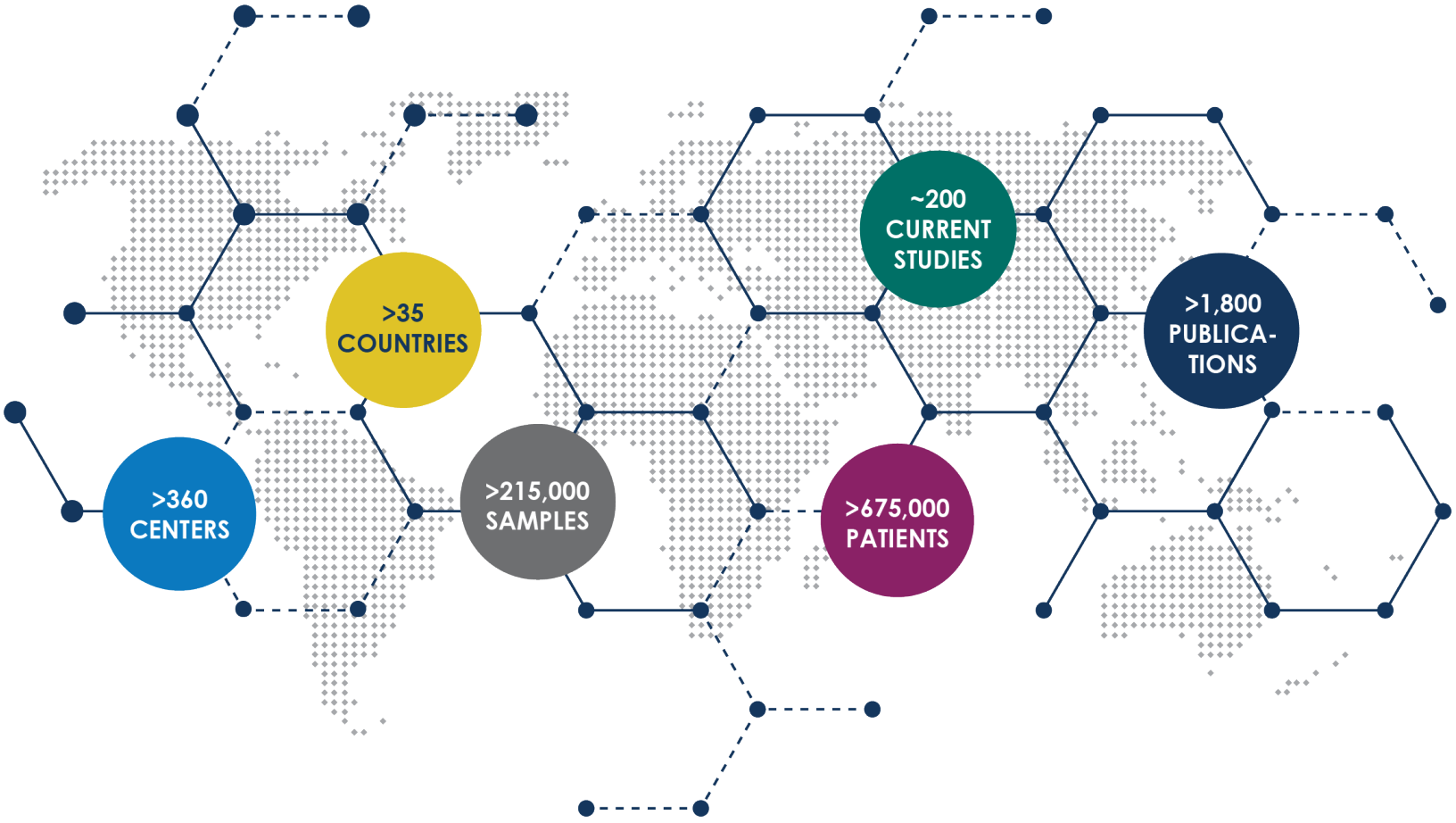

CIBMTR® (Center for International Blood and Marrow Transplant Research®) is a research collaboration between the Medical College of Wisconsin and NMDP.

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CHAPTER 1: ORGANIZATION

1.1 STRATEGY

CIBMTR® (Center for International Blood and Marrow Transplant Research®) is a research collaboration between the Medical College of Wisconsin (MCW) and NMDP.

1.1.1 Mission

CIBMTR is a collaborative resource of data and experts supporting research in cellular therapies to improve patient outcomes.

1.1.2 Vision

The vision of CIBMTR is to be the premier data and resource solution for cellular therapy.

1.1.3 Strategic Pillars

- **Data**. Acquisition, analysis, sharing, and visualization of diverse data.
- **Research**. Transformational, interventional, and observational research.
- **Equity**. Elimination of barriers to ensure health equity.
- **Innovation**. Operational innovation and excellence.
- **Next Generation**. Fostering the next generation of cellular therapy research professionals.

1.2 HISTORY

In July 2004, CIBMTR was formed through an affiliation of the International Bone Marrow Transplant Registry (IBMTR) / Autologous Blood and Marrow Transplant Registry (ABMTR) of MCW and NMDP. The purpose of the affiliation was to establish a formal working relationship for collaborative research to advance the field of hematopoietic cell transplantation (HCT) and related research areas, including adoptive cellular therapies (ACT). In 2004, the IBMTR / ABMTR (MCW) and NMDP agreed to conduct all HCT-related research activities jointly, and a Joint Affiliation Board maintains high-level oversight (**Figure 1.1**). CIBMTR continues to integrate with MCW and NMDP at many levels; this document includes references to the support provided by both parent organizations' Human Resources, Legal, Information Technology (IT), and Finance Departments.

Prior to the affiliation, the IBMTR / ABMTR and NMDP had broad research expertise in HCT, including observational research and clinical trials. The IBMTR began in 1972 as a voluntary organization of 12 transplant centers involving 50 transplant patients worldwide. In 1989, the IBMTR began collaborating with the ABMTR in its research efforts. By 1994, more than 400 institutions in more than 40 countries were involved in sharing patient data and conducting scientific studies with the IBMTR / ABMTR (MCW). NMDP was established in 1987 to provide unrelated donors for patients in need of HCT. NMDP also conducted outcomes research and developed the CIBMTR Biorepository of donor-recipient samples. At the time of the affiliation, the NMDP network included 164 transplant centers, 80 donor centers, 101 collection centers, 89 apheresis centers, and 17 cord blood banks. CIBMTR was formed in an effort to unite the research efforts and complementary strengths of both organizations.

IBMTR / ABMTR strengths included:

- A strong record of clinical research, including publications in HCT and statistical methodology
- A long history of effective collaborations with a large network of international centers
- Key personnel with acknowledged leadership in the field and combined training in both clinical HCT and biostatistics

- An extensive database of clinical information on autologous as well as related and unrelated donor allogeneic transplant recipients

NMDP strengths included:

- Experience with a large network of donor, collection, and transplant centers
- A database that included almost all unrelated donor transplants in the United States (US) with donor-recipient biorepository samples for a large subset of these transplants
- A business office experienced in contractual relationships with biorepository samples, contract laboratories, pharmacies, and other organizations essential for trial-related activities
- A patient advocacy office experienced in providing educational materials for patients treated in or considering participation in clinical trials and in conveying information derived from CIBMTR studies

In 2005, the US Congress passed legislation to establish the C.W. Bill Young Cell Transplantation Program, a component of which is the Stem Cell Therapeutic Outcomes Database (SCTOD) (**Chapter 6**). The purpose of the SCTOD is to increase the availability, safety, and efficacy of allogeneic HCTs and to collect data on all allogeneic HCTs performed in the US as well as all HCTs performed outside the US using products procured through the Program. CIBMTR was awarded the contract to operate the SCTOD in 2006. As a result, CIBMTR was established as the national registry to which data on all allogeneic transplants performed in the US must be reported. This manual includes a description of the changes that were made to successfully execute the requirements of the contract.

CIBMTR's Research Database has been used to demonstrate safety and efficacy of diverse HCT approaches, optimize selection of donor and graft sources, evaluate new drugs and strategies to increase efficacy and prevent complications, assess center-specific outcomes, and predict patient outcomes based on clinical and treatment characteristics. Based on this successful model, in 2014 CIBMTR adapted its infrastructure to meet the need to assess the real-world safety and efficacy of ACT, including chimeric antigen receptor T cell (CAR-T) therapies, and gene therapies.

1.3 OVERVIEW

CIBMTR collaborates with the global scientific community to advance cellular therapy research worldwide. It facilitates research with important effects on clinical practice. This prospective and observational research is accomplished through medical, scientific, and statistical expertise; a large network of centers; a comprehensive biospecimen repository; and a Research Database containing clinical data for more than 675,000 patients.

CIBMTR's network includes more than 360 active centers worldwide. Most centers report patient outcomes data electronically through FormsNet^{SM}, CIBMTR's web-based application. Centers are also able to report data through paper data collection forms if they are unable to access the electronic system. CIBMTR's Research Database is a large repository of information on patients who have been treated with allogeneic or autologous HCT or ACT in which hematopoietic stem cells were used for clinical applications other than HCT. In addition to maintaining this Research Database, CIBMTR provides expert statistical support to investigators analyzing these data. The data and the analytic support available through CIBMTR's Coordinating Center have contributed to the successful completion of more than 1,800 publications.

1.3.1 Programs

CIBMTR has six major research programs:

- **Statistical Methodology Research Program (Chapter 5).** This program facilitates development of new statistical approaches to cellular therapy research, prepares educational review articles on data analysis, and provides input to other scientific projects. The Chief Statistical Director serves as head of this program, a unique asset of which is the expertise of partner Statistical Directors from the MCW Division of Biostatistics. A Statistical Director is assigned to advise each of the 11 CIBMTR Working Committees **(Chapter 2)** and oversees the work and participates in the training of Statisticians.
- **Clinical Outcomes Research Program (Chapter 6).** This program focuses on the effects of cellular therapy on recipients and donors as well as the clinical and treatment factors influencing the effectiveness of the therapy. These topics often cannot be addressed in single-center studies or randomized trials, and the Research Database is a key component of this research. The program includes research conducted within the Scientific Working Committees (**Section 6.1**) and SCTOD (**Section 6.2**) as well as research related to other cellular therapies (**Section 6.3**), Medicare Coverage with Evidence Development studies (**Section 6.4**), and patient-reported outcomes (**Section 6.5**).
- **Immunobiology Research Program (Chapter 7).** This program facilitates studies using the CIBMTR Biorepository and associated CIBMTR data, provides immunobiology expertise for testing and validation strategies from human cell sources, and conducts research with an impact on operations.
- **Clinical Trial Programs (Chapter 8)**:
    - **Blood and Marrow Transplant Clinical Trials Network (BMT CTN)**. The Data and Coordinating Center (DCC) coordinates the activities of the BMT CTN, which was established in October 2001 to conduct large, multi-center clinical trials. DCC activities include overseeing the implementation and completion of clinical trials, facilitating effective communication and cooperation among participating centers and collaborators, and coordinating patient enrollment to trials nationwide. The DCC is overseen by MCW, NMDP, and The Emmes Company (a contract research organization). BMT CTN collaborates and integrates with CIBMTR for data and expertise.
    - **CIBMTR Clinical Research Organization Services (CRO Services)**, formerly known as the Resource for Clinical Investigations in Blood and Marrow Transplantation (RCI BMT). CRO Services, established as a formal program in 2001, provides sponsors, institutions, and researchers with infrastructure and expertise in clinical trial design, conduct, and analysis. CRO Services provides full-scale and a la carte research operations for multi-center studies of all phases.
- **Health Services Research Program (Chapter 9).** This program facilitates studies in a variety of focus areas, including economic analyses, inequities in and barriers to access, treatment decision-making and support, health care utilization, quality and value of care, and survey research. Its overall objectives are to increase access to and utilization of cellular therapy and to improve patient outcomes through health services and policy research.
- **Bioinformatics Research Program (Chapter 10).** This program conducts research with molecular data, develops new methodologies, builds prediction models from integrated data sources, characterizes diverse genetic population needs and

potential, drives new technology applications, and translates research findings into practice to save lives.

CIBMTR research activities are supported by several sources, including:

- U24 Resource Grant jointly funded by the National Cancer Institute (NCI) (lead institute); National Heart, Lung, and Blood Institute (NHLBI); and National Institute for Allergy and Infectious Diseases (NIAID)
- BMT CTN U24 cooperative agreement jointly funded by NHLBI (lead institute) and NCI
- SCTOD contract from the Health Resources and Services Administration (HRSA)

Additional support is provided by NMDP, MCW, foundations, and corporate organizations. See **Chapters 18** and **19** for more information.

1.3.2 Sources and Uses of Data

CIBMTR represents an international group of centers that provide data on consecutive HCT and ACT to its bi-campus Coordinating Center. CIBMTR performs and supports studies using these data, in some cases linking the data to research samples in the CIBMTR Biorepository. Researchers can propose studies to, or request data from, CIBMTR for their own investigations.

Data are collected at two levels using data collection forms developed by CIBMTR:

- Transplant Essential Data (TED) and Cellular Therapy Essential Data (CTED) level
- Comprehensive Report Form (CRF) level

TED and CTED forms include internationally accepted standard data fields focusing on critical HCT and CAR-T variables. CRFs capture extensive patient, disease, treatment, and outcome data for a subset of patients. Data collected for patients treated with gene therapies are collected on the CRF level. For more information about data collection processes, see **Chapter 12** and the *Data Management* webpage.

Requests for CIBMTR data must adhere to CIBMTR rules for releasing data (**Chapter 14**). Investigators requesting CIBMTR data must follow appropriate procedures for:

- Submission of proposals (**Chapter 6**)
- Investigator engagement in developing and completing research studies (**Chapter 6**)
- Rules of authorship (**Chapter 3**)
- Submission of data (**Chapter 12**)

Data can also be requested through the *HRSA Bone Marrow and Cord Blood Donation and Transplantation* website.

1.4 ORGANIZATIONAL STRUCTURE

CIBMTR represents an international network of more than 360 centers that submit data for patients. CIBMTR's Coordinating Center is staffed by approximately 250 employees who work within its functional areas:

- Statistical Operations
- Immunobiology Research
- Clinical Trials
- Health Services Research
- Bioinformatics Research
- Data Operations

- Human Research Protection
- Quality Assurance
- Information Technology
- Advancement
- Business Operations
- Industry Relations
- Finance and Administration MCW

CIBMTR's Executive Leadership Team (**Section 1.4.1**) provides oversight of the organization and is responsible for administrative and scientific operations. The team reports to the Joint Affiliation Board (**Figure 1.1**), which is comprised of members from both NMDP and MCW. CIBMTR committee governance structure (**Chapter 2**) ensures the organization meets the needs and priorities of its medical and scientific communities. CIBMTR's organizational structure is depicted in **Figure 1.2** and outlines the integration of scientific oversight within key operational areas.

1.4.1 CIBMTR Executive Leadership Team

CIBMTR's Executive Leadership Team is comprised of four members:

- Chief Scientific Director, CIBMTR MCW
- Chief Scientific Director, CIBMTR NMDP
- Executive Scientific Director, Policy and Governance, CIBMTR MCW
- Vice President, CIBMTR and Clinical Services, NMDP

This group is responsible for setting the research strategy and aligning the operations of CIBMTR. The Executive Leadership Team meets weekly to discuss tactical and strategic items.

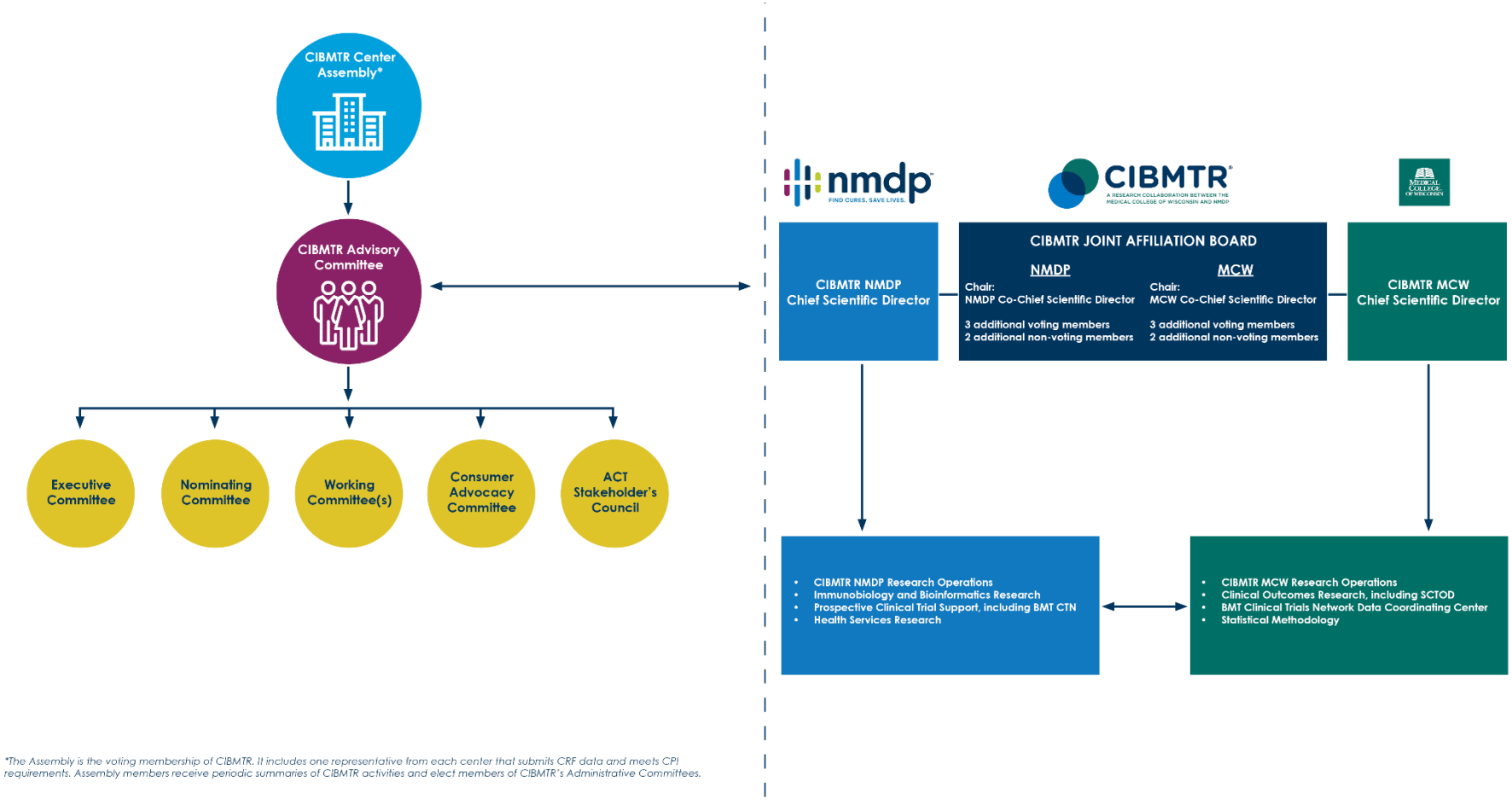
1.4.2 CIBMTR Bi-Campus Senior Leadership Team

CIBMTR Bi-Campus Senior Leadership Team comprises eight members:

- Chief Scientific Director, CIBMTR NMDP
- Chief Scientific Director, CIBMTR MCW
- Vice President, CIBMTR and Clinical Services, NMDP
- Executive Scientific Director, Policy and Governance, CIBMTR MCW
- Senior Scientific Director, CIBMTR NMDP
- Senior Scientific Director, CIBMTR NMDP
- Senior Scientific Director, CIBMTR MCW
- Senior Scientific Director, CIBMTR MCW

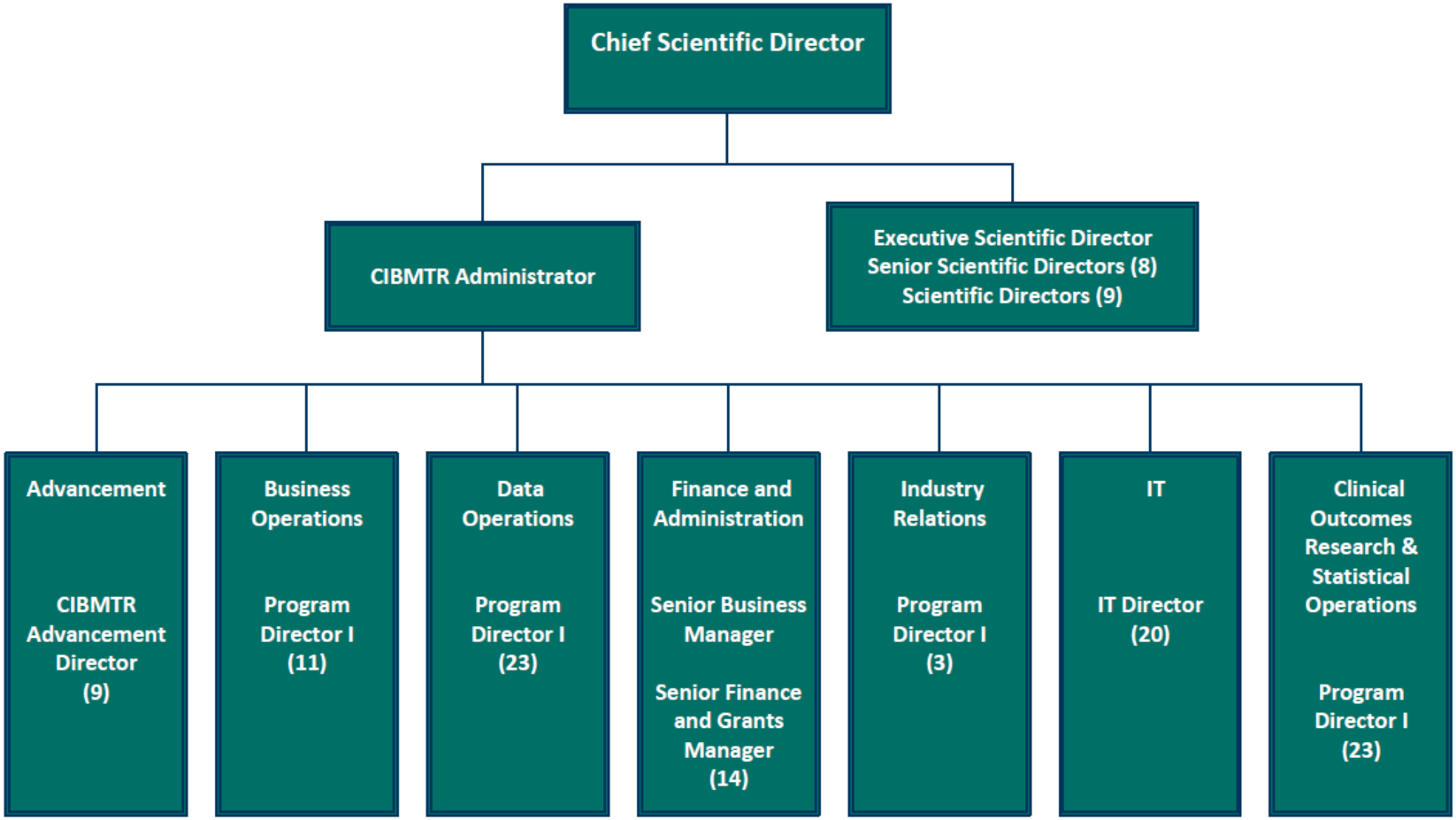
This group is responsible for providing input into the research agenda of CIBMTR, and its members also serve on CIBMTR's Joint Affiliation Board (**Section 2.2.1**). The Bi-Campus Senior Leadership Team meets monthly.

Figure 1.1: CIBMTR Governance Structure



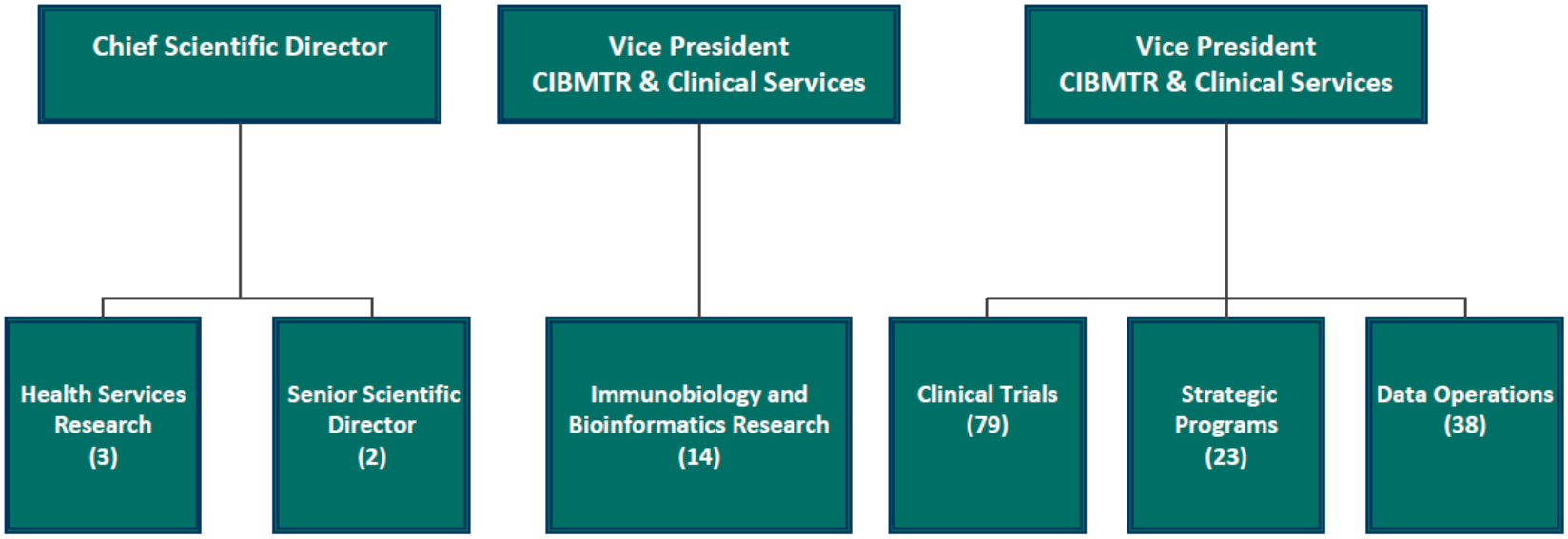
*The Assembly is the voting membership of CIBMTR. It includes one representative from each center that submits CRF data and meets CPI requirements. Assembly members receive periodic summaries of CIBMTR activities and elect members of CIBMTR's Administrative Committees.

Figure 1.2: (Page 1 of 2): CIBMTR MCW Organizational Structure



Note: Numbers in parentheses indicate number of staff reporting to the given leader.

Figure 1.2: (Page 2 of 2): CIBMTR NMDP Organizational Structure



Note: Numbers in parentheses indicate number of staff reporting to the given leader.

CHAPTER 2: COMMITTEE STRUCTURE

CIBMTR committee structure is designed to elicit broad input from the cellular therapy community. It ensures the activities of the organization, and its use of resources, are consistent with the priorities of this community. CIBMTR committees include experts in various disciplines and related diseases. Committees may also include patient and caregiver representatives as well as representatives from CIBMTR's federal funding agencies, including the National Institutes of Health (NIH) and HRSA.

Eligible members must meet one or more of the below criteria:

- In most cases, Administrative Committee and Working Committee Chairs should be from member centers or organizations that submit HCT and ACT research data and/or collaborate with CIBMTR. Centers are also required to meet continuous process improvement (CPI) requirements and not be in the status of "audit consequences" (**Chapter 12**).
- Eligible individuals from non-US centers will show evidence of commitment to CIBMTR's mission. Examples of this may include but are not limited to representing organizations with collaborative data sharing agreements, regular attendance and participation at the Tandem Meetings | Transplantation & Cellular Therapy Meetings of American Society for Transplantation and Cellular Therapy (ASTCT) and CIBMTR (Tandem Meetings), participation in task forces or other initiatives, active membership in CIBMTR committees, and/or authorship on CIBMTR publications.
- Advisory Committee Chair-Elect nominees are typically US-based, may not be from the same institution as the Immediate Past Chair or current Chair, and should be from a center that makes a substantive contribution to CIBMTR.
- All individuals serving on CIBMTR committees will be asked annually to disclose any potential Conflict of Interest and to adhere to CIBMTR's Conflict of Interest Policy (POL-0001).

All committees, except the Joint Affiliation Board, have staggered terms of succession to preserve continuity. Administrative support for committee activities is provided by CIBMTR's Coordinating Center. Committee membership is evaluated periodically to ensure adequate representation. The overall CIBMTR organizational structure, including its committees, is shown in Figure 1.1.

2.1 CIBMTR ASSEMBLY

The Assembly is CIBMTR's voting membership. It includes one representative from each center that submits data and meets CPI requirements (**Chapter 12**). The Assembly meets annually during the Tandem Meetings. Assembly members receive periodic summaries of CIBMTR activities and submit nominations for candidates for CIBMTR committee leadership positions, the Distinguished Service Award, and the Tandem Meeting's Mortimer M. Bortin Lecturer.

2.2 ADMINISTRATIVE COMMITTEES

2.2.1 Joint Affiliation Board

As noted in Chapter 1, CIBMTR was formed through an affiliation of the IBMTR/ABMTR at MCW and NMDP. A Joint Affiliation Board, with representation from both organizations, was established to provide general oversight of CIBMTR's budget and operations. The Joint Affiliation Board:

- Reviews and approves an annual budget
- Reviews and approves a research plan

- Assesses CIBMTR productivity
- Amends, as necessary, terms of the Affiliation Agreement
- Reviews and approves data access and confidentiality policies

The Chief Scientific Directors (CIBMTR NMDP and CIBMTR MCW) serve as Co-Chairs of the Joint Affiliation Board. Each organization has three additional voting members and two non-voting members who serve as part of the Board. The Board meets three times per year.

2.2.2 Advisory Committee

The Advisory Committee is a multi-stakeholder group of experts representing the range of CIBMTR's activities. The major responsibility of this committee is to advise CIBMTR's leadership on scientific direction, policy, and priority use of resources in the context of the larger cellular therapy environment. In this capacity, its scope of activities includes:

- Reviews the scientific strategy for CIBMTR
- Advises on CIBMTR international strategy
- Advises on CIBMTR data use and sharing strategies
- Advises on key CIBMTR contracts including SCTOD
- Participates in promoting CIBMTR mission
- Supports grant and contract applications and renewals
- Approves leadership positions in all CIBMTR committees as proposed by the Nominating Committee, including:
    - Approves Working Committee Chair appointments
    - Approves Advisory and Nominating Committee appointments
    - Oversees Advisory Committee subcommittee, including ensuring representation of appropriate topics from these committees, this includes Nominating Committee, Consumer Advocacy Committee, and Working Committees
    - Supports the structure, activities, and metrics associated with the Working Committees and has the authority to remove and replace Working Committee Chairs who are not participating adequately
    - Reviews audit results and recommends global measures to correct deficiencies
    - Approves the recipient of the Distinguished Service Award, presented annually at the Tandem Meetings [Standard Operating Procedure (SOP)-0238]
    - Approves the annual Mortimer M. Bortin lecture following the procedure: Mortimer M. Bortin Lecturer Selection for Tandem Meetings (SOP-0237)
    - Participates in task forces
    - Advises CIBMTR on the development of diversity and inclusion strategies and community involvement

Individuals appointed to the Advisory Committee should represent stakeholders broadly, including:

- Expertise in adult and pediatric clinical care
- Expertise in HCT, ACT, and gene therapies
- Expertise in donor selection and graft collection and manipulation
- Representation of US and non-US centers
- Familiarity with CIBMTR operations

- Representation of patient, family, and donor interests

Appointed terms are three years in length and begin on March 1 following year-end elections. Exceptions are the shorter, two-year Chair term and one-year terms of the Chair-Elect and Immediate Past Chair (see below). Appointed individuals may serve more than one term but not consecutively. The terms of ex officio voting members are indefinite based on indicated position in their organization.

Members appointed by the Advisory Committee include:

- Chair (1): Two-year term
- Chair-Elect (1): One-year term prior to serving as Chair
- Immediate Past Chair (1): One-year term after serving as Chair
- At Large Members (~8), at least 3 with ACT expertise and at least 3 with HCT expertise
- International Members (~4)
- Consumer Advocacy Committee Co-Chairs (2)*
- ACT Stakeholders Council Chair (1)*
- Cord blood representative (1)

*Term on the Advisory Committee follows the members' terms on the Consumer Advocacy Committee or ACT Stakeholders Council.

Ex officio voting members include:

- ASTCT President (1)
- Office of Naval Research representative (1)
- NCI Project Officer (1)
- NHLBI Project Officer (1)
- NIAID Project Officer (1)
- Nominating Committee Chair (1), (does not vote on Nominating Committee tasks)
- Other ad hoc members as needed to fulfill requirements

Ex officio non-voting members include:

- HRSA Contracting Officer Representative
- CIBMTR Leadership and invitees

A call for nominations for positions occurs in the spring of each year for those positions with terms expiring the following spring. With these nominations, the Nominating Committee recommends appointments for approval by the Advisory Committee. The current ASTCT President serves as the ASTCT representative, the current Nominating Committee Chair serves as Nominating Committee representative and the current ACT Stakeholders Council and Consumer Advocacy Committee Chairs serve as representatives, respectively.

If a committee member relinquishes their position on the Advisory Committee prior to the end of the term and within the annual nomination cycle, the replacement of that committee member follows the standard appointment process, and the committee member is appointed to a three-year term. Except for the Chair, if a committee member relinquishes their position outside the annual nomination cycle, the position will remain open until it can be filled during the next nomination cycle. If the Chair is not able to complete the term, the Chair-Elect will move into the Chair position.

The Advisory Committee Chair may choose to convene an Executive Session when deliberations pose confidentiality issues, such as individual conflict of interest or center

performance. Required attendees include the Chair, Past Chair, or Chair-Elect along with a minimum of three other committee members. Members will be invited based on their expertise in the topic of discussion.

2.2.2.1 Leadership Responsibilities and Meeting Frequency

Advisory Committee Chair:

- Leads the Advisory Committee meetings throughout their term, including in person at the annual Tandem Meetings
- Agrees and approves meeting agendas and minutes with CIBMTR Leadership
- Reviews committee leadership Conflict of Interest disclosures
- Approves the appointment of CIBMTR representatives, including a Program Chair, to the Tandem Meetings Scientific Organizing Committee
- Performs functions on behalf of CIBMTR at the annual Tandem Meetings, including participating as part of the Joint Senior Leadership Team, on monthly planning calls, and in the Scientific Organizing Committee as well as introducing certain speakers, such as the Mortimer M. Bortin lecturer, and presenting awards
- Contributes materials to CIBMTR newsletters or other communications
- Chairs any executive sessions of the Advisory Committee that are convened
- Participates in annual onboarding of new Advisory Committee members
- Fulfills all other roles of the Advisory Committee as needed
- Attend an onboarding prior to their first year on the Advisory Committee
- Attend at least 75% of the annual Advisory Committee meetings

Advisory Committee Chair-Elect:

- Replaces the Chair to lead meetings in the unusual situation that the Chair is unavailable or has declared a conflict of interest
- Moves to the Chair role early in the event that the Chair should unexpectedly leave the position
- Approves the appointment of CIBMTR representatives, including a Program Chair, to the Tandem Meetings Scientific Organizing Committee
- Participates, as able, in any executive sessions of the Advisory Committee that are convened
- Participates in annual onboarding of new Advisory Committee members
- Fulfills all other roles of the Advisory Committee as needed

Advisory Committee Past Chair:

- Supports the incoming Chair in their role
- Participates, as able, in any executive sessions of the Advisory Committee that are convened
- Fulfills all other roles of the Advisory Committee as needed

Advisory Committee Member:

- Agrees with and approves meeting minutes
- May be asked to contribute materials to CIBMTR newsletters or other communications
- May participate in annual onboarding of new Advisory Committee members
- Fulfills all other roles of the Advisory Committee as needed

- Attend an onboarding prior to their first year on the Advisory Committee
- Attend at least 75 percent of the annual Advisory Committee meetings

Advisory Committee Member representing a subcommittee (Consumer Advocacy Committee, Nominating Committee):

- Represents their subcommittee on the Advisory Committee, including raising topics of interest to the committee
- Fulfills all other roles of the Advisory Committee as needed

A meeting of the Advisory Committee is held annually during the Tandem Meetings. Additional meetings take place by conference call at least two times annually. CIBMTR's Coordinating Center takes minutes at each meeting, following the Administrative Committee Meeting Minutes Standard Operating Procedure (SOP-0196).

2.2.3 Nominating Committee

The Nominating Committee is responsible for:

- Reviewing nominee information for those who are interested and willing to serve as members of Working Committees, Administrative Committees, the Data and Safety Monitoring Committee of CIBMTR CRO Services, and CIBMTR's Working Committee Training and Leadership Program, and recommending nominees to the Advisory Committee for appointment approval.
- Assisting with the selection of the Distinguished Service Award and the Tandem Meetings Mortimer M. Bortin Lecturer. A request for nominees is solicited by a survey following the Tandem Meetings and is presented and deliberated at the spring Nominating Committee meeting. The committee then recommends a candidate to the Advisory Committee. The Advisory Committee approves the final recipient.

The committee seeks input from CIBMTR's Assembly, Advisory Committee, and Working Committee Chairs for Administrative Committee and Working Committee Chair recommendations and for the Distinguished Service Award and the Mortimer M. Bortin Lecturer. It receives input from CIBMTR CRO Services program staff regarding Data and Safety Monitoring Board positions and the Working Committee Training and Leadership program staff regarding nominees for the leadership program. The Coordinating Center distributes email requests for nominees. Nominating Committee deliberations are held by teleconference. The committee considers overall expertise and junior investigators interested in becoming more involved in CIBMTR activities as well as researchers from international centers.

The diverse nature of the cell therapy community must be reflected in all CIBMTR committees. In this regard, the Nominating Committee prioritizes representation from all candidate backgrounds and works to ensure heterogeneous center representation and that candidate and center diversity aligns with the commitment of CIBMTR to ensure health equity and to improve access to cellular therapies. The Nominating Committee also seeks to avoid single-center over-representation and, to the extent possible, to identify suitable candidates with racial, ethnic, and gender diversity. All nominees must provide a conflict-of-interest disclosure prior to consideration.

The Nominating Committee includes six members appointed by CIBMTR's Advisory Committee for three-year terms. One member is selected based on specific expertise in ACT research. If a committee member relinquishes their position on the Nominating Committee before the end of the term and within the annual nomination cycle, the replacement of the committee member follows the standard appointment process. Except for the Chair, if a committee member relinquishes the position outside the annual nomination cycle, the

position remains open until it can be filled during the next scheduled nomination cycle. Due to the need to maintain staggered terms, the term of the new / replacement committee member is independently assessed. If possible, a full three-year term is offered. However, a shorter term may be offered to prevent the loss of multiple committee members at the same time. The term of this committee member then ends at the date of the original position, and the new member is eligible for nomination to a second term.

The Nominating Committee Chair is elected by the committee. When elected, the Chair will retain the role throughout the term of their committee membership. If the Chair is not able to complete the full term, the committee will be asked to elect someone from the remaining members. The Nominating Committee Chair also serves as the committee's representative on the Advisory Committee.

2.2.3.1 Leadership Responsibilities and Meeting Frequency

Nominating Committee Chair

- Leads Nominating Committee meetings
- Ensures CIBMTR leadership positions are filled per Nominating Committee guidelines
- Advises on Nominating Committee procedures
- Fulfill other Nominating Committee duties as needed
- Represents the Nominating Committee on the Advisory Committee
- Attend at least 75% of the annual Nominating Committee meetings

Nominating Committee Members

- Ensures Nominating Committee responsibilities are fulfilled
- Fulfill other Nominating Committee duties as needed
- Ensures broad representation across all CIBMTR leadership roles
- Attend at least 75% of the annual Nominating Committee meetings

This committee meets by teleconference three times annually (generally in early spring, mid-summer, and late summer) and as needed throughout the year.

2.3 OTHER COMMITTEES

2.3.1 Consumer Advocacy Committee

The Consumer Advocacy Committee provides valuable patient and donor perspectives during the development of CIBMTR's research agenda. It also helps coordinate initiatives for presenting CIBMTR research outcomes to the public.

Committee representatives participate in three Scientific Working Committees per the Consumer Advocacy Committee Charter:

- Graft-versus-Host Disease Working Committee
- Donor and Recipient Health Services Working Committee
- Morbidity, Recovery, and Survivorship Working Committee

Consumer Advocacy Committee members may participate in other Working Committees as desired.

Consumer Advocacy Committee membership includes a CIBMTR Scientific Director; seven patient representatives (patients, family members, and donors); two Co-Chairs (who serve as patient / family representatives on the Advisory Committee); and ex officio members.

Center directors and coordinators nominate patient representatives for committee membership. Then a panel of Consumer Advocacy Committee Co-Chairs, CIBMTR

representatives, and NMDP Patient Services representatives conduct phone interviews and recommend specific candidates for membership. Finally, the Advisory Committee approves recommended candidates.

Members serve as many as two three-year terms, which are staggered to maintain continuity. If elected as Co-Chair, a member may serve one additional three-year term. The Scientific Director provides scientific support and oversight; CIBMTR provides administrative support, and NMDP Patient Services representatives provide subject matter expertise.

Ex officio members include:

- CIBMTR Leadership and invitees
- NMDP Patient Services representatives
- HRSA representatives

The committee meets in person annually at the Tandem Meetings and by teleconference as needed.

2.3.2 ACT Stakeholders Council

The ACT Stakeholders Council acts as a specialized group in cell and gene therapies that provides input to the Advisory Committee and CIBMTR leadership on relevant topics in the field. It also serves a liaison between CIBMTR and different stakeholders, including the cell and gene therapy community, professional societies, payors, and industry, to better position CIBMTR as a resource to the field.

ACT Stakeholders Council membership includes:

- CIBMTR Scientific Director
- One Chair (who also serves on the Advisory Committee)
- Three core members with ACT expertise
- At least three affiliate members depending on the topic being discussed
- Ex officio members
- CIBMTR Leadership and invitees
- NCI project officer
- CAC representative

Affiliate members are assigned and approved by the Advisory Committee, including the NIH project officers.

The responsibility of the ACT Stakeholders Council is to serve as a standing task force to provide guidance to CIBMTR. The Advisory Committee selects and prioritizes topics to be addressed by the ACT Stakeholders Council. Topic ideas may come from the CIBMTR Assembly, CIBMTR Leadership, ACT Stakeholders Council, and Advisory Committee. After the ACT Stakeholders Council researches and discusses selected topics, committee members present their recommendations to the Advisory Committee.

The committee meets in person annually at the Tandem Meetings and by teleconference as needed.

2.3.3 Working Committees

Most clinical outcomes research, a core activity of the organization, is conducted under the auspices of 11 Scientific Working Committees (Chapter 6). The major responsibilities of these committees are specific to their research areas.

Working Committee leadership positions include:

- Chairs (3-4)
- CIBMTR Scientific Director(s) (1-2)
- CIBMTR Statistical Director (1)
- CIBMTR Statistician(s) (1-2)

Chairs are experts in their fields and have demonstrated commitment to the work of CIBMTR. A Coordinating Center administrative staff member requests nomination in the spring of each year for Working Committee Chair terms expiring in the following spring. Nominees provide biographical information if they are interested in being considered for the role. Current Working Committee leadership provides input regarding the nominees, and the Nominating Committee puts forth recommendations to the Advisory Committee. Once appointed, Chairs hold non-renewable, three-year terms to maintain continuity throughout study lifecycles and research agendas. Chairs must wait three years after they have completed a term to be eligible for another.

If a Working Committee Chair relinquishes their position before the end of the term and within the annual nomination cycle, the replacement will follow the standard appointment process. If a committee member relinquishes their position outside the annual nomination cycle, the position will be filled as soon as possible. Due to the need to maintain staggered terms, the term of the new / replacement committee member will be independently assessed. If possible, a full three-year term will be offered. However, if a three-year term would cause too many Chairs to leave the committee at the same time, the new / replacement committee member's term will end at the date of the original position. The new / replacement committee member who served a shorter term would then be eligible for nomination to serve a second consecutive term, waiving the three-year wait period required of previous Chairs.

