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

Introduction to CIBMTR

NEW CENTER MEMBERSHIP

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WHO WE ARE & WHAT WE DO

CIBMTR® (Center for International Blood & Marrow Transplant Research®) is a research collaboration between the Medical College of Wisconsin (MCW) and NMDP. CIBMTR is funded through a variety of sources, including National Institutes of Health (NIH) awards, United States (US) Office of Naval Research grants, industry sponsors, NMDP and MCW.

In addition to its large Outcomes Database, CIBMTR provides multiple other resources important for worldwide cellular therapy research, including:

- A prospective clinical trial network focused on cellular therapy research
- A biorepository of donor and recipient cells and DNA
- Innovative biostatistical methodologies for analyzing cellular therapies
- Collaboration with worldwide organizations to exchange and increase data worldwide, including as a founding member of the Worldwide Network for Blood and Marrow Transplantation
- Expertise in Patient-Centered Research and Implementation Sciences methodology and qualitative analysis

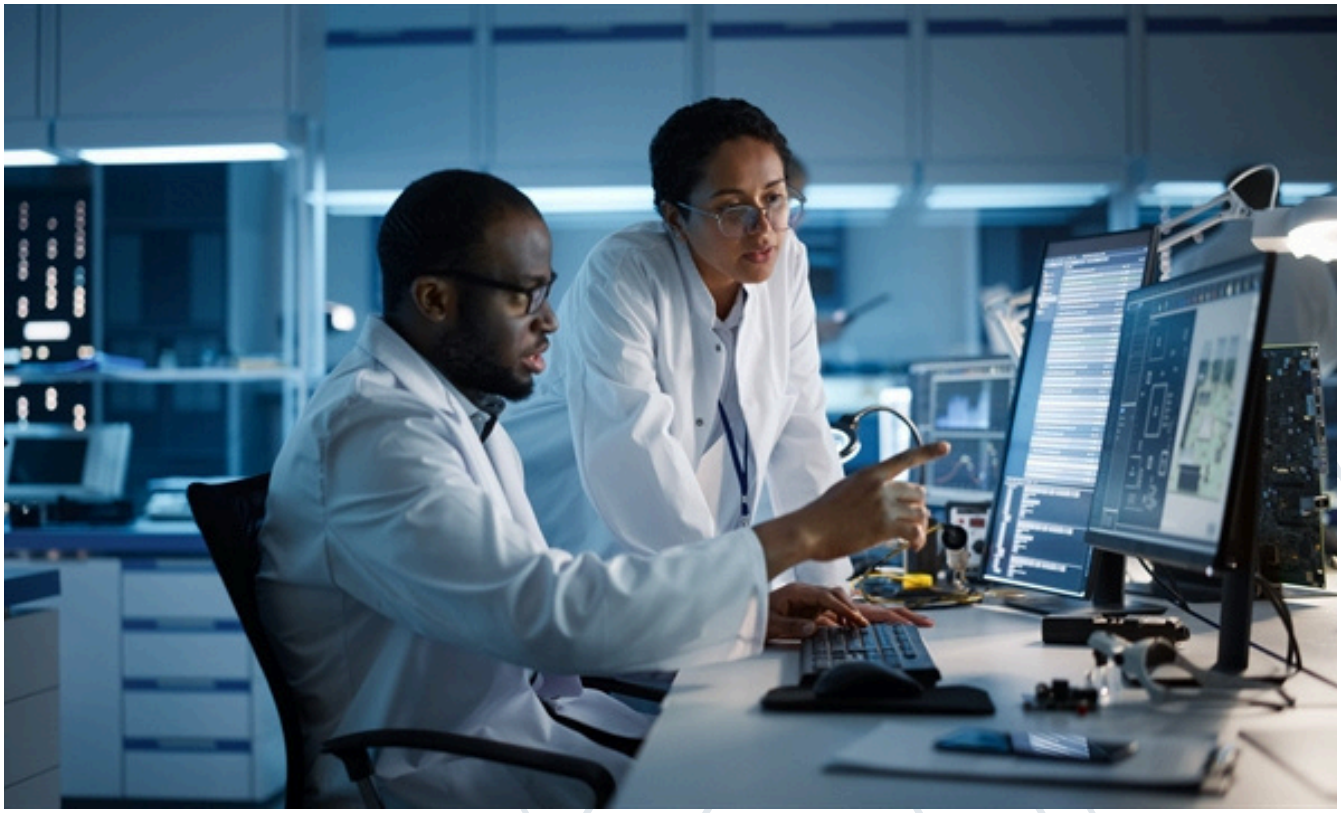
OVERVIEW

WHO WE ARE & WHAT WE DO

MISSION
To lead transformative and collaborative research to improve outcomes in cellular therapy

VISION
To be the premier research organization for cellular therapy

VALUES
Integrity Curiosity Boldness Accountability Equity Connectivity



OVERVIEW

WHO WE ARE & WHAT WE DO

CIBMTR has established an extensive clinical database of patient outcomes. Through the submission of timely and accurate data, center administrators and clinical research professionals play a key role in helping CIBMTR maintain—and grow—this critical database that has led to increased survival for recipients. Participating center staff who submit data to CIBMTR are called data managers. Data managers are vital to the success of CIBMTR as they report all source data for our research.

The collaboration and dedication of more than **310 participating centers** in the US and throughout the world have:

- Built a tremendous resource of data from more than **700,000 patients**
- Provided more than **225,000 paired related and unrelated donor/recipient biologic samples**
- Provided **thousands of hours** of volunteer service to continue the progress in this field

HOW WE COLLECT DATA

DATA SUBMISSION PLATFORM & DATA REPORTING TRACKS

To ensure that the most relevant data are collected, CIBMTR, in collaboration with the global cellular therapy community, has developed a standard set of data elements to be collected for all transplant recipients.