2.3.3.1 Leadership Responsibilities and Meeting Frequency

- Facilitate the committee's research portfolio to ensure its highest possible quality.
- Consider important study questions that have not yet been suggested, and develop new scientific ideas.
- Recruit new CIBMTR study investigators.
- Participate in data collection development and revision process; review content and agree with changes before they are finalized.
- Attend a minimum of 80% of all meetings and teleconferences.
    - Participate in CIBMTR Statistical Meeting teleconferences.
    - Meet every 4-8 weeks by phone with assigned Coordinating Center Statistician, Statistical Director(s), and Scientific Director(s) to guide studies, encourage Principal Investigators (PIs) to meet expected timelines, and keep the committee's portfolio moving forward.
    - Participate in CIBMTR Coordinating Center Pre-Tandem Meetings call with all Chairs.
    - Participate in conference calls with CIBMTR scientific and statistical staff to review Working Committee materials, discuss / finalize the agenda, and plan the Working Committee session.
    - Lead the annual Tandem Meetings Working Committee Meetings.
    - Attend the CIBMTR Leadership Reception at the Tandem Meetings.

    - Meet with the Scientific Director, Statistical Director, and Statistician to prioritize the studies (ongoing and proposed) and discuss the assignment of Coordinating Center hours.
- Recommend the specific Working Committee portfolio studies to be targeted for abstract submission to national and international meetings.
- Participate in the nomination process for replacement positions, with special consideration given to more junior investigators to promote ongoing leadership for the work of CIBMTR.

CHAPTER 3: AUTHORSHIP

3.1 GENERAL RULES OF AUTHORSHIP

CIBMTR has long valued collaboration with external scientists and clinicians to produce and publish high-quality, practice-changing research. All researchers are required to follow guidelines for developing and completing research studies (**Chapter 4**), submitting proposals (**Chapter 6**), and submitting data (if applicable, **Chapter 12**). The general rules of authorship also apply to any investigator or group, including industry collaborations, using information from CIBMTR's Research Database. The *rules of authorship* described in this chapter are consistent with the International Committee of Medical Journal Editors (ICMJE), updated in January 2024.

The main criteria for authorship are commitment and contributory engagement throughout the project's life cycle. These expectations can best be outlined and assessed if the authorship roles are outlined at the initiation of a study. Generally, the person who proposes the study is listed as the study PI. An exception might occur if the person proposing a study is not associated with a center or has only a small proportion of the cases from their center and a member of a center with a large proportion of the patients' requests to lead the study at an early stage (e.g., during protocol development). These rare situations are adjudicated by CIBMTR Leadership, including the Working Committee leadership and CIBMTR Senior Leadership. Most cases are resolved by appointing Co-PIs with an agreement about authorship order made in advance.

Many CIBMTR studies require patients with detailed CRF data, which affects author-related considerations as detailed below. For more information about data management and CRFs, see **Chapter 12**.

3.2 AUTHORSHIP RULES FOR INDUSTRY-SPONSORED STUDIES AND MANUSCRIPTS

Authorship rules for manuscripts related to a retrospective, industry-funded project will be determined based upon contribution of effort and cases within the study population. For non-interventional prospective clinical studies, or when supplemental data are required, the study team or study Steering Committee will determine final authorship. Final determination may be delayed until accrual is complete. Other considerations include:

- Most industry projects will involve sponsor input in manuscript development.
- Rules for authorship may be outlined within the project plan.
- When a Steering Committee does not exist, CIBMTR Senior Leadership will oversee authorship decisions.
- When publication is not included in the sponsored project plan, the study team may still choose to develop a manuscript; however, all CIBMTR oversight requirements must be met, and sponsor input will generally still be required.
- The manuscript will include acknowledgement of the member centers (SOP-0072: Working Committee Manuscript Preparation).

3.3 ESTABLISHING THE WRITING COMMITTEE FOR WORKING COMMITTEE STUDIES

3.3.1 Center Volume Assessment

Numbers of patients from each contributing center are included in the materials prepared by Statisticians during proposal and protocol development; these data are used later to facilitate assessment of the PI center's level of participation (e.g., data submission)

pertinent to that study. Numbers of cases with TED-, CTED-, and CRF-level data submitted are considered for research studies.

If a center that is among the five centers with the largest numbers of cases in the study, or a center that contributes 10% or more of the cases, is not represented on the Writing Committee, then a separate memo is sent to the center director to determine whether the center wishes to designate a representative for the Writing Committee, although authorship is still dependent on meeting other author participation guidelines.

3.3.2 Solicitation for Writing Committee Members

An important milestone in the life cycle of a study is the point at which the PI's draft protocol is approved by the Working Committee leadership and undergoes final review by the Coordinating Center. This document is then distributed by the Coordinating Center to all Working Committee members on record. CIBMTR invites these individuals to participate on the study Writing Committee by commenting on each section of the protocol. The comments are gathered in an electronic form that aims to solicit substantive review of each section of the protocol. The automated form and its comments are then reviewed by Working Committee leadership and the study PI. Only individuals providing comments that are deemed most useful will qualify for inclusion in the Writing Committee, unless there are other mitigating circumstances, such as a center contributing a large number of patients to the analysis:

- 1 – **Extremely useful** and critical comments. Help avoid fatal flaws in the study design and analysis. Comment led to a critical change in the analysis plan or study design. For example, "I think the primary endpoint should be X because Y."
- 2 – **Very useful.** Improved the analysis substantially. Important comments that were incorporated into the analysis plan or study design. For example, "I would include bone marrow because…."
- 3 – **Useful**. Changed something in the analysis. Improved the analysis plan or study design. For example, "I would look at the subset of X and Y because another paper reported they were important."
- 4 – **Not useful** but comments were substantive. Not incorporated or minor clarifications. For example, "I would also look at [variable x that we do not have]" or mere suggestion of a subset not already examined.
- 5 – **No substance to comments.** For example, "This is an important study."

CIBMTR expects everyone who agrees to participate on a Writing Committee to provide timely and substantive contributions to study design, data analysis, interpretation of results, and preparation of the manuscript for publication. It is important to note that sometimes with dozens of Working Committee members commenting, after the first comments are in, it becomes difficult to generate additional meaningful contributions. It is not a goal to make authorship a race to be insightful, but to appreciate all meaningful additions to an analysis or publication.

3.3.3 Consideration in Special Situations

- **CIBMTR studies evaluating rare diseases or new and / or novel therapy indications.** As with other diseases, Medical Directors of centers that are among the five with the most patients reported, or that have provided the majority of patients reported and included in a study, are solicited to contribute to authorship at the protocol development stage. Authorship will generally be granted to a representative from each of those centers. However, these center representatives must make contributions to the study that are consistent with other authorship guidelines.

- **CIBMTR studies evaluating cord blood.** Some studies evaluate outcomes of transplantation using cord blood as the graft source, in which graft handling or processing are relevant issues. Representatives from cord blood banks whose graft products are substantially represented in the proposal are eligible to join the Writing Committee. Scientific Directors and Statisticians are charged with remaining cognizant of these special cases and extending invitations as appropriate.
- **CIBMTR studies that use biologic samples.** Writing Committees for studies that use research samples from the CIBMTR Biorepository operate slightly differently because the PI typically has made a substantial investment in the samples and the testing performed **(Chapter 7).** In these cases, the PI works with the assigned Working Committee Scientific Director(s) and Chairs to define the Writing Committee at study initiation. The Writing Committee is typically composed of the assigned CIBMTR Working Committee statistical analysis team and collaborators identified by the PI. Writing Committees for these studies may be opened to full Working Committee participation at the request of the PI.

3.4 AUTHOR LIST DEVELOPMENT

As noted above, to assure co-authorship status, members of the Writing Committee must make timely and substantive contributions to study design, execution, data analysis, interpretation of results, and preparation of the manuscript for publication, including any requested changes. The study PI and Working Committee leadership review comments collected at the protocol, analysis, and manuscript stages to determine continued inclusion on the Writing Committee based on the criteria outlined above. The Statistician typically monitors all comments and shares this information with the PI / Scientific Director. In consultation with the Scientific Director and Statistician, the PI determines which members of the Writing Committee do not fulfill these requirements and will not be included in the author list. This section describes important considerations in the process of compiling author lists.

3.4.1 Number of Authors

Because the number of authors permitted for any given study is sometimes limited by the journal, first authors are encouraged to consider selecting journals in which multi-center authorship and journal policy permit multiple authors. To decide which authors should be listed in the manuscript, study PIs should consider potential authors' engagement in and contribution to protocol development, data analysis and interpretation, and manuscript preparation. In addition, a consensus of the study PIs, Scientific Director(s), and Working Committee Chairs may consider the following factors. Decision makers should mitigate potential conflict of interest regarding institutions, mentees, colleagues, etc. if possible.

- Usefulness of comments on the protocol, analysis, and manuscript
- Number of cases contributed to the analysis
- Special expertise
- Junior investigator status
- First-time CIBMTR authors
- International authors
- Number of potential authors per center

If the total number of authors exceeds the journal maximum, the PI may request that Coordinating Center staff correspond with the journal, requesting the inclusion of a few additional individuals on the primary author list. If this is not permitted, CIBMTR recommends one of the two following options in the "author contribution section" of the manuscript:

- If acknowledging specific individuals, please state as follows: "We would like to acknowledge additional contributing authors from the Writing Committee."
- If acknowledging the entire Working Committee, please state as follows: "On behalf of CIBMTR's _____ Working Committee."

If a paper is rejected by one journal and resubmitted to another, the author list rules may change, requiring reassessment of the primary author list. In these cases, authors must be notified by the study leadership of changes before submission.

3.4.2 First Author Designation

The study PI is usually the First Author and is typically the person proposing the study and leading the project. This person should be engaged and passionate about the study and willing to take on the majority of writing and editing. The First Author partners with the Last Author to complete the study. An exception is if the center of the person proposing a study has provided only a small proportion of the cases to be studied and a member of a center with a large proportion of the patients also requests to be PI. These decisions are best made prior to initiation of the project (**Section 3.1**), and authorship positions for these individuals are designated at that time. Since many studies include only patients with detailed CRF data, this gives preference to investigators from centers submitting CRF data (**Chapter 12**). If, for some reason, the First Author is unable to fulfill a project responsibility, the Working Committee leadership and Scientific Director should determine if the Last Author or another motivated junior author should step in and complete the task to keep the project moving forward.

3.4.3 Last Author Designation

The Last Author partners with the First Author throughout the project to complete the study. The Last Author will be committed to active collaboration with the First Author throughout the study, irrespective of their academic rank. If there is only a single PI on the proposal, a discussion between the Working Committee leadership team and PI should occur to determine who the Last Author will be. This may be another knowledgeable and involved colleague, a Working Committee Chair, a CIBMTR Scientific Director, or a member of the Writing Committee who provides significant input at the protocol stage and is willing to contribute meaningfully to the role. The Last Author may be a:

- **Mentor to the First Author**. In this circumstance, the Last Author will help guide the First Author in developing the protocol, reviewing data analysis, and preparing the manuscript.
- **Partner to the First Author**. The Last Author should divide tasks with the First Author to ensure timely completion of the study.
- **Working Committee Leader**. This role should not typically be taken by a CIBMTR Scientific Director or a Working Committee Chair; however, there may be circumstances in which either might take the role of the Last Author; this should be clarified with the agreement of the PI and Working Committee leadership.

3.4.4 Authorship Ranking

Authorship ranking is weighted towards Writing Committee members who participate in the development of the study and those from centers that have contributed substantial data for the study and helped with study development. Authorship ranking may vary depending on the complexity of a study and overall level of involvement required of Working Committee leadership, including the Scientific Director (often but not always the Corresponding Author) and the Statistical Director. Sometimes authorship is given, on a case-by-case basis, for contributing unique or specialized expertise to a project.

Working Committee Chair status does not automatically guarantee inclusion on the author list of any CIBMTR manuscript. Working Committee Chairs must make substantive contributions to the design, implementation, and interpretation of a study to merit authorship, similar to the measurable requirements for all other authors as noted above.

Working Committee Chairs and Scientific Directors will adjudicate differences of opinion about authorship, with a final decision made by CIBMTR Leadership, if necessary.

3.5 CONTRIBUTION EXPECTATIONS

Typically, contributions made to the progress of a study by the PI and / or Writing Committee member, from proposal to journal acceptance, are based on the participation criteria described in this section.

First Author / PI responsibilities:

- Present their proposal during a Working Committee meeting (typically held during the annual Tandem Meetings) following CIBMTR Coordinating Center guidelines
- Upon proposal acceptance, return a signed, study-specific Letter of Commitment (**Appendix D1 or D2**) by the deadline noted in the letter (includes Co-PIs)
- Assist the Working Committee Chairs and Coordinating Center staff to develop and meet a reasonable timeline for study completion
- Prepare the study protocol based on discussions with the Last Author and CIBMTR Working Committee leadership, incorporating comments from the Writing Committee at all stages
- Participate actively in teleconferences and meetings, and typically present the study at CIBMTR Statistical Meetings (at both the protocol and analysis stage)
- Participate actively in data file preparation and analyses, as needed
- Prepare study materials, as necessary, for submission for meeting presentation
- Review manuscript formatting high-level guidelines for the target journal
- Prepare a first draft of the manuscript within three months of receiving Writing Committee comments on the final study results
- Submit the final draft of the manuscript to a journal within six months of receiving Writing Committee comments on the final study results
- Collaborate with CIBMTR Coordinating Center in submitting the manuscript, or (rarely) submit per CIBMTR guidelines (**Chapter 4**)
- Address comments from reviewers, with input from Working Committee leadership and other co-authors
- Respond to editorial questions and approve galley proofs

Last Author responsibilities:

- Coordinate the study and help keep it on track and on time
- Review protocol and manuscript comments from the Writing Committee with the First Author, and help identify the substantial comments that should be incorporated
- Review statistical results with First Author and the Working Committee statistical team, and assist in presenting their interpretation to Working Committee leadership and at CIBMTR statistical team meeting
- Communicate regularly with First Author to ensure the study is following the appropriate timeline, and partner with them to complete all study tasks
- Respond promptly to email communication with Statisticians and Working Committee leadership

Considerations for joint First and Last Author positions:

- If multiple PIs are listed on a proposal or if similar proposals have been merged, they will determine among themselves who will assume the role of First and Last Author. If PIs are unable to make this determination, the Scientific Director and Working Committee leadership will help mediate.
- If Co-First or Co-Last authorship is desired by PIs, clearly stated roles for co-authorship will be discussed between authors and Working Committee leadership.
- Other authorship positions should be decided upon at the outset and earned by ongoing participation in all steps of the project.
- CIBMTR Scientific Director or a Working Committee Chair may merit a Co-Last author position (Second Last Author). This should be decided when the authorship is defined or if they have significant input during the life of the study.

First Author (PI), Last Author, and Writing Committee member responsibilities:

- Engage in the protocol development process as evidenced by substantive and timely comments and suggestions (generally within two weeks of receiving the circulated document or query), particularly regarding scientific merit and / or statistical design
- Engage in interpretation of data analysis as evidenced by substantive and timely comments
- Engage in manuscript preparation as evidenced by substantive and timely comments
- Engage in the journal review process by providing substantive and timely responses to journal queries and comments

Corresponding author (usually CIBMTR Working Committee Scientific Director) responsibilities:

- Review final draft, ensuring the interpretations are accurate, and contribute to the fundamental message of the manuscript
- Participate in determining fair and equitable author ranking per CIBMTR guidelines (see above)
- Communicate with the journal editorial staff, with support from CIBMTR Coordinating Center
- Manage communication between co-authors
- Coordinate, as point of contact, queries following publication
- Ensure compliance with CIBMTR and NIH procedures to acquire a PubMed Central ID (PMCID) number* with support from CIBMTR Coordinating Center
    - Assure the proper steps are taken by the journal to submit the article to PubMed Central for assignment of a PMCID number. If the accepting journal does not provide this service (many do), the Corresponding Author must do so or should solicit help from the Coordinating Center. This is required of CIBMTR (by NIH Public Access policy) and is relevant to any peer-reviewed paper that uses data generated by CIBMTR. For more information, see **Chapter 4**.

* This is a US based mandate by the NIH; see **Appendix C** for further details.

Scientific Director and Working Committee leadership responsibilities:

- Support authors throughout the study process
- Ensure First Author understands and signs commitment letter after proposal acceptance
- Ensure Last and any Co-First / Last Authorship is defined soon after the protocol is finalized and the Writing Committee is formed
- Monitor progress with First and Last Author to ensure the project is on track
- Reach out to authors if they are not meeting expectations or there is delay in completing tasks
    - Address reasons for delays and help problem solve
    - Consider reassigning authorship if authors are not fulfilling expectations
- Ensure that meeting minutes describe study discussions and state the next tasks for authors to complete

3.6 MANUSCRIPT PREPARATION

The First Author (with Last Author) have primary responsibility for manuscript preparation (SOP-0072: Working Committee Manuscript Preparation) and are expected to prepare a first draft manuscript within three months of receiving comments from the Writing Committee comments on the final study results. This draft is then reviewed, revised as necessary, and approved by Working Committee leadership.

The First Author ensures that description and interpretation of the results are accurate and contributes to the fundamental message of the manuscript. A CIBMTR Administrative Assistant or Coordinator, under the direction of the study Statistician, distributes the first draft manuscript to the pre-identified Writing Committee for their comments.

The First Author incorporates relevant comments into a subsequent draft. As with the analysis, this is an iterative process until all involved agree that the manuscript is ready for submission. Writing Committee members generally have two weeks to respond to each circulated draft. The approved final draft manuscript is the version submitted to the identified journal (SOP-0073: Working Committee Manuscript Submission). See **Chapter 4** for submission details.

The final author list is determined at submission stage since it depends largely on the value and extent of contribution of each individual throughout the study process.

3.7 CIBMTR FACULTY AND STAFF AUTHOR CITATIONS

To address the manner in which CIBMTR faculty and staff indicate their respective institutions when they are cited in author lists, CIBMTR recommends a standardized format (SOP-0072: Working Committee Manuscript Preparation).

CHAPTER 4: MANUSCRIPT SUBMISSION

This chapter describes the PI's fundamental responsibilities during the life cycle of a study. Specifically, it focuses on the final steps in submitting an approved manuscript to a scientific journal for peer review and publication (SOP-0073: Working Committee Manuscript Submission).

For additional guidelines and helpful hints for a PI conducting a study with CIBMTR, see "Guidelines for Study Principal Investigators" in **Appendix B**. These guidelines are provided to each PI upon study acceptance. For more information about authorship, see **Chapter 3**.

4.1 PI RESPONSIBILITIES

CIBMTR expects active involvement on the part of the study PI to minimize the time from study activation to submission. The time required to move a study forward to manuscript submission is dependent on the PI completing the following:

- Read the "Guidelines for Principal Study Investigators" (**Appendix B**)
- Read the "CIBMTR Guidelines for acquiring PMCID Numbers" (**Appendix C**)
- Prepare a first draft of the manuscript within three months of receiving Writing Committee comments on the final study results
- Submit the final draft of the manuscript to a journal within six months of receiving Writing Committee comments on the final study results (SOP-0072: Working Committee Manuscript Preparation)
- Incorporate comments of Writing Committee members at protocol, analyses, and manuscript stages
- Submit the *International Committee of Medical Journal Editors (ICMJE) form* regarding conflicts of interest to CIBMTR Coordinating Center
    - Potential conflicts of interest include, but are not limited to, employment; consultancies; stock ownership; honoraria; paid expert testimony; ownership interests, including stock options; and membership on another entity's Board of Directors or its Advisory Committee
- Collaborate with CIBMTR Coordinating Center in submitting the manuscript
- Assess journal reviewer comments and respond to editorial questions prior to the deadline in collaboration with Working Committee leadership and other co-authors
- Prepare a response letter in collaboration with Working Committee leadership
- Respond to editorial questions and approve galley proofs

4.2 FINAL SUBMISSION STEPS

4.2.1 Immediate Pre-Submission Phase

CIBMTR Coordinating Center employs a Medical Writer who, upon request, reviews meeting abstracts and final draft manuscripts prior to journal submission. This review is limited to items such as a check for standardized usage of acronyms and abbreviations, correct grammar and spelling, etc. Upon completion, the reviewed, edited manuscript is then returned (with tracked changes, if any) to the corresponding author, copying the Scientific Director and Study Statistician, for final approval prior to submission by either the corresponding author or CIBMTR's Coordinating Center staff.

4.2.2 Manuscript Submission

There are two approaches for submitting manuscripts:

- CIBMTR submits the manuscript (preferred, **Section 4.2.2.1**)
- PI / Corresponding Author submits the manuscript (not preferred, **Section 4.2.2.2**)

4.2.2.1 CIBMTR Submits the Manuscript (preferred)

Due to critical NIH requirements for acquisition of PMCID numbers (**Appendix C**) for all published, peer-reviewed works funded by the NIH (e.g., when CIBMTR data are used), CIBMTR prefers that manuscript submissions and resubmissions be processed centrally. If CIBMTR submits the manuscript, the administrative staff requests and uses the username / password of the corresponding author for the relevant journal to complete the submission.

When handled centrally, a CIBMTR Administrative Assistant or Research Coordinator submits the approved final draft manuscript (using the corresponding author's username / password for the specified journal) to the pre-identified scientific journal and is responsible for any correspondence with the selected journal's editorial staff during the submission procedure. The corresponding author forwards subsequent editor and reviewer comments to the PI, Scientific Director (if not the corresponding author), Statistical Director, and study Statistician. The PI is expected to prepare a response, working with Coordinating Center staff to obtain additional data analyses if needed.

4.2.2.2 PI / Corresponding Author Submits the Manuscript (not preferred)

If the PI / corresponding author prefers to submit their own paper, they must agree to follow the required *NIH processes for obtaining a PMCID number*. CIBMTR provides PIs with proper guidelines (**Appendix C**) upon request and when:

- "Letter of Commitment" is distributed
- Manuscript is submitted
- Manuscript is accepted

When PIs submit their own papers on behalf of CIBMTR, they are urged to notify CIBMTR of the submission (e.g., via the relevant Working Committee Statistician, central office, etc.) due to CIBMTR's obligations regarding the NIH Public Access policy.

When a study PI, or collaborating partner group, submits the manuscript, they should be reminded by Working Committee leadership of these NIH requirements and of proper acknowledgements (see below). In all cases in which CIBMTR data are used within the study (most cases) and the study PI or a collaborating group member submits the paper, they should, throughout the process, respond "yes" when asked to confirm NIH funding. Enter the applicable grant numbers:

- NHLBI, NIAID and NCI: U24CA076518
- HRSA: 75R60222C00011
- ONR: N00014-23-1-2057
- ONR: N00014-24-1-2057

For example, the grant is #U24-CA076518, and Bronwen Shaw, MD, PhD, is the PI for this grant. Her name is automatically associated with the grant number in the NIH Manuscript Submission procedures when a paper is accepted and submitted to PubMed Central.

4.2.2.3 Additional Submission Requirements

Regardless of who submits the manuscript, submission information should include:

- "CIBMTR Data Sources" statement (Appendix E)
- CIBMTR Support List for the research study (SOP-0072: Working Committee Manuscript Preparation and SOP-0073: Working Committee Manuscript Submission)
- Acknowledgement of NIH funding (i.e., "CIBMTR NIH Support Verification Letter") (Appendix F)

- MCW recommends, to maintain compliance with NIH Public Access policy, whoever submits the paper should also submit an "NIH Support Verification Letter" at the time of submission to alert the editor that the paper qualifies as one that must be made available to the public via PubMed Central.

Current versions of these documents are available to PIs and other submitting groups upon request to the central office. They are maintained at the Coordinating Center Milwaukee Campus (414-805-0700), updated periodically, and approved by the Executive Scientific Director, Policy and Governance for CIBMTR MCW, and Vice President, CIBMTR and Clinical Services, NMDP.

4.2.2.4 Journal Submission to PubMed Central

Most, but not all, journals to which CIBMTR submits research papers forward the final peer-reviewed manuscript or the final published article to PubMed Central. There are a variety of submission methods available to journals and authors; review *the NIH When and How to Comply Public Access Policy* or *the National Center for Biotechnology (NCBI) Navigating the National Institutes of Health Manuscript Submission (NIHMS) Process* for specific directives depending on the journal to which the paper is being submitted. The submission method specifies which manuscript version is permitted. The version options are:

- **Final Peer-Reviewed Manuscript.** The investigator's final manuscript of a peer-reviewed paper accepted for journal publication, including all modifications from the peer review process.
- **Final Published Article.** The journal's authoritative copy of the paper, including all modifications from the publishing peer review process, copyediting and stylistic edits, and formatting changes.

If the journal does not offer this submission service, the corresponding author has primary responsibility for *submitting papers through the NIHMS* using Method D. CIBMTR Coordinating Center can also submit on behalf of the corresponding author by using Method C.

Another helpful resource is the NIH webpage *Frequently Asked Questions about the NIH Public Access Policy*.

4.3 PUBLICATION LISTS

CIBMTR publications are posted online monthly. Listings date back to inception of the IBMTR in 1972. Beginning January 1, 2010, the publication list also includes articles published by NMDP dating back to its inception in 1987 as well as statistical methodological papers authored by CIBMTR partner Statistical Directors and relevant articles authored by BMT CTN, CRO Services, and Bioinformatics. All works since the 2004 affiliation of the IBMTR and NMDP (**Chapter 1**) are identified as CIBMTR publications.

To accommodate frequent and assorted reporting requirements, information is maintained internally to monitor numerous data elements relevant to CIBMTR publications (authors, author institutions at time of publication, grant information, duration of study lifecycle to time of publication, journal impact factors, relative citation ratio, etc.). This internal, comprehensive *publications document* is updated monthly and available to both campus staff members on SharePoint and via monthly emails (AID-0091 CIBMTR Publications List).

4.4 PUBLICLY AVAILABLE DATASETS

Starting in July 2019, analysis datasets for certain CIBMTR publications are publicly available on CIBMTR's *website* in accordance with the NIH Data Sharing Policy and NCI Cancer Moonshot Public Access and Data Sharing Policy (SOP-0119: Shared Publication Datasets Standard Operating Procedure).

CHAPTER 5: STATISTICAL RESOURCES

5.1 COLLABORATION WITH THE MCW DIVISION OF BIOSTATISTICS

Since 1985, CIBMTR has benefitted from a unique and collegial partnership with Biostatistics Faculty from the MCW Division of Biostatistics in the Data Science Institute. This distinctive relationship contributes substantially to CIBMTR's success. The collaboration is funded in part by an NCI grant and the SCTOD contract (**Chapter 6**). The MCW Biostatistics Division mission is threefold:

- Provide basic biostatistical support to MCW's community of biomedical researchers
- Commit to high-quality research in statistical and data science methods
- Commit to its PhD and MA programs in biostatistics

This long-standing association between CIBMTR and MCW Division of Biostatistics faculty:

- Ensures the statistical integrity of CIBMTR scientific activities
- Results in articles on statistical issues related to cellular therapy for clinical audiences
- Supports Working Committee members and investigators in developing scientific study protocols using CIBMTR data and provide multivariate analysis for each study

The MCW PhD Faculty Biostatisticians who work with CIBMTR have substantial experience in assessing the unique statistical problems associated with cellular therapy. They collaborate with CIBMTR MD Scientific Directors (most of whom also hold MS degrees in statistics, epidemiology, or public health) and network investigators in each CIBMTR Research Program. In addition, Biostatistics Faculty have developed an active Statistical Methodology Research Program investigating new approaches and techniques for analyzing cellular therapy data. Finally, during the annual Tandem Meetings, Biostatistics Faculty host a statistics session focusing on statistical design and analysis. In addition, they provide one-on-one statistical consultation to researchers writing proposals or developing protocols for both CIBMTR studies and external studies.

The CIBMTR Coordinating Center employs more than 20 Statisticians, some with more than 20 years of experience with cellular therapy studies. MCW PhD Biostatisticians are significantly involved in training these Statisticians, overseeing ongoing studies, and collaborating with them on univariable analyses and multivariable regression analyses.

Following is a detailed description of how the Division of Biostatistics integrates with the mission of CIBMTR to improve the outcomes of cellular therapy.

5.1.1 Biostatistics Leadership

MCW PhD Biostatisticians are Statistical Directors within CIBMTR organizational structure and report directly to CIBMTR's Chief Statistical Director. In addition to the Chief Statistical Director, six PhD Statistical Directors from the MCW Division of Biostatistics participate in CIBMTR research activities under a part-time, subcontracted arrangement with the following foci:

- Lead Statistician for the BMT CTN and as a Statistical Consultant to NMDP; this person led the statistical development approach for NMDP's current Center-Specific Analysis (now the purview of CIBMTR)
- Survival analysis and expertise in analysis of cellular therapy data that involve censored and / or truncated time-to-event data and competing risk events
- Research with an emphasis in statistical genetics; this person provides statistical service for analyzing immunogenetic data (**Chapter 7**)
- Other expertise in biostatistics and support of CIBMTR research in their respective focus areas

- Occasionally visiting professors also participate in analysis of CIBMTR data

CIBMTR's Program Director of Clinical Outcomes Research and Statistical Operations leads the MCW Statistical team and provides overall statistical oversight and administration for the activities associated with the MCW Statistical Operations Area, Clinical Outcomes Research Program, and training for the Statisticians within MCW. This team supports:

- Working Committees (**Section 6.1**)
  - Acute Leukemia
  - Chronic Leukemia
  - Infection and Immune Reconstitution
  - Graft-vs-Host Disease
  - Lymphoma
  - Morbidity, Recovery, and Survivorship
  - Non-Malignant Diseases
  - Pediatric Cancer
  - Plasma Cell Disorders
- BMT CTN (**Section 8.1**)
- Industry contracts facilitated by CIBMTR MCW's Industry Relations Program (**Chapter 11**)
- Statistical Methodology Research Program (**Chapter 5**)
- SCTOD (**Section 6.2**)
- Cure Sickle Cell Initiative (**Section 6.7**)

The Program Director of Clinical Outcomes Research and Statistical Operations works in collaboration with CIBMTR MCW's Leadership team and the Chief Statistical Director.

Biostatistics Leadership at NMDP provides statistical oversight, coordination, and training for the Statisticians within NMDP. This team supports:

- Working Committees (**Section 6.1**)
  - Immunobiology
- Donor and Recipient Health Services
- NMDP-driven research initiatives
- Patient-Reported Outcomes Research
- Immunobiology Research Program (**Chapter 7**)
- CRO Services (**Section 8.2**)
- Bioinformatics Research team (**Chapter 10**)
- Health Services Research team (**Chapter 9**)
- Other NMDP analytical groups

NMDP Biostatistics Leadership works in collaboration with CIBMTR NMDP's Leadership team.

The MCW and NMDP Statistical Teams also collaboratively support CIBMTR standard reports, information requests, and CIBMTR research initiatives as identified by Senior Leadership. The team collaborates with other CIBMTR operational areas to support the database infrastructure and quality of data.

5.2 STATISTICAL METHODOLOGY

The Chief Statistical Director and his staff actively participate in the development and adaptation of statistical methodology for optimal analysis of CIBMTR and other cellular

therapy-related data. This group has expertise in right-censored data analysis and clinical trials and publishes methodological papers that address issues in the analysis of post-HCT outcomes.

CIBMTR has an important role in guiding the research community in appropriate application and interpretation of sophisticated statistical models required for analyzing cellular therapy survival data. Thus, CIBMTR statistical research is twofold: Development of new statistical methodologies and subsequent application of these methodologies to studies using CIBMTR clinical data.

The most common outcomes of interest being studied are hematopoietic recovery, acute and chronic graft-versus-host disease (GVHD, the most important obstacle to a successful outcome), toxicities of CAR-T cell therapy, transplant-related mortality, disease recurrence, and disease-free and overall survival.

Cellular therapies are complex procedures with multiple competing risks; therefore, analyzing outcomes can pose statistical challenges that are not amenable to standard methods. The post-therapy period, in particular, is complex to model, with patients transitioning between numerous intermediate states and the terminal state. These include episodes of engraftment, GVHD, relapse, application of post-treatment therapies, and occurrence of secondary cancer. In some analyses, models fit on final outcomes must be synthesized with models fit on intermediate events in order to derive a model that predicts patient outcomes based on their history at a particular point in time. Censoring, through loss to follow-up, and truncation, through delayed entry, further complicates analyses.

Statistical challenges are numerous. The common competing risks problem results when the occurrence of one outcome (e.g., death from regimen toxicity) precludes occurrence of another (e.g., relapse). Another challenge with data analysis is that covariates, such as GVHD, toxicities, or immune suppressive treatment, may change over time. When comparing cellular therapy to other therapies, it is necessary to consider differential start times for the treatments, using statistical adjustments such as delayed entry into the study cohort or time-dependent stratification.

These statistical problems require development or extension of new statistical tools by investigators with expertise in both the clinical and statistical problems of cellular therapy. This is the unique feature provided by CIBMTR Statistical Directors.

Certain methodology approaches are required or must be considered for analyzing right-censored data in CIBMTR's Research Database, including:

- Competing risks
- Multistate models
- Techniques for censored and truncated data
- Clinical trials design

These data are often used to teach clinicians and other researchers how to properly analyze such complicated information. Lessons include descriptions of results in various disease states and patient groups; determining prognostic factors (including immunogenetic factors); defining inter-center variability in diagnosis, practice, and outcome; evaluating long-term outcomes, including quality of life; and developing analytic approaches to evaluating outcomes.

5.2.1 Comparative Approaches in Cellular Therapy

As noted above, reliably assessing outcomes is complex. Outcomes are influenced by many patient- and disease-related factors such as age, disease stage, and prior treatment as well as transplant-related factors such as graft source, conditioning regimen, and GVHD

prophylaxis. CIBMTR addresses issues in large randomized clinical trials, but clinical trials present specific challenges related to cellular therapy. (CIBMTR's Clinical Trials Support Program is presented in **Chapter 8**.) For example, enrolled patients may represent only a small proportion of the target population and may not be representative of the larger group. Also, most clinical trials focus on short-term and intermediate-term outcomes, yet there is need for long-term follow-up of recipients since cellular therapy may be associated with important effects, such as therapy-related cancers, which occur many years after treatment. CIBMTR leverages its Research Database to conduct studies that address these challenges after cautious interpretation and acknowledgement of methodological restrictions.

This research can also be used to evaluate new regimens and compare cellular therapy with other therapies. Results of various strategies among concurrently treated patients using observational data can be compared, provided that appropriate adjustments are made to ensure that comparable patients receiving the alternative strategies are evaluated. CIBMTR Statistical Directors analyze the detailed clinical information for each patient, allowing adjustment for potentially confounding effects of important prognostic variables. To compare the results of different treatment regimens, their approach is to:

- Define the therapies to be compared
- Compare the characteristics of patients treated with each therapy
- Compare the results after adjusting for variables that differ significantly among the treatment groups

This adjustment can be done either by stratifying important prognostic factors, matching for important factors or propensity scores, or multivariable regression. The approach is dependent on the outcome, the explanatory variables to be evaluated, and the size of the population to be studied. Sometimes all of these techniques are used to demonstrate that the results are not dependent on a particular method.

In some instances, cellular therapy is used to treat diseases where there is no other effective therapy. Often, large, randomized trials are not possible in these instances due to the rarity of the disease; variable treatment philosophies; and the limited availability of donors, technologies, and resources. There are also other potentially curative treatments that raise the question of relative effectiveness. It is difficult to compare published results of cellular therapy versus other treatments directly. Differences in patient selection and inherent delay in performing treatments can lead to truncation of early failures from most series (time-to-treatment bias).

Comparisons of cellular therapy to alternative treatments can be done by combining CIBMTR data with primary data compiled by groups studying other regimens. These comparisons use regression or matching techniques to adjust for patient differences. They handle time-to-treatment differences in a variety of ways, all of which have the net effect of giving less weight to events occurring at a point in the disease when few patients have proceeded to transplant. Coordinating Center personnel have conducted simulation studies to compare methodologies for conducting these studies.

Comparing treatments, whether they are different cellular therapy regimens or compared to chemotherapy in non-randomized studies, requires careful consideration of potential biases, not all of which can be addressed by statistical techniques. There are limitations to this approach, and the Statistical Directors address potential biases in presentations of results. However, such studies contribute to understanding treatment effects, provide valuable data for planning and interpreting trials, and, in some situations, are the only feasible means of comparing strategies in a controlled fashion.

5.3 CIBMTR BIOSTATISTICAL ACTIVITIES

5.3.1 CIBMTR Working Committee Support

The primary way in which the Statistical Directors oversee and influence the integrity of CIBMTR data analysis is in their role as members of the Working Committees. They guide the analytical assessment of data extracted from the large database that are relevant to the scientific question(s) of each ongoing study.

Statistical meetings are held weekly and attended by all Scientific Directors, Statistical Directors, Coordinating Center Statistical Staff, and, in most cases, study PIs and Working Committee Chairs. During the meeting, attendees discuss protocol design, selection of the study population, proper variables and those that need to be adjusted in the analysis, the approach to statistical analysis, and final analyses. Statistical Directors are available to the members of their Working Committees for in-person or phone consultation, and they attend their Working Committee's monthly leadership teleconferences. Statistical Directors approve analyses completed by the Statisticians and usually perform the multivariable regression analyses for each study. Scientific Directors and assigned Statistical Directors work closely with study PIs during all phases of study development, including final approval of the manuscript that is submitted to peer-reviewed journals for publication.

The Immunobiology Working Committee (**Chapter 7**) has a unique and independent mission. It addresses scientific questions about the association between genetic factors and successful transplantation outcomes. The committee's studies include comparisons of clinical outcomes from different donor types (e.g. mismatched related versus unrelated donors).

5.3.2 Center-Specific Survival Analysis

NMDP has been analyzing center outcomes for unrelated donor HCTs since 1994. Since 2006, these analyses are under the purview of CIBMTR as required by the SCTOD contract (**Chapter 6**), and since 2010 they include data on related donor HCTs. Reports provide one-year survival statistics for all US centers doing allogeneic HCT, both related (since 2008) and unrelated, using a three-year rolling window. The reports compare observed and expected survival rates with a 95% confidence interval. Because centers vary considerably in the risk level of the cases they treat, CIBMTR developed a statistical model to adjust for risk factors known or suspected to influence outcomes. Reports are submitted to HRSA each year, and copies are distributed to center medical directors and payers. Results are published on the NMDP *Transplant Center Search* webpage and used to populate the Center Performance Analytics and Survival Calculator applications on the CIBMTR Portal. These reports are useful for improving quality of HCT and informing the public about them.

Since 2008, CIBMTR has conducted forums at least every other year to discuss and develop plans to conduct these center-specific survival analyses with center representatives and experts in outcomes reporting and statistical analysis as well as patient and payer representatives. The last forum was held in October 2023. Recommendations generated during these forums are used to guide the center-specific survival analyses. CIBMTR distributes these recommendations to US center medical directors and posts them on its *Center Outcomes Forum* webpage.

5.3.3 Public Website Display of Survival and Center Volumes Data

As part of the SCTOD contract, CIBMTR provides information about related and unrelated allogeneic transplants performed by US centers. Data on autologous transplants are submitted voluntarily by centers and are also included in these reports. The reports provide a moving five-year window of data:

- ***US Patient Survival Report***. Published approximately every three years, this report provides patient survival estimates by disease at the following time points after

transplant: 100 days, 1 year, and 3 years. Survival estimates are also available by patient age, patient sex, patient race, cell source, and the year the transplants were performed.
    - The window for these data includes five years of "accrual" into the cohort and three years of follow-up.
    - Sample sizes for some categories are quite small, so statistically valid estimates of overall survival outcome cannot be calculated where there is not enough patient data available for analysis.
- ***Transplant Activity Report*.** Published annually, this report provides tables with the number of transplants performed at US centers. These data include all types of transplants, categorized by patient's age, cell source, disease, donor type, sex, race, state of center, and year of HCT. The dataset supporting these reports is also available for download.

5.3.4 BMT CTN and CRO Services

A CIBMTR designated Statistical Director plays a lead role in the activities of both the BMT CTN and CRO Services, which comprise CIBMTR's Clinical Trials Support Program (**Chapter 8**). A Lead Statistician is assigned to each clinical trial, and a Statistician is assigned to each BMT CTN or CRO Services study. Throughout the course of the study, Statisticians are responsible for:

- Designing the trial
- Advising on sample size
- Completing power calculations
- Defining randomization plans, including blinding procedures if relevant
- Developing the statistical analysis plan
- Defining study tables, listing, and figures
- Programming and data analysis
- Interpreting the results

Designing clinical trials that produce meaningful results requires special consideration to be given to:

- Sample size
- Randomization procedures
- Eligibility criteria
- Multiple, competing outcomes
- Center effects (e.g., those affecting patient outcomes due to practices / approaches unique to center transplant teams)
- Early stopping guidelines
- Overall analysis plans
- Other issues

Adequate sample sizes are needed to detect meaningful differences in treatment strategies. Selecting eligibility criteria that control for the heterogeneity of the patient population while allowing for reasonable patient accrual is also essential. Using CIBMTR's Research Database, Coordinating Center personnel explore the effects of specific eligibility criteria on the potential for enrollment in clinical trials. Staff members also use the Research Database in trial design and when considering amendments to enhance accrual.

Assessing multiple, competing outcomes can be challenging, as they can also interfere with assessment of the primary endpoint of a trial. Center effects, which can confound statistical analyses, are particularly important when evaluating complex treatments like cellular therapy, in which substantial differences in supportive care-related practice patterns among centers exist (e.g., prophylactic and preemptive therapy for infection, nutritional support, isolation practices). Study data are stratified by center whenever feasible to minimize center effects on study results.

Detailed study design and analysis plans vary from the larger Phase II-III trials (randomized or not) to the smaller Phase I-II studies. In both cases, CIBMTR's Research Database provides fundamental data supporting design of these trials.

5.3.5 Health Services Research

CIBMTR Health Services Research Program (**Chapter 9**) also benefits from the statistical expertise of the Coordinating Center in conducting cellular therapy-related research. The Senior Scientific Directors, Operational Leaders, Investigators, and health services analysts of the Health Services Research Program collaborate with Statistical Directors on a variety of studies.

Studies accomplished through this unique initiative, in partnership with Statistical Directors, fall into three broad categories: Health economics and outcomes research, treatment decision-making support, and survivorship and patient-reported outcomes.

CHAPTER 6: CLINICAL OUTCOMES RESEARCH

Clinical outcomes research using CIBMTR's Research Database is a core activity of the organization. These studies address a wide range of issues, focusing on questions that are difficult or impossible to address in single-center studies or randomized trials because diseases treated with cellular therapy are uncommon and single centers treat few patients with a given disorder. Additionally, clinical outcomes research databases facilitate long-term follow-up, permitting studies addressing quality of life and late effects of cellular therapy. All research studies are approved by the NMDP's Institutional Review Board (IRB) before initiation (SOP 0323 – Clinical Outcomes Research Program – Research Database Protocol IRB Determination).

Clinical outcomes research focuses on the effects of cellular therapy on recipients and donors as well as the clinical and treatment factors influencing the effectiveness of the therapy. CIBMTR adheres to a high standard of scientific and statistical rigor in selecting, planning, and conducting observational research, as described in this chapter.

See **Chapter 12** and **Chapter 15** for more information about CIBMTR's Research Database.

6.1 CIBMTR SCIENTIFIC WORKING COMMITTEES

CIBMTR conducts most clinical outcomes research under the auspices of 11 Scientific Working Committees, listed in **Table 6.1** below. Members include assigned Coordinating Center leadership and staff (discussed further in this section) as well as basic and clinical scientists with expertise in cellular therapy and related disciplines. The major responsibilities of Working Committees are to:

- Review and score study proposals that use CIBMTR data relevant to the committee's subject area and assist leadership in the proposal approval process
- Design and conduct studies relevant to their subject area involving CIBMTR data, statistical resources, networks and / or centers
- Periodically assess and revise relevant sections of CIBMTR data collection forms
- Plan and conduct workshops at CIBMTR meetings

Working Committees meet in person annually during the Tandem Meetings (**Chapter 17**), at which time current studies are discussed and new proposals are presented and considered using a scoring mechanism standardized by CIBMTR (**Section 6.1.5.1**).

6.1.1 Working Committee Leadership and Staff

Membership in Working Committees (**Table 6.1**) is open to any individual willing to take an active role in the development of studies that involve CIBMTR data and / or resources [SOP-0195: Working Committee Membership or Study in Data and Information for Statistical Center Operations (DISCO)]. To join a Working Committee, visit the *committee webpage* or email CIBMTRStatsOps@mcw.edu.

6.1.1.1 Chairs

Each Working Committee is generally staffed with two to four Chairs who are appointed by the Advisory Committee to non-renewable, three-year terms. Three-year terms allow Chairs to become familiar with their role, provide continuity over time, and increase the likelihood of guiding studies from proposal to manuscript submission or acceptance for publication. Terms are staggered to facilitate succession while maintaining continuity. Individuals may serve as Chair more than once but not consecutively on the same Committee. Active Chairs are expected to participate in the nomination process for replacement positions with special consideration given to more junior investigators to promote ongoing leadership for the work of CIBMTR.

Table 6.1: Scientific Focus of CIBMTR Working Committees

Working Committee	Scientific Focus
Acute Leukemia	The Acute Leukemia Working Committee provides scientific oversight for studies related to HCT and ACT for acute leukemias.
Chronic Leukemia	The Chronic Leukemia Working Committee provides scientific oversight for studies related to HCT and ACT for chronic leukemias, myelodysplastic disorders, and myeloproliferative disorders.
Graft-versus-Host Disease	The Graft-versus-Host Disease Working Committee provides scientific oversight for studies related to biology, prevention, and treatment of GVHD and its complications.
Donor and Recipient Health Services	The Donor and Recipient Health Services Working Committee focuses on social and economic determinants of health as well as quality of care for the donor and recipient.
Immunobiology	The Immunobiology Working Committee provides scientific oversight for studies related to histocompatibility and other genetic and immunologic issues related to HCT.
Infection and Immune Reconstitution	The Infection and Immune Reconstitution Working Committee provides scientific oversight for studies about the prevention and treatment of post-transplant / cellular infusion infections and issues related to the recovery of immune function.
Lymphoma	The Lymphoma Working Committee provides scientific oversight for studies related to HCT and ACT for Hodgkin and non-Hodgkin lymphoma.
Pediatric Cancer	The Pediatric Cancer Working Committee provides scientific oversight for studies related to HCT and ACT for childhood cancers, including solid tumors.
Plasma Cell Disorders	The Plasma Cell Disorders Working Committee provides scientific oversight for studies related to HCT and ACT in multiple myeloma, light chain amyloidosis, and other plasma cell disorders.
Non-Malignant Diseases	The Non-Malignant Diseases Working Committee provides scientific oversight for studies related to HCT and gene therapy / gene editing for immune deficiencies, inborn errors of metabolism, autoimmune diseases, aplastic anemia, hemoglobinopathy, and other non-malignant hematopoietic disorders.
Morbidity, Recovery, and Survivorship	The Morbidity, Recovery, and Survivorship Working Committee provides scientific oversight for studies related to preparative regimens, prevention, and treatment of early non-GVHD toxicities and supportive care in the early post-transplant or post-cellular therapy period as well as studies regarding issues of long-term survivors of HCT and ACT, including clinical and psychosocial effects of transplantation.

Chairs are selected for expertise in their topic area as well as to ensure adequate expertise in the field of cellular therapy, including autologous or allogeneic HCT or ACT, and adequate experience with CIBMTR activities. In general, Chairs must be members of CIBMTR centers

that submit CRFs unless an exception is granted by the Advisory Committee. Exceptions are granted to allow individuals without an association with a center but with demonstrated expertise and commitment to serve as Chair (e.g., PhD Director of a histocompatibility laboratory, apheresis center, or donor registry).

Working Committee Chairs are responsible for facilitating the committee research portfolio to ensure its highest possible quality. This is accomplished through familiarity with all committee studies, CIBMTR data collection forms, and knowledge of key variables that are typically used in CIBMTR research studies. Chairs demonstrate leadership throughout the year to guide studies, encourage PIs to meet expected timelines, and keep the portfolios moving forward. In addition, Working Committee Chairs represent their committee to a wider audience through the committee reports section of CIBMTR's Newsletter (**Section 16.4.9**).

Working Committee Chairs lead the annual Working Committee Meetings. Chairs are expected to be present and provide direction to the discussion so that it is productive and respectful and encourages new member involvement. In preparation for the Tandem Meetings, Chairs participate in conference calls with CIBMTR scientific and statistical staff to review proposals and protocols, discuss and finalize the agenda, and plan the Working Committee session; they also participate in the Coordinating Center pre-meeting call with all Chairs and attend CIBMTR's Leadership Reception at the Tandem Meetings. Immediately after the Working Committee Meetings, Chairs meet with the Scientific Director and Statisticians to prioritize the studies (ongoing and proposed) and discuss the assignment of Coordinating Center hours. A significant responsibility of a Chair is to recommend specific Working Committee portfolio studies to be targeted for abstract submission at national and international meetings.

While study PIs hold ultimate responsibility for their studies, every 4-8 weeks Working Committee Chairs lead committee conference calls (SOP-0076: Working Committee Conference Call) and communicate via email to shepherd the Working Committee portfolio of studies through the process. Chairs provide thoughtful and expert input on specific study issues. They review the Committee's studies as they progress from concept to proposal and on to analysis and manuscript submission. Throughout this process, they provide timely input to study PIs. If a study stalls, Working Committee Chairs intervene directly with a PI. When a study from their Working Committee portfolio is being presented, the Chair attends and participates in CIBMTR's Statistical Meeting teleconference. Working Committee Chairs are expected to attend a minimum of 80% of all meetings and teleconferences. If this criterion is not met and repeated attempts to reconcile the issue have failed, the Working Committee Scientific Director may ask the Executive Committee to consider appointing a new Chair. In collaboration with the Working Committee Coordinating Statistician and Scientific Director, Chairs are responsible for facilitating and approving meeting minutes of in-person meetings and teleconferences.

If forms relevant to the Committee's area of interest are under revision, Chairs are asked to participate in the new form development process, review content, and agree with changes before the form is finalized. Chairs provide input and review any study-specific supplemental data request. Chairs are also asked to consider important study questions that have not yet been suggested. Developing new projects and recruiting new investigators are important aspects of the Working Committee Chair role. Chairs should make every effort to involve a wide group of committee members as PIs and spread both the work and the rewards.

6.1.1.2 Scientific Director

Each Working Committee is assigned a Scientific Director. Scientific Directors are generally active cellular therapy physicians with master's degree level training in biostatistics or a related area. The Scientific Director provides medical oversight and analytic expertise for

committee activities and facilitates communication among investigators, Chairs, Statistical Directors, and statistical staff (SOP-0070: Scientific Director Guidelines).

6.1.1.3 Statistical Director

Faculty members of the MCW Division of Biostatistics provide biostatistical support for all CIBMTR's scientific efforts (**Chapter 5**). The Chief Statistical Director assigns one Statistical Director to each Working Committee. Statistical Directors participate in all committee meetings / calls and provide guidance in study design. They participate in weekly Coordinating Center meetings to critique statistical methodology and data interpretation during various milestones in the progress of each study. They perform most multivariate analyses for CIBMTR clinical outcomes studies and participate in the Statistician training program.

6.1.1.4 Statisticians

Statisticians on both campuses coordinate the activities of Working Committees, prepare data sets, and perform analyses for individual studies. Each Working Committee is assigned a Statistician. CIBMTR Senior Leadership, in consultation with the Program Director of Clinical Outcomes Research and Statistical Operations and CIBMTR NMDP Manager of Biostatistics, allocates a specific amount of effort for Working Committee activities. Statisticians are responsible for:

- Serving as primary Statistician for a Scientific Working Committee, including developing a timeline for each committee study and monitoring its progress in collaboration with Working Committee Chairs and Scientific Directors, setting up teleconferences with Working Committee Chairs, and communicating with the PIs
- Conducting proposal feasibility assessments
- Directing approximately 10-15 studies of HCT and/or ACT patient data, including preparing the study data set, performing univariate and occasionally multivariate analyses, and assisting in preparing the manuscript
- Preparing materials for annual Working Committee in-person meetings

6.1.1.5 Statistician Training

The Coordinating Center maintains a formal training program for Statisticians to ensure uniform procedures in the coordination of requests and research study implementation. The training program, which includes workshops, led by CIBMTR Statistical Directors and/or Scientific Directors, focus on the following areas:

- Overview of HCT and ACT (e.g., common indications for treatment, conditioning regimens, general outcomes, and other disease-specific topics)
- Organizational structure of CIBMTR (includes SOPs)
- Clinical Trials-BMT CTN and CIBMTR CRO Services (includes program-specific SOPs for BMT CTN and CRO Services)
- Introduction to clinical trials
- Introduction to statistical support of clinical trials
- Data management principles for statisticians
- ICH E9 and E6
- Introduction to Phase I/II study designs in cell therapy research
- Adaptive designs
- Safety evaluation via stopping rules
- CIBMTR data collection forms and processes

- Use of and access to CIBMTR databases
- SAS programming environment
- Information requests and rules for releasing CIBMTR data (SOP-0119: Shared Publication Datasets Standard Operating Procedure; SOP-0069: Data Sharing to Non-MCW or Non-NMDP Employees; SOP-0065: Information Requests; Form-0080; CIBMTR Data Use Agreement Template)
- Preparation for national and international professional meetings
- Standard reports preparation (SOP-0153: HRSA US Patient Transplant Survival Report; SOP-0154: Summary Slides; SOP-0205: US Center Volumes Dataset for Corporate Use; SOP-0244: US Transplant Activity Report; SOP-0249: CIBMTR Report of Survival Statistics for Blood and Marrow Transplant)
- Working Committee coordination, management, and written communications (SOP-0078: CIBMTR Working Committee Folder Structure; SOP-0195: Working Committee Membership or Study in DISCO; SOP-0076: Working Committee Conference Call; SOP-0313: Working Committee Protocol, Analysis, and Manuscript Circulation)
- Procedures to perform a research study at CIBMTR
- Evaluation of proposals
- Study protocol development
- Supplemental forms development
- Data quality
- Data file preparation (SOP-0077: Haploidentical Donor Transplant Selection; SOP-0281: Data Inclusion for Use; SOP-0221: Assessment for European Union Data)
- SAS codes library (SOP-0066: Library of SAS Codes)
- Definition and analysis of transplant outcomes
- Completeness index for evaluating adequacy of follow-up
- Creation of Statistical Analysis Plans (
- Statistical methods of survival analyses (e.g., cumulative incidence function, proportional hazards regression, adjusted survival curves, completeness index, logistic regression, propensity score)
- Univariate and multivariate statistical analyses using *SAS software*
- Presentation and summary of results at internal meetings (SOP-0068: Statistical Meetings)
- Manuscript preparation and submission (SOP-0072: Working Committee Manuscript Preparation; SOP-0073: Working Committee Manuscript Submission)
- CIBMTR Biorepository resources and HLA typing
- FormsNet and SQL/OBIEE access to Research Database
- Tandem Meetings overview and preparation
- CIBMTR Master List of Studies

Training plans are individualized based on the statistician's role and may encompass a subset of the exhaustive list above. Comprehensive educational manuals are provided to each Statistician for their personal reference. A code library is maintained on GitHub; the Data Sharing to Non-MCW or Non-NMDP Employees SOP (SOP-0069) details the specific steps in this process.

A Senior Statistician or higher-level staff member is assigned to junior staff members to provide mentoring and answer questions (GUIDE 0012 - Supervisory Guidelines for Senior Statisticians). There is also a monthly bi-campus Statistician meeting to discuss updates on

Working Committee management, study issues, SAS codes, policies and procedures, data, and other issues as needed (SOP-0075: Bi-campus MS Statistician Meetings). As part of their continuing education, Statisticians attend annual CIBMTR data management meetings, the annual Tandem Meetings, periodic topical lectures led by Statistical and Scientific faculty, and short courses on statistical techniques that can be applied to the cellular therapy field.

The Statistical Manager of Education and Support (NMDP) and the Manager of Biostatistics (MCW) develop and maintain the educational manual and the Biostatistician Reference Guide. This guide is updated periodically and used primarily as a resource tool for the Statisticians while in training and thereafter.

6.1.2 Working Committee Metrics

The Advisory Committee (**Section 2.2.2**) reviews Working Committee metrics three times annually. The executive summary prepared for the Advisory Committee includes:

- Annual Working Committee Overview and Project Plan report summarizing standard metrics related to Working Committee efficiency
- Standardized rating systems used at Working Committee meetings to evaluate new proposals and re-evaluate those previously approved studies not yet initiated
- Annual standardized study impact factor assessment (by Working Committee leadership)
- Annual characterization (by Working Committee leadership) of new studies by major topic, methodology type, and scientific merit to facilitate continuous review of Working Committee portfolios
- Monthly reports to Working Committee leadership to identify study-specific delays, when appropriate

Standard Working Committee metrics in various categories are listed below.

Process Metrics (completed by Working Committee leadership):

- Create an annual Working Committee Overview and Project Plan with a clear division of labor and responsibilities about leadership
- Evaluate responses to questionnaires regarding the effectiveness of their committee's annual meeting at the Tandem Meetings
- Conduct calls monthly or every other month, as documented by brief, action-oriented minutes
- Adequately prepare for and conducts face-to-face meetings before and after the committee's annual meeting at the Tandem Meetings

Productivity and Impact Metrics:

- Study Progress: Given the current Unified Data Model data centralization and transfer process, developing additional metrics based on study acceptance date alone is challenging. Current metrics are based on availability of Working Committee comments on the final analysis:
    - Time from Working Committee comments on final analysis to first manuscript draft <3 months
    - Time from Working Committee comments on final analysis to manuscript submission <6 months
- Manuscript Submission:
    - Total number of submitted papers >75% of planned submissions

    - Very low tolerance for manuscripts in preparation >1 year
- Publications:
    - Number of publications
    - Impact factors of journals in which manuscripts published
    - Relative citation ratios and total number of citations
- Presentations:
    - Number of abstracts presented at conferences

6.1.3 Master Study List and Statistical Hour Allocation

A fundamental resource of CIBMTR is its Research Database, developed through the collaboration and good will of a very large segment of the cellular therapy community over a period of more than 50 years. An equally important resource is the statistical support provided to investigators to allow them to use the Research Database to address important issues in the field. Although some investigators have local statistical support available for studies, most rely on CIBMTR Statisticians for study design, implementation, and interpretation. Statistical support is a limited resource and must be allocated based on need and merit (MCW SOP-0152: Time Tracking). Experience shows that each study typically requires approximately 290 statistical hours to complete if it does not require supplemental data or form development. The average number of statistical hours required for each study phase, based on estimates of past CIBMTR studies, is shown below:

- Form development (for studies requiring supplemental data): 40 hours
- Data collection (for studies requiring supplemental data): 20 hours
- Protocol development: 100 hours
- Data file preparation: 100 hours (140 hours if CIBMTR data are to be combined with an external database)
- Analyses: 60 hours
- Manuscript: 20 hours
- Submission and response to reviewers: 10 hours

Prior to the Tandem Meetings, statistician hours for the next academic year are allocated to each of the Working Committees by CIBMTR Leadership. These allocations depend on the number of available Statistician hours, number of studies in progress and proposed studies, availability of supplementary funding, Working Committee productivity, and overall activity. An initial estimate of hours required for new studies to be proposed to the Working Committee is also made prior to the Tandem Meetings. The Working Committee leadership and staff prioritize proposals and studies in progress and determine study timelines based on these allocated hours.

A Master Study List is maintained throughout the year, tracking all observational study titles, study numbers, Chairs, assigned Statisticians, allotted hours, current status, fiscal year (July 1-June 30) remaining hours, hours remaining to completion, dates on which milestones are achieved to measure progress, and more. The Master Study List is updated three times per year by the Program Director of Clinical Outcomes Research and Statistical Operations in consultation with CIBMTR Senior Leadership and CIBMTR NMDP Manager of Biostatistics. Studies remain on the list until published or officially dropped. As new proposals are accepted, they are assigned a study number and inserted on the list. Studies may be deferred for a variety of reasons (e.g., pending accrual, requiring supplemental data, financial support, etc.) These studies remain on the list and are reassessed annually. The time to completion of observational studies is a key performance metric of CIBMTR, with a goal of completing all studies within 18 months of initiation.

The Master Study List represents CIBMTR's Clinical Outcomes research agenda and is reviewed three times annually by the Advisory Committee. This committee provides the highest level of oversight for study progress and Working Committee activities in general. It makes recommendations as needed to Working Committee leadership.

6.1.4 Statistical Meetings

CIBMTR Scientific and Statistical Faculty and Staff members meet regularly by teleconference to assess active studies and new proposals (SOP-0068: Statistical Meetings). These weekly, one-hour sessions are attended by CIBMTR Leadership, Scientific Directors, Statistical Directors, Program Directors, and Statisticians. Working Committee Chairs and Study PIs for studies to be discussed are also invited and frequently attend. The Program Director of Clinical Outcomes Research and Statistical Operations approves the meeting agenda for presentation using the following study-ranking schema:

- Study presentation requires a second review based on recommendations from a previous meeting (highest priority)
- Multivariate analysis is complete, and results are to be distributed to the Writing Committee
- Protocol is ready for distribution to the Working Committee (this generally includes a preliminary description of the data file)
- Study proposal requires review if Working Committee leadership feels additional input is needed

Generally, only three studies are evaluated per meeting to permit adequate time for discussion. Studies must be approved by the Statistical Director and Scientific Director before being referred to the Coordinating Center weekly statistical meeting. Relevant study materials (e.g., protocol documentation, descriptive / univariate / multivariate analyses, summaries of findings, and specific questions) are distributed with the agenda four business days in advance of each meeting.

Study PIs are encouraged to attend these meetings to present their study, highlight specific issues, and participate in the statistical discussion. The Scientific Director for the relevant Working Committee presents the study if the PI is unable to attend. The assigned Statistical Director presents results of multivariate analyses. One of three actions may follow the discussion:

- **Protocol is approved for release to the Working Committee.** The protocol will be sent to the Working Committee as-is or after implementing minor recommendations.
- **Limited review is recommended.** The Statistical Director or Statistician will implement recommended changes. These changes will be reviewed by the Working Committee Scientific Director, Statisticians, and PI, who will either approve distribution of the results to the Writing or Working Committee or will request a second discussion at the Coordinating Center weekly statistical meeting.
- **Another Statistical Meeting review is required.** Major changes will be made, and a subsequent Coordinating Center review will be scheduled within one month of initial presentation.

Each study is presented at least twice at the weekly statistical meetings: Before finalization of the study protocol and before release of results. When necessary, additional weekly statistical meetings are scheduled to ensure timely discussion of studies and other business. CIBMTR's Statistical Meetings SOP (SOP-0068) details the specific steps in this process.

6.1.5 Study Development

See **Appendix G** for a two-page summary of the study development cycle.

6.1.5.1 Proposal Process

Anyone may submit a proposal to use CIBMTR's Research Database at any time. Each fall, CIBMTR extends a formal invitation to center clinicians and basic scientists to submit proposals. This communication includes website links to proposal submission instructions, including those that require CIBMTR Biorepository specimens, patient-reported outcomes (PRO), and/or machine learning. To guarantee consideration by the Working Committees at the Tandem Meetings, proposals must be submitted at least two months before the meetings, generally no later than mid-October.

Before submitting a proposal, investigators are encouraged to view CIBMTR *data collection forms* to verify that critical data are available for their proposed study and review the *Study Proposal Guidance*. Depending on the time-period considered in the proposed study, PIs should also review previous versions of forms. Investigators should likewise review the current online listing of studies in progress to avoid proposals for ideas / studies previously accepted. Lastly, a preliminary discussion with Working Committee leadership can be helpful in determining the feasibility of studies and the level of enthusiasm for the research idea.

On occasion, studies are proposed in collaboration with other registries, cord blood banks, or professional transplant groups / societies. During the proposal process, details must be clarified related to merging of data and who will provide analytical support as these matters affect assignment of statistical resource hours, the study plan, and projected timeline.

When a proposal is first received, the investigator is notified of receipt, and a proposal number is assigned for tracking purposes. The proposal is then forwarded to the appropriate Scientific Director and Statistician, who review the proposal for feasibility with CIBMTR data and potential conflict with active studies. The Statistician then forwards the proposal to the Chairs for discussion. In cases of conflict or feasibility issues, the Scientific Director or Committee Chair communicates with the PI regarding modifying or withdrawing the proposal. When such determinations are not straightforward, the proposal may be discussed at a Coordinating Center weekly statistical meeting (**Section 6.1.4**). Numerous proposals are approved for presentation at the annual Working Committee meeting. However, Chairs may consider certain proposals for expedited approval and implementation after discussion with CIBMTR Leadership. Such expedited approval requires delaying progress on other studies and is considered only for proposals with potential for high-impact or time-sensitive funding opportunities.

Prior to presentation of a proposal at the annual Working Committee meeting, the Statistician prepares a table describing the study population, as specified within the proposal, to allow assessment of potential sample size and feasibility. This may be presented at the Coordinating Center weekly statistical meeting (prior to the annual meeting) if the Working Committee leadership request additional Coordinating Center input. Such discussions may result in suggestions to the PI for amending the proposal prior to presentation. These suggestions are communicated by the Working Committee Chair or Scientific Director.

Working Committee members in attendance at the Tandem Meetings score proposals via electronic ballots to help prioritize them based on researcher interest and scientific value (e.g., novelty of idea, clinical relevance, and the chance of it being published in a high-quality journal). Working Committee Chairs and CIBMTR Leadership, charged with final decisions, consider this input in preparing an agenda for the committee's activities for the next academic year. The primary approval criteria for evaluating proposals are scientific merit and feasibility. When deciding among proposals of similar merit, preference is given to

those proposed by investigators from CRF-submitting centers in good standing. (See **Chapter 3** for more information).

CIBMTR encourages PIs who submit proposals to attend the Tandem Meetings and personally present their ideas to Working Committee members. This enables the investigator to answer committee members' questions, convey enthusiasm for the proposal, and explain its clinical relevance. Investigators are notified within approximately one month of the results of the deliberations of the Working Committee and after final Advisory Committee approval of the complete CIBMTR research agenda. If a proposal is rejected, the Working Committee Chair(s) or Scientific Director inform the PI of the decision and explain the fundamental issues resulting in the rejection. If a proposal is accepted and assigned a study number, a PI (typically the individual who proposed the original concept) is assigned and informed of their responsibilities throughout the duration of the study process.

If a proposal addresses the same scientific question as an ongoing study, the proposer may be asked to join the Writing Committee of that study, if it is in an early stage. Additionally, the scope of an ongoing study may be amended to accommodate a different population (e.g., pediatric vs adult) suggested by a new proposal.

PI responsibilities are best understood when familiar with CIBMTR's study process. Guidelines describing these processes and instructions for preparing a protocol are provided to each PI upon study acceptance (**Appendix B**). PIs are asked to read the guidelines and follow the contribution expectations listed in **Section 3.5**.

The study PI, in collaboration with the Coordinating Center, ensures that the specified deadlines at each phase of the study are met. Time to produce the data sets is dependent on:

- How much accrual is needed to have an adequate sample
- Quality of data, such as volume of missing data for key variables
- Overall follow-up of patients resulting in unanticipated, but reasonable, delays in the study.

Occasionally studies are raised to a higher priority, or studies do not progress as planned. In these cases, resources may be reallocated as needed. Every attempt is made to maximize productivity with limited resources. Generally, CIBMTR expects studies to be completed within 18 months. Delayed studies are monitored closely, and if necessary, actions are taken to facilitate speedy completion or removal.

CIBMTR's Review and Approval of Working Committee Studies SOP (SOP-0067) details the specific steps in this process.

6.1.5.2 Assignment of the PI

After acceptance by the Working Committee, each study is assigned a study number identifying it by Working Committee abbreviation and year of acceptance. The person proposing the study generally becomes the study PI. An exception to this policy may be made if the person proposing a study has only a trivial proportion of the cases to be studied and a member of a center with a large proportion of the patients also requests to lead the study. These situations are uncommon and adjudicated by CIBMTR Leadership, including Working Committee leadership and the Chief Scientific Directors. Investigators from centers contributing a high proportion of the data are given preference. Most disputes are resolved by appointing Co-PIs with agreement about authorship order made in advance (**Chapters 3 and 4**).

6.1.5.3 Protocol Development

The first step in study implementation is protocol development. The study protocol is an essential tool that clarifies the study objectives to Working and Writing Committee participants, and it guides Statisticians and Statistical Directors to ensure study objectives will be met by the analyses conducted at the Coordinating Center. When notified of acceptance, each PI is asked to submit a draft protocol by a date specified by the Coordinating Center in the Letter of Commitment (**Appendix D1** or **D2**). A guideline for preparing the draft is provided. The draft must include:

- **Research Hypothesis**. Scientific assumption that is the basis for the study.
- **Objectives**. Specific aims that will be achieved by the proposed analysis.
- **Scientific Justification**. Summary of the study rationale that conveys the study's importance.
- **Study Population**. Definition of selection criteria.
- **Outcomes**. Clear definition of study outcomes, including any relevant time points.
- **Variables to be Analyzed**. Listing of explanatory variables, based on biological principles, available in the Research Database and proposed format / categories for analysis.
- **Data Collection**. Specification of supplemental data required and a plan for data collection.
- **Study Design**. Statistical approach to achieving each objective (this will be refined with support of Coordinating Center Statisticians).
- **References**.

Once received by the Coordinating Center, this draft protocol is further refined in collaboration with the Working Committee Statistician, Statistical Director, and Scientific Director. A table including a preliminary description of the proposed population is added, and the draft protocol is presented at a Coordinating Center weekly statistical meeting.

6.1.5.4 Establishing a Writing Committee

Writing Committees are formed early to supervise study progress. After approval by CIBMTR's Scientific and Statistical group, Coordinating Center staff invites interested investigators to participate when they distribute the final draft protocol to all Working Committee members and center directors who contributed data for substantial numbers of patients meeting the eligibility criteria for the study. Numbers of patients from each contributing center are included in the materials prepared earlier by Statisticians to facilitate discussion about center participation during proposal / protocol development, as noted below.

After distribution of the invitation soliciting Writing Committee membership, Working Committee Chairs and Scientific Directors review the Writing Committee membership and study population. If a center that is among the five centers with the largest numbers of cases in the study or a center that contributes 10% or more of the cases is not represented on the Writing Committee, Coordinating Center staff sends an additional memo to the center director to determine whether the center wishes to designate a representative for the Writing Committee.

To assure co-authorship (**Chapter 3**), members of the Writing Committee must make timely and substantive contributions to study design, data analysis, interpretation of results, and preparation of the manuscript for publication. CIBMTR expects all Writing Committee members to provide substantive input and timely commentary during subsequent developmental stages of the study. Writing Committee members who do not fulfill this

requirement are expected to withdraw as a co-author or, alternatively, the PI may remove their names.

6.1.5.5 Supplemental Forms / Data Collection

If the study requires supplemental data collection (i.e., data not collected on CIBMTR report forms), supplemental form development may be required. Coordinating Center staff design supplemental forms in collaboration with the PI and Working Committee leadership. All but the simplest forms must be piloted before implementation, and time must be allowed for the appropriate data entry screens to be added to FormsNet. In general, this step tends to delay the study timeline by one year and typically results in an increase in the number of statistical hours required for study completion. For these reasons, studies requiring this step are not encouraged.

6.1.5.6 Data File Preparation

The objective of study file preparation is to have a data file of eligible patients who are consecutively treated at participating centers with adequate follow-up, minimal missing data items, and in large enough numbers to give the analysis sufficient statistical power to meet the stated study objectives. This process involves a series of steps on the part of the Statistician, sometimes working together with a Clinical Research Coordinator, to ensure data quality. It often involves consultation with the PI as well as Scientific Directors and Statisticians at the Coordinating Center. These steps include:

- Finalizing selection criteria
- Determining the adequacy of follow-up and taking steps to obtain additional follow-up information if necessary
- Evaluating the extent and nature of missing values and their potential effect on the study and takings steps to obtain missing data if necessary and feasible
- Identifying data discrepancy / outliers and reconciling these by examining data collection forms or communicating with centers
- Determining appropriate groups for continuous and categorical variables, if not already specified in the protocol
- Describing the included and excluded patients so that the investigators can determine whether the final study population is representative of the target population (unbiased sample)

6.1.5.7 Analysis

Analysis proceeds in several phases. The first analysis generally includes a detailed description of the patient population and univariate analyses of study endpoints. Sometimes a preliminary multivariate analysis is also performed. These data are distributed to Writing Committee members requesting their suggestions and comments. An iterative process then ensues. The PI works with Working Committee leadership to discuss and address comments raised by the Writing Committee. Revised analyses, with a description of steps taken to address comments, are then distributed to the Writing Committee. It is the PI's responsibility to draft this memo with input from the Working Committee leadership. If additional substantive comments are made by the Writing Committee, the process is repeated until a final analysis is available. This final analysis serves as the basis for the manuscript.

6.1.5.8 Manuscript Preparation and Submission

See **Chapter 4**, SOP-0072: Working Committee Manuscript Preparation, and SOP-0073: Working Committee Manuscript Submission.

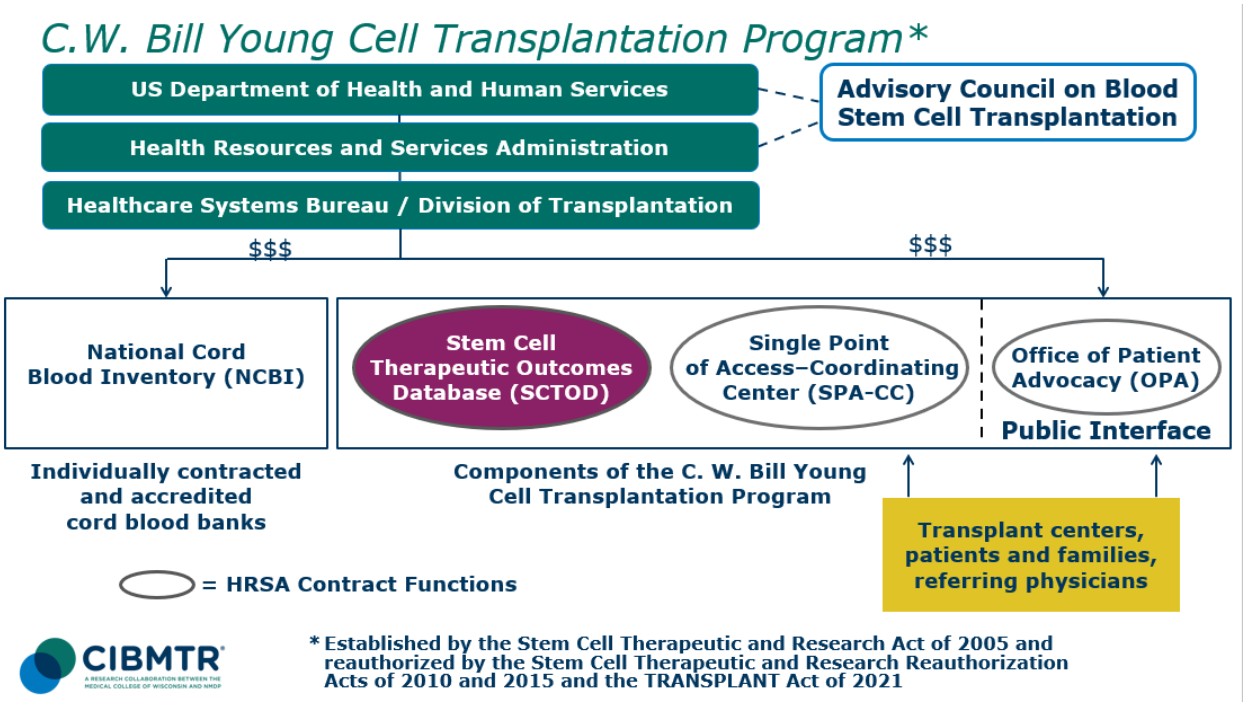
6.2 STEM CELL THERAPEUTIC OUTCOMES DATABASE

In 2006, CIBMTR was awarded a contract from HRSA to create and manage the SCTOD. The SCTOD is a national registry for allogeneic transplant information. It is a component of the C.W. Bill Young Cell Transplantation Program (the Program), which was established and then subsequently reauthorized by:

- Stem Cell Therapeutic and Research Act of 2005 (passed by Congress and signed by President Bush in December 2005 as Public Law 109-129)
- Stem Cell Therapeutic and Research Reauthorization Act of 2010, Public Law 111-264 (signed by President Obama in October 2010)
- Stem Cell Therapeutic and Research Reauthorization Act of 2015, Public Law 114-104 (signed by President Obama in December 2015)
- TRANSPLANT Act of 2021, Public Law 117-15 (signed by President Biden in May 2021)

CIBMTR renewed the contract in 2012, 2017, and 2022. **Figure 6.1** shows an overview of the Stem Cell Acts.

Figure 6.1: Overview of the Stem Cell Therapeutic and Research Acts



The Program was designed to help patients who need a transplant from an unrelated adult marrow, peripheral blood stem cell, or cord blood unit donor. Its goal is to increase the numbers of unrelated marrow donors and available cord blood units, expand research to improve patient outcomes, and provide information about HCT to patients and their families, health care professionals, and the public. There are three components of the Program, each with its own HRSA contract:

- Single Point of Access - Coordinating Center (Program contractor is NMDP)
- Office of Patient Advocacy (Program contractor is NMDP)
- SCTOD (Program contractor is CIBMTR)

The three components of the Program, including the SCTOD, work together to:

- Operate a system for identifying, matching, and facilitating distribution of blood stem cells
- Allow transplant physicians, health care professionals, and patients to search online for available cord blood units and adult donors
- Support studies, demonstrations, and outreach projects for the purpose of increasing cord blood donation and volunteer adult donors, to ensure genetic diversity
- Carry out informational and educational activities to increase cord blood donation, promote cord blood units as a transplant option, and increase the number of adult donors

CIBMTR accomplishes Program requirements directly or through subcontracts. CIBMTR subcontracts with NMDP to provide some services, including IT, maintenance of the related donor-recipient CIBMTR Biorepository (**Chapter 7**), auditing, and CPI support for data management and quality assurance (**Chapter 12**).

In addition to the three components of the Program, HRSA has awarded contracts to individual cord blood banks for the National Cord Blood Inventory, which collects, stores, and provides high-quality umbilical cord blood units to patients and, in some cases, to researchers. The Advisory Council on Blood Stem Cell Transplantation advises the Secretary of the US Department of Health and Human Services and the Administrator of the HRSA on the activities of the C.W. Bill Young Cell Transplantation Program and the National Cord Blood Inventory Program. For more information, see the *HRSA Program* website.

6.2.1 SCTOD Oversight

CIBMTR staff members oversee the administration of the SCTOD.

Key staff members:

- **Project Director (CIBMTR Senior Scientific Director)**. The Project Director has overall responsibility for successful execution of the contract. This person monitors progress of data collection, research, business, and communications activities, assisted by the Research Director, Deputy Project Director Subcontract Operations, Senior Statistician, Liaison Officer, and Contracts and Administration Manager. The Project Director works closely with CIBMTR Scientific Directors and Medical Consultants and is the primary point of contact for the SCTOD.
- **Research Director (CIBMTR Chief Scientific Director)**. The SCTOD Research Director oversees CIBMTR technical and scientific activities with input from the Advisory and Working Committees. This person reports to the Project Director for oversight of the work of the SCTOD and has primary responsibility for preparing and supervising its research agenda.
- **Deputy Project Director Subcontract Operations (Associate Scientific Director)**. The Deputy Project Director Subcontract Operations oversees CIBMTR technical and scientific activities of the subcontract scope of work. This person reports to the Project Director for oversight of the subcontract work of the SCTOD.
- **Senior Statistician (CIBMTR Statistical Director)**. The Senior Statistician reports to the Research Director for all contractual matters related to statistical analyses. This person has primary responsibility for ensuring that the methodology used for analytic and research tasks of this contract is sound, and for developing innovative approaches to analytic issues.
- **Database Administrator / Security Officer (CIBMTR IT Director – CIBMTR MCW Information System Security Officer)**. The Database Administrator / CIBMTR Information System Security Officer reports to the Project Director and has

primary responsibility for ensuring the integrity and security of the Research Database to comply with federal security regulations. This person also develops data query tools, disseminates data to Program components and centers, provides datasets to the Statistical team for use in CIBMTR analyses, and assists in development of systems to receive data from other registries or data sources. This individual collaborates with the Information System Security Officer in Minneapolis.

Additional SCTOD personnel (with CIBMTR titles in parentheses, if different):

- **Administrator (Executive Scientific Director, Policy and Governance, CIBMTR MCW).** The Administrator reports to CIBMTR Chief Scientific Director and, working with the Vice President, CIBMTR and Clinical Services, NMDP, supervises the IT, Statistics, Data and Business Operations functional areas as well as data collection, training programs, quality control and audit activities to ensure the availability of high-quality data.
- **Liaison Officer (Program Manager for SCTOD).** The Liaison Officer reports to the Project Director via the Administrator. This individual coordinates communications with HRSA and among CIBMTR, NMDP, and other Program contractors. The Liaison Officer also tracks and prepares deliverables to ensure deadlines are identified and met, coordinates and schedules meetings and action items, and provides administrative support to the Project Director.
- **Contracts and Administration Manager (CIBMTR Administrator).** The Contracts and Administration Manager reports to the Project Director via the Administrator and is responsible for ensuring that all required financial and administrative reports for the contract and NMDP subcontract are completed in a timely manner. The MCW Grants and Contracts Office and Office of Sponsored Programs assist with administrative, contractual, and reporting requirements.
- **Associate Statistical Director (Program Director of Statistical Operations).** The Associate Statistical Director reports to the Senior Statistician, Administrator, and Project and Research Directors. This person is responsible for supervising, training, and coordinating Statisticians and monitoring Working Committee progress. The Associate Statistical Director also analyzes outcomes data, helps develop data collection tools, and participates in the design and generation of required reports.
- **CIBMTR Statistical Directors.** Statistical Directors report directly to the Senior Statistician and provide statistical direction for SCTOD-related studies.
- **Statisticians.** Statisticians report to the Project Director, Research Director, Administrator, and Senior Statistician. They perform analyses of Program data, support Working Committee research under the direction of the Chief Scientific and Statistical Directors, coordinate Working Committee activities including ensuring communication with Working Committee Chairs and other members, and monitor Working Committee studies.
- **Scientific Directors.** Scientific Directors report to the Research Director. They provide unique clinical perspective as HCT physicians with MS degrees in biostatistics, epidemiology, and / or clinical research and immunology. They communicate with investigators seeking to use Program data, serve as the primary liaison with Working Committee Chairs, and provide guidance to statistical personnel. They consult on the design of data collection forms / systems, data elements, and studies. Scientific Directors also supervise scientific aspects of Working Committee studies, evaluate proposals that use the SCTOD, provide medical input for data collection issues, and ensure that studies involving the SCTOD are efficiently completed with scientific rigor.

- **Vice President of Data Operations (Vice President, CIBMTR and Clinical Services, NMDP)**. The Vice President of Data Operations reports to the Deputy Project Director Subcontract Operations. This person, working with the Administrator, supervises (through Directors of Data Operations) data collection, training programs, and quality control and center audit activities to ensure availability of high-quality research data. This individual also provides assistance in day-to-day SCTOD operations, ensuring activities comply with applicable federal privacy and human subjects regulations.
- **Database Administrator (CIBMTR NMDP Director of IT).** The Database Administrator reports to the Vice President of Data Operations. This person leads development of FormsNet and A Growable Network Information System (AGNIS) (**Chapter 15**). This individual partners with the Database Administrator / Security Officer in Milwaukee to oversee SCTOD functions and activities.
- **Immunobiology / Research Repository Director (Scientific Director).** This Director reports to the Deputy Project Director Subcontract Operations and provides Repository management services through NMDP. This individual oversees activities related to development, management, and maintenance of the CIBMTR Biorepository, including integration with the Clinical Database.

6.2.1.1 Policies and Technical Direction of the SCTOD

The Advisory Committee functions as a Board of Directors for the SCTOD (**Section 2.2.2**). The committee establishes policies and technical direction for CIBMTR, including the SCTOD. It is comprised of experts in the HCT / ACT field and two representatives of the Division of Transplantation of HRSA that serve as ex officio members. This assures government representatives are aware of all proposed policy changes and have adequate time to review significant policies impacting the Program.

If a proposed policy change is recognized to be significant and have conflict with policies of the Program, CIBMTR will provide an assessment of the policy impact along with recommendations to the HRSA Contracting Officer Representative at least 30 days in advance of Advisory Committee notification.

6.2.2 Key Activities

The SCTOD contract requirements are to:

- Collect HCT outcomes data on:
  - All allogeneic HCTs performed in the US using related or unrelated donors
  - All allogeneic HCTs worldwide that use grafts procured through the Program
  - Clinical applications other than hematopoietic cell recovery
- Use the data collected for the SCTOD to evaluate the performance of centers
- Provide certain SCTOD data to the public
- Collect a basic set of data for analyses of Program use, center-specific outcomes, donor registry, cord blood inventory size, and patient access to HCT
- Establish and maintain a related donor-recipient CIBMTR Biorepository

Basic information is collected for all allogeneic and autologous HCTs on the TED form (**Chapter 12**). TED forms were initially developed by CIBMTR in collaboration with international partners to capture the most essential data for understanding the transplantation procedure and its outcomes. TED forms were also designed to meet SCTOD requirements, including collection of data considered important for center-specific outcome reporting. TED forms require Office of Management and Budget (OMB) approval every three years or as changes are made. Form review occurs at least annually and incorporates a

broad group of expert stakeholders, representing an international consensus on a basic data set to be collected for all HCT recipients.

FormsNet, a web-based application designed specifically for the SCTOD, provides a single platform for US and non-US centers to submit federally required outcomes data to CIBMTR. FormsNet allows bi-directional communication between CIBMTR and centers. For more information, see **Chapter 15**.

6.2.2.1 Completing SCTOD Contract Performance Requirements

The SCTOD contract includes a Performance Work Statement with nine performance requirements, which are further categorized into specific deliverables to be submitted to HRSA. These are updated with each five-year contract renewal, and some may already be complete in fulfillment of the current contract. The following performance requirements are associated as numbered and named below with the contract effective 9/27/2022-9/26/2027:

2.1 Fulfill Contract Administration Requirements

- 2.1.1 Attend Initial / Kick-off Meeting
- 2.1.2 Attend Quarterly Contracting Officer's Representative Meetings
- 2.1.3 Attend Special Contracting Officer's Representative Meetings
- 2.1.4 Establish Policy and Technical Direction of the SCTOD
- 2.1.5 Follow Privacy Act of 1974
- 2.1.6 Records Management Training
- 2.1.7 System Of Records Notice

2.2 Collect Stem Cell Therapeutic Outcome Data

- 2.2.1 Collect and Maintain Outcomes Data
- 2.2.2 Evaluate Data Collection Process and Assess Gaps in Data
- 2.2.3 Develop a Data Validation and Verification Plan
- 2.2.4 Implement Process to Maintain Historical Data Sets and Programming Code

2.3 Disseminate Data

- 2.3.1 Disseminate Data to the Public and C.W. Bill Young Cell Transplantation Program-Participating Organizations
- 2.3.2 Create Standard Analysis Files (SAFs)

2.4 Provide Analytic Support to and in Collaboration with HRSA

- 2.4.1 Provide Analytic Support to HRSA

2.5 Report on Study Activities

- 2.5.1 Report on Study Priorities in the Field of Stem Cell Transplantation and Cellular Therapy
- 2.5.2 Report on the Current State of Quality of Life for Transplant Recipients and Analysis to Improve Patient Late Effects
- 2.5.3 Compare Treatment Options and Outcomes

2.6 Submit Routine Reports

- 2.6.1 Submit Progress Reports
- 2.6.2 Provide a Quarterly SCTOD Function Report
- 2.6.3 Submit Annual Statistical Report on SCTOD Activities
- 2.6.4 Develop and Disseminate Transplant Center Survival Rates
- 2.6.5 Provide Cord Blood Bank Reports

2.7 Use Plain-Language Guidelines and Other Government Laws and Regulations for all Products

- 2.7.1 Comply with Plain-Language Guidelines
- 2.7.2 Comply with Other Government Laws and Regulations

2.8 Optional Task

- 2.8.1 Submit Transition Plan

2.9 Security and Privacy Requirements

6.2.2.2 Conducting Specialized Research

In fulfillment of its SCTOD contract deliverables, as discussed above, CIBMTR conducts specialized research in the following areas.

- **Inventory and Adult Donor Model Analyses.** The SCTOD requires collaborating with the Single Point of Access – Coordinating Center contractor on analysis of the ideal size and composition of both the NCBI and the Program's adult donor registry. The analysis must include an estimate of the effect of different scenarios of Program growth on the probability that a patient in each of several racial / ethnicity categories would find a specified number of potentially matched cord blood units / adult donors. The approach and specific methodologies were developed with NMDP, CIBMTR, external modeling experts, the Single Point of Access Coordinating Center, the Office of Patient Advocacy, and HRSA project staff.
- **Center-Specific Survival Analyses.** See **Section 5.3.2**.

Since 2008, CIBMTR has conducted forums at least biennially to discuss and develop plans to conduct these center-specific survival analyses with center representatives and experts in outcomes reporting and statistical analysis as well as patient and payer representatives (**Section 17.2**). The last forum was held in October 2023. Recommendations generated during these forums are used to guide the center-specific survival analyses. These recommendations are distributed to US center medical directors and made available on the CIBMTR *Center Outcomes Forum* webpage.

6.3 CAR-T AND OTHER CELLULAR THERAPY RESEARCH

In addition to receiving data on transplant recipients, CIBMTR receives data from more than 300 centers for patients who received other cellular therapies. Indications for treatment include malignant hematologic disorders, suboptimal donor chimerism, prevention of disease relapse, neurologic disease, infection and GVHD treatment and prophylaxis, and other conditions. CIBMTR receives ACT data via a suite of CTED forms. These forms, harmonized with the European and Japanese registries, undergo real-time review and revision.

6.3.1 ACT Stakeholders Council

In June 2023, CIBMTR received funding from NIH to create the ACT Stakeholders Council to act as a specialized group in cell and gene therapies that will provide input to the Advisory Committee and CIBMTR Leadership on relevant topics in the field. To better position CIBMTR as a resource to the field, the ACT Stakeholders Council serves a liaison between CIBMTR and various stakeholders, including the cell and gene therapy community, professional societies, payors, and industry.

The ACT Stakeholders Council serves as a standing task force to guide CIBMTR. Topics to be addressed by the ACT Stakeholders Council are selected and prioritized by the Advisory Committee and can originate from the CIBMTR Assembly, CIBMTR Leadership, the ACT Stakeholders Council, or the Advisory Committee. The ACT Stakeholders Council reviews the selected topics and presents recommendations to the Advisory Committee.

The ACT Stakeholders Council meets in person annually at the Tandem Meetings and by teleconference as needed.

6.3.2 Long-Term Follow-Up

The FDA requires pharmaceutical companies that commercialize genetically engineered cellular therapies to follow recipients of these therapies for 15 years in order to evaluate their safety and efficacy. CIBMTR supports this requirement and is currently partnered with several pharmaceutical companies to track these long-term outcome data.

6.4 MEDICARE COVERAGE WITH EVIDENCE DEVELOPMENT (CED) STUDIES

Some Americans were denied access to cellular therapy in the US due to lack of Medicare insurance coverage by the Centers for Medicare and Medicaid Services (CMS). To help secure Medicare coverage for these patients, CIBMTR, NMDP, ASTCT, and other organizations partnered with CMS to launch CED studies. The CED approach allows CMS to provide coverage for procedures and to advocate for clinical studies that inform policy decisions. CIBMTR is currently engaged in four CMS CED studies:

- Multiple Myeloma (17-CMS-MM): NCT#03127761
- Myelofibrosis (16-CMS-MF): NCT#02934477
- Sickle Cell Disease (17-CMS-SCD): NCT#01166009
- Sickle Cell Disease (BMT CTN 1503): NCT#02766465

In December 2023, CMS released a National Coverage Analysis Proposed Decision Memo, which proposes expanding coverage for allogeneic HCT for Medicare patients with high-risk myelodysplastic syndromes (MDS). CIBMTR's CMS CED study (10-CMS-MDS) provided critical evidence for this decision and officially closed on March 6, 2024.

6.5 PATIENT-REPORTED OUTCOMES

CIBMTR implemented an electronic patient-reported outcomes (ePRO) system to support the collection of PRO data, to be linked with clinical data, in the registry. Instruments in the NIH Patient-Reported Outcomes Measurement Information System (PROMIS*)* form the backbone of PRO data collected by CIBMTR. The PROMIS measures capture patient-reported health status using a set of valid, generic, and adaptable assessment tools that cover a variety of domains related to physical, mental, and social health and functioning.

CIBMTR may utilize multiple modes to collect PRO data, including electronic, pen-and-paper, or phone. When collected electronically or over the phone, PROMIS measures are administered as computer adaptive testing through the PROMIS Application Programming Interface (API) and are validated in multiple languages. Computer adaptive testing is a flexible, computer-driven measure that presents a respondent with items from an item

bank. As a patient completes the initial question of a measure's item bank, the computer adaptive testing algorithm selects only those next items that sharpen the estimate of the patient's score in the domain being measured, thus decreasing respondent burden as patients only see questions that are relevant to them.

In addition to PROMIS measures, CIBMTR also collects measures to assess financial well-being, occupational functioning, and social determinants of health. PROs for specific clinical trials may include other measures that are relevant to the study aims. All PRO data are stored in CIBMTR's Integrated Data Warehouse, which can be linked by CIBMTR Recipient ID Assignment (CRID) to clinical data. Data are then available to be shared for observational research studies, including with clinical trial investigators or to centers through existing CIBMTR data sharing portals and functionality, with the patient's permission (**Section 15.2.2**).

CIBMTR's ePRO system is managed by staff members of the Survey Research Group and CIBMTR's IT group. This system integrates several applications. The ePRO Configuration and Maintenance SOP (SOP-0229) describes how each application is configured and integrated together.

- **Qualtrics**. A cloud-based survey platform and the interface for building PRO surveys, generating unique survey links, and for patients to complete PRO surveys.
- **Salesforce**. The client-relationship management system used by CIBMTR for tracking PRO participants, time points, and activities.
- **Assessment Center API**. Delivers PROMIS measures using computer adaptive testing functionality and provides automated scoring of PROMIS measures.
- **FormsNet**. Pushes patient contact information and study enrollment and event dates to Salesforce to initiate PRO data collection time points, and supports direct patient contact from Survey Research Group staff.
- **Integrated Data Warehouse**. Pulls PRO data and scores from Qualtrics, and links them with clinical data.

The ePRO system is flexible and scalable, allowing additional measures at a variety of time points as relevant to individual clinical trials and long-term follow-up of patients. The Patient-Reported Outcomes (PRO) Collection SOP (SOP-0232) describes how staff members in the Survey Research Group contact study participants to collect PRO data.

6.6 GENE THERAPY INITIATIVES

CIBMTR formed an internal Gene Therapy Working Group in 2020 to design and implement data collection requirements for patients receiving gene therapies. The Gene Therapy Working Group collaborated with a national task force comprised of gene therapy experts to determine how to leverage CIBMTR infrastructure to efficiently collect data considered necessary for gene therapy products and for long-term follow-up of gene therapy recipients. New and revised data collection forms, including a gene therapy product form and new thalassemia disease-specific forms, were released to centers in Fall 2021 and Spring 2022. A post-transplant Gene Therapy Persistence form was released in October 2023.

6.7 CURE SICKLE CELL INITIATIVE

The Cure Sickle Cell Initiative builds a community of patients, advocates, researchers, and scientists to accelerate promising genetic therapies to cure sickle cell disease. Launched in 2018 by NHLBI, the initiative encourages collaboration among researchers, nonprofit organizations, and policy-making agencies focused on curing the disease. Since 2019, CIBMTR has worked with the Cure Sickle Cell Data Consortium to build a research data ecosystem designed to support investigator-initiated collaborative research. Each year

CIBMTR delivers to the data ecosystem a shareable research dataset of sickle cell disease HCT outcomes.

CHAPTER 7: IMMUNOBIOLOGY RESEARCH

Established in 2010, CIBMTR's Immunobiology Research Program leverages NMDP's investment in developing an unrelated donor-recipient specimen repository of research samples known as the CIBMTR Biorepository with the NIH's investment in CIBMTR's Research Database. These resources facilitate studies that link genetic and immunobiological data with clinical phenotype data and outcomes.

The related donor-recipient collection of research samples, an SCTOD contract requirement (**Chapter 6**), is a newer program that offers a unique opportunity to enhance immunobiology research. With recent increases in the number of haploidentical procedures performed worldwide, it has also become important to develop a robust repository of these samples to enable future research. Together, the unrelated and related donor-recipient specimen research sample collections of the CIBMTR Biorepository facilitate a broad approach to studying transplant biology across the full spectrum of allogeneic HCT. The overall goal of immunobiology research is to facilitate studies that focus on:

- Improving outcomes after cellular therapy through a better understanding of the immune response pathways, HLA, and other genetic determinants of outcomes
- Increasing the efficacy of unrelated donor HCT through a better understanding of donor and recipient genetic determinants
- Understanding the role of HLA-matched or mismatched related and unrelated donor HCT compared to other sources and factors

Examples of research supported by this program include:

- Genes and gene products of the major histocompatibility complex (MHC)
- Natural killer cell biology
- Cytokines and other immune response determinants
- Minor histocompatibility loci
- Other immune regulatory genes and products, such as anti-HLA antibodies
- Comparative studies that involve related donors, unrelated donors, and cord blood units

7.1 PROGRAM OVERSIGHT

The Immunobiology Research Program is overseen by the Director of Immunobiology & Bioinformatics Research. The program is managed by the Manager, Immunobiology Research. Input into the program is provided by Senior CIBMTR Leadership and the Immunobiology Working Committee.

The Director of Immunobiology & Bioinformatics Research is a co-scientific Director of the Immunobiology Working Committee. Observational research studies that focus on immunobiology are typically conducted through the Immunobiology Working Committee using the clinical outcomes research process (**Section 6.1**) and directly facilitated by the Immunobiology Research program. The committee is unique in that it may have a Chair who is a PhD Scientist from a histocompatibility-focused laboratory background rather than an MD. In addition, the committee is assigned two Scientific Directors, ad hoc additional Statistical Directors, and Statisticians to accommodate the large number of studies it conducts.

7.2 KEY ACTIVITIES

7.2.1 Collaborative Research

To meet its research goals, the Immunobiology Research Program collaborates with researchers in the clinical and basic sciences communities on prospective and observational

research. Proposals to the Immunobiology Working Committee are submitted via a formal mechanism for submission and review, and specific instructions can be found on CIBMTR's *Propose a Working Committee Study* webpage. Ancillary and correlative proposals using data and samples from clinical trials are also reviewed and coordinated by the Immunobiology Research leadership.

Proposals to the Immunobiology Working Committee are initially reviewed by the Chairs and Scientific Directors before being presented and discussed at the annual Tandem Meetings, during which committee members provide input regarding the scientific agenda and priorities for their committee. In addition, meritorious studies may be reviewed mid-cycle and approved if adequate support is available. For up-to-date information on committee structure, research proposal criteria and submission processes, biospecimen inventories, and contact information, refer to *CIBMTR's Immunobiology Research* webpage. Studies are approved based on scientific merit, originality, feasibility, and biostatistical considerations, including statistical power and the need for additional resources. Investigators with expertise to contribute are invited and encouraged to become actively involved in the Immunobiology Working Committee. Additional resources to support the planning and development of research proposals can be found on *CIBMTR's Resources* webpage.

7.2.2 CIBMTR Biorepository

The CIBMTR Biorepository provides a unique resource to investigators for retrospective analysis of immune response determinants and transplant outcomes. A quality-controlled biorepository, the CIBMTR Biorepository links pre-transplant donor and recipient research samples collected from multiple institutions with comprehensive clinical outcome data and provides access to the cellular therapy research community. NMDP has developed and actively maintains this repository; sample types and an inventory summary are posted on *CIBMTR's Biospecimen Inventories* webpage. As a condition for access to the samples and data analysis support, investigators are required to submit the data and interpreted results of all assays performed on the samples back to NMDP. This data submission requirement helps ensure all sample testing yields information that is readily available to the research community for subsequent analyses and reduces or eliminates duplicate testing to conserve resources and sample inventory.

7.2.3 Donor / Recipient Pair Project

CIBMTR conducts research that supports the objectives of the Immunobiology Research Program. The Donor / Recipient Pair Project is a retrospective HLA typing initiative to characterize class I (HLA-A, B, and C) and class II (HLA-DRB1, DQB1, and DPB1) alleles and other immunobiological data of interest from transplant donor / recipient paired samples stored in the CIBMTR Biorepository.

The data are stored in a database developed by NMDP and are valuable for evaluating the impact of matching, as either the focus of or as a variable in a CIBMTR-approved research study (**Chapter 6**). Allele-level data are also used to assess genetic diversity within populations. Genetic diversity analyses have focused on the evaluation of HLA haplotypes within the donor and recipient data set, made possible by the completeness of the loci characterized, the level of resolution achieved, and the high level of quality control. Statistical models developed using project data are also applied to NMDP's HapLogic™ search algorithm, which originated with Bioinformatics Research as an NMDP resource supporting the identification of optimal donors for patients in need of transplant. HapLogic continues to contribute to selection strategies for improved patient outcomes.

7.3 SIGNIFICANCE TO CIBMTR

CIBMTR's Immunobiology Research Program is significant to CIBMTR in several ways:

- **Histocompatibility Expertise**. The Immunobiology Research team contributes to assignments and validation of HLA matching data and other genetic factors for inclusion in CIBMTR research studies. The Immunobiology Working Committee ensures the research priorities associated with histocompatibility in related and unrelated transplants (adult donor and umbilical cord blood) are addressed through the Immunobiology Research Program. The results of these research program studies are directly integrated into the histocompatibility matching guidelines promoted through NMDP.
- **Research Materials Stewardship**. The Immunobiology Research Program facilitates utilization of research materials contained within the CIBMTR Biorepository through collaboration with researchers across the cellular therapy community, including samples collected from donors and recipients pre-transplant in addition to samples collected through clinical trial protocols. The program maintains a comprehensive record of donor and recipient HLA profiles and match grades at transplant to facilitate retrospective analysis of HLA concordance in transplant outcomes. Subject matter experts within the program link investigators with the research materials necessary to perform novel immunobiology research while providing oversight to ensure appropriate and judicious use of valuable resources.
- **Strategic, Diverse Data Resource.** Studies of the genetic diversity of donors and recipients using the CIBMTR Biorepository and strategically collected molecular and cellular data are translatable to clinical practice through the development of improved search and selection algorithms used to identify hematopoietic stem cell sources for patients in need of transplant. These resources also inform models and tools for diagnosis and prediction of patient disease and projected outcomes from cellular therapies.

CHAPTER 8: CLINICAL TRIALS

CIBMTR participates in and supports a variety of clinical trial activities to accomplish its mission of improving the success of cellular therapy. CIBMTR supports investigators in planning these trials by providing resources, access to its Research Database, and statistical expertise. In addition to its clinical outcomes research (**Chapter 6**), CIBMTR also supports two active clinical trials programs, the BMT CTN (**Section 8.1**) and CRO Services (**Section 8.2**).

8.1 BMT CTN

The BMT CTN, or the Network, was established in October 2001 to conduct large, multi-institutional Phase II and III trials addressing important issues in cellular therapy. The Network includes the BMT CTN DCC; 20 Core Clinical Centers, some of which are consortia of 2 or more centers; and about 80 Affiliate Centers. BMT CTN collaborates and integrates with CIBMTR for data, expertise, and network management activities.

8.1.1 BMT CTN DCC and CIBMTR

The BMT CTN DCC coordinates all Network activities including operations, data management, communication, and statistical support. It is funded by a cooperative agreement from the NIH, with the NHLBI as the lead institute. The award is held and managed by CIBMTR at MCW.

Administration and leadership of the DCC is shared by MCW, NMDP, and The Emmes Company, each with extensive research expertise. See the *BMT CTN Manual of Procedures* for a list of these shared responsibilities.

The DCC plays a key role in developing and facilitating study proposals and is responsible for statistical planning and collection of data from participating clinical centers. It manages all BMT CTN protocols, maintaining version control during development and after approval. It organizes, schedules, and prepares minutes and agendas for meetings and conference calls for the Steering Committee, Executive Committee, and others as requested. The DCC also maintains a private, password-protected website and a *public website* for the Network. For more information about the BMT CTN, including policies and procedures, see the annual BMT CTN Progress Report and Manual of Procedures on the *public website*.

8.1.2 Data Collection and Statistical Resources Provided by CIBMTR

CIBMTR's Research Database is a key source of data for all BMT CTN studies, especially for accrual projections and statistical design. CIBMTR makes data and statistical resources available to support several of the Network's activities:

- **Trial Planning**. CIBMTR's extensive Research Database of clinical information is used to assess the availability of appropriate patient populations for the specific eligibility criteria of each trial.
- **Data Collection Instruments**. The Network uses data collection forms developed by CIBMTR. These include the TED forms used by most centers for submitting data and the CRFs used to collect more detailed information about transplants from a select group of centers (**Chapter 12**). Centers must provide CRFs for Network studies, even if they are required to provide only TED forms under the SCTOD (Chapter 6) guidelines.
- **Statistical Consultation**. CIBMTR Statistical Staff provide design support and analytical review for BMT CTN protocols.
- **Trial Interpretation**. CIBMTR data are used to evaluate the results of clinical trials by providing matched controls for patients treated in single and multi-institutional studies of transplant strategies, as required by the study protocol.

8.1.3 Data Submission

There are four primary ways to submit data to the BMT CTN:

- **AdvantageEDC℠ and Advantage eClinical℠ Systems**. These Web-based interactive data entry (electronic data capture, EDC) systems are housed at The Emmes Company. The Network uses their systems to record real-time study data. The DCC and centers can use these systems to generate lists of submitted, due, or delinquent forms for each patient and center. AdvantageEDC and Advantage eClinical forms include additional data fields that are not on CIBMTR CRFs.
- **FormsNet**. This CIBMTR web-based system allows centers to electronically submit data to CIBMTR using TED forms and CRFs, which are occasionally used as the main mechanism for data collection in BMT CTN trials. In the context of BMT CTN studies, data collected via this mechanism are merged with data collected by the Emmes platform.
- **ePRO**. This CIBMTR system utilizes NIH-funded PROMIS measures as its backbone and is administered as computer adaptive testing. The system is scalable, allowing additional measures to be collected, as identified by study needs. See **Section 6.5** for more information. All BMT CTN studies use this platform to collect PRO.
- **Medidata Rave and Veeva Vault EDC**. These cloud-based data entry and monitoring systems are utilized by CIBMTR CRO Services for trials requiring prospective data capture beyond what is required within FormsNet. See **Section 15.2.1.1.2** for details.

8.1.4 Statistical Expertise

CIBMTR and Emmes Statistical Staff are responsible for developing statistical designs, analytical methodology, and data analysis. CIBMTR and Emmes PhD Biostatisticians provide statistical review of clinical trial protocols and serve as expert resources for the protocols.

8.1.5 Accrual Planning, Monitoring, and Intervention

Adequate accrual is crucial to the success of the Network's clinical trials. The BMT CTN Program Manager, a CIBMTR staff member, assists in launching BMT CTN trials and develops, implements, and supports patient accrual strategies. The Program Manager works with Protocol Teams to assess accrual barriers prior to study launch and throughout the course of the trial and to develop protocol-specific accrual plans. This person also has ready access to CIBMTR databases, helps oversee all DCC activities, and coordinates key projects.

8.2 CRO SERVICES

CIBMTR formed CRO Services to provide support for a wide array of clinical studies, including multi-center trials, surveys, and quality of life assessments. CRO Services, which conducts prospective research within CIBMTR, provides organizations and researchers with infrastructure and expertise in clinical trial design, conduct, and analysis. CRO Services supports studies of all phases and offers full study support or a la carte options.

Clinical trial services available through CRO Services include full-scale or a la carte options for research sponsored by CIBMTR / NMDP, industry organizations, academic consortia, or investigators. Team capabilities include:

- Protocol development
- Regulatory support
- Study management
- Site management and monitoring
- Study database development and oversight

- Statistical support and data analysis
- PROs
- Clinical sample research
- Contract and financial administration

Organizations or PIs may also contract for specific services as needed, such as support with surveys, site selection and management, sample management, and more. For academic studies, investigators may request assistance with funding applications from a variety of sources, such as government agencies, foundations, and private corporations. CRO Services is led by the CIBMTR NMDP Chief Scientific Director and Vice President of Clinical Trials. Its research portfolio is overseen by CIBMTR's Executive Leadership Team.

CRO Services is supported by operational managers and team members within survey research, research sample oversight, program and project management, monitoring, data management, biostatistics, site operations, and quality. Staff members are responsible for the daily operation of prospective and observational studies conducted through CRO Services. It is also supported by CIBMTR Statistical Directors, who are faculty members of the MCW Division of Biostatistics, as well as other NMDP departments, including regulatory, IT, immunobiology, legal, contracts and purchasing, regulatory, and finance. Protocol Officers, Study Chairs, and PIs are frequently CIBMTR faculty from either campus. CRO Services staff members work with the study Sponsor PI and/or Protocol Chair and Protocol Teams to:

- Collaborate with the sponsor to develop study protocols and materials
- Prepare and submit applications and continuing reviews to the Data and Safety Monitoring Board, FDA, and NMDP IRB (**Chapter 13** and **Section 8.2.4**)
- Perform site selection, initiation, interim, and close-out monitoring visits
- Coordinate contracts with selected investigational sites
- Identify and contract with suitable labs and repositories for study support
- Coordinate communications among laboratories and repositories
- Develop case report forms, and build and host the study-specific electronic data capture
- Develop statistical analysis plans
- Coordinate study and site training
- Coordinate with selected sites for informed consent form review and local and single IRB submission
- Coordinate site activation, including site initiation training
- Review data submitted on CRFs for completeness and accuracy
- Communicate with participating centers regarding missing, delayed, incomplete, or erroneous data
- Review and file regulatory documents within the electronic trial master file (eTMF)
- Coordinate meetings and conference calls, including site locations, travel arrangements, and call-in information
- Coordinate communications among participating centers, NMDP representatives, and other stakeholders
- Coordinate analysis of study data
- Prepare study data for publication and data submission

8.2.1 CRO Services Trial Centers

All CIBMTR centers in the US are eligible to participate in trials, although not all trials are opened in all centers. Participation in specific protocols is determined by:

- Study design and requirements
- Level of center commitment, including availability of research staff
- Accrual targets
- Competing protocols
- Previous record of participation and compliance in multi-center trials

8.2.2 Trial Selection and Progress Oversight

CRO Services leadership reviews and prioritizes proposals based on scientific merit, feasibility, and alignment with scientific agenda / mission.

8.2.3 Data and Safety Monitoring Board

CRO Services has its own Data and Safety Monitoring Board, which serves as an independent advisory body for studies that require review and are not already reviewed by another data and safety monitoring mechanism. The primary function of the Board is ongoing assessment and monitoring of CRO Services studies for their validity, safety, and efficacy. The Data and Safety Monitoring Board includes an interdisciplinary membership with expertise in cellular therapy and the conduct of clinical trials.

8.2.4 NMDP IRB

The NMDP IRB reviews all applicable CRO Services protocols as CIBMTR staff members are engaged in the trial research activities. It is an administrative body established to protect the rights and welfare of human subjects recruited to participate in NMDP and CIBMTR research activities. The IRB has the authority to approve, require modifications in, or disapprove all research activities that fall within its jurisdiction, as specified by both federal and state regulations and NMDP policies and procedures. The IRB must approve all applicable CRO Services protocols before they can be distributed to participating sites for their respective site IRB approvals. See **Chapter 13** for more NMDP IRB information.

8.2.5 Survey Research Group

The Survey Research Group is a team within the CRO Services created to assist researchers in developing and conducting research involving questionnaires, direct subject interviews, and PRO. The group is responsible for collecting high-quality, scientifically valid data from donors, patients, and their families. The Survey Research Group utilizes standardized and semi-structured telephone interviews, self-administered questionnaires, and its ePRO system to support clinical trials, long-term follow-up, and other research studies with patients and donors (**Section 6.5**).

8.2.6 Study Proposals

Investigators or organizations may submit study proposals to CRO Services at any time by outreach to CIBMTR Leadership or directly to the Vice President of Clinical Trials.

8.2.7 Study Budget Management

Budgets are prepared and approved for each project. As noted above, all funding must include internal labor, travel, and protocol-specific expenses including items contracted to outside organizations such as laboratory, central pharmacy, or other products and services needed to accomplish the study objectives. Study budget management includes:

- **Study budget preparation and development**. CRO Services staff members collaborate with NMDP's Finance Department, including Contracts and Purchasing, to prepare and develop budgets. This includes developing individual protocol budgets and coordinating funding for studies with external support.
- **Budget review process**. The final budget must be approved by the Vice President of Clinical Trials. CRO Services staff members may work with NMDP's Contracts and Finance Departments to create a Request for Proposals and contracts for centralized services, to finalize contributions, and to review the budget.
- **Expense tracking**. NMDP Contracts and Purchasing tracks and reconciles CRO Services protocol-related funds, makes payments to suppliers, makes payments to investigational sites per executed study riders, and reconciles all costs quarterly.
- **Budget revisions**. When significant changes are made to a protocol budget, either because of contributions or a change in costs, a new budget must be approved by the Vice President of Clinical Trials.

8.2.8 Other Systems

CRO Services also utilizes the following systems:

- **Veeva Vault CTMS** (clinical trial management system). This Web-based metrics system allows patient enrollment and milestone tracking, site monitoring, and issue management.
- **Veeva Vault eTMF**. This Web-based electronic trial master file system provides regulatory document exchange, tracking, and storage.
- **Florence eTMF**. This Web-based electronic trial master file system provides regulatory document exchange, tracking, and storage as well as remote site access capabilities through its eBinders.
- **LabVantage**. This Web-based system allows biorepository management for oversight of research sample collection, processing, storage, and distribution.

8.2.9 Data Submission

While the CRO Services offers a la carte services and can support study activities without data management oversight, it utilizes four systems to collect trial data:

- **Veeva Vault EDC**. This Web-based interactive data entry system is custom built for each study. Veeva Vault EDC provides an end-to-end environment to collect, review, and process trial data.
- **Rave platform**. This Web-based interactive data entry system is custom built for each study utilizing the Medidata cloud-based system. Rave allows real-time study data collection and immediate validation checks; query management and forms status functionality are built into each study.
- **FormsNet**. This CIBMTR web-based system allows centers to electronically submit data to CIBMTR using TED forms and CRFs. It was developed by CIBMTR in fulfillment of SCTOD requirements for submission of outcomes data and also serves the CRO Services for certain studies for collecting pre-treatment, survival data, and selected cellular therapy data. See **Section 15.2.1.1.1** for more information.
- **ePRO**. This CIBMTR system utilizes NIH-funded PROMIS measures as its backbone and is administered as computer adaptive testing. The system is scalable, allowing additional measures to be collected, as identified by study needs. See **Section 6.5** for more information.

8.2.10 Publications

CRO Services leadership is responsible for developing and approving all publication and presentation policies. They also review all proposed publications and presentations to ensure protection of proprietary information and study participant confidentiality and to determine the public impact of publication and / or presentation of incomplete or premature results. No participating institution, protocol team, or other individual may present or publish individual findings from work performed on study protocols or work related to CRO Services meetings and conference calls without approval of the CRO Services leadership. This includes methodologic or position papers related to CRO Services protocol development or operations.

See **Chapter 3** for more information about authorship guidelines and **Chapter 4** for manuscript submission policies.

CHAPTER 9: HEALTH SERVICES RESEARCH

Health services research is the multi-disciplinary field of scientific investigation that studies how socioeconomic factors, financial systems, organizational structures and processes, technology, and behavior affect treatment outcomes, quality, and cost. The Health Services Research Program was established in 2009. Its overall objectives are to:

- Increase access to and utilization of cellular therapy
- Improve patient outcomes through evidence-based and real-world data-driven health services and policy research

Multiple research methods are used to help meet these objectives:

- Observational (retrospective and prospective) research designs
- Primary and secondary data analysis
- Data management and dataset linkage
- Survey design and administration
- Qualitative, quantitative, or mixed methods analytical approaches

Examples of research supported by this program:

- Inequities in access to and utilization of cellular therapies resulting from social determinants of health-related barriers and genetic risk factors
- Survivorship and PRO, such as quality of life
- Treatment decision-making support, including for clinical practice and quality / value of care
- Health economics and outcomes research, including healthcare utilization

9.1 PROGRAM OVERSIGHT

9.1.1 Program Leadership

The Health Services Research Program is led by the Manager, Implementation Science. Oversight for the program is provided by the Chief Scientific Directors, CIBMTR MCW and NMDP. The Scientific Directors and Statistical Directors of CIBMTR Donor and Recipient Health Services Working Committee also serve as ad hoc advisors (**Figure 1.1**).

9.1.2 Collaboration with CIBMTR Working Committees

CIBMTR Working Committees, including the Donor and Recipient Health Services Working Committee and the Morbidity, Recovery, and Survivorship Working Committee, conduct studies using CIBMTR's Research Database. The Health Services Research Program complements the research of these Working Committees, conducting studies that require additional resources and methods (e.g., surveys, focus groups, and studies involving use of data from regional and national databases, such as administrative claims).

9.2 KEY ACTIVITIES

9.2.1 Research and Collaboration

Intramural: The Health Services Research Program identifies new research opportunities, and it conducts and supports research studies that fulfill the missions and expand the research portfolios of CIBMTR and NMDP. Additionally, it collaborates with other CIBMTR programs and NMDP departments to provide subject matter expertise for research proposals that address health policy and health services issues related to cellular therapy.

Extramural: The Health Services Research Program works with external investigators interested in conducting health policy and health services research related to cellular

therapy. External collaborators are invited to contribute expertise and resources as appropriate. Studies are prioritized based on relevance to CIBMTR and NMDP missions, potential for extramural funding, and available resources. The Health Services Research Program also participates in and partners on research through the ASTCT Survivorship, Palliative and Supportive Care, Biobehavioral, and Value and Health Economics Special Interest Groups.

Collaboration occurs in many ways:

- Study development and support, including design, analysis, visualization, and reporting
- Program planning, development, evaluation, and management of organizational and community initiatives
- Through relationships with stakeholders, including patients, caregivers, donors, patient advocacy organizations, government agencies, health professionals, payers, and center financial staff

9.2.2 Development and Dissemination

In addition to the Tandem Meetings (**Chapter 17**), health services researchers regularly participate in the American Society of Hematology (ASH) Annual Meeting & Exposition. *ASH* is the world's largest professional society for clinicians and scientists in hematology. The annual meeting provides education and highlights the latest topics in hematology.

CHAPTER 10: BIOINFORMATICS RESEARCH

The Bioinformatics Research team drives high-impact research and produces strategic applications to bridge the transition from research to operations. At the intersection of science and technology, this team moves in the direction of Computational Biomedicine in the following main areas: Precision medicine and omics analytics, machine learning and clinical predictions, cellular therapy selection, and therapy source inventory modeling.

10.1 PROGRAM OVERSIGHT

10.1.1 Program Leadership

Bioinformatics research is led by the Director of Bioinformatics & Immunobiology Research. Input into the program is provided by Senior CIBMTR Leadership and advisory groups.

10.1.2 Collaborations

The program works closely with senior leaders at NMDP and MCW and collaborates with other internal programs and with external organizations, such as academic centers, registries, corporations, and other associations, on a project-specific basis.

10.2 KEY ACTIVITIES

10.2.1 Precision Medicine and Omics Analytics

Program staff develop processing and annotation workflows to characterize variation in donors and cellular therapy products, patients, and transplant donor-recipient pairs. The team leverages technology platforms that enable integrated, scalable data analysis and high-throughput bioanalytics on a variety of omics sources, including whole-genome, exome, proteome, and methylome sequencing and array data. Staff members analyze sample variation from donors and recipients to identify novel molecular factors that impact transplant outcomes and prognostic factors that contribute to event-free survival. The team performs analyses and creates tools to extract and annotate immunogenetic data to facilitate improved selection diverse therapies and treatments tailored to patient needs.

10.2.2 Machine Learning and Clinical Predictions

The Bioinformatics Research Program prepares platforms for data science applications and builds and trains models for analysis of business and clinical data collected in daily operations at CIBMTR and NMDP and through network partners and research trials. The team investigates patient searches, donor availability, cellular therapy product collection, and disease impacts, among others, to provide strategic insight for NMDP operations. Staff members apply machine learning and research and develop models to improve transplant outcome predictions and provide tools to improve survival outcomes and quality of life for all patients.

10.2.3 Cellular Therapy Selection and Therapy Source Inventory Modeling

The Bioinformatics Research Program investigates algorithms and develops services to improve the prediction of missing immunogenetic data and the selection of cellular therapies for patients toward best survival and quality of life outcomes. Program researchers improve the collection, analysis, validation, and utilization of data on donors and patients with diverse ancestry for feature improvements. Novel approaches are tested for accuracy, flexibility, and scalability to produce applications for NMDP and to ensure critical research results can be incorporated into the matching algorithm as soon as possible. Finally, the translation of research and evidence-based guidelines to user interfaces by the Bioinformatics Research team helps to optimize cellular therapy matching and donor selection for physicians, transplant centers, and other stakeholders.

To determine how to best meet the needs of all patients in need of cellular therapy, the Bioinformatics Research Program curates HLA frequencies in global populations and models the composition of the Donor Registry, Cord Blood Banks, and other Biobanks in order to project needs and optimize the availability of cellular therapies for patients. These and related projects help to increase the likelihood of finding a match for patients and identify cellular products with high potential (e.g., SOP-0148: Custom Donor Search Process for the Development of Allogeneic Cell and Gene Therapies). In addition, these applications inform strategies to prepare a ready source of cellular therapy in case of acute radiation emergency. The Bioinformatics Research Program ensures CIBMTR and NMDP are at the forefront of innovative research and applications so that new technologies and clinical findings can be incorporated into the operational side of CIBMTR and NMDP as swiftly and seamlessly as possible.

CHAPTER 11: INDUSTRY PROGRAM

CIBMTR's Industry Program supports non-grant-supported industry relationships through initial contact, proposal development and design, study development, and delivery of industry-sponsored non-interventional research. These activities support CIBMTR's mission and generate revenue to support and enhances industry awareness of CIBMTR and its ongoing research initiatives. CIBMTR's service portfolio includes:

- Real-world data non-interventional research solutions
  - Data licensing
  - De-identified datasets
  - Control populations for clinical trials
  - Long-term follow-up studies
  - Use of CIBMTR's multi-study protocol
- Real-world evidence non-interventional research solutions
  - Post-authorization safety studies
  - Post-authorization efficacy studies
- Non-interventional regulatory research consulting
- Non-interventional research planning and optimization consulting

11.1 PROGRAM LEADERSHIP AND STAFF

11.1.1 Senior Scientific Director for Industry Program

The Senior Scientific Director for CIBMTR's Industry Program is responsible for facilitating the Industry Program's portfolio, aligning it to CIBMTR's mission and ensuring CIBMTR maintains data integrity. This is accomplished through familiarity with all industry studies, both before and after execution; Data Operations capabilities and processes; observational study and statistical practices; IT infrastructure; CIBMTR budgets and finances; and MCW and NMDP grants and contracts operations. The Scientific Director facilitates studies, encourages PIs to meet expected timelines, and keeps the portfolios moving forward. The Scientific Director provides medical oversight and analytic expertise and facilitates CIBMTR Leadership visibility of Industry Program activities (SOP-0070: Scientific Director Guidelines).

11.1.2 Industry Relations Program Director Responsibilities

- Along with the Senior Scientific Director, provide strategic leadership for the expansion of CIBMTR's industry portfolio aligned with CIBMTR's mission
- Initiate new opportunities with pharmaceutical, biotechnology, insurance, and consulting companies, and renew existing and lapsed relationships
- Understand market landscape and determine how to best position CIBMTR to create opportunities for revenue development
- Collaborate with CIBMTR Advancement to develop an industry marketing strategy
- Oversee CIBMTR Industry Relations responsibilities
- Develop collaborative agreements with partnering organizations
- Establish and strengthen working relationships with business leaders at all levels
- Document and report the status of all industry funding secured, including annual contract value, customer lifetime value, new leads in pipeline, average age of leads in pipeline, conversion rate of initial conversations to executed contracts, and number of new project requests from existing clients
- Collaborate with NMDP BioTherapies commercial portfolio

11.1.3 Industry Relations Program Managers' Responsibilities

- Gather preliminary information about clients' requests
- Collaborate cross-functionally to shepherd requests through intake and proposal development
- Manage accounts externally by representing CIBMTR with clients and internally by working with direct reports and supporting positions
- Develop a thorough understanding of clients' positions in the market, their products / services, points of difference, and competitive landscape
- Manage client input and feedback for all projects with detailed direction and timelines
- Establish and build strong working relationships with business leaders at all levels
- Manage day-to-day client communication and ongoing relationships as they relate to current, new, and upcoming projects
- Proactively remain connected to clients and the market to access new opportunities and ensure all viable clients are engaged on a regular and effective basis

11.2 INDUSTRY RELATIONS KEY ACTIVITIES

11.2.1 Project Intake and Engagement

CIBMTR's Industry Program receives requests from its website information request form, emails directly from clients, and emails from CIBMTR Scientific Directors and staff members.

Before submitting a proposal, prospective clients are encouraged to view CIBMTR publicly available data sets and CIBMTR data collection forms to verify that critical data are available for their proposed study. The Industry Relations Program Director and Senior Scientific Director, along with a statistician depending on the maturity of the request, meet clients to define needs.

Once the request is sufficiently defined, the Senior Scientific Director presents the request to CIBMTR's Executive Leadership Team (**Section 1.4.1**) to confirm alignment with CIBMTR's mission. Leaders consider the study's potential to improve outcomes and access directly as well as the study's potential to improve the ability to perform studies or change practice that will improve outcomes and/or access.

11.2.2 Proposal Feasibility Assessment

Once CIBMTR's Executive Leadership Team (**Section 1.4.1**) approves a preliminary proposal to proceed, CIBMTR begins feasibility assessment, determining:

- Feasibility of variables:
    - Length of time data have been collected
    - Need for supplemental data collection
    - Availability of data for the years requested
    - Data Operation's and IT's ability to provide the requested data
- Need for additional IRB approvals
- Ability to perform every study aspect within the client's timeline

The Data Operations Study Manager reviews the study for accuracy of data collection methods and business rules. If the Manager determines supplemental data collection is appropriate, the study will follow the supplemental data processes described in **Section 6.1.5.5 and Appendix B**.

A feasibility assessment generally includes a table describing the patient population, patient availability for the study, and a high-level assessment of infrastructure readiness and

timeline. Complex feasibility discussions should prompt a request for Corporate Membership (**Section 18.2.1.1**), and a Scientific Director should not commence work on a project outline or proposal without an appropriate-level Corporate Membership in place. A contract for a planning phase is required for study requests that require protocol development (**Section 11.3.2.1**).

11.2.3 Proposal and Statement of Work Development

A completed Statement of Work includes a preliminary project proposal, preliminary budget, and deliverables and timeline.

For a retrospective project, CIBMTR creates an initial project proposal and shares it with the client for approval or amendments. Then CIBMTR uses the approved proposal to generate a Statement of Work. A proposal and contracted Statement of Work may be sufficient for outlining study objectives and analysis plans for an observational study using existing registry data for non-regulatory purposes.

For a prospective study, CIBMTR creates a draft task list using the Prospective Projects definition and budgeting tools. Then CIBMTR uses the task list to create the Statement of Work and budget. If a data license is needed, the Director of Technology is involved. Once the client approves the Statement of Work, the project may move on to Procurement and Delivery.

11.2.4 Procurement and Delivery

Depending on the type of project, CIBMTR may execute a research services agreement, master services agreement, research services agreement with data license, or Corporate Membership. All proposals and budgets must follow appropriate approval processes. As CIBMTR is a partnership of MCW and NMDP, contracts are routed through the applicable legal entity. Industry funding proposals contracted on the Milwaukee campus must comply with MCW Grants and Contracts policies, so CIBMTR develops contracts in conjunction with MCW's Grants and Contracts Office.

Once CIBMTR and the client approve the contract and Statement of Work, the Industry Relations team submits a proposal to CIBMTR's Finance team and Authorized Department Representative. When the proposal is ready for final Grants and Contracts Office review, CIBMTR completes an eBridge Proposal Request, and CIBMTR's Finance team submits the proposal to MCW's Grants and Contracts Office. After all stakeholders review and redline the contract, CIBMTR routes a clean copy of the contract for signatures and execution. Following contract execution, project management shifts to CIBMTR's Industry Operations team.

11.3 INDUSTRY OPERATIONS KEY ACTIVITIES

Once a contract is executed, the Industry Relations Program Manager notifies the Industry Operations Program Manager of the new project and provides study documents.

11.3.1 Initiation Phase

During the Initiation Phase, the study team creates a master file in the Business Operations Collaborate / SharePoint Site to collect essential documents. The team also confirms and aligns documents and confirms IRB status. Finally, the team submits study information to CIBMTR's Master List of Studies.

11.3.2 Planning Phase

In the Planning Phase, the study team develops a Project Overview and communication plan and schedules internal and external kick-off meetings. The Project Overview includes:

- Study name and ID
- Sponsor

- Agenda
- Study team introduction
- Brief summary of the Statement of Work
- Data collection, including forms and supplemental form development as applicable
- Statistical Analysis Plan (**Section 11.3.2.2**)
- Milestone / deliverable list and due dates

At the external kick-off meeting, the study team confirms expectations regarding publication (**Section 2.2**) and regulatory submission. If there is a planned change in scope, the study team will determine if an amendment is warranted. After the kick-off meetings, the study team finalizes the study calendar tracker and project overview. If needed, the team completes a Project Plan, Statistical Analysis Plan, and/or Data Transfer Agreement.

11.3.2.1 Protocol Development (SOP-0314)

CIBMTR may develop a protocol as a contracted deliverable for a post-approval study, post-authorization safety study, or long-term follow-up study. Members of the study team, including the Industry Operations Project Manager, Scientific Director, Statistical Director / Statistician, and Data Operations Program Coordinator, meet to discuss the Statement of Work, protocol development, statistical analysis, and timeline. The Scientific Director and Statistical Director are responsible for drafting the protocol based on the objectives, selection criteria, outcomes, and variables that are specified in the Statement of Work. The client's templates may be used, but CIBMTR templates are strongly preferred. The study team reviews and addresses comments for the draft protocol, and they may present the draft protocol at the weekly Coordinating Center statistical meeting for additional comments.

11.3.2.2 Statistical Analysis Plan Preparation (SOP-0242)

A Statistical Analysis Plan describes planned analyses for a clinical trial or an observational study; it contains study objectives, study design, an analysis plan, and statistical methods of analyses. SOP-0242 outlines the procedure for creating a Statistical Analysis Plan for industry studies if the contract specifies.

If contracted, members of the study team, including the Industry Operations Program Manager, Statistical Director, Statistical Operations Manager / Senior Statistician, Study Statistician, and Scientific Director, prepare the draft Statistical Analysis Plan. The study team may meet with the client to discuss the protocol and plan and to answer questions. The Statistical Director is responsible for drafting the Statistical Analysis Plan based on the objectives, selection criteria, outcomes, and variables specified in the protocol. The Statistical Operations Manager / Senior Statistician reviews and provides comments to the plan.

If a study has a Statement of Work that is sufficient for outlining the project's objectives and analysis plan, a separate Statistical Analysis Plan is not needed. If the client already has a Statistical Analysis Plan, CIBMTR reviews and signs off on the plan.

11.3.3 Execution / Monitoring and Controlling Phase

In the Execution / Monitoring and Controlling Phase, the Industry Operations Program Manager monitors and tracks study progress using the Project Overview and Study Tracker. The Manager ensures effort is aligned with the Statement of Work, patient enrollment is stopped once accrual is met, and deliverable work is progressing. Once a deliverable is completed, the study team conducts quality checks to ensure all requirements are met. Once the Scientific Director approves the deliverable, the Industry Operations Program Manager or Business Operations Director delivers it to the client using an approved

platform. The Industry Operations Program Manager notifies CIBMTR's Finance team to send an invoice. If the client requests changes or clarification that are related to delivering the data as stated within the Statement of Work and/or it can be completed within minimal effort, the team may revise the deliverable. If the changes are out of scope or require significant effort to fulfill the request, the contract or Corporate Membership should be amended.

11.3.4 Closing Phase

At the end of the project, the study team facilitates a "Lessons Learned" discussion and confirms completion of all contractual requirements, payment of all invoices, closure of all contracts, and archival of all documents in the master file.

11.4 DATA OPERATIONS KEY INDUSTRY ACTIVITIES

Once a contract has been executed, Data Operations reviews the final executed protocol or Statement of Work. The Data Operations Program Coordinator creates a template study folder on the Data Operations SharePoint page and saves in it:

- Data Operations-specific study documents
- Center agreement forms
- Center participation email, if applicable
- Data Operations section of the project plan
- Data Operations study master file
- Study synopsis
- Documents / workbooks used for data quality efforts
- Meeting minutes
- Reports

After the internal planning meeting, the Data Operations Program Coordinator begins setting up the study. For prospective studies, the coordinator enrolls eligible centers that agree to participate in the study. The coordinator also maintains:

- **Industry Studies Dashboard**. Includes logic to determine required forms and follow-up length.
- **Corporate Studies OBI Dashboard**. Contains information on enrollment, events, study forms, due dates and past due information, "CT specific reports," lost-to-follow-up rate, and summaries of FormsNet study tables.

Based on the timeline communicated by the Industry Operations Program Manager, the Data Operations Program Coordinator creates the Data Operations reports with deliverables two weeks prior to the due date. Reports may include accrual reports, quarterly reports, data sets, annual reports, and final reports.

CHAPTER 12: DATA MANAGEMENT

Data collection is a core activity of CIBMTR that requires a comprehensive and sophisticated data management system. CIBMTR works with federal government and international authorities to collect essential cellular therapy data, develop data collection requirements, and minimize the burden of data collection. These organizations (**Chapter 20**) include:

- ASTCT
- EBMT
- Asia-Pacific Blood and Marrow Transplantation Group (APBMT)
- Foundation for the Accreditation of Cellular Therapy (FACT)
- World Marrow Donor Association (WMDA)
- Cord blood banks worldwide
- Other organizations in the international cellular therapy community

In 2006, CIBMTR was awarded the contract for the SCTOD of the C.W. Bill Young Cell Transplantation Program (**Chapter 6**). This contract requires specialized collection and analyses of data that resulted in many changes to CIBMTR's data management practices. Of significance, CIBMTR and NMDP developed an electronic data collection system, FormsNet (**Chapter 15**), and custom forms, which are described in this chapter, for data collection including contract requirements.

Effective December 2007, CIBMTR implemented the revised data collection forms and the FormsNet application for electronic data collection. These tools are used to collect data for the SCTOD contract requirements and all other research activities.

12.1 PROGRAM OVERSIGHT

Data management activities are shared across CIBMTR's two campuses and supervised by the Executive Scientific Director, Policy and Governance, CIBMTR MCW, and the Vice President, CIBMTR and Clinical Services, NMDP. Data Operations staff members provide first line assistance for CPI compliance (**Section 12.7.1**), study queries, and data submission questions. The Milwaukee Program Director and Minneapolis Senior Managers of Data Operations, with support from Scientific Directors, provide leadership to data support staff regarding data management activities. Data Operations is also supported by IT (**Chapter 15**) staff.

12.2 HCT REPORTING REQUIREMENTS

Participating centers submit HCT data to CIBMTR at two levels:

- **TED level**. TED forms contain an internationally agreed upon set of essential data elements collected for all transplant recipients. TED-level data, with some additional details of donor and graft characteristics, comprise the obligatory data to be submitted to the SCTOD.
- **CRF level**. CRFs capture additional patient, disease, and treatment-related data.

All CIBMTR reporting forms and other related materials are available on the *CIBMTR Data Collection Forms* webpage.

Generally, research studies require the more detailed CRF data rather than TED data. When appropriate, CIBMTR shares these data with other entities.

12.2.1 TED Centers

A center designated as TED-only is required to submit the following forms:

- CIBMTR Research ID (CRID) Assignment (Form 2804), due only for a recipient's first CIBMTR-reported HCT
- Indication for CRID Assignment (Form 2814)
- Pre-TED form (Form 2400)
- Pre-TED Disease Classification form (Form 2402)
- Post-TED form (Form 2450) at 100 days, 6 months, and annually post-treatment through 6 years, then biannually thereafter
- Infectious Disease Markers (Form 2004), Confirmation of HLA Typing (Form 2005), and HCT Infusion Form (Form 2006) for any recipients participating in the related specimen Biorepository and for all recipients of non-NMDP cord blood units, including autologous, related, and non-NMDP unrelated cord blood units
- HCT Infusion Form (Form 2006) for all recipients of NMDP products [marrow, peripheral blood stem cell (PBSC), or cord blood]
- Recipient Death (Form 2900), if applicable
- Subsequent Neoplasms (Form 3500), if applicable

12.2.2 CRF Centers

A center designated as a CRF center is required to submit the following forms:

- CRID Assignment (Form 2804), due for a recipient's first CIBMTR-reported HCT
- Indication for CRID Assignment (Form 2814)
- Pre-TED (Form 2400), Pre-TED Disease Classification (Form 2402), and disease-specific Pre-Infusion (Form 20xx)
- Follow-up forms: Either the Post-TED (Form 2450) or a CRF (Form 2100), and a disease-specific Post-Infusion (Form 21xx), as determined by CIBMTR forms selection algorithm (**Section 12.2.2.1**), at 100 days, 6 months, and annually post-treatment through 6 years, then biannually thereafter
- Infectious Disease Markers (Form 2004), Confirmation of HLA Typing (Form 2005), and HCT Infusion (Form 2006) for:
    - All recipients assigned to the CRF track with one exception:
        - Form 2004 and Form 2005 are not required for recipients of NMDP products as that information is reported to NMDP
    - Any recipient participating in the related specimen Biorepository
    - All recipients of non-NMDP cord blood units (including autologous, related, and non-NMDP unrelated cord blood units) assigned to the TED-track
- HCT Infusion (Form 2006) for all recipients of NMDP products (marrow, PBSC, or cord blood) assigned to the TED-track
- Recipient Death (Form 2900), if applicable
- Subsequent Neoplasms (Form 3500)
- Pregnancy (Form 3501)

The CRID Assignment (Form 2804), Pre-TED form (Form 2400), and Pre-TED Disease Classification form (Form 2402) are required on all reported infusions. All personally identifiable information entered on Form 2804 is sequestered in a secured and entirely separate database and not used for research studies. These data are accessible only to CIBMTR Leadership and selected IT personnel.

12.2.2.1 Forms Selection Algorithm

CIBMTR developed a weighted-randomization selection algorithm for CRF centers that determines which set of forms (TED versus CRF) is required for each HCT recipient. The algorithm randomly selects an epidemiologic sample of recipients for whom a CRF is to be requested. The algorithm considers the type of HCT, age of the recipient, disease, and other factors. It gives higher weights to patients receiving HCT for rare indications, to very young and very old patients, and novel treatment approaches. It aims to provide representative, adequately sized subsets of patients for studies requiring detailed data. The algorithm is periodically reviewed to assess the burden of data submission for centers.

If any recipient consents to participate in research, the algorithm determines the HCT follow-up data submission level: Post-TED forms or the CRFs. If an allogeneic recipient does not consent to participate in research, then HCT follow-up data must be submitted on the Post-TED form.

12.2.3 Other Cellular Therapy Reporting

Other cellular therapy reporting can occur pre-HCT, post-HCT, or independent of HCT. Participating centers submit cellular therapy data to CIBMTR at two levels (similar to HCT reporting):

- **TED level**. TED forms contain a set of essential data elements collected for cellular therapy recipients.
- **CRF level**. CRFs capture additional product, recipient, and toxicity data.

Selection of TED or CRF level depends on infusion-level characteristics, such as product name and details. All CIBMTR reporting forms and other related materials are available on the *CIBMTR Data Collection Forms* webpage.

Cellular therapy data collection incorporates the following forms. Those marked with as asterisk (*) are only required for CRF-level reporting.

- CRID Assignment (Form 2804), due for a recipient's first CIBMTR-reported cellular therapy treatment
- Indication for CRID Assignment (Form 2814)
- Pre-Cellular Therapy Essential Data (Form 4000)
- *Cellular Therapy Baseline Data (Form 4001)
- Disease Classification (Form 2402) for malignant and non-malignant indications
- Post-CTED Follow-up (Form 4100) at designated intervals, which varies by indication, along with Disease-Specific forms for certain indications
- *Post-Cellular Therapy Follow-Up (Form 4101)
- Cellular Therapy Product (Form 4003)
- Cellular Therapy Infusion (Form 4006)
- Subsequent Neoplasms (Form 3500)
- *Pregnancy (Form 3501)
- Recipient Death (Form 2900), if applicable

12.2.4 Reporting Guidelines for Prior HCT or Other Cellular Therapy Infusions

If at the time a new patient is registered with CIBMTR and a prior *autologous* HCT or other cellular therapy infusion (not known to CIBMTR) is reported on the Pre-TED (Form 2400) or Pre-CTED (Form 4000), then the center is not required to complete any additional forms specifically related to the prior infusion. However, due to the mandatory reporting of allogeneic HCT in the US, if a prior *allogeneic* HCT is reported on the new patient Pre-TED

(Form 2400) that is determined to have not been previously reported, a Data Operations staff member will reach out to the center that performed the prior allogeneic HCT to collect data associated with the prior infusion.

12.3 CIBMTR-APPROVED PROTOCOLS AND CONSENT FORMS

Research protocols exist for the Database and the CIBMTR Biorepository(**Sections 12.3.1 and 12.3.2**, respectively). Complete participant eligibility requirements are also outlined in each study protocol.

A signed, informed consent is required of all participants on research protocols **(Chapter 13)**. If the recipient of an allogeneic (related or unrelated) HCT does not consent to the use of their data for research, the center is still required, by US federal law, to submit TED-level data on the recipient. In this case, the recipient's data are used only for federally required analyses and reporting, such as the Center-Specific Analysis for outcomes as mandated by CIBMTR's contract to operate the SCTOD (**Section 6.2**). The recipient's data are not included in observational research studies.

TED-level data may also be used in research. Therefore, if a center only submits TED-level data to CIBMTR, the center must still approach all HCT recipients for consent to CIBMTR's Research Database. If a recipient consents, their TED-level data may be used in research.

For autologous recipients who do not consent to participate in research, CIBMTR requests only the Pre-TED (Form 2400) and Pre-TED Disease Classification (Form 2402) be submitted. This information helps maintain the epidemiological integrity of the Research Database and does not require provision of protected health information that could identify the recipient, nor is this information used in any analysis.

12.3.1 CIBMTR Research Database Protocol

CIBMTR's Research Database is a comprehensive data source for studying HCT and ACT issues including:

- Post-transplant recovery
- Long-term outcomes after cellular therapy
- Barriers to treatment access
- Donor issues, including recovery from collection procedures
- Marrow-toxic injuries
- Outcomes of other cellular therapies

The "Protocol for a Research Database for Hematopoietic Stem Cell Transplantation, other Cellular Therapies, and Marrow Toxic Injuries" and *corresponding consent forms* are reviewed and approved by NMDP's IRB (**Chapter 13**). Centers must also submit these documents to their local IRB for review and approval or have their local IRB delegate review authority to NMDP's IRB. CIBMTR allows the consent forms to be formatted according to each site's requirements, but the protocols must be submitted as written.

12.3.2 CIBMTR Biorepository

The CIBMTR Biorepository stores samples for research projects intended to:

- Improve the understanding of cellular therapy selection
- Determine and evaluate factors that affect cellular therapy outcomes
- Study the distribution of immunogenetic factors and HLA types in different populations

The "*Protocol for a Research Sample Repository for Allogeneic Hematopoietic Cell Transplantation, other Cellular Therapies, and Marrow Toxic Injuries*" and *corresponding*

consent forms are reviewed and approved by NMDP's IRB. The CIBMTR Biorepository contains samples from allogeneic cellular therapy recipients and / or their adult volunteer or related donor or cord blood unit.

12.4 IRB REQUIREMENTS

12.4.1 US Centers

All US centers must obtain IRB approval for both the "Protocol for a Research Database for Hematopoietic Stem Cell Transplantation, other Cellular Therapies, and Marrow Toxic Injuries" and the "Protocol for a Research Sample Repository for Allogeneic Hematopoietic Stem Cell Transplantation, Other Cellular Therapies, and Marrow Toxic Injuries."

Upon obtaining IRB approval, the center must send a copy of the IRB's approval letters, approved protocols, and informed consent documents to CIBMTR to remain compliant with CPI (**Chapter 13**). NMDP's IRB tracks IRB approval for CIBMTR's Research Database and the CIBMTR Biorepository at each participating center. Centers that did not transition the protocols to the 2018 Common Rule requirements will receive a renewal reminder approximately two months in advance of their local continuing review date. IRB approval for these protocols must be consistent at all times with the Common Rule requirements that apply to the protocols at their center. Failure to follow the Common Rule requirements for IRB approval may affect a center's ability to meet CPI requirements for data and sample submission.

As noted in **Chapter 13,** to be compliant with US federal regulations for human research subject protection, all centers must obtain IRB-approved informed consent from recipients to allow data submitted to CIBMTR's Research Database to be used for observational research studies, regardless of the level of data (TED or CRF) the center submits to CIBMTR.

12.4.2 International Centers

International centers must follow their country's laws and regulations governing human subjects and privacy protection. The center is responsible for obtaining the necessary institutional review and approval for participation in CIBMTR's Research Database. If the recipient does not consent to participate according to the respective country's laws and regulations, CIBMTR requests that centers provide acknowledgement of the infusion and limited patient information (disease, year of birth, month of infusion, and donor type) as part of their annual transplant list verification (CTA) instead of reporting these data to FormsNet. This information helps maintain the epidemiological integrity of the Research Database and does not require provision of any protected health information that could identify the recipient, nor is this information used in any analysis. This request applies to recipients of allogeneic (related and unrelated) and autologous HCT.

12.5 DATA COLLECTION FORMS

CIBMTR data collection and management activities are fully integrated across both CIBMTR campuses. A harmonized set of TED forms and CRFs is used for collecting HCT data. A new and expanding suite of CTED forms is used for collecting other cellular therapy data. All *data collection forms* can be viewed on and downloaded from CIBMTR's website.

12.5.1 Data Capture

CIBMTR conducts form revisions on a regular basis in response to rapidly changing technologies (e.g., molecular markers, cytogenetic prognostic factors, etc.) and internationally accepted criteria updates for disease response. The process is comprehensive, involving many internal and external individuals and three levels of review. The first level involves scrutiny of data field details by subject matter experts, Statisticians, volunteer Working Committee members, Center Data Managers, and a CIBMTR Metadata

Analyst who assures consistency across all forms. CIBMTR Scientific Directors, Working Committee members, and IT staff then review from a scientific and logistical standpoint. Review concludes with assessment by CIBMTR Data Operations leadership, Scientific Directors, and Senior Leadership. Forms are released into production on a date mutually agreed upon by CIBMTR Data Operations and IT staff.

12.5.2 Forms Training

Forms training is conducted in many venues including an annual Clinical Research Professionals Data Management conference held at the Tandem Meetings in February. Conference materials, including audio recordings from selected sessions, are available from CIBMTR.

CIBMTR's *Data Management webpage* provides detailed information regarding SCTOD reporting requirements, protocols and the consent process, data manager education, and past communications to all external users.

Forms Instruction Manuals are provided for

- Pre- and Post-HCT / cellular therapy forms, including, but not limited to:
  - Pre-TED (Form 2400)
  - Post-TED (Form 2450)
  - Post-HCT Follow-Up CRF (Form 2100)
- Some disease-specific forms, such as forms for:
  - Acute myeloid leukemia
  - Multiple myeloma
  - Non-Hodgkin lymphoma

CIBMTR also provides a *Data Management Guide* that includes information about participation in CIBMTR research, center membership, protocols and consent, CPI Program, data collection and forms submission process, Corporate Studies and Registries, Center Volume Data Reports, Transplant Center-Specific Analysis, and many other helpful tips and resources. In addition, CIBMTR maintains the *FormsNet Training Guide*.

CIBMTR Data Operations staff addresses issues and answers questions submitted to CIBMTR's Customer Support Center that may not be covered in the Forms Instruction Manuals or the Data Management Guide.

12.5.3 Forms Submission

FormsNet allows centers to electronically submit data to CIBMTR using TED forms, CTED forms, and CRFs. It includes real-time error validation, override capabilities, and access to the Forms Due Report. The center's primary contact is authorized to set up new users through CIBMTR's Center Information Management webpage. When the request is complete, the primary contact then activates the new user in FormsNet. Periodic FormsNet updates are released to address revisions and enhancements. FormsNet also includes:

- **Verify Mobile App**. This feature enhances FormsNet security by requiring a second identity authentication.
- **Override Codes**. Override codes allow users to force entry of data fields that are flagged as errors in FormsNet. Errors should be assigned an override code only if the data field is confirmed as correct by center staff (e.g., Data Manager) by comparing the data field with the appropriate source document. CIBMTR monitors each center's use of override codes.
- **Queries**. Using query functionality, CIBMTR can place an error check on a field in FormsNet to request additional information, supporting documentation, or correction.

Queries require review by CIBMTR staff to resolve to ensure updates and comments addressed the data question.

Any validation errors detected by FormsNet can be corrected by the center directly through FormsNet.

AGNIS, which was created by CIBMTR, also supports secure, electronic data sharing across diverse database systems and assists centers in collecting data for internal research, patient care requirements, and reporting purposes. For more information, view *CIBMTR's AGNIS* webpage and **Chapter 15**.

For a select and expanding number of centers, CIBMTR deployed the CIBMTR Reporting Application, which uses an API known as the HL7 Fast Healthcare Interoperability Resources (FHIR) standard to enable automated acquisition of data from electronic health records and other real-world evidence source systems deploying within reporting centers. The CIBMTR Reporting Application is deployed in the Epic App Orchard and is available to all centers who deployed the Epic foundation electronic health record.

12.5.4 Forms Reimbursement

CIBMTR reimburses centers for all completed CRFs through funds that support the Research Database. Reporting of TED-level data is not reimbursed. However, some CRF forms may be requested that could be reimbursed. Examples include Infusion (Forms 2003 and 2006) and Supplemental Disease Forms (for studies). When a form is designated as accurate and complete in FormsNet, CIBMTR reimburses the center according to a *fee schedule*.

CIBMTR can neither receive nor reimburse for CRFs until it has a current, signed Data Transmission Agreement or Master Healthcare Data and Sample Submission Agreement on file. These agreements allow centers (both US and non-US) to transfer patient data to CIBMTR for use in its research. This is in addition to the center's IRB approval for CIBMTR research protocol and associated consent forms. Data Transmission Agreements are submitted to NMDP's contracts department designees, who are assigned to specific centers. CIBMTR Data Operations staff members also help with forms reimbursement questions and issues.

12.6 DATA MANAGEMENT REPORTS

Data management reports support efficiency and accuracy in data collection management activities. These reports include:

- **Data Quality Checks / Reports**. CIBMTR has developed >120 data quality checks in its Data Quality Mart to identify discrepant data more readily. Companion reports are developed in OBIEE (Oracle Business Intelligence Tool) to enable staff to place queries on the discrepant data and have centers correct or verify the data much earlier in the process.
- **CPI Summary Reports**. The Recipient CPI Forms Due report is automatically sent to current primary data managers and staff indicated as cc-PDC. Centers may use this report to understand the current completion percentages and identify the most urgent forms to address. CPI compliance is tracked with nine metrics, including target completion percentages. For more information, review the Data Management Guide.
- **Study and Registries Forms Due List**. This report details forms that are due for patients enrolled on CIBMTR-managed studies. The report is intended to reflect real-time form expectations, which are more rigid than CPI expectations. If a form is past its due date, it may be represented on both this list and the CPI list. For more information, review the Data Management Guide.

- **Query Report**. This report details forms which currently have unresolved queries still requiring action by the center. At a minimum, each center will receive this report on a weekly basis.
- **Daily Status Report** (internal use only). This daily quality assurance report identifies all forms entered into FormsNet by CIBMTR data support staff. The report identifies both error-free forms ready to be sent for imaging as well as forms with errors.
- **Discrepancy Report** (internal use only). This quality assurance report displays discrepancies between the first and second data entry or double data entry process (**Section 12.7.3**). Designated staff members use this report to resolve any discrepancies.

12.7 QUALITY ASSURANCE PROGRAMS

12.7.1 CPI for Forms Submission

CIBMTR monitors forms submission according to its CPI standards. To maintain CPI compliance, a center must meet target completion metrics for five categories of forms / queries and participate in an annual verification of transplant activity. Forms must be error-free with all applicable inserts completed. Centers that are not CPI compliant enter a due-process procedure.

For centers unable to meet CPI requirements, an exemption program is available. To be granted an exemption from a CPI requirement(s), centers must implement a center-specific strategy to return to good standing. Center / CIBMTR meetings and milestone reporting may also be required as part of the exemption process.

12.7.2 Data Audit Program

CIBMTR data audit program includes the following steps and processes:

- **Audit Cycle**. CIBMTR audit cycles span four years. Eligible centers, within and outside the US, are assigned an audit year within that cycle. To be eligible for an audit, the center must complete a minimum of 20 HCTs, including allogeneic related, unrelated, and / or autologous procedures. CIBMTR schedules the audit for the year following the performance of the center's 20th HCT. Once audited, the four-year cycle begins again for the center. The Scheduling Transplant Center Audits SOP (SOP-0149) outlines the processes for determining center eligibility for audit as well as the steps required to complete audit scheduling.
- **Recipient Selection and Eligibility Requirements**. A pre-selected number of HCTs are audited at each center. If a center has performed more than the pre-selected number of HCTs, eligible recipient records are randomly selected (only once) for audit. A recipient record is eligible for audit only if the TED or required CRFs were submitted to CIBMTR and designated as complete and error-free. The Transplant Center Audit Preparation SOP (SOP-0150) details the processes for randomizing eligible recipients that will be audited, generating audit worksheets, and scheduling travel to the center, as applicable.
- **Consent Form Review**. Auditors select and review treatment recipients' completed Research Database and Biorepository consent forms to ensure proper completion, as applicable.
- **Forms and Data Fields**. All data elements on all forms are subject to audit. However, the audit concentrates on "critical" data, i.e., data most likely to be included in a research study. Auditors review randomly selected "non-critical" data elements, as well, to increase the validity of the audit error rates. On average, auditors review 11,000 fields per audit.

- **Methodology**. Auditors compare data submitted to CIBMTR's Research Database with data from the source documentation. They categorize discrepancies into one of three groups: audit error, missing documentation, and non-audit errors. If any systemic errors are identified during the audit, auditors may review those findings directly with the Data Manager. Auditors make all data corrections in the Research Database and provide the center with a Data Change Summary report, which documents all changes; the Medical Director signs the Data Change Summary to acknowledge the changes made to the database as part of the audit. The Transplant Center Audit Process SOP (SOP-0151) outlines the processes auditors complete while conducting a data audit.
- **Audit Analysis and Reports**. Centers receive a detailed audit report and may be required to submit a Corrective Action Plan in response to issues identified during the audit. Issues include:
    - Critical field error rates >3%
    - Systemic errors, e.g., consistent errors in reporting (GVHD, product analysis, etc.) even if the overall rate is not >3%
    - Consent form issues

  The Transplant Center Audit Process SOP (SOP-0151) details the processes for entering data corrections in the Research Database, calculating audit error rates, and completing and sending the audit report. The Corrective Action Plan Development Evaluation and Approval SOP (SOP-0269) details the corrective action plan process.
- **Data Review**. If a center requests that the data field changes made as part of the audit be reviewed post-audit, the center submits their questions along with any applicable source documentation regarding the data changes. The audit team reviews the information and shares it with CIBMTR Leadership, if necessary. If the review results in data field changes, CIBMTR updates the originally calculated error rates and describes the data changes and new error rates in a summary letter. If a center's pass / fail status changes based on the data review, CIBMTR sends an amended audit report to the center.
- **Consequences**. Any center's audit(s) resulting in a critical field error rate of >3% for two consecutive audits will result in audit consequences. Audit consequences are implemented on a case-by-case basis.

12.7.2.1 Consolidation of FACT-CIBMTR Audits

Previously, CIBMTR and FACT individually audited data management at centers. To reduce duplicative efforts and ease the reporting and compliance burdens for centers, the organizations agreed in 2016 to consolidate data management audit efforts. Within this collaboration, CIBMTR conducts data management audits and evaluations on behalf of both organizations, and FACT determines whether the results of a data management audit are satisfactory for the purpose of accreditation.

CIBMTR audit teams verify accuracy of submitted data against source data, using the practices and schedules described above. FACT verifies at each annual report and at each application for renewal accreditation the status of CIBMTR data accuracy by requiring submission of centers' most recent CIBMTR audit results for error rates (critical, random, and overall error rates). FACT verifies completeness of data by requiring each center to annually submit the most recent CPI report from CIBMTR that demonstrates "in good standing" related to the on-time submission of completed forms at the target completion rate.

A FACT-CIBMTR Data Audit Committee meets regularly to coordinate the evaluation of center data audits performed by CIBMTR. This committee is comprised of two Co-Chairs

(FACT Chief Medical Officer and CIBMTR Scientific Director) and a minimum of 10 members, including representation from FACT, CIBMTR, and individuals at transplant centers with exceptional CIBMTR data audits who have demonstrated strong data collection and management abilities. The committee tracks and monitors transplant center data reporting, assesses FACT inspection findings related to data audits, and incorporates findings into training and development programs.

12.7.3 Verification and Validation

Data verification and validation are important processes to assure data accuracy and are accomplished in several ways, both manually and electronically.

Double data entry of paper forms is a verification process in which two CIBMTR data support staff members manually enter the same fields from the paper form into FormsNet and their supervisor reconciles any differences between the two entries. This ensures accuracy, but also tracks the proficiency of CIBMTR data support staff. Any form fields can be manually entered into FormsNet as many times as needed for verification.

When a form is entered into FormsNet, either by the center or CIBMTR, FormsNet performs a series of automated validation checks including:

- **Mandatory Field Validation**. This step verifies that all required fields are completed, including primary questions and their dependent fields (e.g., selecting "yes" for "developed acute graft-versus-host disease" requires answering all acute GVHD questions).
- **Range Validation**. This step verifies laboratory values, drug doses, heights, and weights against established upper and lower limits.
- **Consistency Among Forms**. This step verifies consistency between data reported on the current form and related data reported on a previous form. For example, on all forms, the contact date is validated against the HCT date.
- **Consistency Within a Form**. This step verifies each form for consistency among related data reported on the same form. For example, all dates are validated against the "date of last contact."

If a form fails any of these online validations, FormsNet prompts the center to correct any issues before submitting the form to CIBMTR. For example, if a lab value reported on a form is outside CIBMTR's established validation range, the center must verify the value with the source documentation and either correct it or use an override code to remove the error. Override options include:

- NA: Not asked
- NT: Not tested
- UK: Unknown
- VC: Verified correct
- UA: Unable to answer

12.7.4 Document Control

CIBMTR data collection forms are stored in a protected SharePoint site, and data management SOPs are managed through MasterControl; all controlled documents are approved, implemented, and communicated consistently. Previous versions of the documents are archived. CIBMTR forms manuals are managed through the Manula software.

12.8 ADDITIONAL DATA COLLECTION

If additional data collection is approved, Statisticians coordinate special observational study requests with a CIBMTR Research Program Coordinator to request additional data from the

center. These requests may also include resolving incomplete CRFs and / or missing and inconsistent data, or additional data.

12.9 CONTACT MANAGEMENT AND PERSONNEL CHANGES

CIBMTR tracks information about organizations and key contacts in DISCO (Data and Information for Statistical Center Operations), a contact management system built on the Salesforce platform. This system has been customized to track CIBMTR center and contact information, Working Committee participation, studies, and publication information. A select group of staff members on each CIBMTR campus has editing privileges.

The Network Partner Portal (https://nmdp.service-now.com/partner) allows primary data managers and medical directors at centers to request new accounts and modify security access for their staff. The information submitted is sent to CIBMTR's Center Maintenance team and updates are made in the database. For questions regarding the Network Partner Portal, centers submit a ticket via CIBMTR Center Support (CIBMTR Center Maintenance > Center Information Change) at *https://nmdp.service-now.com/csm*. For questions before becoming a CIBMTR center, centers contact cibmtr-centermaintenance@nmdp.org.

CHAPTER 13: HUMAN RESEARCH PROTECTION PROGRAM

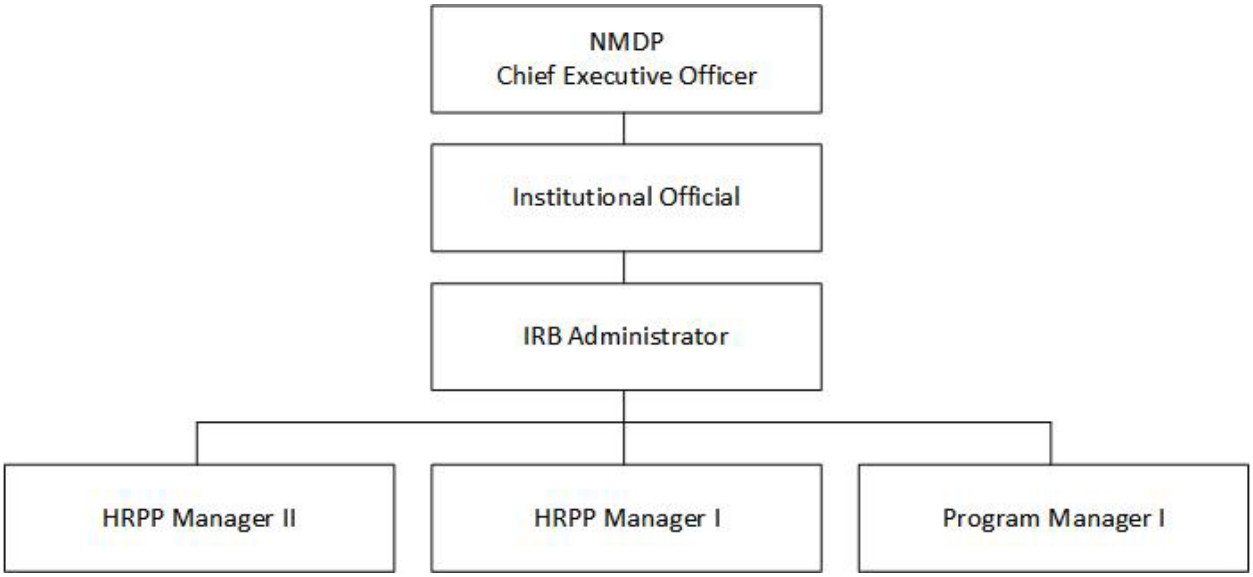
CIBMTR works within the NMDP-maintained comprehensive Human Research Protection Program to protect the rights and welfare of its research participants and to ensure compliance with all pertinent US federal regulations.* In 2014, NMDP's Human Research Protection Program was fully accredited by the Association for the Accreditation of Human Research Protection Programs; it was re-accredited in December 2017 and December 2022.

Since 2011, under an IRB Authorization Agreement between MCW and NMDP, NMDP's IRB serves as the IRB of record for all research conducted by CIBMTR. NMDP's IRB has the authority to approve, require modifications in, or disapprove all research activities within its jurisdiction as specified by both federal and state regulations as well as NMDP policies and procedures. NMDP's IRB reviews protocols from individual centers at which the NMDP unrelated donor is considered a research subject by virtue of the research the recipient is participating in. NMDP's IRB also serves as the single IRB for the BMT CTN and CRO Services. However, only CIBMTR-sponsored research is addressed in this chapter. All CIBMTR staff members are required to complete initial and continuing education and training in the protection of human subjects through the *Collaborative Institutional Training Initiative*.

13.1 PROGRAM OVERSIGHT AND STAFF

Day-to-day operational activities of NMDP's IRB are overseen by an IRB Administrator and three staff members, as shown in **Figure 13.1.**

Figure 13.1: NMDP IRB Organizational Structure



* These are the Office for Human Research Protection common rule regulations [45 Code of Federal Regulations (CFR) Part 46] and the FDA regulations (21 CFR Part 50 and 21 CFR Part 56).

Members of NMDP's IRB are appointed based on their capacity to participate fully in NMDP's IRB process, and they are qualified through education and experience to assure a comprehensive review of the research. There are nine primary members of NMDP's IRB, including four stem cell physicians, two hematology / oncology physicians, a donor advocate, a patient advocate, and an ethicist. Each NMDP IRB member is appointed for a three-year term, which may be renewed once.

13.2 KEY ACTIVITIES

NMDP's IRB reviews all human subject research involving CIBMTR staff. CIBMTR research activity subject to this oversight includes all research efforts within its major Programs, which are described in detail in **Chapters 6-10**. These include:

- Observational studies (projects implemented within the structure of its Working Committees)
- Immunobiology Research Program
- Clinical Trials Support (i.e., CRO Services specifically, including all Survey Research projects, and BMT CTN studies where NMDP's IRB serves as the single IRB)
- Health Services Research Program
- Bioinformatics Research Program
- NMDP-initiated research objectives

Observational studies implemented through the Scientific Working Committee structure that utilize data from CIBMTR's Research Database or specimens from the CIBMTR Biorepository are conducted under the *Research Database protocol* and / or *Research Sample Repository protocol*. All CIBMTR centers and NMDP donor centers are required to maintain IRB approval for the Database and Repository protocols and seek consent from patients and donors for use of their data or samples in CIBMTR research. Clinical outcomes studies approved by a Scientific Working Committee under one or both of these protocols do not need additional IRB approval.

Human subjects research conducted through CIBMTR's CRO Services or Health Services Research Programs are also subject to oversight by NMDP's IRB. Protocols conducted through these Programs must be approved by NMDP's IRB prior to implementation. Once NMDP's IRB has approved the study, it is released to participating sites for approval by their local IRBs or for approval of their site by NMDP's IRB if NMDP's IRB is serving as their IRB of record for the study. The overall PIs of these studies also seek IRB approval for their own participating sites.

13.2.1 Monitoring Center IRB Compliance

As noted above, to be compliant with US federal regulations for human research subject protection, all transplant centers and donor centers participating in a CIBMTR-sponsored research protocol must obtain IRB approval for the study. IRB approval letters and consent forms for all other CIBMTR-sponsored research, including the Database and Repository protocols, must be submitted to CIBMTR staff designated for the specific study.

CIBMTR staff members track the IRB approval at each participating center. Sites receive a renewal reminder approximately two months in advance of the center's continuing review date. The center's IRB approval for CIBMTR protocols must be current for continued participation in the protocol.

13.2.2 Investigator Support for Completing NMDP IRB Application

CIBMTR staff members involved in CRO Services or health services research assist PIs of CIBMTR-sponsored research in completing the NMDP IRB initial and continuing review applications. In addition, IRB staff members assist in NMDP's IRB application process by

reviewing all submissions prior to NMDP IRB review to ensure the application is complete. Investigators with current NMDP IRB-approved studies are notified of the study's upcoming continuing review approximately two months prior to the scheduled review of the study.

CHAPTER 14: DATA – ACCESS AND RELEASE

CIBMTR manages one of the world's largest cellular therapy outcomes research databases and is a unique information resource for clinicians, researchers, and the general public interested in cellular therapy. It is CIBMTR's policy to provide maximum access to and use of its data (POL-0003: CIBMTR Data Release Policy; SOP-0281: Assessment for Inclusion of Data Based on Embargo and Consent Status).

14.1 ACCESS TO CIBMTR DATA

Access to CIBMTR information falls into five major categories:

- Publicly available data
- Requests for datasets from previous CIBMTR research
- Customized information requests
- Proposal to conduct a CIBMTR clinical outcomes study or custom dataset
- Center access to their own data

The processes CIBMTR follows for handling these requests, and their timelines for completion, vary depending on the type of request, complexity, need for statistical resources, and availability of external funding.

CIBMTR provides summarized, general information through its websites, described below and in **Chapter 16**. In order to efficiently handle all requests, CIBMTR has a few common pathways to receive and triage the requests.

14.1.1 Publicly Available Data

CIBMTR regularly publishes information in a variety of report formats and makes these data available through the CIBMTR, NMDP, and *HRSA* websites or upon request. Examples of information readily available include the annual CIBMTR Summary Slides and the SCTOD Reports (US Patient Survival Report, Transplant Data by Center Report, US Transplant Data by Disease Report, and Transplant Activity Report) as well as synopses of studies published by CIBMTR. CIBMTR shares these data to support both research and general informational uses. In July 2019, CIBMTR started publicly sharing analysis datasets of certain publications on its website in accordance with the NIH Data Sharing Policy and NCI Cancer Moonshot Public Access and Data Sharing Policy (SOP-0119: Shared Publication Datasets Standard Operating Procedure). More information about CIBMTR websites is available in **Chapter 16**.

14.1.2 Requests for CIBMTR Datasets from Previous Research

When the analysis dataset is not publicly available, CIBMTR supports requests for datasets assembled for previously published studies and the annual Center-Specific Survival Analysis to conduct additional, independent analyses. Requestors submit a study proposal using the format noted in **Section 14.1.4** to define their planned analysis and study design. These requests are for external use of the data and do not require CIBMTR statistical resources to conduct the proposed analyses. Coordinating Center staff members review and approve these requests for existing datasets, and they often need to review and update the datasets before they can provide them to the requestor. When they distribute the datasets, staff members will include a corresponding data dictionary, as well.

CIBMTR typically responds to these requests in three to four weeks but may take longer depending on complexity, verification, and approval.

14.1.3 Customized Information Requests

Requests that cannot be addressed using existing reports or publicly available datasets require a customized response. Reasons for these requests include self-education, patient counseling or clinical decision-making, presentation support, and center assessments. They

range from simple queries of patient, disease, and frequencies to those with greater complexity involving specific data combinations and / or statistical analysis of survival outcomes. Interested parties submit these requests by email or via the online *Custom Information Request Form*. A Statistician is the first to receive, triage, and respond to information requests that are received via the web-based *Data Request System* (SOP-0065: Information Requests). CIBMTR Scientific Directors work with the Statistician to provide scientific input, address questions, and, when appropriate, review information prior to release.

CIBMTR responds to requests related to clinical decision-making within three business days and results from other simple requests within one week. Requests requiring a more complex custom analysis may take additional time, up to four weeks. If a request will take more than the estimated one to four weeks to fulfill, CIBMTR will notify the requestor of the new time estimate. Most requests will require Scientific Director review prior to sending the response.

Industry requests follow the guidelines of the Industry Program and may require a Statement of Work and budget **(Chapter 18).** Research-related requests will require a formal study proposal for approval and prioritization (**Section 14.1.4**). Center requests may be referred to the Data Back to Centers (DBtC) application on CIBMTR's Portal site to obtain their own center data (**Section 13.1.5**).

14.1.4 Proposal to Conduct a CIBMTR Clinical Outcomes Study or Custom Dataset

The most common request to access CIBMTR data and statistical resources is through submission of a study proposal to a CIBMTR Working Committee (**Chapter 6**). Information on how to propose a study is on CIBMTR's *How to Propose a Study* webpage. A list of previously published CIBMTR research, studies that are in progress, and copies of data collection forms are available on CIBMTR's *Data Collection Forms* webpage; CIBMTR encourages investigators to review these before submitting a proposal.

Working Committee members evaluate new proposals based on their scientific merit and feasibility as well as CIBMTR's ability to complete the study in a timely fashion. Feedback from Working Committee members at the annual meeting is considered in deciding the relative merits of proposals. Final decisions regarding which studies to pursue are made by Working Committee Leadership, CIBMTR Leadership, and CIBMTR's Advisory Committee. Proposals may also be submitted for review by Committee leadership between meetings and may be assigned resources if deemed to be of exceptionally high impact and timeliness.

14.1.5 Center Access to Their Own Data

Centers that submit data to CIBMTR often request datasets specific to their own center. CIBMTR asks centers to first determine if they can access requested data using the DBtC application (**Chapter 15**). CIBMTR Data Operations and IT staff members individually address any requests for existing data that are more complex.

CIBMTR typically responds to requests for centers' existing data within two weeks but may take longer depending on the complexity of the request.

14.2 RELEASE OF CIBMTR DATA

CIBMTR releases only datasets that comply with all relevant federal regulations regarding privacy and confidentiality. It has standard policies and procedures in place for protecting CIBMTR data; these are addressed in further detail in **Chapters 12 and 13,** CIBMTR's Data Use and Processing Policy, and CIBMTR's Data Release Policy (POL-0003).

When releasing data, CIBMTR is obligated to ensure that datasets do not contain protected health information or personally identifiable information (PII). CIBMTR staff members follow

a standard procedure for creation of de-identified datasets that specifies removal of all patient, donor, and center identifiers, which could lead to the identification of a patient or center from data files (SOP-0069: Data Sharing to Non-MCW or Non-NMDP Employees). CIBMTR does not release to the PI or any other member of their research team personally identifiable information, personal data, or identifiable patient or center variables unless these data are critical to the approved study / project or will be used for linking to another data file via an established honest broker relationship. In these cases, special procedures are outlined in the Approval to Disclose PII for Linking or Computerized Matching Person Data to External Data Sources SOP (SOP-0100), documented with a Data Transfer and Use Agreement (**Appendix D2**), and established prior to final approval of the request.

CIBMTR prepares datasets with SAS statistical software and generally contain a standard set of essential data with pre-defined categories. A data dictionary defining each variable, valid values, and labels accompanies the dataset. Other file formats are provided upon request.

In cases of an approved traditional clinical outcomes study (**Section 14.1.3**) or when datasets are requested from previous research that will not utilize CIBMTR statistical resources for analysis (**Section 14.1.4**), the PI must submit a Data Transfer and Use Agreement that specifies the requirements for using CIBMTR data (**Appendix D1** or **D2**) before CIBMTR will provide final approval of the project. Staff members provide the PI, or requester of data, with the Data Transfer and Use Agreement when they submit a study protocol or Statement of Work.

14.3 PUBLISHING CIBMTR DATA

Authors requesting to reproduce CIBMTR figures or unpublished data, data in manuscripts, or other printed or online media must first receive permission from CIBMTR and must acknowledge use of CIBMTR's data. These requests require the use of disclaimer text and completion of the *Publication Permission Request Form* prior to publication or presentation. A letter granting the requestor permission to publish CIBMTR data includes the disclaimer text.

CIBMTR typically responds to these requests within one to two weeks.

CHAPTER 15: INFORMATION TECHNOLOGY SERVICES

CIBMTR's IT team is responsible for managing CIBMTR data and information, facilitating data acquisition, implementing commercial software products, developing custom software, sharing data, and providing technical support. Responsibilities are shared between the Minneapolis and Milwaukee campuses. The IT team supports CIBMTR's scientific research objectives through the following activities, which are described in this chapter:

- Developing, maintaining, and ensuring high-quality data acquisition, data exchange, and data analytics systems
- Developing and maintaining data transmission solutions for electronic exchange of data with centers and networks
- Extracting datasets from CIBMTR's Integrated Data Warehouse
- Enabling team collaboration and information dissemination by maintaining and enhancing CIBMTR's web presence (**Section 15.2.3**)
- Facilitating secure data sharing through CIBMTR Portal Applications
- Providing technical services
- Maintaining overall security of all information systems and components and supporting protection of data in these systems in accordance with federal requirements and information security best practice

15.1 PROGRAM OVERSIGHT AND GOVERNANCE

CIBMTR IT functionally reports to the CIBMTR Administrator, CIBMTR MCW, and the Chief Digital and Information Officer of NMDP in Minneapolis. The program is overseen by the following committees, advisory groups, and project teams.

15.1.1 CIBMTR IT Steering Committee

CIBMTR's IT Steering Committee authorizes project prioritization and scope, oversees projects, and sponsors key initiatives. Membership includes CIBMTR Executive Leadership and CIBMTR IT Directors. CIBMTR Program Directors and CIBMTR Functional Area Managers may be invited, as needed, based on topic areas. This committee meets monthly.

15.1.2 Advisory Groups

- **IT Quarterly Portfolio Roadmap Committee**. This group reviews project objectives, drives business process changes, and makes recommendations to CIBMTR IT Portfolio Committees regarding project prioritization. Projects occur within four program areas:
    - Data collection, e.g., FormsNet (**Section 15.2.1.1.1**)
    - Data sharing, e.g., Data Warehouse (**Section 15.2.2.3**)
    - Web presence (**Section 15.2.3**)
    - Bioinformatics (**Section 15.2.4**)

  The IT Quarterly Portfolio Roadmap Committee also helps coordinate staff participation in IT project teams and promotes communication. The group is empowered to take immediate action to resolve defects or issues that affect critical operations or data integrity. Membership includes internal leadership from functional areas who are users of CIBMTR IT systems in data collection, Data Warehouse, Bioinformatics, and web presence program areas; subject matter experts; and CIBMTR IT Managers, Project Managers, and Scrum Masters.
- **Electronic Data Exchange Sponsorship Group**. This group manages electronic data exchange initiatives, including AGNIS (**Section 15.2.1.2**) and data collection and transfer tools (**Section 15.2.1.3**), as well as project objectives. The group

makes recommendations to CIBMTR's IT Steering Committee regarding resource allocation and prioritization. It also provides guidance in fostering relationships with external partners for AGNIS and data collection and transfer tools. Membership includes internal leadership representing functional areas (e.g., Data Operations, IT) responsible for the electronic data exchange applications.

- **Web Advisory Team**. This team provides ongoing management and strategic oversight of CIBMTR websites. Membership includes cross functional CIBMTR leadership representatives, ad hoc member representatives from NMDP Marketing and Communication, and technical representation. Membership is evaluated annually. The Website Advisory Team:
    - Approves changes to messaging standards, graphic standards, the home page, programmed content, and templates
    - Conducts an annual review and audit of the websites to ensure compliance with defined standards and maintenance expectations
    - Updates the governance and maintenance plan to support changing organizational needs or processes
    - Identifies and proposes future development initiatives to improve site content, functionality, and site management processes

15.1.3 Project and Scrum Teams

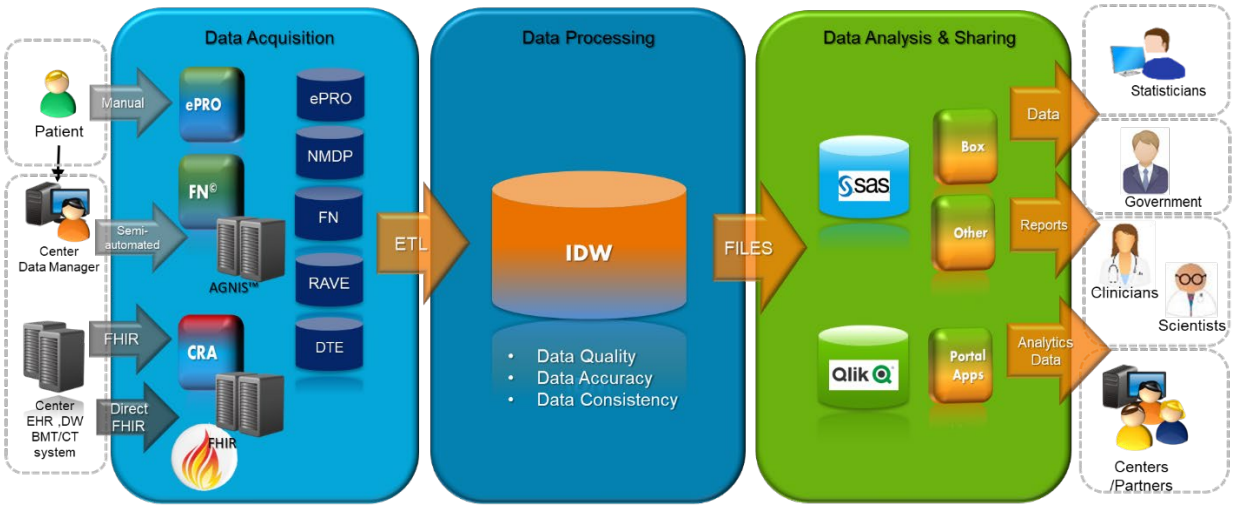
CIBMTR IT resources are organized based on the type of work and whether the work is part of a defined product. Project teams are responsible for the successful planning and execution of a project, which has a defined scope, beginning, and end. CIBMTR's IT team follows the CIT System Development Lifecycle SOP (SOP-0125) when developing and implementing systems within MCW and NMDP's Software Development Lifecycle when developing and implementing systems within NMDP's domain. CIBMTR also employs Agile Scrum to iteratively or incrementally plan and deliver work that supports one or more products. Project teams and scrum teams are comprised of a number of different specialties: Product owners / subject matter experts, IT architects, project managers / scrum managers, business system analysts, programmer analysts, data analysts, quality assurance analysts, developer leads, database and system administrators.

- Activities common to both project and scrum teams:
    - Facilitating ongoing team communication
    - Collaborating on design and architecture
    - Building business readiness
    - Managing information requests
- Project team activities:
    - Defining business processes and requirements
    - Completing technical design, development, and testing activities
    - Installing and configuring software
    - Training users on systems and processes
    - Managing releases
- Scrum team activities:
    - Managing scope requests, enhancements, and fixes in a product backlog
    - Planning, designing, and executing a defined scope of work in iterative or incremental sprints

15.2 KEY ACTIVITIES

CIBMTR data systems reside within the IT structure of NMDP and MCW, as shown in **Figures 15.1 and 15.2**.

Figure 15.1: Research Data Flow for Data

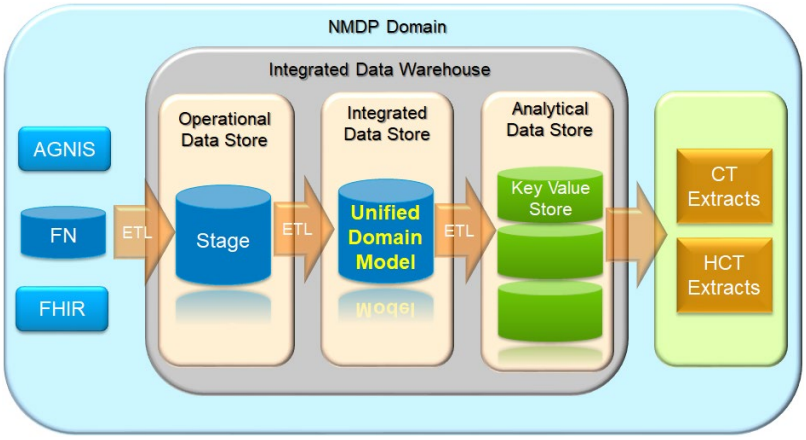


CIBMTR IT is responsible for managing all systems that facilitate data production for research activities. Centers provide patient treatment and outcome data via one or more of the following primary methods:

- Manual entry to a secure electronic data capture application known as FormsNet
- System transfer to an open-source messaging system specifically designed to exchange HCT data using a secure, standards-based system, known as AGNIS
- For a select and expanding number of centers, an application that uses an API known as the HL7 FHIR standard to enable automated acquisition of data from electronic medical records and other real-world evidence source systems deployed within reporting centers

All methods are hosted and maintained at NMDP and require that users of these systems provide credentials and authentication. CIBMTR has also been innovating with centers to apply automation to read data directly from the center (**Section 15.2.3**). All transplant data follow similar lifecycles. CIBMTR's Research Database contains data for recipients and donors.

Figure 15.2: Research Data Flow through CIBMTR's Integrated Data Warehouse



Aligned with the goal to achieve a single trusted version of truth for its data, CIBMTR has undertaken a significant initiative to centralize and collocate its data. Since shortly after IBMTR was established in 1972, CIBMTR has stored its HCT data in its Research Database. CIBMTR maintains its other cellular therapy data in its Integrated Data Warehouse, which is hosted at NMDP. Bringing these data together lays the groundwork for CIBMTR's data management, data analysis, and data sharing work (**Section 15.2.1.3**). During the transition period, CIBMTR will revise existing SOPs and develop new SOPs.

At defined intervals, data in source systems are transposed into CIBMTR's Integrated Data Warehouse where they are validated for consistency, quality, and accuracy, and they are normalized and arrayed for analysis and use. These data are routinely locked as of a defined date, extracted, and securely transferred to other analytic and data visualization platforms to support CIBMTR deliverables. These systems include QlikView, which supports data sharing with external parties, such as centers and commercial partners, and SAS, which primarily supports internal stakeholders, namely biostatisticians. Data dictionaries are created and maintained to accompany these extracts and visualizations.

15.2.1 Data Collection Technology

15.2.1.1 Web-based Electronic Data Collection

15.2.1.1.1 FormsNet

Most data are either entered into FormsNet by Data Managers at centers or are submitted electronically to FormsNet, directly from databases or systems at the centers, via AGNIS. The FormsNet application suite is CIBMTR's web-based application for data collection, submission, and forms-based storage for cellular therapy donors and recipients. It includes the following key functions:

- Electronic data submission from centers to CIBMTR for both TED forms and CRFs, including real-time error validation and forms due listings (**Chapter 12**)
- Collection of donor clearance / suitability and follow-up data to ensure donor safety
- Support for data collection, and quality control, via the Management Reporting function
- Support for auditing and event reporting

15.2.1.1.2 CIBMTR Reporting Application

The CIBMTR Reporting Application registers HCT / ACT patients to CIBMTR for outcomes research and displays and reports laboratory data found in the electronic health record. This allows transplant centers that currently register transplant recipients manually through CIBMTR FormsNet to instead register these patients directly from the Epic electronic health record, increasing efficiency and decreasing the possibility of error. Further details regarding overall automated data exchange from centers' electronic health records are described below (**Section 15.2.1.3**).

15.2.1.1.3 Medidata Rave

Medidata Rave is a web-based electronic data capture system used for clinical trials and other prospective research projects (**Chapter 8**). Rave is also used for monitoring submitted data.

15.2.1.1.4 Veeva Vault EDC

Veeva Vault EDC is a web-based electronic data capture system also used for clinical trials. It has functionality for study monitoring and querying.

15.2.1.1.5 Electronic Patient-Reported Outcomes

CIBMTR's ePRO system integrates Qualtrics online surveys with PROMIS computer adapted test measures and a Salesforce Customer Relationship Management platform to administer quality of life and other PRO with follow-up support by the Survey Research Group. For more information, see **Section 6.5**.

15.2.1.2 AGNIS

AGNIS is a messaging middleware that permits electronic submission and retrieval of forms data with FormsNet. CIBMTR created this messaging conduit to assist centers in collecting data for internal research, to track patient data to assist in care management, and for reporting purposes. AGNIS supports secure data sharing across diverse database systems. The AGNIS software is an open-source web service.

Data are transmitted via AGNIS using common data elements (CDEs) from the Cancer Data Standards Registry and Repository (caDSR), a metadata repository operated by the NCI Center for Biomedical Informatics and Information Technology. It is compliant with government standards for electronic data transmission. Nearly all data fields collected in FormsNet are represented as CDEs within caDSR.

15.2.1.3 CIBMTR Tools for Data Collection and Transfer

CIBMTR has been innovating with centers to apply automation to read from centers' real-world sources of data, such as an electronic health records, lab systems, cell therapy specialty systems, or data warehouses.

Centers may select the best option within the suite of tools for their technical landscape. CIBMTR will work with the partner to perform initial configuration to source data systems and testing. Data collected with the new tools are reviewed to ensure data quality before they are accepted into production at CIBMTR. At present, a limited number of data variables are processed through the tools; however, CIBMTR continues to expand the data variables that can be collected and transferred through the tools. The latest information is available on *CIBMTR's Data Transformation Initiative webpage*.

15.2.2 Data Sharing

CIBMTR's Data Release Policy (POL-0003) is reviewed and approved annually by Senior Leadership.

15.2.2.1 Research Database

CIBMTR's Research Database contains HCT data collected by CIBMTR as well as historical data collected on IBMTR and NMDP forms before 2008. The Research Database has not been updated with new HCT content since June of 2020 and has not been refreshed with existing follow-up data throughout 2022. CIBMTR has instead focused on centralizing and collocating HCT data to CIBMTR's Integrated Data Warehouse. As HCT data centralization is more completely processed within the Data Warehouse, the Research Database will be archived for specific research and contract needs as well as pre-FormsNet era, legacy data (HCT data acquired prior to January of 2008), which is expected to occur in 2023-2024.

15.2.2.2 SAS

CIBMTR biostatisticians perform analyses using third-party *SAS software* applications for clinical data analyses and reporting. To simplify study dataset preparation, CIBMTR IT staff members create SAS datasets of the most commonly analyzed data fields and most commonly used computed variables. Staff members extract data from CIBMTR's Integrated Data Warehouse and format them to be SAS-compatible. As shown in **Table 15.1**, staff members create nine datasets with different levels of frequency throughout the year. The

Data Retrieval SOP (SOP-0048) and the Cellular Therapy Data Extract SOP (SOP-0200) detail the specific steps in these processes.

Table 15.1: Study Datasets

Study Datasets	Description
TED	Transplant Essential Data; all transplants (legacy NMDP, IBMTR, and FormsNet). Includes data on Pre-TED (Form 2400), Pre-TED Disease (Form 2402), and Post-TED (Form 2450) as well as equivalent data derived from CRF track, cord blood data(Forms 2004, 2005, 2006).
Cellular Therapy Extract*	All other cellular therapy infusions for which at least a Form 4000 has been received. Includes data on Pre-CTED (Form 4000), Disease forms [Form 2402, Plasma Cell Disorders Pre- / Post-HCT (Forms 2016 / 2116), Lymphoma Pre- / Post-HCT Forms (2018 / 2118)], and Post-CTED (Form 4100) as well as equivalent data derived from HCT tracks, HLA (Form 2005). *This extract is not in a SAS retrieval format.
HCT Allogeneic	All transplants for patients on CRF track who had an allogeneic transplant and a follow-up form was submitted. Includes data from CRFs (Forms 2000, 2100, 2900, 2004, 2005) and disease forms.
HCT Autologous	All transplants for patients on CRF track who had an autologous transplant and a follow-up form was submitted. Includes data from CRFs (Forms 2000, 2100, 2900, 2004, 2005) and disease forms.
HLA Save	HLA data for all transplants known to CIBMTR. Includes data on Pre-TED (Form 2400), Pre-TED Disease (Form 2402), HLA (Form 2005), NMDP data, computed match grade data, and other computed variables. This dataset is used by CIBMTR statisticians, Bioinformatics Research Group members, and other interested NMDP operational groups.
Study	All patients in certain studies for which immediate access to all data submitted is critical; examples include industry studies and BMT CTN trials. Includes data from CRFs (Forms 2000, 2100, 2900, 2004, 2005) and disease forms.
TED Download for HRSA to support SCTOD	Allogeneic transplants performed after 12/03/2007. Includes only Pre-TED, Pre-TED Disease, Post-TED (including equivalents from CRF track), and cord blood data. Submitted quarterly to HRSA.
DBtC Download	DBtC and DBtC Download are integrated applications developed within the QlikView platform, which is hosted on CIBMTR's Portal site for access by authorized center users. DBtC provides visualization, interaction, and analytics on key cellular therapy data variables while DBtC Download provides users with the ability to download transplant and non-transplant cellular therapy data sets. Transplant data for centers in MyTED include legacy IBMTR since 1972 and legacy NMDP to 1987. Includes only Pre-TED, Post-TED, and equivalents from the CRF track. Retrieval is completed monthly and posted on CIBMTR's Portal site for access by authorized users of centers. Other cellular therapy data for centers in MyCTED includes all data for variables on the cellular therapy data extract (above) and is also generated monthly.

Study Datasets	Description
DBtC	All transplants for centers since 1/1/2008. Includes select HCT data from Pre-TED and Post-TED forms, HCT data from CRFs (2000, 2100, 2900, 2004, 2005, disease), and select non-transplant CAR-T data from CTED forms (4000, 4100) submitted by participating centers. Data are extracted monthly and populate the DBtC data model in the QlikView data analytics application.

15.2.2.3 Integrated Data Warehouse

CIBMTR continues to implement its Integrated Data Warehouse to consolidate CIBMTR systems and support the utilization of quality data that meet the diverse administrative and scientific needs of CIBMTR stakeholders. CIBMTR has pursued an evolutionary approach to implementing its Integrated Data Warehouse in a way that does not compromise its ability to fulfill existing obligations. When complete, CIBMTR's Integrated Data Warehouse will provide data sharing products that fulfill desired capabilities, including:

- Access to and export of data for research analysis
- Performance management
- Quality data monitoring
- Compliance with requests from regulatory bodies, accrediting organizations, and payers

CIBMTR's Integrated Data Warehouse will support these capabilities through different information delivery methods, including reports and dashboards, applications, data extracts, and self-service analytics.

15.2.3 Web Presence

The primary goals of CIBMTR's web presence are to optimize and enhance CIBMTR websites to:

- Provide better online access to cellular therapy information for both the scientific community and the public
- Provide training and support to centers who provide outcomes data to CIBMTR
- Create a shared communications and networking environment for centers and CIBMTR Working Committees
- Provide web-based access to CIBMTR databases and other resources

CIBMTR's web presence initiative comprises three distinct websites, each with its own purpose and security model:

- Public website (**Section 15.2.3.1**)
- CIBMTR Hub website (**Section 15.2.3.2**)
- Portal website (**Section 15.2.3.3**)

15.2.3.1 Public Website

The *CIBMTR.org* website provides anonymous access to the public and disseminates information about CIBMTR, its data collection process, research activities, committee structure, how to get involved, news, and publications. CIBMTR posts its annual Summary Slides on the site in a downloadable PowerPoint format. These frequently requested slides summarize outcomes and current uses of cellular therapy and provide answers to questions posed by the research community. The public website also provides information from

CIBMTR's studies, publications, and authors database, which includes detailed information about studies, publications (since 1972), and historical information on authors and their institutions.

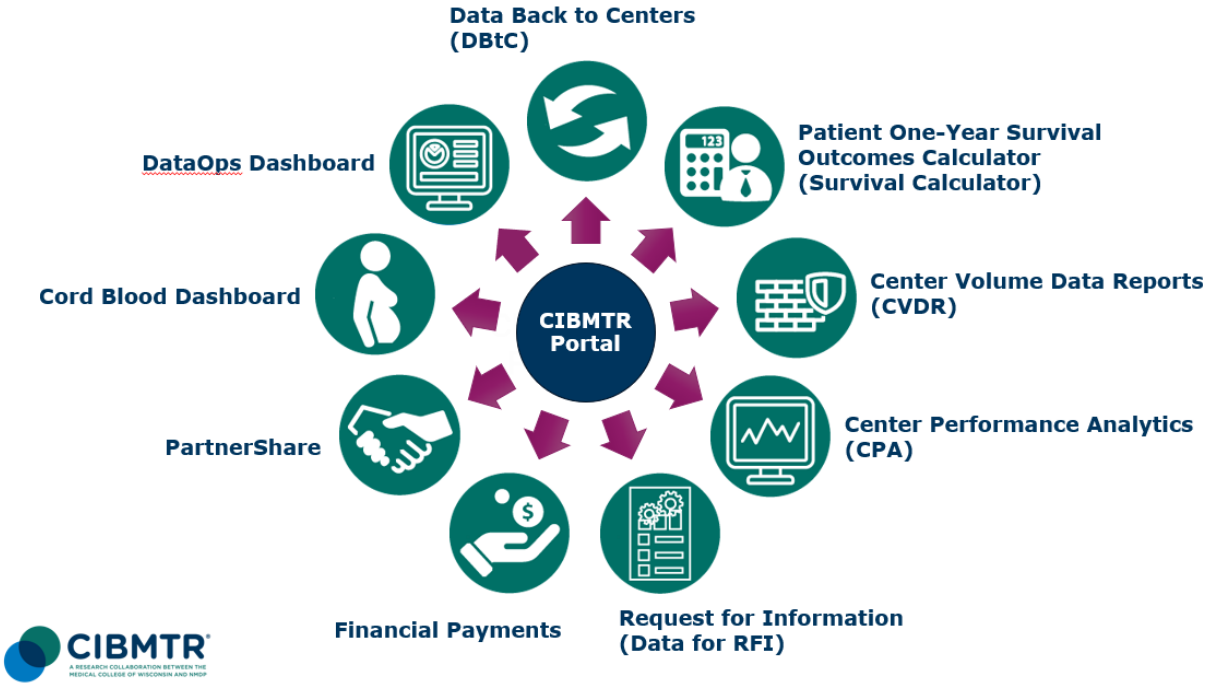
15.2.3.2 CIBMTR Hub Website

CIBMTR Hub functions as CIBMTR's intranet and primary collaboration portal and is restricted to internal users. Deployed in SharePoint, the Hub provides features that promote cooperation among CIBMTR staff and serves as a communication platform for specific studies and initiatives. This secure site requires a username and password. Access is based on a user's assigned role.

15.2.3.3 Portal Website

CIBMTR's *Portal* website functions as a secure extranet that delivers custom applications and data to CIBMTR staff and partners (including investigators), centers, and research coordinators. Authorization and access to the Portal requires all users to be registered within NMDP's Active Directory; NMDP uses Okta Verify multifactor authentication. CIBMTR's Portal provides access to a suite of applications developed in QlikView, as well as additional custom developed applications:

Figure 15.3: QlikView Data Sharing Applications on CIBMTR Portal



15.2.3.3.1 Data Back to Centers (DBtC)

DBtC is a data analytics application that provides users with self-service access to a subset of their most commonly used data, including functionality to analyze and view descriptive statistics and outcomes. Pre-defined filters permit analysis of subsets of interest, and robust visualization features provide options for viewing data in a chart or table. An ad hoc query tab permits users to create and implement custom queries. Users can export data in Excel file formats. DBtC includes HCT data from 2008 to present and CAR-T infusion data from 2020 to present for participating centers. Outcomes include five-year overall survival, acute and chronic GVHD, and more for HCT patients as well as neurotoxicity for non-transplant CAR-T patients. DBtC also provides a Risk Evaluation and Mitigation Strategy (REMS) report

for CAR-T patients. DBtC data are extracted, validated, and refreshed monthly. The DBtC Monthly Data Load Process SOP (SOP-0051) details the specific steps in this process. All data that support the tables and charts can be easily downloaded. DBtC data are extracted, validated, and refreshed monthly.

DBtC Download also permits users to download data in either Excel or comma-separated value format. These data have been validated by CIBMTR data quality processes. Transplant data, found in MyTED, include Pre-TED, Post-TED, and imputed TED equivalents from the CRF track as well as legacy IBMTR data since 1972 and legacy NMDP data to 1987. Other cellular therapy data, found in MyCTED, include Pre-CTED, Post-CTED, and relevant aggregations calculating in the cellular therapy extract from the Integrated Data Warehouse. Both transplant data and other cellular therapy data are updated monthly (SOP-0051: DBtC Monthly Data Load Process). Data dictionaries are provided with definitions for each field and coded values in the datasets.

15.2.3.3.2 Patient One-Year Survival Calculator

The Patient One-Year Survival Calculator for Allogeneic Transplants is deployed on CIBMTR's Portal site for access by extranet users. The intent of this online survival calculator is to provide centers with a tool to predict one-year survival for individual allogeneic HCT recipients. Data taken from CIBMTR's Center-Specific Survival Analysis for 2022 is used to calculate the expected probability of one-year survival for individual recipients of first allogeneic HCT in the US. Patient, disease, and transplant characteristics of allogeneic HCT recipients at US centers between 2018 and 2020 are currently used to generate these estimates. The Survival Calculator Information and Update Process SOP (SOP-0055) details the specific steps in this process. The calculator is updated annually to reflect new information contained in the center outcomes analysis.

15.2.3.3.3 Center Volume Data Report (CVDR)

The CVDR allows centers to review and approve center volume data that is published annually to the *Bone Marrow and Cord Blood Donation and Transplantation* website to which CIBMTR is required to provide data. This public website, under the Department of Health and Human Services banner, is required by the SCTOD contract (**Section 6.2**) and includes the center-specific outcomes data collected by the SCTOD. The CVDR displays and permits download of the previous two years of volume data in addition to the current year. Subsequent reports show additional HCTs performed since the data were last approved.

15.2.3.3.4 Center Performance Analytics (CPA)

CPA supports center performance and quality initiatives using the dataset from the Center-Specific Survival Analysis. Authorized (by center) users can compare their center's data relative to aggregated data from other centers using pre-defined filters that include geographic region, historical performance, volume of HCTs, and patient population served. Centers can visualize and filter their center's own one-year survival rate, based on the rolling three-year period of data included in the Analysis dataset. Like DBtC, users can create and implement customized, ad hoc queries and export a download of the source dataset for their center. CPA is updated annually, and the Refresh Data for Center Performance Analytics SOP (SOP-0117) details the specific steps in this process.

15.2.3.3.5 Data for Request for Information (RFI)

Data for RFI is a QlikView / Microsoft Excel solution that utilizes the standard reporting format developed by the ASTCT. It provides US centers with the ability to access, view, reconcile, and format data previously submitted to CIBMTR to fulfill the center's annual obligation to share outcomes data with third-party payers and external organizations. Accessible from within the Portal or from within the DBtC application, Data for RFI leverages

the same CIBMTR data available in DBtC but translates it to the standard RFI format developed by the ASTCT, including but not limited to risk classification by disease. It also incorporates the standard ASTCT rules for determining survival, differentiating between adult and pediatric populations, and more. Data for RFI is not a report but a data extract that centers can export in an Excel document that conforms to the standard format developed by the ASTCT. It only contains data collected on CIBMTR forms and provided to CIBMTR.

15.2.3.3.6 Financial Payments

Centers receive reimbursement for submitting certain forms to CIBMTR. The Financial Payments app offers authorized users within centers self-service access to securely download their financial reimbursement reports. This app not only provides the most current and up-to-date reports but also serves as an archive of prior reports, allowing users to actively monitor the changes of their data from month-to-month in a convenient web-based interface.

15.2.3.3.7 PartnerShare

PartnerShare is available to research collaborators and study sponsors that have obtained required approvals and executed contracts with CIBMTR. It provides authorized individuals with self-service access to data on patients submitted across centers based on specific protocol criteria, such as therapeutic product used, disease indication, or cohort characteristics. Data are refreshed monthly. Users can export data in Excel file formats. Initial data visualization features provide accrual information by study and center query status. Pre-defined filters permit analysis of subsets of interest, and robust visualization features provide options for viewing data in a chart or table.

15.2.3.3.8 Cord Blood Dashboard

The Cord Blood Dashboard provides a secure portal for cord blood banks to download formatted reports and data extracts in Excel format. These data include chimerism, data quality, submitted queries, inclusion reports, exclusion reports, and adverse event reports. These reports are updated quarterly along with a data dictionary with definitions for each variable and any coded values.

15.2.3.3.9 Data Ops Dashboard

The Data Operations Dashboard is a secure self-service portal with which transplant centers can access documents that were historically emailed to each center. These documents consist of consecutive transplant audit reports, Final CPI Standing memos, and Center-Specific Analysis reports. CPI memos provide a formal status to centers that includes a review of a center's IRB standing and form submission completions for each trimester. The consecutive transplant audit reports provide a simple audit for patient records selected for the consecutive transplant audits. This is an annual process, and the reports are updated weekly during the several months-long initiative. The Center-Specific Analysis reports allow centers to compare their performance to benchmarks established by a consensus of other transplant centers. These reports are assembled annually.

15.2.4 Bioinformatics Supported by IT Services

Bioinformatics Research is described in **Chapter 10**. CIBMTR IT services provide data, infrastructure, security, and systems administration support for many Bioinformatics Research needs. CIBMTR IT provides data to help with research, such as the HLA Save Extract, a summary of the HLA Data and related variables for all the transplants known to CIBMTR and NMDP. CIBMTR IT also provides assistance with other data integrations and can provide data from many domains. Support for registry and donor selection optimization was recently moved to NMDP Enterprise Analytics.

15.2.5 Technical Services

CIBMTR IT departments on both campuses work collaboratively with the parent IT departments at MCW and NMDP to provide technical service support for servers, networking equipment, and personal computers. This includes shared file directories, email systems, operating systems, software patches, service monitoring, firewalls, and user accounts and permissions. Staff service requests are submitted to the respective IT departments.

15.2.6 Information Security

CIBMTR maintains a comprehensive and rigorous information security and data protection program composed of overlapping and complementary controls—policies, plans, procedures, and practices implemented locally within CIBMTR, and more broadly, within its parent institutions, MCW and NMDP.

CIBMTR has aligned with the National Institute of Standards and Technology (NIST 800-53) Security and Privacy Control for Federal Systems framework, currently revision 4, and transitioning to revision 5 in 2024. Both institutions that comprise CIBMTR also comply with numerous laws, administrative regulations, and directives.

Administrative, operational, and technical controls and practices implemented in each organization are unified within respective organizational system security plans, and their implementation is continuously monitored and subject to annual assessment by a qualified, independent third-party auditor, which was most recently completed in September 2022 by Baker Tilly Virchow Krause, LLP. Assessment findings and a statement of fact are reported to CIBMTR Information Security and Data Oversight for acceptance and, upon request, are made available as part of a security assurance package to key stakeholders, including HRSA.

The hallmarks of these plans include, but are not limited to:

- **Security and Data Privacy Awareness**. Upon hire and annually thereafter, CIBMTR staff members are required to complete security and data privacy awareness training, as set forth by CIBMTR's Security Awareness and Training Policy (POL-0005).
- **Identification, Authentication, and Access Control**. NMDP and CIBMTR MCW implement standardized credential authentication methods aligned to the NIST 800-53 framework and NIST 800-63 guidelines, requiring industry-leading multifactor authentication across system boundaries, critical, and personally identifiable information or protected health information holding systems. (SOP-0161) details the specific steps in affecting access to key CIBMTR systems.
- **Incident Response**. CIBMTR implemented incident response policies and plans consistent with NIST 800-53, NIST 800-61, and OMB M-17-12, which undergo regular testing and updating, as appropriate. CIBMTR POL-0019 establishes incident response policy, and PLAN-0002: CIBMTR Incident Response Plan delineates response handling of incidents that may occur.
- **Continuous Monitoring**. CIBMTR implemented continuous monitoring plans to protect hosts, endpoint systems, and networks. Practices include vulnerability scanning, malware detection, intrusion detection, event monitoring, and annual penetration testing. These plans support rapid discovery of unanticipated threats or hazards as well as checks and balances for detecting whether these are operating as expected. Vulnerability Scanning and Remediation SOP (SOP-0059) details the specific steps in this process.
- **Configuration and Change Management**. With these practices, CIBMTR reviews and authorizes any system changes released in production. Configuration

Management for Systems / Data Policy (POL-0009) details the specific steps in this process.

- **Contingency Planning**. CIBMTR's contingency plans include business continuity as well as contingency and disaster recovery plans. They are aligned to NIST 800-34, properly documented, and annually tested. The Contingency Planning Policy (POL-0018) details the specific steps in this process.
- **Risk Assessments**. CIBMTR conducts risk assessments annually, or more frequently as needed, on systems with sensitive data. CIBMTR and MCW are expanding assessments to assess privacy risk and supply chain risk.
- **Governance and Oversight**. CIBMTR's Information Security Oversight Committee is comprised of senior and executive CIBMTR administrative and scientific leaders. This committee is responsible for fulfilling CIBMTR information security governance and for assuring alignment with CIBMTR's mission critical functions and operational obligations.

CIBMTR's system security plans and their complementary controls, maintained by CIBMTR MCW and NMDP, and CIBMTR's IT security plans ensure similar standards of information security are applied to systems. These security plans and controls represent robust information security risk management beyond those established by the Health Insurance Portability and Accountability Act of 1996 (HIPAA), which provides federal protections for personal health information (**Chapter 13**).

15.2.7 Data Use and Protection

In response to changing global personal data protection requirements, CIBMTR updated and continues to refine its *Data Use and Processing Policy (PDF)* to align data privacy regulations in the US with those of other countries and regions, including the European Union General Data Privacy Regulation (GDPR). A *Personal Data Protection Statement* is publicly posted on CIBMTR's website along with additional information regarding CIBMTR security infrastructure and how it protects personal data. CIBMTR understands the importance of its role as a steward of the data it collects and continues to work with partners within and outside the US to ensure its systems meet all standards.

CHAPTER 16: COMMUNICATION

This chapter defines how CIBMTR communicates internally as well as externally to key partners, including center staff, physicians, working group members, and the general public. The communication strategies for these activities are to:

- Build a consistent image and understanding of CIBMTR and related organizations
- Develop simplified, succinct, and clear communications about research, research services, data, and expertise
- Develop benefit- and action-focused communications to motivate stakeholders

16.1 OBJECTIVES AND STRATEGIES

To promote its research efforts and meet the needs of its various audiences, CIBMTR defines and prioritizes communication objectives to raise awareness about CIBMTR, develop meaningful content, implement key activities, and increase stakeholder and resource support. These objectives seek to:

- Increase understanding of CIBMTR and its contributions (e.g., supporting high-quality studies including proposals, trial enrollment, and timely completion of research)
- Increase participation in and commitment to CIBMTR research (e.g., encouraging current and new leaders to submit studies and collaborate on research projects)
- Improve efficiency and engagement in data submission (e.g., ensuring that data managers are well-trained and efficient)
- Increase use of CIBMTR data and expertise to advance cellular therapy (e.g., promoting use of the CIBMTR Biorepository)

To accomplish these objectives, communication strategies:

- Raise awareness of CIBMTR, CIBMTR studies, and study impacts leading to practice-changing findings
- Raise awareness of availability of and methods for accessing CIBMTR research services, data, and expertise
- Engage young physicians in CIBMTR by offering CIBMTR services to help them perform research and meet publishing goals
- Simplify and improve training, communications, and support for data submission
- Generate interest in increasing the level of participation in CIBMTR research / Working Committees by emphasizing benefits to clinicians (individually and institutionally)
- Engage corporations and organizations in supporting CIBMTR research and meetings

16.2 STANDARDS

CIBMTR uses a standardized brand, or appearance, which represents the organization and makes it recognizable to its various audiences. An ongoing committee with bi-campus representation helps develop and maintain these brand standards and makes recommendations for graphics (including logos), numerical displays, documentation, and language. The Website Advisory Team, which oversees the public and two private websites (**Chapter 15**), maintains consistent appearance and processes. *CIBMTR's Brand Standards* are available for download in the Knowledge Center.

16.2.1 Acknowledging CIBMTR in Publications

CIBMTR encourages use of the following standard texts, as applicable, whenever CIBMTR is described in print materials:

- **General Acknowledgement**. CIBMTR collaborates with the global scientific community to advance cellular therapy research worldwide. A research collaboration between the Medical College of Wisconsin and NMDP, CIBMTR facilitates critical, cutting-edge research that has led to increased survival and an enriched quality of life for thousands of patients. Its prospective and observational research is accomplished through scientific and statistical expertise, a large network of centers, and a clinical outcomes Research Database of more than 600,000 patients.
    - **Negative Acknowledgement** (used when CIBMTR does not agree with published findings or interpretations). CIBMTR did not review and / or approve the study results presented in this publication.
- **Data Sources Statement** (**Appendix E**).

Use of the appropriate acknowledgement in the publication is approved by the Senior Scientific Director for Research Operations.

16.3 KEY PERSONNEL

Key personnel within the Advancement functional area, as well as staff and leadership on both campuses, provide input to and approval for a variety of CIBMTR materials prior to publication. Additionally, NMDP's Patient Services and Marketing staff members contribute to the development and support of objectives and strategies, including content development of internal and external communication tools for certain CIBMTR outreach activities.

16.4 KEY ACTIVITIES

Development and dissemination of information is a core activity of CIBMTR. To promote high-quality cellular therapy research, information must move effectively and efficiently from the Coordinating Center as well as between and within Working, Steering, and Advisory Committee members; investigators; center staff; and others.

CIBMTR is committed to collaborative work with all its partners and works to overcome communication barriers, including geographical and time zone differences, language, security concerns, and research goals. To ensure productive communication among collaborators, CIBMTR encourages face-to-face meetings when feasible as well as teleconferences, and it supports several communication mechanisms.

16.4.1 SharePoint

CIBMTR uses a collection of SharePoint Online websites for secure document sharing, internal communication between campuses, and use by employees working off-campus. These websites are password-protected via single sign-on and require multifactor authentication. CIBMTR staff members use SharePoint for departmental, functional, process-related, and collaborative project activities.

CIBMTR continues to enhance and organize SharePoint on an ongoing basis to optimize and strengthen internal and external communication. For example, CIBMTR utilizes SharePoint for collaboration on:

- Product enhancement, including FormsNet, AGNIS, and other application developments
- Strategic and operational projects, such as the Data Transformation Initiative, Data Centralization, and Integrated Data Warehouse
- Data governance

- Data quality management
- SOP process and document management
- Tandem Meetings and other meeting administration
- Working Committee collaboration
- Knowledge management

CIBMTR is also expanding workflow processes and Working Committee study collaboration features (**Chapters 6, 12, 15**,and **17**). SharePoint is only available to registered users, and users are assigned privileges for specific site and / or file access depending on their role and credentials.

16.4.2 Conference Attendance

National conferences are key opportunities to interact in person with many audiences. These conferences not only provide a wide range of educational opportunities for CIBMTR staff members but also educate others about the organization's range of research and educational activities. CIBMTR hosts exhibit booths at selected conferences, which provide opportunities to share its publications and informational marketing materials and to network with colleagues and interested investigators.

16.4.3 Websites

CIBMTR's Web Presence Initiative includes three distinct websites, each with its own purpose and security model:

- CIBMTR's public website, *CIBMTR.org,* supports anonymous access by the public and provides information about CIBMTR and its research.
- *SharePoint* promotes connectivity among authorized and approved CIBMTR staff members and provides a communication platform for specific studies and initiatives.
- CIBMTR's *Portal* website requires multifactor authentication; it securely delivers applications and data to authorized and approved CIBMTR staff and partners, including investigators, centers, Clinical Research Coordinators, and commercial partners.

CIBMTR staff members request updates to any of CIBMTR websites via the *Web Change Request Form* or, in the case of CIBMTR's Portal site, the *CIT Project Intake Form*. The Website Advisory Team processes each request and seeks necessary approval for each change. Additional questions regarding a website change should be sent to *cibmtr-webmaster@mcw.edu.*

For more information about these websites, see **Chapter 15**.

16.4.4 Summary Slides

Each year, CIBMTR publishes Summary Slides on the state of the art in cellular therapy. Using information from CIBMTR's Research Database, a Statistician and a CIBMTR Senior Scientific Director prepare these charts summarizing current uses and outcomes of allogeneic and autologous HCT as well as other cellular therapies. These valuable and highly anticipated slides are used by clinicians and researchers in the cellular therapy community. *Summary Slides* are posted on CIBMTR Slides and Reports webpage (under Resources).

16.4.5 Publications

CIBMTR produces increasing numbers of peer-reviewed publications as well as book chapters. Most are submitted from the Coordinating Center. Staff members follow all NIH requirements, including PubMed citations, and specific journal guidelines, such as proper acknowledgement of funding resources. See **Chapter 3** for authorship rules. CIBMTR

maintains a *current list of publications with citations* on CIBMTR's Publication list webpage (under Resources).

16.4.6 Plain-Language Summaries

For the public, CIBMTR creates easy-to-read summaries of CIBMTR and BMT CTN publications. Summaries are created through a collaborative process involving CIBMTR Consumer Advocacy Committee members, a CIBMTR MCW Medical Writer, a CIBMTR MCW Communications Consultant, an NMDP Patient Education Specialist, and CIBMTR Scientific Directors / BMT CTN Protocol Chairs. Additional information can be found in the Patient Summaries of CIBMTR Research Publications SOP (SOP-0172). Once finalized, CIBMTR posts the summaries on the *Study Summaries* webpage.

16.4.7 Post-Transplant Guidelines

CIBMTR, along with several other organizations, publishes recommended post-transplantation treatment strategies. NMDP converted these strategies into an easy-to-use reference guide for physicians and patients. It is available in print, online, and in a mobile application (for iPhone and Android). The guidelines can be accessed on CIBMTR's *Post-Transplant Guidelines* webpage (Rotz SJ et al. International Recommendations for Screening and Preventative Practices for Long-Term Survivors of Transplantation and Cellular Therapy: A 2023 Update. Transplantation and Cellular Therapy. 2024. Epub 2024/02/28. PMID: 38413247. doi:10.1016/j.jtct.2023.12.001.)

16.4.8 Annual Reports

CIBMTR publishes several annual reports. Government versions of the reports fulfill requirements of cooperative agreements with NCI, NHLBI, and NIAID, as the major source of funding for the fundamental work of CIBMTR as well as with the NHLBI and NCI for the DCC of the BMT CTN (**Section 8.1**).

The primary audience for the public versions of the reports is the scientific community, researchers, and the general public. CIBMTR creates and distributes printed copies of the public versions. Electronic copies are available on the *Administrative Reports* webpage and the BMT CTN *Progress Reports* webpage.

CIBMTR's annual research performance progress report to the government details accomplishments and goals of the previous calendar year. CIBMTR publishes the public version and distributes it in February in time for the Tandem Meetings. CIBMTR Annual Report SOP (SOP-0311) details the process for creating and distributing the public annual report, and CIBMTR RRPP Development SOP (SOP-0165) details the process for creating and submitting to NIH CIBMTR's research performance progress report each year.

The BMT CTN also creates a research performance progress report for submission to NIH and an annual report for the public each year. These reports detail accomplishments and goals of the DCC during the previous 12-month reporting period. The BMT CTN Annual Report (public version) is distributed during the annual summer meeting of the BMT CTN Steering Committee.

16.4.9 Newsletters

CIBMTR publishes a quarterly external newsletter for the cellular therapy community. Staff members distribute the external newsletter via email and post it on CIBMTR's *Newsletters* webpage. The primary audience is center physicians and staff who participate in CIBMTR research by submitting data. Newsletters feature updates on CIBMTR Working Committees, research programs, data collection and management, and newsworthy events in the cellular therapy community. CIBMTR Quarterly External Newsletter SOP (SOP-0173) details the process for creating and distributing the newsletter.

16.4.10 Social Media

CIBMTR maintains X (*@CIBMTR*), Facebook (*@theCIBMTR*), and LinkedIn (*theCIBMTR*) accounts to increase awareness of the organization, collaborate with various individuals both within and outside the cellular therapy research community, and share resources. CIBMTR MCW Communications Consultant monitors, updates, and posts content to these accounts on a regular basis, providing information and supporting CIBMTR's network.

16.4.11 Informational Marketing Materials

Any program, department, or committee may need informational or marketing materials. The communications staff at either campus may produce these materials with input from appropriate personnel on either campus. These materials may include flyers for distribution at meetings, CIBMTR's overview brochure, documents for Working Committee members and centers, and other items.

16.4.12 Phone, Video, and Web Conferences

Many CIBMTR functional areas utilize conference calls, videoconferencing, and web conferences to optimize communication and productivity between groups that may be spread apart geographically. Teleconferencing helps create interpersonal relations and increased collaboration among CIBMTR, its associate institutions, and its research partners. For example:

- CIBMTR Working Committees utilize conference calls among Scientific Directors, PIs, and various committee members to discuss current studies and proposals for future studies.
- CIBMTR has staff members on two different campuses as well as in the Department of Biostatistics at MCW. Leaders bring many of these members together for weekly teleconferences to discuss ongoing statistical development of research protocols.
- Clinical Research Coordinators, Data Support staff, Program Coordinators, and Administrative staff utilize conference calls to complete a wide range of responsibilities.
- The following groups also use conference calls and videoconferencing as a primary interface: Executive Committee, Consumer Advocacy Committee, Affiliation Board, Protocol Writing Committees, and many more.

16.4.13 Dissemination through NMDP

Through its medical education activities, NMDP routinely highlights CIBMTR research results and outcomes data. NMDP reaches US and international audiences online at BeTheMatchClinical.org, through newsletters, during medical education programs, via clinical resources, and more.

16.5 EDUCATIONAL OUTREACH

16.5.1 Data Management Education

CIBMTR has provided Data Operations training to contributors for more than 20 years:

- **New Data Manager Onboarding**. CIBMTR offers live, virtual New Data Manager Onboarding training twice per year. These sessions offer an invaluable opportunity for CIBMTR and center staff to interact and share best practices. Onboarding sessions include interactive training in the FormsNet training environment and CIBMTR Portal along with comprehensive topics that are pertinent to new data managers to submit high-quality data.
- **Self-Guided Onboarding**. CIBMTR offers self-guided onboarding training for new data managers that is available at any time on its Portal site. This self-guided course

provides all the eLearnings and information about CIBMTR's data submission requirements and field knowledge as well as two suggested timelines, standard or accelerated, for completing the self-guided learning materials.

- **Recorded Data Manager Trainings**. In 2023, CIBMTR began offering a recorded version of New Data Manager Onboarding for new data managers who are not able to attend the training live. Additionally, the Data Operations training team began offering a free, virtual Intro to CIBMTR Resources and TED-Level Reporting training to introduce new data managers to all the training resources that are available to them. CIBMTR also offers free, live webinars for experienced data managers on advanced reporting topics, as many as four times per year.
- **eLearnings**. The Data Operations Training Specialist creates web-based training modules to assist data contributors around the world. The currently available training modules address core competencies such as the general process, basic review of applicable science including pertinent diseases, medical terminology, immunology, hematology, histocompatibility, reporting documents and schedules, and CIBMTR policies and procedures. There are currently more than 40 eLearnings available.

Ongoing, comprehensive web-based training helps address the problems caused by turnover in data management staff at centers, the wide geographic distribution of centers, and limited resources overall for supporting attendance of all data management staff at in-person meetings. Detailed documentation also helps train center staff to report in an accurate and timely manner. CIBMTR has produced a detailed instruction manual for the HCT CRFs, HCT Pre- and Post-TED forms, and cellular therapy suite of forms. There are disease-specific instruction manuals on *CIBMTR's Forms Instructions Manual* webpage including:

- Acute lymphocytic leukemia
- Acute myeloid leukemia
- Aplastic anemia
- Chronic lymphocytic leukemia
- Chronic myeloid leukemia
- Fanconi anemia / constitutional anemia
- Hemophagocytic lymphohistiocytosis
- Hodgkin / non-Hodgkin lymphoma
- Immune deficiencies
- Juvenile myelomonocytic leukemia
- Leukodystrophies
- Myelodysplastic syndrome
- Myeloproliferative neoplasms
- Neuroblastoma
- Plasma cell disorders
- Sickle cell disease
- Thalassemia
- Waldenstrom's macroglobulinemia
- Wiskott-Aldrich Syndrome
- X-linked lymphoproliferative syndrome

Additional disease-specific instruction manuals are posted as they are completed.

16.5.2 BMT CTN Coordinator Education

The first BMT CTN (**Section 8.1**) Coordinators Meeting was held in conjunction with the BMT Tandem Meetings in February 2008. The goal was to present a variety of logistical and scientific information geared towards Center Research Coordinators. This popular meeting is scheduled annually during the Tandem Meetings and is now offered in hybrid format. BMT CTN coordinators typically meet for a day, during which they cover a variety of topics ranging from data entry and quality control issues to review of procedures and protocol requirements. Coordinators provide the DCC with useful feedback from centers. The BMT CTN also provides protocol-specific training to participating sites, as described for CRO Services below (**Section 16.5.3**).

16.5.3 CRO Services Training

CRO Services (**Section 8.2**) staff members provide protocol-specific training to sites participating in a protocol. Prior to activation of a clinical trial at a selected site, CRO Services will hold a site initiation to train the PI, coordinator, and supporting study staff on the objectives and procedures of the study. The training will take place remotely via conference call, web-based conferencing, e-learning training sessions, or during an onsite face-to-face training. If applicable, the meeting may take place in person either at the site or another location. Training content may include study overview and purpose, summary of Good Clinical Practices, summary of the study design and study procedures, review of inclusion and exclusion criteria, subject enrollment procedures, assessments, follow-ups, reporting of adverse events and unanticipated problems, case report form review, and electronic data capture system training along with any other study-specific procedures (e.g., labs, drug accountability). If staff changes occur during the protocol, training will be conducted.

CHAPTER 17: MEETINGS

CIBMTR hosts and participates in many national and international meetings to promote and disseminate its research worldwide. The largest meeting hosted by CIBMTR is The Tandem Meetings | Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR (Tandem Meetings), which has been co-hosted since 1993 by CIBMTR in collaboration with the ASTCT. These meetings are a well-recognized forum for the full cellular therapy team: Physicians, scientists, advanced practice providers, data managers, and others. Discussions focus on idea generation, works in progress, and reporting of completed projects.

CIBMTR personnel also participate in other scientific meetings as attendees, presenters, and booth hosts. These meetings include:

- NMDP One Forum held annually in November
- ASH Annual Meeting held in December
- EBMT Annual Meeting held in April
- American Society of Clinical Oncology (ASCO) Annual Meeting held in June
- Cord Blood Connect annual meeting held in September

17.1 TANDEM MEETINGS

The Tandem Meetings are the combined annual meetings of CIBMTR and ASTCT. They are the largest North American gathering of worldwide experts in cellular therapy patient care, clinical investigation, and laboratory research. Reports on recent progress and updates in basic science, translational research, and clinical studies target worldwide physicians and scientists with an interest in cellular therapy.

The Tandem Meetings are held in February to avoid schedule conflicts with other meetings. Four days of plenary scientific sessions, concurrent scientific sessions, and satellite symposia present the latest and best of basic, translational, and clinical cellular therapy research. Tracks convene for nurses; center administrators; clinical research professionals, data managers, and coordinators; pharmacists; IT professionals; and others working in the field. Equally important are the ancillary meetings and collegial sharing of ideas within the cellular therapy community.

Many CIBMTR committees meet in person during the Tandem Meetings, including the Advisory Committee (**Section 2.2.2**) and its Working Committees (**Sections 6.1 and 17.1.3**). The Scientific Organizing Committee for the following year is formed and meets shortly after the Tandem Meetings conclude (**Section 17.1.2**).

Attendance at the Tandem Meetings increases annually to current levels of more than 5,000 registrants. A limited number of travel grants are provided for selected attendees.

The educational objectives of the Tandem Meetings are to:

- Report on the state of the art in cellular therapy and HCT
- Analyze new methods and controversial issues in clinical management strategies for reducing toxicity and improving transplant and other cellular therapy outcomes
- Assess new basic science information in areas of immunogenetics, molecular biology, stem cell biology, and immunology as it relates to HCT
- Review CIBMTR research accomplishments and contribute to setting the organization’s scientific agenda for the next year
- Review accomplishments of ASTCT, including progress on organizational, societal, and regulatory issues in HCT and ACT

- Report on contemporary principles in HCT and ACT nursing, pharmacy, data management, clinical research analysis, pediatric transplantation, and transplant center administration

17.1.1 Relationship with ASTCT

Holding the Tandem Meetings jointly with ASTCT helps reduce travel costs and schedule conflicts of attendees, while also promoting networking for members of both organizations. CIBMTR and ASTCT share the following responsibilities:

- Financial management, including grant procurement and industry support, monitoring educational exhibits, and satellite symposia
- Agenda coordination
- Internal and ancillary meeting management
- Awardee / speaker benefits and travel
- Abstract submission and selection process for oral and poster presentations
- Strict adherence to continuing medical education and Accreditation Council for Continuing Medical Education requirements
- Venue and vendor negotiations and contracting
- Transportation
- Online registration services and registration fee setting
- Online housing services
- Audio / visual, live streaming, and expo management
- Food and beverage management
- Website and general logistical conference management

17.1.2 Scientific Organizing Committee

The Tandem Meetings Scientific Organizing Committee is comprised of 16 appointed individuals who work collaboratively to select topics and Chairs for the upcoming year. CIBMTR and ASTCT each propose six members, one fellow, and a meeting Co-Chair.

In addition to the individuals listed above, the members of the Tandem Meetings' Joint Senior Leadership Team, listed below, participate in the Scientific Organizing Committee:

- CIBMTR MCW Chief Scientific Director
- CIBMTR NMDP Chief Scientific Director
- CIBMTR Advisory Committee Chair
- CIBMTR Executive Scientific Director, Policy and Governance
- Vice President, CIBMTR and Clinical Services, NMDP
- ASTCT Executive Director
- ASTCT President
- ASTCT Immediate Past President
- ASTCT President-Elect
- ASTCT Vice President
- Scientific Organizing Committee Immediate Past Co-Chairs

A representative from each accredited track also participates in the Tandem Meetings Scientific Organizing Committee. CIBMTR's Executive Committee may appoint additional committee members to represent both US and non-US CIBMTR-participating centers. The ASTCT President may appoint additional representatives, which are confirmed by the ASTCT

Board of Directors. Committee members are chosen to represent a wide spectrum of clinical and laboratory science interests.

This Scientific Organizing Committee is formed and meets after the conclusion of the previous Tandem Meetings. After making its recommendations for the upcoming meetings, the ASTCT / CIBMTR Tandem Team Leads, the Scientific Organizing Committee Co-Chairs, and the Joint Senior Leadership Team meet during the year to coordinate planning and scheduling details.

17.1.3 CIBMTR Working Committee Meetings

All conference registrants are encouraged to attend and actively participate in meetings of the 11 CIBMTR Working Committees (**Sections 2.4 and 6.1**) and their Collaborative Session, which are scheduled during the Tandem Meetings. During these meetings, Working Committee leadership and members of each Working Committee review the past year's research accomplishments, discuss current studies, review new proposals, and establish priorities by setting the scientific agenda for the coming year. This is the only time the Working Committees meet in person, and these sessions are a core activity of the annual scientific meeting. Working Committee meetings are planned to avoid conflict with scientific sessions (**Section 17.1.4**).

17.1.4 Scientific Sessions (Plenary and Concurrent)

At plenary and concurrent scientific sessions, leading authorities from around the world present the latest developments in cellular therapy. Topics include but are not limited to:

- Acute and chronic GVHD
- Cellular therapy
- Basic science and biology of hematopoietic cell engraftment
- Best treatment practices
- CAR-T
- Disease-specific issues
- GVHD
- Graft sources
- Health services research
- Non-transplant cellular therapies
- Prevention
- Relapse
- Transplantation-specific issues

17.1.5 Satellite Symposia

CIBMTR and ASTCT schedule popular satellite symposia sessions during mealtimes to minimize conflict with other scientific sessions or Working Committee meetings. Third-party medical education companies submit symposia topics, Chairs, and speakers to a subcommittee of the Tandem Meetings Scientific Organizing Committee. Meetings staff members publish an annotated list of proposed symposia topics and an application form on the Tandem Meetings website and circulate it to health care companies.

Industry partners provide funding to support symposia and a variety of presentations; however, CIBMTR and ASTCT structure symposia so that scientific and educational content are separated from commercial interests and comply with rules and guidelines for continuing education. The competitive bidding process ensures:

- Separation between symposia content and financial support
- Transparency in the development of symposia content and faculty selection
- Uniformity in symposia design, planning, execution, and outcomes assessment
- Simplified and economical processes for companies wanting to support symposia

17.1.6 Tracks and Ancillary Meetings

During the Tandem Meetings, tracks are held concurrently. Tracks incorporate specialized sessions for nurses, clinical research professionals (data management), advanced practice providers, pharmacists, center administrative directors, medical directors, BMT CTN coordinators and investigators, IT professionals, infectious disease specialists, and pediatric cancer specialists.

Other cellular therapy-related societies and associations often hold annual Board and training meetings during the Tandem Meetings. Examples include NMDP, journal review boards, and pharmaceutical companies. These ancillary meetings must be approved to ensure a lack of conflict with the scientific agenda. Typically, more than 60 ancillary meetings are held during the Tandem Meetings.

17.1.7 Abstract Review and Awards

Interested parties submit abstracts online each year. Abstract Review Teams review all abstract proposals, decide which ones will be accepted for presentation, and determine which ones will be presented as posters and orally. There are approximately 24 abstract Review Teams, each with its own assigned topics. The Tandem Meetings Abstract Manager contacts previous reviewers to nominate new reviewers each year. Each Review Team is led by a Review Team Chair invited by the Co-Chairs of the Scientific Organizing Committee. Review Team Chairs typically include experienced volunteers with related expertise, members of the Scientific Organizing Committee, and CIBMTR and ASTCT leadership.

Reviewers evaluate each abstract for its impact on the field of transplantation and cellular therapy. All research must be original and not previously reported in the medical literature or at another medical meeting. Exceptions are sometimes made for work also submitted to the ASH Annual Meeting because these meetings have overlapping abstract deadlines. Reviewers complete their review and scoring online in October, with final decisions made by early November. Review Teams review the composite score report and make final decisions by conference call. Review Teams also recommend their top abstracts for consideration for the Best Abstract awards.

Several hundred individuals submit abstracts for consideration annually. Reviewers accept about 10-15% for oral presentation and invite most of the rest for poster presentation. CIBMTR and ASTCT sometimes award travel grants to junior investigators whose abstracts are selected for oral presentations. ASTCT manages the travel grants program for all those who had an abstract accepted to the Tandem Meetings. Meetings staff members post all accepted abstracts on the Tandem Meetings website and publish them in a digital abstract book. *Transplantation and Cellular Therapy Journal* (formerly known as *Biology of Blood and Marrow Transplantation*) also publishes abstracts in a supplement to its February issue, enabling the accepted abstracts to be indexed in medical literature.

Leadership selects three clinical abstracts and three basic science abstracts each year to receive Best Abstract awards. Leadership included in this selection process include the Scientific Organizing Committee Co-Chairs and the Joint Senior Leadership Team. Selected speakers present their abstracts orally during the Best Abstracts Session. The principal author of the top choice receives a substantial monetary prize.

In addition to the clinical and basic research abstracts, there are several special categories of abstracts for advanced practice providers, quality and transplant program administration,

information technology and informatics, oncology nursing, pharmacy, and data management. The organizers of those educational tracks review these abstracts separately since these oral abstracts are also presented in the education track. All special category abstracts are presented in special sessions and categorized separately in the digital abstract book and online postings.

General guidelines to follow when selecting Oral Abstract Session Moderators:

- Moderators must be from different institutions
- Include moderators who are not already moderating plenary or concurrent sessions
- Involve people from as many different institutions as possible
- Attempt to include fewer senior moderators whenever possible and emphasize junior or early career moderators

17.1.8 Meeting Planning and Venues

The Tandem Meetings' Joint Senior Leadership Team (**Section 17.1.2**) meets with members of the Tandem Meetings Planning Team monthly. The Joint Senior Leadership Team provides direction regarding future meetings sites. They evaluate proposed venues based on size and location of the facility, security, and accessibility by air and ground transportation, among other considerations. The Tandem Meetings Planning Team subcontracts registration and housing services for the meetings to outside vendors. Tandem Meetings planners work with vendors to negotiate conference venue contracts. Members of the legal staff from MCW and ASTCT review contracts prior to signatures from both organizations. For information about past and upcoming meetings, view the *Tandem Meetings* webpage.

17.2 CENTER OUTCOMES FORUM

In support of its SCTOD contract deliverables (**Section 6.2**), CIBMTR hosts the Center Outcomes Forum (formerly Center-Specific Analysis Outcomes Forum) at least biannually to increase transparency and understanding of center outcomes reporting in HCT. CIBMTR invites representatives of the cellular therapy community, including transplant physicians and center directors, ASTCT, governmental funding agencies, patients, private payers, and statisticians; the solid organ transplant community; and experts in hospital and quality outcomes reporting. The meeting's purpose is to review the current approach to center-specific outcomes reporting and to provide meaningful recommendations for future reports. Additional information, including meeting summaries and recommendations, are available on CIBMTR's *Center Outcomes Forum* webpage.

17.3 OTHER MEETINGS

CIBMTR participates in a variety of meetings to promote communication, team building, continuing education, staff training, etc. Some of the meetings in which CIBMTR participates include:

- AcademyHealth Annual Research Meeting
- Advanced Placement Program Statistics Conference
- American Society for Histocompatibility and Immunogenetics Annual Meeting
- American Society of Clinical Oncology Annual Meeting
- American Society of Hematology Annual Meeting
- Asia-Pacific Blood and Marrow Transplantation Group Annual Conference
- Association of American Cancer Institutes and Cancer Center Administrators Forum
- BMT CTN Steering Committee
- Sociedade Brasileira de Terapia Celular e Transplante de Medula Óssea Meeting

- Congress on Controversies in Stem Cell Transplantation and Cellular Therapies
- Cord Blood Connect
- EBMT Annual Meeting
- European Federation for Immunogenetics Annual Meeting
- European Immunogenetics and Histocompatibility Conference
- European Hematology Association Annual Meeting
- Health Resources and Services Administration Advisory Council Meeting
- INSPIRED Symposium
- International Congress of Blood and Marrow Transplantation
- International Conference on Malignant Lymphoma Annual Meeting
- International Donor Registry Conference
- International Society for Quality of Life Research
- Japanese Society for Transplantation and Cellular Therapy Annual Meeting
- Latin American Bone Marrow Transplantation Group Meeting
- Minnesota Developer Conference
- Minnesota Health Services Research Conference
- National Council of University Research Administrators
- The ONE Forum
- Patient-Centered HCT Outcomes Research Symposium
- Psychoneuroimmunology Research Society
- SAS Users Conference
- Sickle Cell Disease Research and Education Symposium
- Society of Clinical Research Associates Chapter Meeting
- The Tandem Meetings | Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR
- University of Minnesota Bioinformatics and Computational Biology Annual Meeting
- Worldwide Network for Blood & Marrow Transplantation Meeting

CHAPTER 18: FOUNDATION FUNDING

CIBMTR maintains a diverse revenue portfolio, including funds from fundraising activities. CIBMTR's Advancement Program Director identifies, cultivates, and solicits prospective donors, corporate philanthropic gifts, and foundation funding for CIBMTR infrastructure support.

18.1 ROLES AND RESPONSIBILITIES

The Advancement Program Director oversees donations and membership revenue. Staff at NMDP Foundation also help raise awareness and funding for CIBMTR. Any corporate opportunity secured, on either campus, is coordinated with CIBMTR's Industry Relations Program.

CIBMTR's Business Operations team tracks deliverables for executed awards. CIBMTR MCW Finance and Administration or NMDP Finance is responsible for payment schedules, invoices, and tracking of secured funds.

18.2 ADVANCEMENT TEAM'S KEY ACTIVITIES

CIBMTR's Advancement Team oversees Corporate Membership (**Section 18.2.1**), seeks support from foundations (**Section 18.2.2**), and connects with individual contributors (**Section 18.2.3**).

18.2.1 Corporate Membership

The rapidly increasing use of cellular and gene therapies and the introduction of new technologies make frequent updates essential for information about transplant use and outcomes. CIBMTR's Corporate Membership program provides a variety of resource materials to corporations related to the most current and comprehensive data on cellular therapy and an opportunity to participate in CIBMTR annual meetings. Corporate partners may use Corporate Membership levels to access a variety of CIBMTR services, including protocol development and customized data reports describing cellular therapy to patients, physicians, hospitals, pharmaceutical companies, insurance companies, and others involved in healthcare.

The annual membership program also provides access to the most current cellular therapy and center reports, including the Report on Survival Statistics for Blood and Marrow Transplants, Center Volumes Dataset, US AlloHCT Activity Report, CIBMTR newsletters, and CIBMTR Summary Slides on the state of the art in cellular therapy. CIBMTR invites Corporate members to attend its meetings and educational forums and to access CIBMTR databases for simple analyses. These resources are useful for marketing managers, medical directors, research directors, product managers, case managers, and transplant coordinators.

There are five Corporate Membership levels available, each described on CIBMTR's *Corporate Membership Program* webpage.

18.2.2 Foundation Support

CIBMTR's Advancement Team seeks funding from foundations to support specific studies or to support the infrastructure of any CIBMTR major program.

18.2.3 Individual Contributions

CIBMTR relies on individual contributions to continue its research to seek better treatments and outcomes in cellular therapy. Contributions made to CIBMTR are used in the following ways:

- **General Support.** Donations support the overall operations of CIBMTR and can be applied to any of its ongoing research projects.
- **Mortimer M. Bortin Endowment.** Donations are applied to the principal of the Mortimer M. Bortin Endowment fund. CIBMTR may use investment earnings each year to support its research efforts.

18.3 TRANSPLANTATION AND CELLULAR THERAPY MEETINGS

CIBMTR co-sponsors the annual Tandem Meetings (**Section 16.1**) with ASTCT, with which it shares meeting revenue and expenses. The Tandem Meetings are accredited by MCW in compliance with the standards of the Accreditation Council for Continuing Medical Education. Commercial support agreements are negotiated between CIBMTR MCW, the MCW Continuing Medical Education office, and the commercial supporter. The Tandem Meetings include:

- **Commercially Funded Continuing Medical Education Symposia**. CIBMTR solicits educational grants from companies to support mealtime symposia related to cellular therapy.
- **General Corporate Support**. CIBMTR solicits educational and promotional grants from companies to support various meeting activities and scientific presentations.
- **Exhibits**. Pharmaceutical and biotech companies, patient and caregiver support groups, and foundations can exhibit at the Tandem Meetings for a fee.

18.4 RESPONSIBILITIES OF EACH CAMPUS

The following general guidelines are applied to foundation support. However, because each request is unique, approval must be given by CIBMTR's Chief Scientific Director, CIBMTR's Advancement Director, and the President of NMDP Foundation, as described in this section.

CIBMTR Advancement Director in Milwaukee:

- Coordinates and solicits funding, including individual contributions, for the Tandem Meetings and other CIBMTR meetings, for donor support, and for endowments, such as the Mortimer M. Bortin Endowment
- Works with CIBMTR Leadership Committee members to solicit lapsed donors and identify new development opportunities
- Informs and educates current CIBMTR donors and research participants about the research being conducted by CIBMTR
- Establishes agreements for infrastructure funding of CIBMTR major programs
- Documents and reports the status of all meeting, donor, and endowment support

NMDP Contracts and Procurement staff in Minneapolis:

- Negotiates contracts, grants, and other agreements with health care companies or other organizations that provide funding for specific BMT CTN and CRO Services studies or CIBMTR NMDP research program infrastructure
- Develops collaborative agreements with partnering organizations
- Documents and reports the status of all agreements

CHAPTER 19: FEDERAL FUNDING

Federal grants and contracts provide funds for CIBMTR activities that improve cellular therapy outcomes and patients' quality of life. This chapter describes the processes for handling federal funding. See **Chapters 11 and 18** for information about non-federal funding.

CIBMTR facilitates all day-to-day management of financial, personnel, and operational activities for its research activities. In addition to CIBMTR's Business Office, the MCW Offices of Research, Grants and Contracts, and Sponsored Programs provide oversight of grants and contracts at the MCW Campus, and NMDP's Office of General Counsel, Contracts & Procurement provides oversight of grants and contracts at the NMDP office.

Budget approval for CIBMTR rests with the Joint Affiliation Board (**Section 2.2.1**), but systems to create and administer that budget must also address the procedures and processes of the two host institutions: MCW in Milwaukee and NMDP in Minneapolis. In some cases, this creates a higher level of complexity when creating budgets and expenditure reports for various entities that require an accounting, including granting organizations. This section describes how CIBMTR manages these finances.

CIBMTR receives funding from a wide variety of sources. The primary sources are federal grants and contracts that are awarded to both MCW and NMDP. Additional sources include industry contracts, corporate and individual gifts, service agreements, endowments, meeting revenue, and institutional support.

Because all federal grants or contracts must be received by a legal entity, CIBMTR Leadership determines which entity (MCW or NMDP) will apply for each funding opportunity. This decision is based on several factors, including relevance to the core business, likelihood of receiving the award, and availability of appropriate leadership and project personnel. The awardee organization is the "Prime Contractor," and the other organization is the "Subcontractor."

- If MCW is the Prime Contractor, all proposals and funds are received under the umbrella of MCW on behalf of CIBMTR and must be managed within MCW's standard operating procedures. CIBMTR staff members assigned to the contract are responsible for the contract deliverables.
- If NMDP is the Prime Contractor, all proposals and funds are received by NMDP. NMDP Contracts and Procurement Department staff are responsible for contract deliverables. Three-week and six-week notices are issued to the responsible parties, and all submissions are given to NMDP's Contracts Representative for submission.

19.1 BI-CAMPUS MANAGEMENT

19.1.1 MCW Campus

MCW is a private, not-for-profit, academic institution dedicated to leadership and excellence in education, research, patient care, and service. MCW is a nationally recognized research center, the largest research institution in the Milwaukee metropolitan area and the second largest in Wisconsin.

The MCW Office of Grants and Contracts within the Office of Research provides pre-award services, including information regarding budget preparation, the proposal submission process, and federal policies and procedures relating to grant / contract applications. It assists in contract preparation and negotiation, reviews agency budgets prior to submission of grants for processing, and accepts subcontracts from and issues subcontracts to collaborating institutions. The office also serves as a liaison between granting agencies and MCW faculty.

The MCW Office of Sponsored Programs provides post-award financial oversight of projects supported by internal and external funding sources. The terms specified by the sponsor determine the level of restriction placed on the sponsored project. Grants and contracts funded on either a fixed cost or cost-reimbursement basis are assigned a unique project number to segregate financial data in the grant accounting system. For each project, the system tracks a budget, revenue, expenditures, open commitments, and the budget balance. CIBMTR's Business Office prepares monthly reports on each project from data prepared by the MCW Controller's Office. These reports include overall account status, transaction details, open commitment details, and a labor distribution listing. Sponsored Programs also generates monthly or quarterly invoices, periodic Financial Status Reports, and any other financial reports required by the sponsoring agency.

19.1.2 NMDP Campus

NMDP was established in 1986 to create and maintain a registry of volunteer donors who would consider donating hematopoietic stem cells for a patient in need of a stem cell transplant. NMDP is a 501(c)3 not-for-profit organization. Responsibility for financial management at NMDP resides with the Chief Financial Officer, and contractual management resides with the Chief Administrative Officer and General Counsel.

NMDP's Finance / Contract and Award Accounting Department prepares and reconciles budgets, tracks actual costs incurred, and prepares invoices.

NMDP's Contracts and Procurement Department submits and negotiates proposals, negotiates budgets, and establishes terms and conditions of contracts to ensure compliance with government and CIBMTR requirements, working within NMDP's Office of General Counsel to ensure compliance. The department also works with NMDP Finance to maximize budgets and revenue.

19.1.3 Financial Relationship Between MCW and NMDP

In 2004, MCW and NMDP established a formal Affiliation Agreement to create CIBMTR (**Section 1.3**). The organizations collaborate on a variety of awards and service agreements to provide and share resources, such as staff support, patient care costs, travel funds, and other expenses. In 2020, the organizations reviewed and updated the Affiliation Agreement.

CIBMTR's Business Office and NMDP's Finance Department together manage the organization's finances and prepare various reports for CIBMTR Leadership at each respective institution as well as research partners and federal agencies. They also develop a combined CIBMTR financial report to aid in strategic planning.

The Joint Affiliation Board (**Section 2.2.1**) has final approval on all budget items. Voting members of the Board include

- From CIBMTR MCW:
    - Chief Scientific Director
    - Executive Scientific Director, Policy and Governance
    - Senior Scientific Directors (2)
    - MCW Executive Vice President
    - MCW legal counsel
- From CIBMTR NMDP:
    - Chief Scientific Director
    - Vice President, CIBMTR and Clinical Services
    - Vice President of Research
    - Chief Medical Officer NMDP

- NMDP Chief Financial Officer
- NMDP legal counsel

19.2 PROJECT BUDGETS

Contract, grant, and study budgets are prepared by CIBMTR's Business Office or NMDP Finance, as appropriate. Tasks include:

- **Preparing the Budget**. CIBMTR staff prepare preliminary and final budgets in cooperation with the Project Director and any other relevant personnel, in accordance with the sponsoring institution guidelines.
- **Determining Labor Costs**. CIBMTR staff review similar past projects for applicable actual costs. They apply standard or approved federal labor rates, as applicable.
- **Assessing Travel and Meeting Expenses**. CIBMTR staff carefully estimate travel expenses, which can comprise a substantial part of a project budget. Working, Advisory, and Executive Committee Chair travel stipends, as well as operational staff travel expenses, affect these travel costs.
- **Estimating Other Direct Costs**. CIBMTR staff work with MCW or NMDP Contracts and Purchasing to obtain cost estimates or bids from external product and service providers.
- **Determining Government or Institutional-Approved Fringe and Indirect Rates**. CIBMTR staff use these rates for all project budgets, unless otherwise directed by management or the granting agency.

Proposed budgets must be approved by MCW or NMDP. Proposals are negotiated by the respective institution, supported by the scientific personnel and NMDP Finance or CIBMTR Business Office. MCW budget proposals are submitted by CIBMTR's Business Office to the Grants and Contracts Office via the online eBridge system. This site allows MCW faculty and research staff to submit, track, report, and archive applications involving funding proposals as well as human subject and animal research conducted at MCW. All proposal approvals, budgets, and awards are managed through this system, including sub-awards issued and received. Upon award, the MCW Office of Sponsored Programs or NMDP Finance assigns unique general ledger / project account numbers to track expenses and billing. NMDP Finance prepares fee schedules for projects such as the SCTOD (**Section 6.2**) in collaboration with the applicable CIBMTR personnel.

19.3 INVOICING AND CONTRACT MANAGEMENT

NMDP and MCW prepare invoices based on actual costs incurred and / or projections of costs (if advance invoicing is allowed) and upon the terms of the grant or contract. Staff members issue invoices to the appropriate agency, and NMDP Finance or the MCW Office of Sponsored Programs tracks to ensure prompt payment. NMDP and MCW CIBMTR also internally track payments processed by detailed category to provide CIBMTR Leadership with timely reporting of costs incurred as well as ongoing projections for the entire grant / contract period.

Any revisions or amendments to contracts must be approved by CIBMTR Leadership and processed with respective institutional approvals. All contracts are closed out in accordance with the terms in the contract and the relevant government regulations, and they adhere to the standard operating procedures of each institution.

CHAPTER 20: INTERNATIONAL PARTNERS

The cellular therapy field has benefitted from an international collaboration of organizations that collect, analyze, and share data to address important clinical research efforts that affect the global community. Hundreds of centers worldwide submit outcome data to CIBMTR, many since the time of its inception in 1972. The IBMTR, precursor to CIBMTR, established research and data sharing relationships first with the European transplant groups / registries and has since developed strong collaborative relationships with other groups worldwide. CIBMTR and EBMT established a Memorandum of Understanding that supports project-specific data sharing under the guidelines of the General Data Protection Regulation.

CIBMTR often collaborates on research studies with cellular therapy groups within and outside the US. The lead researcher or group proposes the study and presents it to CIBMTR's Working Committees, and CIBMTR and its collaborator(s) determine issues such as data sharing plans, analyses, and writing / authorship early in the process. **Chapters 3, 6,** and **14** address this in more detail.

CIBMTR is one of the four founding members of the WBMT along with the APBMT, EBMT, and WMDA. The WBMT's mission is to promote excellence in HCT through collaboration of existing international societies using coordination, communication, and advocacy. It engages in charitable, scientific, and educational activities to promote and foster scientific and clinical disciplines, information exchange, and recipient and donor research relating to cellular therapy. Learn more about the WBMT and its 21 Member Societies on the *WBMT* website.

In addition to the Member Societies of the WBMT, CIBMTR has relationships with many other international organizations (**Table 20.1**). These relationships include, but are not limited to advocacy, policy, data sharing, and standards.

Table 20.1: International Organizations with which CIBMTR Collaborates

Organization	Description
American Society for Transplantation and Cellular Therapy (**ASTCT**) *astct.org*	ASTCT is an international association dedicated to improving the application and success of HCT and related cellular therapies.
American Society of Hematology (**ASH**) *hematology.org*	ASH is a professional society fostering high-quality, equitable care, transformative research, and innovative education to improve the lives of patients with blood and bone marrow disorders.
American Society for Histocompatibility and Immunogenetics (**ASHI**) *ashi-hla.org*	ASHI is an international society of professionals dedicated to advancing the science, education, and application of immunogenetics and transplant immunology.
Asia-Pacific Blood and Marrow Transplantation Group (**APBMT**) *apbmt.org*	APBMT is an international organization promoting all aspects associated with HCT and related therapies in the Asia-Pacific region.

Organization	Description
Australasian Bone Marrow Transplant Recipient Registry (**ABMTRR**) *abmtrr.org*	ABMTRR operates under the auspices of the Bone Marrow Transplant Society of Australia and New Zealand to record details of bone marrow, PBSC, and cord blood stem cell transplants throughout Australia and New Zealand.
Cord Blood Association *cb-association.org*	The Cord Blood Association is an international nonprofit organization that promotes both public and family cord blood banking and accelerates the use of cord blood and birthing tissues to benefit patients and advance medicine.
Cell Therapy Transplant Canada (**CTTC**) *cttcanada.org*	CTTC is leading national efforts to improve patient lives in HCT and cell therapy through education, clinical care, research, and advocacy in Canada and worldwide.
Children's Oncology Group (**COG**) *childrensoncologygroup.org*	COG is a National Cancer Institute-supported clinical trials group devoted exclusively to childhood and adolescent cancer research.
Deutsche Knochenmarkspenderdatei (**DKMS**) dkms.org	DKMS is an international nonprofit organization dedicated to the fight against blood cancer and blood disorders by creating awareness, recruiting bone marrow donors to provide a second chance at life, raising funds to match donor registrations costs, and supporting the improvement of blood cancer therapies by its own research.
Eastern Mediterranean Blood and Marrow Transplantation (**EMBMT**) *embmt.org*	EMBMT promotes all aspects of patient care, academic, and research activities associated with HCT in Eastern Mediterranean countries with the goal of sharing experience, initiating cooperative trials, and establishing common strategies to achieve optimization in the HCT field.
Eurocord eurocord.org	Eurocord is a clinical research group dedicated to studying cord blood transplantation and innovative therapy in both malignant and non-malignant diseases. The organization seeks to develop new indications for stem cell therapy.
European Federation for Immunogenetics (**EFI**) efi-web.org	EFI promotes the advancement of immunogenetics in Europe and supports research and training in the field. It also supports research in histocompatibility testing and HCT.

Organization	Description
EBMT (formerly known as the European Society for Blood and Marrow Transplantation) *ebmt.org*	EBMT aims to improve outcomes of cellular therapy and provide information to the public about developments in the field by sharing the experience of European centers and encouraging cooperative research among scientists and physicians in the field.
Foundation for the Accreditation of Cellular Therapy (**FACT**) *factglobal.org*	FACT is a nonprofit organization that establishes standards for high-quality medical and laboratory practice in cellular therapies for the purposes of voluntary inspection and accreditation in the field of cellular therapy.
International Histocompatibility Working Group (**IHWG**) *fredhutch.org/en/research/institutes-networks-ircs/international-histocompatibility-working-group.html*	IHWG provides a comprehensive inventory of HLA reference genes to support worldwide research in immunogenetics. They also offer selected cell lines and DNA from their substantial DNA Bank of more than 1,000 cell lines from selected families, as well as individuals with diverse ethnicity and immunologic characteristics.
International Society of Blood Transfusion (**ISBT**) *isbtweb.org*	ISBT is an international professional society that facilitates knowledge about transfusion and transplantation science and medicine.
International Society for Cell and Gene Therapy (**ISCT**) *isctglobal.org*	ISCT is a global association that promotes cellular therapy research by fostering international translational research, driving commercialization strategies, and providing education.
Japan Data Center for Hematopoietic Cell Transplantation (**JDCHCT**) *jdchct.or.jp*	CIBMTR and the JDCHCT have collaborated to develop a structure to capture data from patients treated with CAR-T in Japan. This collaboration includes translating forms to Japanese and collecting data. The JDCHCT has access to all data collected from Japanese centers, and they operate the cellular therapy registry using this infrastructure.
Japanese Society for Transplantation and Cellular Therapy (**JSTCT**) *jstct.or.jp/modules/en/index.php*	JSTCT's research aim is to provide safe and effective therapies for patients with intractable hematological disorders by working in collaboration with other academic societies, non-government organizations, industry, and administration. JSTCT members play key roles in steering the Japan Marrow Donor Program, Japan Cord Blood Bank Network, APBMT, and WBMT.

Organization	Description
Joint Accreditation Committee – ISCT (Europe) & EBMT (**JACIE**) *jacie.org*	JACIE is a nonprofit organization that assesses and provides accreditation in the field of HCT and cellular therapy. Its primary aim is to promote high-quality patient care and laboratory performance in collection, processing, and transplantation centers through an internationally recognized system of accreditation.
Latin American Bone Marrow Transplantation group (**LABMT**) *wbmt.org/member-societies-of-wbmt/labmt*	The purpose of LABMT is to provide a mechanism through which Latin American HCT and hematology groups can collaborate and engage in scientific and educational activities. LABMT promotes excellence in HCT, stem cell donation, cellular therapy, and accreditation in Latin America. Activities include data collection and sharing outcome information.
Pediatric Transplantation and Cellular Therapy Consortium (**PTCTC**) *theptctc.org*	The purpose of PTCTC is to support research and education to improve the availability, safety, and efficacy of HCT and other cellular therapeutics for children and adolescents.
Primary Immune Deficiency Treatment Consortium (**PIDTC**) *pidtc.rarediseasesnetwork.org*	PIDTC consists of 47 centers in North America whose shared goal is to improve the outcome of patients with rare, life threatening, inherited disorders of the immune system. The immediate focus of the consortium is to concentrate on four severe immune disorders, which can be cured by HCT, enzyme replacement, and/or gene therapy by bringing together physicians and scientists who evaluate and care for the majority of children with PID in North America. The PIDTC developed a centralized computerized registry with the eventual aim of including all patients diagnosed with inherited immune diseases in North America.
Sociedade Brasileira de Terapia Celular e Transplante de Medula Óssea (**SBTMO**) *sbtmo.org.br*	The SBTMO and CIBMTR have a long-standing relationship to assist in promoting registry activities in Brazil. Initial collaborations included active participation at their annual meetings through education for data managers about CIBMTR and to health care professionals about clinical research methodology. CIBMTR and SBTMO started a project to develop a national registry using FormsNet, whereby centers report data to CIBMTR and these data are shared with SBTMO to run analysis on transplant activities and outcomes.

Organization	Description
Society for Immune Polymorphism *immunepolymorphismsociety.org*	The Society for Immune Polymorphism is an international membership organization of scientists dedicated to understanding the genetic and functional variation of the vertebrate immune system and the immune system's role in evolutionary biology, disease, and health. Together with its members, the Society's vision is increased collaboration, engagement, and sharing of domain knowledge among scientists focused on any aspects of immune-related genomics.
Worldwide Network for Blood and Marrow Transplantation (**WBMT**) *wbmt.org*	The WBMT promotes excellence in HCT, stem cell donation, cellular therapy, and accreditation as well as access to HCT worldwide through collaboration of existing international societies using coordination, communication, and advocacy. The purpose of this cooperation is to engage exclusively in charitable, scientific, and educational activities and endeavors, including promoting and fostering among the many scientific and clinical disciplines, the exchange and diffusion of information and ideas relating to HCT and other cellular therapies, and encouraging investigations on these matters.
World Marrow Donor Association (**WMDA**) *wmda.info*	WMDA is a global association whose mission is to assure that high-quality stem cell products are available for all patients in need, while maintaining the health and safety of volunteer donors. WMDA incorporates all functions previously undertaken by Bone Marrow Donors Worldwide and Netcord.

APPENDIX A: GLOSSARY / ACRONYMS

Term / Acronym	Definition
ABMTR	Autologous Blood and Marrow Transplant Registry
ABMTRR	Australasian Bone Marrow Transplant Recipient Registry
ACT	adoptive cellular therapies
AGNIS	A Growable Network Information System®
APBMT	Asia-Pacific Blood and Marrow Transplantation Group
API	Application Programming Interface
ASCO	American Society of Clinical Oncology
ASH	American Society of Hematology
ASHI	American Society for Histocompatibility and Immunogenetics
ASTCT	American Society for Transplantation and Cellular Therapy
BMT	blood and marrow transplant
BMT CTN	Blood and Marrow Transplant Clinical Trials Network
caDSR	Cancer Data Standards Registry and Repository
CAR-T	chimeric antigen receptor T cell
CDE	common data elements
CED	Coverage with Evidence Development
CFR	Code of Federal Regulations
CIBMTR	Center for International Blood and Marrow Transplant Research
CIT	CIBMTR Information Technology group
CMS	Centers for Medicare and Medicaid Services
COG	Children's Oncology Group
CPA	Center Performance Analytics
CPI	Continuous Process Improvement – CIBMTR's form completion compliance program
CRA	CIBMTR Reporting Application
CRF	Comprehensive Report Form
CRID	CIBMTR Recipient ID Assignment
CRO Services	CIBMTR Clinical Research Organization, formerly known as the Resource for Clinical Investigations in Blood and Marrow Transplantation (RCI BMT)
CTED	Cellular Therapy Essential Data
CTTC	Cell Therapy Transplant Canada
CVDR	Center Volume Data Report

Term / Acronym	Definition
DBtC	Data Back to Center
DCC	Data and Coordinating Center (of the Blood and Marrow Transplant Clinical Trials Network)
DISCO	Data and Information for Coordinating Center Operations
EDC	Electronic Data Capture
EFI	European Federation for Immunogenetics
EHA	European Hematology Association
ELN	European Leukemia Network
EMBMT	Eastern Mediterranean Blood and Marrow Transplantation
EMDIS	European Marrow Donor Information System
ePRO	electronic patient-reported outcomes
ETL	extract, transform, and load
FACT	Foundation for Accreditation of Cellular Therapy
FDA	Food and Drug Administration
FHIR	Fast Healthcare Interoperability Resources
GOCO	government-owned, contractor-operated
GVHD	graft-versus-host disease
HCT	hematopoietic cell transplantation
HIPAA	Health Insurance Portability and Accountability Act
HLA	human leukocyte antigen
HRSA	Health Resources and Services Administration
IBMTR	International Blood and Marrow Transplant Registry
ICMJE	International Committee of Medical Journal Editors
ICML	International Conference on Malignant Lymphoma
IDW	integrated data warehouse
IOTN	Immuno-Oncology Transplantation Network
IRB	Institutional Review Board
ISBT	International Society of Blood Transfusion
ISCT	International Society of Cellular Therapy
IT	Information Technology
JACIE	Joint Accreditation Committee-ISCT (Europe) & EBMT
JDCHCT	Japanese Data Center for Hematopoietic Cell Transplantation
JAMA	The Journal of the American Medical Association

Term / Acronym	Definition
LABMT	Latin American Bone Marrow Transplantation group
MCW	Medical College of Wisconsin
MDS	myelodysplastic syndrome
MHC	major histocompatibility complex
MS	Master of Science (-level Statistician)
NCBI	National Center for Biotechnology
NCI	National Cancer Institute
NHLBI	National Heart, Lung, and Blood Institute
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NIHMS	National Institutes of Health Manuscript Submission
NIST	National Institute of Standards and Technology
OMB	Office of Management and Budget
PBSC	peripheral blood stem cell
PI	Principal Investigator
PID	primary immune deficiency
PIDTC	Primary Immune Deficiency Treatment Consortium
PII	personally identifiable information
PMCID	PubMed Central Identification
PRO	patient-reported outcomes
PROMIS	Patient-Reported Outcomes Measurement Information System
RFI	Request for Information
SBTMO	Sociedade Brasileira de Terapia Celular e Transplante de Medula Óssea
SCTOD	Stem Cell Therapeutic Outcomes Database
SOP	Standard Operating Procedure
TED	Transplant Essential Data
US	United States
WBMT	Worldwide Network for Blood and Marrow Transplantation
WMDA	World Marrow Donor Association

APPENDIX B: GUIDELINES FOR CIBMTR STUDY PRINCIPAL INVESTIGATORS

The role of a Study Chair / PI is to behave ethically and do whatever it takes to complete the study that answers your research question. It is easier to accomplish this task if you have an understanding of CIBMTR study process, specifically where and when your efforts are most needed. The following document will explain the life cycle of a CIBMTR observational study and review the responsibilities of a PI. Hints and tips to make the study process as successful as possible are noted with an arrow (→).

STUDY PROPOSAL

The PI is generally the first person who suggests the study and who prepares the *Study Proposal*. Ideally the PI presents his or her proposal during a Working Committee meeting (typically held during the Tandem Meetings). These presentations are very important because they allow the PI to advocate for the study. Successful Working Committee study proposals are feasible and unique, and they have high scientific impact. CIBMTR Working Committee hours and resources are limited, so the committee is very selective in which studies they accept.

→ Before preparing the proposal, please read CIBMTR's *Study Proposal Guide (PDF)*. CIBMTR study proposal guidance will assist you in the development of your proposal. This document is designed to assist in making your proposal successful. Please review to determine if your study question is best answered through CIBMTR.

→ Please look at the data collection forms prior to preparing your proposal. Many people propose studies that require data not collected routinely by CIBMTR. Studies that require additional data collection usually get greater scrutiny because of the extra time and effort required whenever centers have to be contacted for additional data. Additionally, the response rate to requests for supplemental data is often disappointing – ask your own data managers how difficult it is to go back and find data for patients who underwent cellular therapies years ago. The ability to collect supplemental data successfully depends on how complex and / or extensive the data are, the size of the study population, how far back in time the transplants were done, and whether you have resources (people or funds) to assist in the process.

Note that study proposals may be submitted *throughout the year*. The vast majority are submitted just before the deadline, three months before the Tandem Meetings. If you want your proposal to benefit from greater CIBMTR statistical and scientific input, then submitting your proposal far in advance is helpful. Proposals submitted throughout the year will be reviewed by the Working Committee leadership. They have the authority to approve a proposal based on the importance of the scientific question or they may elect to defer it until presentation at the annual meetings of ASTCT and CIBMTR.

PRIORITIZATION AND DISTRIBUTION OF STATISTICAL HOURS

After the Tandem Meetings, the Working Committee Chairs, Scientific Directors, Statistical Directors, and Statistical Staff meet to discuss the results of the meeting and prioritize new and ongoing studies. Studies are assigned Coordinating Center hours according to their need and priority. In general, a study needs 100 hours of Statistical Staff time to finish the protocol, 100-140 hours to prepare the data file (depending on whether additional data collection, follow-up, or excessive data cleaning is necessary), 60 hours for the analysis phase, 20 hours for manuscript preparation, and 10 hours for submission and response to reviewers. PIs are generally notified about Committee decisions (i.e., approval, prioritization) regarding their proposals within one month after the meeting and after final Advisory Committee approval of the complete research agenda. At that time, the Working Committee Statistician serves as the point person for communications.

→ PIs can increase the chance of their proposal being approved by carefully preparing the Proposal Form that is presented to the Working Committee. Discussion with CIBMTR Working Committee leadership in advance of the Working Committee meeting may help clarify the study and address study design questions. Many great concepts fail because PIs do not consider available data, size of the available study population, power calculations, and other statistical issues. The Working Committee is much less receptive to studies that appear to have multiple unresolved issues at the meeting.

STUDY PROTOCOL

The next step in the study's life is generation of the study protocol. This is an important document that is first drafted by the PI based on discussions with the last author and submitted to the Statistician. The draft study protocol should be completed by the date specified by the Coordinating Center in the "Letter of Commitment." In preparing this document, it is crucial to carefully consider the variables to be included in the analysis, because the Statisticians and Scientific Directors use these documents to guide data collection and cleaning. Common pitfalls include failure to include important variables to address study hypotheses and failure to consider potentially confounding variables. A table with a preliminary description of the proposed study population is added, and the draft protocol is presented for discussion at a weekly Coordinating Center meeting. After the initial draft is reviewed and approved by the Coordinating Center, it is circulated to the Working Committee for comment; at that time, Committee members may request to participate in the study and a Writing Committee is formed (see below). Individuals wishing to serve on the Writing Committee provide substantive comments on the study protocol. It is the PI's responsibility to collate and address these comments by either modifying the protocol or providing an explanation for not incorporating suggested changes. Since Writing Committee members earn their authorship by reviewing the study protocol, analyses, and manuscripts, CIBMTR also keeps track of comments and contributions.

→ Each study protocol is reviewed at the weekly Coordinating Center conference call / meeting (held on Tuesdays, 9:00-10:00 am US Central Time) before distribution to the Working Committee; typically, the PI will present the protocol and participate in the discussion of the study's design and implementation. (Studies are again discussed at a Coordinating Center weekly meeting as they reach significant milestones. PI participation in each of these discussions is strongly encouraged.)

→ The most successful PIs respond to Writing Committee critiques as they do journal reviews — by carefully organizing them and responding to each. If a Writing Committee member brought up an issue, it is likely that a reviewer will also bring up the same points. It is expected that the PI will summarize and respond to these critiques within three weeks after the deadline for comments has passed.

→ PIs have a great deal of control over the time between study proposal approval and the completion of a final study protocol. Timely submission of the draft protocol and response to Writing Committee comments can vault your study ahead of others in terms of Coordinating Center priority. If yours is ready to go and another is not, yours may be given priority, even if initially it was planned for the other study to be done first.

DATA COLLECTION

If supplemental data collection is needed for the study, approval from CIBMTR Senior Leadership is required. The PI needs to provide the following information for the approval: 1) number of questions, 2) types of questions, 3) number of cases and 4) the study calendar.

Once the request has been approved, the "CIBMTR Forms Revision Team" will prepare a supplemental form for review within one week. This draft form will be a Word document

listing all the supplemental questions that are relevant, as well as the most frequent response options. This form will have input from the Scientific Director, PI, Study Statistician, Metadata and Data Operations Staff for clarity, length, internal consistency of response options, and feasibility of data extract. The form will be formatted to be consistent with other CIBMTR forms, and a table will be created in the database to receive the data. This step is very important for any study collecting additional data. If the form is long or leaves out critical variables, the ultimate study results could be compromised by missing data.

The supplemental form will go to CIBMTR Senior Leadership, Scientific Director, and PI for final approval. The Scientific Director and PI will prepare a letter detailing the importance of the data needed for the study with a copy to the Medical Director. This letter will be sent with the study request. If terms or concepts on the supplemental data collection form are unfamiliar to the data management teams, an instruction manual that describes the variable and provides examples of how data managers should interpret primary data will have to be written.

Each study is assigned a Clinical Research Coordinator who communicates with centers to facilitate data submission. Most, but not all, centers are very responsive to these requests. If some centers are lagging behind in submitting extra forms, PIs may need to make personal email or phone appeals.

→ Providing the initial draft form and content for the instruction manual is the responsibility of the PI. Delay in putting it together can significantly delay initiating the data collection process. If the process is inordinately delayed so that the data needed for a study is not available in a timely manner, the study may be deferred to the next year.

→ For smaller studies, where every patient counts, personal appeals from the PI to the Transplant Center Director can sometimes be very effective.

DATA FILE PREPARATION

In this step, the Statistician prepares a data file using the finalized study protocol as guidance. Data interpretation issues may arise here, especially if uncommon variables are necessary for the study. Values for common variables have probably already been reviewed and, if missing or out of range or inconsistent, already clarified (data "cleaning") for other studies. If your study is the first to examine a particular variable or study population, then expect to do a lot of data cleaning.

→ The PI can accelerate this process by being available to the Statistician and Scientific Director as questions come up. The PI should also carefully review the frequencies of study variables for outliers and other clinical inconsistencies.

UNIVARIATE ANALYSIS

Once the data file is prepared, the Statistician performs as much of the analysis as possible before handing the data set to the Statistical Director assigned to the project. First, a table of study population characteristics containing all the variables listed in the protocol and preliminary univariate analysis is prepared. This is reviewed by the PI and Scientific Director. When they are satisfied with the population, the study may be scheduled for another Coordinating Center weekly meeting / conference call to confirm final composition of the population and study design and review the univariate analysis before multivariate analyses are performed. Relevant comments from the Coordinating Center review will be summarized by the Statistician and the Scientific Director and relayed back to the PI for comment if the PI cannot participate personally in the meeting.

→ As noted above, the PI is invited to participate in CIBMTR Coordinating Center Meeting (Tuesdays) when his or her study is discussed. It is worth repeating that it is very helpful

for the PI to participate since they can often address questions as they arise so that the statistical input is most helpful.

MULTIVARIATE ANALYSIS

Once the population characteristics and univariate analyses are approved, the data file is transmitted to the Statistical Directors for multivariate and more complex modeling. When completed, results are sent to the PI and Scientific Director who prepare a memo for circulation to the Writing Committee for comments after review at the weekly statistical meeting. The comment period usually lasts two to three weeks. The PI summarizes the comments and prepares another memo for the Writing Committee within three weeks of the close of the comment period. If substantive issues arise, especially related to the study population or analyses, then a conference call involving the PI, Scientific Director, Statistical Director, and Statistician may need to be convened to plan an approach for addressing the comments.

→ The most successful PIs take advantage of the Statisticians' and Statistical Directors' familiarity with the project and the data to finish their analyses quickly. If extended time passes between each phase of the analysis, the Statisticians will need to re-familiarize themselves with the project and coding. A task that could take a couple of hours immediately after the initial results are completed may take much longer a month or two later (and the Statisticians understandably will be less excited about picking up the project again).

ABSTRACTS

Many PIs hope to submit abstracts to national and international meetings. Multivariate analyses must be complete with enough time to allow generation of an abstract. These abstracts must be circulated to the Writing Committee and reviewed by the Coordinating Center staff prior to submission. Please allow enough time to complete these steps before the abstract deadline. If the abstract is accepted for oral presentation, the Coordinating Center staff will also need to review the slides, primarily for accuracy but sometimes also to make suggestions for clarity. CIBMTR has a template for format and background that is required for all presentations.

→ Planning for ASH and other meeting abstracts happens immediately after the Tandem Meetings. If you would like to submit your abstract to one of these meetings, an early declaration of your intentions and demonstrable effort in moving towards that goal will result in your study getting higher priority.

→ In general, studies are only submitted to one meeting; once submitted in abstract form, priority should be placed on writing and submitting the manuscript.

→ Submission of abstracts should not delay preparation of manuscripts. PIs are expected to meet manuscript preparation deadlines independently of abstract submission.

MANUSCRIPT

Once the analysis is completed, drafting the manuscript is the responsibility of the PI and the Last Author. A draft manuscript is expected within three months of receiving Writing Committee comments on the final study results. The draft is circulated to the Writing Committee and comments are again summarized and incorporated. At least one round and sometimes up to three or more rounds are necessary to create a final manuscript. CIBMTR will do the final formatting for journal submission, attach all the co-authors' information (such as institution and contact information), collect any necessary signatures, and submit the paper. CIBMTR has a long list of acknowledgements for funding sources that is attached to the paper.

→ The initial manuscript draft usually causes the greatest delay in study progress and is the step most directly under control of the PI. The most successful PIs recognize that publishing their study results is a critical measure of success for all involved parties—themselves, CIBMTR, and all the collaborators involved in the study. Working Committee Chairs have the authority to reassign a study to a different PI if the delay in manuscript preparation is too long (> 60 days).

ACCEPTANCE

Unless the paper is accepted on the first submission, it will need to be revised or resubmitted. If comments are straightforward, the PI can prepare a response to reviewers for circulation, along with the revised version. Some comments from reviewers require additional analyses or discussion at a Coordinating Center meeting prior to resubmission. CIBMTR will assist with manuscript resubmission. Once the paper is accepted, the PI also handles proof review.

→ Unless a study is completed in record time, it will be "in progress" at the next Tandem Meetings. PIs should plan to present a study update at CIBMTR Working Committee meeting or designate another person on the Writing Committee to do this, as long as the study is active.

→ Any expected or unexpected deviations from the above timetable should be discussed between the PI and the Scientific Director. Sometimes unavoidable delays are due to either CIBMTR or the PI. A proactive plan designed to keep the study moving forward should be devised. Generally, CIBMTR expects studies to be completed within 18-24 months.

APPENDIX C: GUIDELINES FOR ACQUIRING PUBMED CENTRAL IDENTIFICATION (PMCID) NUMBERS

All publications funded by the NIH must comply with the *NIH Public Access Policy*. This policy, which applies to any NIH-funded (including all agencies under the NIH), peer-reviewed material accepted on or after April 7, 2008, requires acquisition of a PubMed Central Identification (PMCID) number. This includes data supported by the NCI, the NHLBI, and the NIAID. The *NIH* website has a complete list of all agencies that are under it.

The PMCID is a unique number assigned to a work that is posted to *PubMed Central*, a free digital archive of biomedical and life sciences journal literature at the NIH, developed and managed by NIH's National Center for Biotechnology Information in the National Library of Medicine. All works applicable under the NIH Public Access policy are posted to PubMed Central.

NIHMS facilitates submission of final, peer-reviewed manuscripts online. When a manuscript is accepted, most but not all journals will then submit the paper to NIHMS. If the journal does not provide this service, the corresponding author, or another designated individual, must do so. If they are unable to do so, then CIBMTR must complete this. View the *NIH* website for more information.

When the manuscript is accepted by NIHMS, a NIHMS identification number is assigned, and the following three steps occur:

- **Approve PDF Receipt**: A PDF version is sent to the Corresponding Author to verify that the correct manuscript was submitted. The NIHMS email subject line is "Approve PDF Receipt" (email displays NIHMS #). The Corresponding Author must approve the PDF.
- **Undergoing NIHMS submission review and file preparation / Undergoing conversion to PubMed Central (PMC) documents**: The PDF version that was approved is being converted into the final web version.
- **Approve Web Version**: A second mailing is sent to the Corresponding Author asking to "Approve Web Version." The PMCID assignment is contingent on final approval of this web version by the Corresponding Author.

CIBMTR employs two methods for submitting manuscripts to a journal to ensure compliance with PMCID requirements:

- CIBMTR submits the manuscript (preferred);
- Principal Investigator / corresponding author submits the manuscript.

If a Principal Investigator / corresponding author prefers submitting their own manuscript, CIBMTR requests that they follow the guidelines outlined below and in **Chapter 4** to inform the Coordinating Center that a paper has been submitted on behalf of CIBMTR. In *either* case, the **designated reviewer is responsible for the required interactions** with NIHMS after paper is accepted.

The following documents should be included with manuscript submissions:

- A CIBMTR "Data Sources Statement" (**Appendix E**);
- CIBMTR Support List for the research study (see SOP-0072: Working Committee Manuscript Preparation and SOP-0073: Working Committee Manuscript Submission); Acknowledgement of NIH funding if applicable (e.g., "CIBMTR NIH Support Verification Letter") (**Appendix F**).

When the journal asks if the manuscript and / or data are NIH-funded, respond "yes if applicable."

The proper CIBMTR grant number is **U24-CA076518**.For other grant numbers (e.g. for BMT CTN), please contact the respective Program Manager.

APPENDIX D1: LETTER OF COMMITMENT TO COMPLETE CIBMTR OBSERVATIONAL STUDIES

Date

PI's name

PI's address

PI's address

Re: PRINCIPAL INVESTIGATOR (PI) COMMITMENT TO COMPLETE A CIBMTR OBSERVATIONAL STUDY

CIBMTR study # and title

Dear Dr. PI's last name:

Congratulations on the approval of your proposal as a CIBMTR study. The commitment and expertise of Principal Investigators (PIs), like you, is vital to our ability to conduct the highest quality scientific analyses. The study process, and preparation of a study dataset in particular, are rigorous, so it is critical for PIs to work closely with CIBMTR scientific and statistical staff to successfully complete their projects in a timely fashion. We recognize that you are likely to commit a substantial amount of time to this project, and we will support your efforts.

Please review the following list of PI expectations. We will begin the study or dataset preparation process after we receive your acknowledgement and acceptance of these responsibilities:

- Read CIBMTR Guidelines for Principal Investigators.
- Read CIBMTR Guidelines for acquiring PubMed Central Numbers (PMCID).
- Assist the Working Committee leadership and Coordinating Center staff in developing a reasonable timeline for study completion.
- Prepare a first Draft Study Protocol by *Date* of this year.
- Prepare the Final Study Protocol (taking into consideration all Writing Committee comments) within four weeks of distribution date to full Working Committee (CIBMTR will remind you two weeks in advance).
- Participate actively in teleconferences and meetings (e.g., weekly Statistical Staff meetings upon invitation). Typically, the PI will be the presenter of the study at the weekly Statistical Meetings.
- Participate actively in data file preparation and analyses.
- Prepare a first draft of the manuscript within three months of receiving Writing Committee comments on the final study results.
- Submit to a journal the final draft of the manuscript within six months of receiving Writing Committee comments on the final study results.
- Prepare study materials, as necessary, for submission for meeting presentation.

- Collaborate with CIBMTR Coordinating Center in submitting the manuscript, or (rarely) submit per CIBMTR guidelines.
- Submit the *International Committee of Medical Journal Editors (ICMJE) form* regarding conflicts of interest to CIBMTR Coordinating Center.
- Address comments from reviewers, with input from CIBMTR Working Committee leadership and other co-authors.
- Respond to editorial questions and approve galley proofs.

If you are unable to meet the responsibilities outlined above, Working Committee or CIBMTR Leadership may assign your role to someone else and/or decline to credit your participation in the finished product. These consequences are unlikely, as most PIs successfully fulfill their responsibilities; however, it is essential that you complete activities in a timely fashion.

By signing this Letter of Commitment, you state that you clearly understand your responsibilities, and you agree to optimize this opportunity to complete a high-quality study in a timely manner. Please know that CIBMTR values your role and is prepared to support your efforts.

Please return this signed *Letter of Commitment* by the deadline noted in the accompanying email message (includes Co-PIs).

I certify that I have read this document and commit to fulfilling the responsibilities described herein.

Agreed by:

_____ _____

Signature of Principal Investigator Date

_____

Printed Name of Principal Investigator

_____

Study Number

PLEASE SCAN SIGNED FORM AND SEND TO CIBMTR

APPENDIX D2: DATA TRANSFER AND USE AGREEMENT

Center For International Blood & Marrow Transplantation Research ("CIBMTR") Data Transfer and Use Agreement ("Agreement")

Provider:	CIBMTR	Recipient:	
CIBMTR Contact		Recipient Contact	
Name/Title:		Name/Title:	
Email:		Email:	
Project Name		Agreement Term	
		Start Date:	Date of last signature
		End Date:	Three (3) years after start date

Terms and Conditions

1) Provider will provide the data set described in Attachment 1 (the "Data") to Recipient for the research purpose set forth in Attachment 1 (the "Project"). Provider shall retain ownership of any rights it may have in the Data, and Recipient does not obtain any rights in the Data other than as set forth herein.
2) If applicable, reimbursement of any costs associated with the preparation, compilation, and transfer of the Data to the Recipient will be addressed in Attachment 1.
3) Recipient shall not use the Data except as authorized under this Agreement. The Data will be used solely to conduct the Project and solely by Recipient Contact and Recipient's faculty, employees, fellows, students, and agents ("Recipient Personnel") and Collaborator Personnel (as defined in Attachment 3) that have a need to use, or provide a service in respect of, the Data in connection with the Project and whose obligations of use are consistent with the terms of this Agreement (collectively, "Authorized Persons"). Recipient must notify Provider of any change in Recipient and/or Recipient Contact listed above and request from Provider an amended agreement with the Recipient and/or Recipient Contact prior to the transfer of any and all responsibility for the Data.
4) Except as authorized under this Agreement or otherwise required by law, Recipient agrees to retain control over the Data, including information derived from the Data, and shall not allow the use of the Data to identify individuals and will not link or combine the data with other patient-level information, make copies of the Data, nor release or permit other to release the files, disclose, release, sell, rent, lease, loan, or otherwise grant access to the Data to any third party, except Authorized Persons, including but not limited to, without the prior written consent of Provider. Recipient agrees to establish appropriate administrative, technical, and physical safeguards to prevent unauthorized use of or access to the Data and comply with any other special requirements relating to safeguarding of the Data as may be set forth in Attachment 2.
5) Recipient agrees to use the Data in compliance with *CIBMTR's Data Use and Processing Policy* and with all applicable laws, rules, and regulations, as well as all

professional standards applicable to such research, including but not limited to obtaining and maintaining appropriate local IRB oversight consistent with the uses of the data where applicable. Documentation of IRB review (or documentation by the relevant IRB as to why review was deemed unnecessary under applicable regulation) must be provided to Provider prior to release of the dataset to the investigator.

6) **Confidentiality**. Recipient agrees that the Data are private and confidential and that Recipient will have in place and shall maintain administrative, technical, procedural, and physical safeguards sufficient to protect the confidentiality of the data, including preventing unauthorized access and use, Recipient will clearly describe any anticipated proprietary use of the Data or the work product that derives from use of the Data. Any proprietary uses of the data will require approval from the Provider prior to the release of the Data.

7) **Publications**. Any publication deriving from these data must contain a statement confirming the study was conducted in accordance with all applicable human subjects' protections laws and regulations. Recipient is encouraged to make publicly available the results of the Project. Recipient agrees to the following:

   - All data, a description of the methodology applied, and conclusions resulting from the Data must be reviewed by the Provider at least forty-five (45) days before any presentation, press release, other display or publication to ensure appropriate interpretation of the analysis and compliance with the terms of this Agreement.
   - A copy of any abstract, publication or presentation of work derived from the Data, along with a complete citation, shall be provided to the Provider within thirty (30) days of its presentation or publication.
   - All publications or presentations of the Data shall acknowledge Provider as a data source and will acknowledge that the findings presented by the author are not the opinion of the Provider or its funding sources without first obtaining approval from the Provider.
   - Should Recipient have sufficient Data and permission from Provider to combine the Data with other data from another group, Recipient agrees to share the final data file and analysis with the Provider.
   - Provider Guidelines regarding required funding source citation and acquisition of PubMed Central Numbers (PMCID) must be followed.

8) **Use of Name**. Neither party shall use the other party's name, trademarks, or other logos in any publicity, advertising, or news release without the prior written approval of an authorized representative of that party. The parties agree that each party may disclose factual information regarding the existence and purpose of the relationship that is the subject of this Agreement for other purposes without written permission from the other party provided that any such statement shall accurately and appropriately describe the relationship of the parties and shall not in any manner imply endorsement by the other party whose name is being used, Recipient agrees to recognize the contribution of the Provider as the source of the Data in all written, visual, or oral public disclosures concerning Recipient's research using the Data, as appropriate in accordance with scholarly standards and any specific format that has been indicated in Attachment 1.

9) **Termination**. Unless terminated earlier in accordance with this section or extended via a modification in accordance with Section 13, this Agreement shall expire as of the End Date set forth above. Either party may terminate this Agreement with thirty

(30) days written notice to the other party's Authorized Official as set forth below. Upon expiration or early termination of this Agreement, Recipient shall follow the disposition instructions provided in Attachment 1, provided, however, that Recipient may retain one (1) copy of the Data to the extent necessary to comply with the records retention requirements under any law, and for the purposes of research integrity and verification.

10) Recipient will destroy all Data or return all Data to Provider within six (6) months of the completion of the approved use; Recipient will certify in writing to Provider such destruction of all copies, including archival copies of the Data.

11) **Status Report**. Recipient will provide a status report to Provider one year after delivery of the dataset and annually thereafter, or upon request from Provider, until the approved use of the Data has been completed; this report will describe the status of the project approved for the use of the Data.

12) Except as provided below or prohibited by law, any Data delivered pursuant to this Agreement is understood to be provided "AS IS." PROVIDER MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESSED OR IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF THE DATA WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER PROPRIETARY RIGHTS. Notwithstanding, Provider, to the best of its knowledge and belief, has the right and authority to provide the Data to Recipient for use in the Project.

13) Except to the extent prohibited by law, the Recipient assumes all liability for damages which may arise from its use, storage, disclosure, or disposal of the Data. The Provider will not be liable to the Recipient for any loss, claim, or demand made by the Recipient, or made against the Recipient by any other party, due to or arising from the use of the Data by the Recipient, except to the extent permitted by law when caused by the gross negligence or willful misconduct of the Provider. No indemnification for any loss, claim, damage, or liability is intended or provided by either party under this Agreement.

14) No modification or waiver of this Agreement shall be valid unless in writing and executed by duly authorized representatives of both Parties.

15) Unless otherwise specified, this Agreement and the below listed Attachments embody the entire understanding between Provider and Recipient regarding the transfer of the Data to Recipient for the Project.

- Attachment 1: Project-Specific Information
- Attachment 2: Data-Specific Terms and Conditions
- Attachment 3: Identification of Permitted Collaborators (if any)
- *CIBMTR Data Use and Processing* by reference

The undersigned Authorized Officials of Provider and Recipient expressly represent and affirm that the contents of any statements made herein are truthful and accurate and that they are duly authorized to sign this Agreement on behalf of their institution.

By: _____ By: _____

(Authorized signature)	(Authorized signature)
(Printed Name)	(Printed Name)
Title:	Title:
Date:	Date:

Attachment 1: Data Transfer and Use Agreement Project-Specific Information

1) Description of Data:

[Instructions to the drafter; delete after completion of this section:

This section of this attachment should provide sufficient information such that each party understands the information that will be transmitted under this Agreement. Examples of information that should be provided include:

- Whether the data is obtained from human subjects and, if so, a description of the population included in the data
- If not from human or animal subjects, a description of the focus of the data
- The number of subjects and/or experiments included
- Name of the study that the data was obtained under

If there is a particular study that needs to be acknowledged/cited as the source of the data, this information should be included here.]

2) Description of Project:

[Instructions to the drafter; delete after completion of this section:

This section of this attachment should provide sufficient information such that each party understands the project that the Recipient will perform using the Data. Content of this section will be very similar to the Statement of Work used in other types of Agreements. Examples of information that should be provided include:

- Objective or purpose of the Recipient's work
- A general description of the actions to be performed by the Recipient using the Data and possibly the anticipated results
- Include whether or not the Recipient is permitted to link the Data with other data sets (If yes, be sure to include any special disposition requirements related to the linked data sets in Section 5 of this attachment).]

3) Provider Support and Data Transmission:

Provider shall transmit the Data to Recipient: (select one) ☐ electronically or ☐ by mail to:

Name:

Address:

Email:

Phone:

Name:

Address:

Email:

Phone:

Agreement ID:

Upon execution of this Agreement, Provider shall send any specific instructions necessary to complete the transfer of the Data to the contact person listed above, if not already included below in this section of Attachment 1.

[Instructions to the drafter; delete after completion of this section.

This section of this attachment should also provide sufficient information such that each party understands the level of support the Provider will supply to the Recipient. Examples of information that may be appropriate to include in this section are:

- Format of Data
- Provision of Data dictionary
- Availability of Provider to assist Recipient in understanding the Data structure (e.g. variables, code lists, etc.)
- If/how Data will be revised and resent if errors are found by the Recipient
- Specific instructions necessary to complete the transfer of the Data, if available/appropriate, and any support supplied by the Provider for the transfer.]

4) Reimbursement of Costs:

☐ None

☐ As governed by a separate written agreement between the parties

Reimbursement Agreement Reference # (if required):

_____

☐ As set forth herein:

5) Disposition Requirements upon the termination or expiration of the Agreement:

[Instructions to the drafter; delete after completion of this section:

This section of this attachment should provide sufficient information such that each party understands the Recipient's obligations with regards to the Data upon the expiration or early termination of this Agreement. If the Recipient is permitted to link the Data with other data sets, be sure to include any special disposition requirements related to the linked data sets in this attachment.]

Agreement ID:

Attachment 2: Data Transfer and Use Agreement Data-Specific Terms and Conditions

Additional Terms and Conditions:

1) If accessing the data from a remote location on a time-sharing Network, computer system or LAN with any statistical package, Recipient will not share with any other individual(s) any logon name or password provided by Provider.
2) The Data will not include personally identifiable information as defined in NIST Special Publication 800-122. If the Data being provided is coded, the Provider will not release, and the Recipient will not request, the key to the code.
3) If Provider is a Covered Entity, the Data will be de-identified data, as defined by the Health Insurance Portability and Accountability Act of 1996 ("HIPAA").
4) Recipient will not use the Data, either alone or in concert with any other information, to make any effort to identify or contact individuals who are or may be the sources of Data without specific written approval from Provider and appropriate Institutional Review Board (IRB) approval, if required pursuant to 45 CFR 46. Should Recipient inadvertently receive identifiable information or otherwise identify a subject, Recipient shall promptly notify Provider and follow Provider's reasonable written instructions, which may include return or destruction of the identifiable information.
5) By signing this Agreement, Recipient provides assurance that relevant institutional policies and applicable federal, state, or local laws and regulations (if any) have been followed, including the completion of any IRB or ethics review or approval that may be required.
6) Recipient shall promptly report to the Provider any use or disclosure of the Data not provided for by this Agreement of which it becomes aware.

Agreement ID:

Attachment 3: Data Transfer and Use Agreement Identification of Permitted Collaborators (if any)

For all purposes of this Agreement, the definition of "Collaborator Personnel" checked below will pertain:

☐ "Collaborator Personnel" means: None. No collaborators are permitted on the Project.

-OR-

☐ "Collaborator Personnel" means as set forth below and agreed upon between the Parties:

Sample definition language for the drafter; delete if the first option is checked or after a final definition has been agreed between the Parties:

"Collaborator Personnel" means: faculty, employees, fellows, or students of an academic institution, which institution (i) has agreed to collaborate in the Project, (ii) has faculty, employees, fellows, or students who have a need to use or provide a service in respect of the Data in connection with its collaboration in the Project, and (iii) has been made aware of the terms of this Agreement and agreed to comply, and to cause its personnel to comply, with such terms.

An alternative option for (iii); "has executed an agreement that is substantially similar to this Agreement"

APPENDIX E: DATA SOURCES STATEMENT

CIBMTR® (Center for International Blood and Marrow Transplant Research®) is a research collaboration between the Medical College of Wisconsin and NMDP. It comprises a voluntary working group of more than 360 participating centers worldwide that contribute detailed data on cellular and gene therapies. Participating centers are required to report all HCTs consecutively; reporting of other cell and gene therapies remains voluntary. Compliance is monitored by Clinical Research Staff and patients are followed longitudinally. Computerized checks for discrepancies, physicians' review of submitted data, and data audits of participating centers ensure data quality. Studies conducted by CIBMTR are performed in compliance with all applicable US federal regulations pertaining to the protection of human research participants. Protected Health Information used in the performance of such research is collected and maintained in CIBMTR's capacity as a Public Health Authority under the HIPAA Privacy Rule.

Globally, as required by that country's laws and regulations governing human subjects and privacy protection, the center is responsible for obtaining any necessary institutional review and approval of the protocols, "Research Database for Hematopoietic Stem Cell Transplantation, other Cellular Therapies, and Marrow Toxic Injuries," "Research Sample Repository for Allogeneic Hematopoietic Cell Transplantation, other Cellular Therapies, and Marrow Toxic Injuries," and "Protocol for Collection of Patient-Reported Outcomes Data," including the informed consent documents. The center must obtain consent of each patient participating in the research Protocol in a manner consistent with the laws and regulations in effect in that country.

CIBMTR collects data at two levels: Transplant Essential Data (TED) level and Comprehensive Report Form (CRF) level. HCT TED-level data are an internationally accepted standard data set that contains a limited number of key variables for all consecutive transplant recipients. TED-level data, with some additional details of donor and graft characteristics, comprise the obligatory data submitted to the SCTOD. When an HCT infusion is registered with CIBMTR, a subset of patients is selected for the CRF level of data collection through a weighted-randomization scheme. The CRF captures additional patient, disease, and treatment-related data. CIBMTR collects gene therapy data at the HCT CRF-level and other cellular therapy data with a suite of Cellular Therapy Essential Data (CTED) forms. CIBMTR selects the level of CTED reporting - TED or CRF - based on infusion-level details.

CIBMTR collects TED-level data for HCT and other cellular therapies and CRF-level data for HCT pre-treatment as well as post-treatment at 100 days, 6 months, annually until year 6, and at least biannually thereafter. CIBMTR collects gene therapy and CRF-level cellular therapy data pre-treatment as well as post-treatment at 100 days, 6 months, and every year annually through 15 years.

APPENDIX F: CIBMTR NATIONAL INSTITUTES OF HEALTH SUPPORT VERIFICATION LETTER

[DATE]

Dear [NAME],

Thank you for your attention to the enclosed submission. This article is based on research at the Medical College of Wisconsin (MCW) that is funded in whole or in part by grants from the National Institute of Health (NIH) and is therefore subject to the mandatory NIH Public Access policy (See *http://publicaccess.nih.gov/policy.htm*). As a matter of US federal regulation, the final, peer-reviewed manuscript must be deposited with the PubMed Central (PMC) database upon acceptance for publication and be made publicly accessible no later than 12 months after publication. In order to ensure compliance with this mandate and to be sure that copyrights are addressed appropriately, we ask that EITHER:

- You, as the publisher, submit the article directly to PubMed Central after acceptance. In this case, we can work with your standard publication contract and need only ask to be informed when submission is complete so that the required reference number(s) that must be used in subsequent NIH applications can be obtained. OR
- If the necessary language is not part of your standard publication agreement or copyright transfer, please include this additional wording, which is suggested by the NIH: "The Journal acknowledges that Bronwen Shaw, MD, PhD, retains the right to provide a copy of the final manuscript to the NIH upon acceptance for Journal publication, for public archiving *in PubMed Central as soon as possible but no later than 12 months after publication by Journal*."

In addition, please inform us of any applicable embargo up to the allowed 12-month delay. We will deposit the article in PMC. It is our hope that one of these options will be employed to ensure that we can cooperate to comply with this mandate. However, since this is a requirement of the current and future NIH funding which supports a great deal of research at MCW, we must ensure that our authors comply with the public access policy. If you accept this article for publication and none of the above options have been implemented, we will ask our authors to include the italicized passage above from the NIH as an additional term of any contract they sign and will proceed with depositing the article in PMC.

Thank you for your consideration and cooperation.

Sincerely,

Bronwen Shaw, MD, PhD

CIBMTR MCW Chief Scientific Director

Center for International Blood and Marrow Transplant Research

APPENDIX G: STUDY DEVELOPMENT CYCLE

This study development cycle pertains to studies for which CIBMTR provides data and statistical support (**Chapter 6**). Data sets are also made available to investigators who have their own statistical resources (**Chapters 14** and **15**). Manuscripts resulting from these analyses are reviewed and approved by CIBMTR prior to journal submission (**Chapters 3** and **4**).

PLANNING STAGE

- **Protocol pending**. Proposals remain in this preliminary stage until a draft protocol is created.
- **Protocol received**. PI sends a draft protocol to the Coordinating Center.
- **Protocol development**. The PI and invited Working Committee members develop a study proposal into a comprehensive study protocol. The protocol is refined in collaboration with the Working Committee study statistician, Statistical Director, Scientific Director, and Chairs. A table with a preliminary description of the proposed study population is added, and the protocol is presented for discussion at a weekly Coordinating Center meeting. When a protocol is approved, Working Committee members are invited to participate in a Writing Committee. Coordinating Center staff use the protocols to prepare data files for analysis and define the detailed study design. This document defines the study and how it progresses.
- **Ongoing**. Ongoing studies are long-term projects that require CIBMTR data and are supported by external funding sources, often multiple grants / renewals. Each study is assigned a Statistical Director.

IN PROGRESS

- **Sample typing**. During sample typing, the PIs perform laboratory tests (e.g., genotyping) on samples from the CIBMTR Biorepository (**Chapter 7**).
- **Supplemental form / data collection**. Most CIBMTR studies use routinely collected data. Use of supplemental data, including data not collected on CRFs (**Chapter 12**), is discouraged unless it will result in a particularly meaningful publication and/or external funding can support the extra burden placed on centers and supplement forms reimbursement costs. If necessary, a supplemental form must be developed and approved prior to soliciting centers for additional data. These forms are prepared by Coordinating Center staff in collaboration with the Principal Investigator and relevant Working Committee Chairs.
- **Data file preparation.** The objective of data file preparation is to create a file of eligible patients who are consecutively treated at participating centers with adequate follow-up, with minimal missing data fields, and in large enough numbers to give the analysis sufficient statistical power to meet the stated study objectives. This process involves a series of steps by the Statistician, sometimes working with the Clinical Research Coordinator, to ensure data quality:
    - Verifying selection criteria
    - Assessing follow-up
    - Determining the extent and nature of missing values and their potential effects on the study
    - Resolving and reconciling data discrepancies / outliers by examining data collection forms and communicating with centers and the Principal Investigator

    - Including and excluding patients so that the investigators can determine whether the final study population is representative of the target population (unbiased sample)
- **Analysis**. Analysis proceeds in several phases. The first generally includes a detailed description of the patient population and univariate analyses of study endpoints. These data are distributed to Writing Committee members for suggestions and comments. An iterative process then ensues, in which the Principal Investigator works with Coordinating Center staff to review comments from the Writing Committee. The process is repeated until final analysis, which serves as the basis for the manuscript.

PRELIMINARY RESULTS

- **Manuscript preparation**. The PI is primarily responsible for manuscript preparation and is expected to prepare a draft manuscript. The manuscript is distributed to Writing Committee members for suggestions and comments. An iterative process then ensues, in which the PI works with Coordinating Center staff to review comments from the Writing Committee. The process is repeated until manuscript is ready for submission. See **Chapter 3** for detailed guidelines regarding authorship.
- **Submitted**. Coordinating Center staff are generally responsible for submitting the manuscript and corresponding with the chosen journal. The Working Committee Scientific Director often serves as corresponding author. See **Chapter 4** for detailed guidelines regarding manuscript submission.
- **In press**. A publication is in press when it has been approved but does not yet have a citation.

COMPLETED

- **Published**. A manuscript is considered published when a citation is available, including a PubMed Central Identification (PMCID) number, if applicable. See **Appendix C** for detailed guidelines regarding PMCIDs.

APPENDIX H: STANDARD OPERATING PROCEDURES (SOP) INDEX

Following is a list of CIBMTR SOPs referenced in this Manual of Operations. For more information regarding CIBMTR SOPs, email *contactus@cibmtr.org*.

Chapter	SOP Title	SOP Number
1. Organization	N/A	
2. Committee Structure	CIBMTR Distinguished Service Award Nomination and Selection	SOP-0238
	Administrative Committee Meeting Minutes	SOP-0196
	CIBMTR Mortimer M. Bortin Lecturer Selection for Tandem Meetings	SOP-0237
	Working Committee Membership or Study in DISCO	SOP-0195
	Working Committee Conference Call	SOP-0076
	Conflict of Interest Policy	POL-0001
	Conflict of Interest Survey	Form-0001
3. Authorship	Working Committee Manuscript Preparation	SOP-0072
	Working Committee Manuscript Submission	SOP-0073
4. Manuscript Submission	Working Committee Manuscript Submission	SOP-0073
	Working Committee Manuscript Preparation	SOP-0072
5. Statistical Resources	N/A	
6. Clinical Outcomes Research	Working Committee Membership or Study in DISCO	SOP-0195
	Working Committee Conference Call	SOP-0076
	Scientific Director Guidelines	SOP-0070
	Haploidentical Donor Transplant Selection	SOP-0077
	Assessment for Inclusion of Data Based on Embargo and Consent Status	SOP-0281
	Assessment for Inclusion of European Union Data	SOP-0221
	Library of SAS Codes	SOP-0066
	Corporate Study Statistical Analysis Plan Preparation	SOP-0242
	Working Committee Manuscript Preparation	SOP-0072
	Working Committee Manuscript Submission	SOP-0073
	Data Sharing to Non-MCW or Non-NMDP Employees	SOP-0069

Chapter	SOP Title	SOP Number
	Statistical Operations Team Monthly Meetings	SOP-0075
	Advisory Committee Annual Working Committee Review Materials	SOP-0246
	Statistical Operations Time Tracking	SOP-0152
	Statistical Meetings	SOP-0068
	Review and Approval of Working Committee Studies	SOP-0067
	ePRO Configuration and Maintenance	SOP-0229
	Patient-Reported Outcomes Data Collection and Management	SOP-0232
7. Immunobiology Research	N/A	
8. Clinical Trials Support	N/A	
9. Health Services Research	N/A	
10. Bioinformatics Research	Custom Donor Search Process for the Development of Allogeneic Cell and Gene Therapies	SOP-0148
11. Industry Program	Scientific Director Guidelines	SOP-0070
	Corporate Office Phase 1 Engagement	SOP-0257
	Corporate Office Phase 2 Feasibility Assessment	SOP-0258
	Data Operations Prospective Studies Process	SOP-0300
	Business Operations Industry Project Management	SOP-0301
	Industry Protocol Development	SOP-0314
	Corporate Study Statistical Analysis Plan Preparation Standard Operating Procedure	SOP-0242
12. Data Management	Scheduling Transplant Center Audits	SOP-0149
	Transplant Center Audit Preparation	SOP-0150
	Transplant Center Audit Process	SOP-0151
	Transplant Center Corrective Action Plan Development, Evaluation and Approval	SOP-0269
13. Human Research Protection Program	N/A	

Chapter	SOP Title	SOP Number
14.Data – Access and Release	Data Release Policy	POL-0003
	Information Requests	SOP-0065
	Shared Publication Datasets	SOP-0119
	Data Sharing to Non-MCW or Non-NMDP Employees	SOP-0069
	Approval to Disclose PII for Linking or Computerized Matching Person Data to External Data Sources	SOP-0100
15.Information Technology Services	CIT System Development Lifecycle	SOP-0125
	Data Retrieval	SOP-0048
	Cellular Therapy Data Extract	SOP-0200
	DBtC Monthly Data Load Process	SOP-0051
	Survival Calculator Information and Update Process	SOP-0055
	Refresh Data for Center Performance Analytics	SOP-0117
	Maintaining CIT Information System Component Inventory	SOP-0160
	FormsNet Account Management	SOP-0163
	CIBMTR Incident Response Plan	Plan-0002
	Incident Response for Data/Systems Policy	POL-0019
	Vulnerability Scanning and Remediation	SOP-0059
	Configuration Management for Systems/ Data	POL-0009
	CIBMTR Contingency Planning Policy	POL-0018
	Security Awareness and Training Policy	POL-0005
16.Communication	Plain-Language Summaries of CIBMTR Research Publications	SOP-0172
	CIBMTR Annual Report SOP	SOP-0311
	CIBMTR RPPR Development	SOP-0165
	CIBMTR Quarterly External Newsletter	SOP-0173
17.Meetings	N/A	
18.Foundation Funding	N/A	
19.Federal Funding	N/A	

Document History

Date	Version	Description of Changes	Completed By
9/27/2012	1.0	First edition (posted to website)	Paula Watry
10/11/2012	1.1	Posted CIBMTR Advisory Committee review	Paula Watry
3/12/2013	1.2	Revised International Organizations with which CIBMTR Collaborates (Table 20.1) Revised Letter of Commitment to Complete CIBMTR Observational Study (Appendix D1) Revised Letter of Commitment for the Use of CIBMTR Datasets (Appendix D2)	Paula Watry Waleska Perez Doug Rizzo
7/1/2015	2.1	Reviewed and updated entire document	Vicki Vlach Jessica Gillis-Smith Patty Steinert
8/12/2016	3.1	Reviewed and updated entire document Added Working Committee Efficiency (Section 6.1.3) Added Bioinformatics Research (Chapter 10)	Jessica Gillis-Smith Waleska Perez Michael Wright Patty Steinert
7/1/2017	4.1	Reviewed and updated entire document Added Cellular Therapy Reporting (Section 12.2.3) Added Consolidation of FACT-CIBMTR Audits (Section 12.7.2.1)	Andrea Kusch Jessica Gillis-Smith Patty Steinert
7/21/17	4.2	Added HRSA Security Assessment SOP (Appendix M)	Jessica Gillis-Smith Patty Steinert
7/1/18	5.1	Reviewed and updated entire document Added SOP references Added CIBMTR Data Release Policy (Section 15.2.2) Added Electronic Patient-Reported Outcomes (Section 15.2.1.1.3) Added Appendix M: Standard Operating Procedures	Andrea Kusch Jessica Gillis-Smith Patty Steinert
8/13/19	6.1	Reviewed and updated entire document Added additional SOP references and numbers Added Cellular Therapy Research (Section 6.3), CMS CED Studies (Section 6.4), and PRO (Section 6.5) Restructured Appendix H: SOP Index	Liz Siepmann Jessica Gillis-Smith Patty Steinert
2/14/20	6.2	Updated CIBMTR Advisory Committee (Section 2.2.2) and CIBMTR Executive Committee (Section 2.2.3)	Liz Siepmann Jessica Gillis-Smith

Date	Version	Description of Changes	Completed By
		Added Reporting Guidelines for Prior HCT or Cellular Therapy Infusions (Section 11.2.4)	Patty Steinert
7/1/20	7.1	Reviewed and updated entire document	Liz Siepmann Jessica Gillis-Smith Patty Steinert
4/26/21	7.2	Updated "CIBMTR Support List for research studies" (Section 4.2.2.1 and Appendix C)	Liz Siepmann Waleska Perez
5/13/21	7.3	Updated governance throughout document (mainly Chapters 1, 2, and 18)	Liz Siepmann Jessica Gillis-Smith Patty Steinert
7/28/21	8.1	Reviewed and updated entire document	Liz Siepmann Jessica Gillis-Smith Patty Steinert
1/3/22	8.2	Updated Section 2.2.2 (removed SCTOD language, updated Advisory Committee description), updated Chapter 3	Liz Siepmann Waleska Perez Patty Steinert
11/22/22	9.1	Reviewed and updated entire document	Liz Siepmann Jessica Gillis-Smith
8/31/2023	10.1	Reviewed and updated entire document, including significant edits to Chapter 2, Committee Structure	Liz Siepmann Jessica Gillis-Smith Jennifer Motl
7/1/2024	11.1	Reviewed and updated entire document, including branding (both CIBMTR and NMDP)	Liz Siepmann Jessica Gillis-Smith