DATA SUBMISSION PLATFORM

The FormsNet3 application is what centers use to electronically submit all data to CIBMTR. One hundred percent of data collection is captured in FormsNet3 using more than 250 forms related to reporting hematopoietic stem cell transplant (HCT), cell therapy (CT) and gene therapy (GT) outcomes for donors and recipients.

CIBMTR is committed to transforming our data and systems by making usable data available faster through innovation. One of those innovations is CIBMTR Data Automation which strives to use technology to collect, integrate, validate and analyze data while minimizing manual intervention. For several years, CIBMTR has piloted automated approaches and processes for data collection including CIBMTR Reporting App (CRA), DirectFHIR, ISCN Cytogenetic parser, HML2FHIR and Upstream CRID.

CIBMTR Reporting Application (CRA) registers HCT or cell therapy patients to CIBMTR for outcomes research and displays and reports select laboratory, vital signs and drug administration data found in the electronic health record (EHR). This allows transplant centers that currently register transplant recipients manually through FormsNet3 to instead register these patients directly from the Epic EHR, increasing efficiency and decreasing the possibility of error.

Upstream CRID is a process in which NMDP patient demographics and infusion information are sent from an application called MatchSource, directly to FormsNet3. It is used to register a recipient in FormsNet3.

HOW WE COLLECT DATA

DATA SUBMISSION PLATFORM & DATA REPORTING TRACKS

DATA REPORTING TRACKS

CIBMTR collects transplant data on donors and recipients with two general sets of forms, Transplant Essential Data (TED) forms and Comprehensive Report Forms (CRF). Cell therapy data are also collected on two sets of forms referred to as CTED and CRF.

TED-level data are used for research when appropriate and evaluation of the Stem Cell Therapeutic Outcomes Database (SCTOD) program operations, including federally required research such as analyses of center-specific outcomes and evaluation of optimal registry and cord blood bank size. This level of reporting includes all mandatory data centers must report to CIBMTR. TED-level reporting assists in fulfilling Foundation for the Accreditation of Cellular Therapy (FACT) accreditation eligibility requirements. For more information on FACT eligibility requirements, click here.

CRF-level data are more thorough and included in research studies, though TED-level data may occasionally be used. These forms collect more detailed data including disease assessments at each follow-up visit, expanded acute and chronic GVHD data, engraftment data and more.

For additional information on reporting levels, please visit the CIBMTR Data Management Guide.

HOW WE COLLECT DATA

DATA SUBMISSION PLATFORM & DATA REPORTING TRACKS

	TED LEVEL FORMS	CRF LEVEL FORMS
Reporting Requirements	Required reporting to CIBMTR, including basic pre- and post-transplant information as part of the SCTOD program operations	Includes TED-level data plus detailed information for research purposes, such as, but not limited to, disease assessments at each follow-up visit, expanded acute and chronic GVHD data, engraftment data
Reporting Level Assignment	The FormsNet3 algorithm assigns either TED forms or CRFs to transplant recipients. All cases are assigned to the TED follow-up track unless CRF reporting is required for a study	The FormsNet3 algorithm assigns either TED forms or CRFs to transplant recipients. CRF assignments are based on factors like study participation, consent, type of transplant, age, disease, and more
Reimbursement	Forms completed for TED reporting are not typically reimbursed, with the exceptions of Gene Therapy Product Form 2003 and HCT Infusion Form 2006	Forms completed for CRF reporting are reimbursed. Centers are reimbursed for forms completed within one year of the due date of the form (due date is shown in FormsNet3). For more information on reimbursement, click here
Benefits	Benefits of TED-level reporting include receiving all CIBMTR general mailings, newsletters, and summary slides, as well as discounted member rates for the CIBMTR annual meeting	Benefits of CRF-level reporting include all benefits of TED-only centers and members may also chair CIBMTR Working Committees, be members of the Executive Committee and have voting privileges

CENTER REQUIREMENTS

CENTER REGULATORY COMPLIANCE: STAFFING, MHA & IRB APPROVAL

STAFFING

Centers must have at least one primary data manager and a medical director to become a CIBMTR center. The size of a center's data management team depends on variables such as the number of infusions performed, type of infusions, diseases treated and type of EMR used. Some centers have specific individuals working as data managers at their centers, whereas many centers have their nursing staff, transplant coordinators, or even attending physicians completing the data forms. This is especially true for centers outside the United States.

MASTER HEALTHCARE DATA AND SAMPLE SUBMISSION AGREEMENT

The Master Healthcare Data and Sample Submission Agreement (MHA) is an agreement that defines responsibilities for both CIBMTR and the center that covers how data and/or samples may be used. It specifies informed consent requirements, privacy and confidentiality obligations and other responsibilities for both parties. In addition, the agreement addresses mandated reporting under the C.W. Bill Young Cell Transplantation Program for US products, as well as the data and/or samples submitted for participation in CIBMTR protocols. For additional information on Protocols & Consents, please visit the CIBMTR Data Management Guide.

INTERNATIONAL CENTERS: INSTITUTIONAL REVIEW BOARD APPROVAL

International transplant centers must follow their country's laws and regulations governing human subjects and privacy protection. The transplant center is responsible for obtaining the necessary Institutional Review Board (IRB) review and approval for the Observational Database.

If a recipient does not consent to participate in the Observational Database according to the laws and regulations of their country, CIBMTR requests the completion of TED-level pre-infusion data, indicating consent to research as 'no.'

- This reporting will help ensure the epidemiological integrity of the database is maintained and the recipient's information will not be used in research
- This applies to recipients of allogeneic (related and unrelated) and autologous HCT

CENTER REQUIREMENTS

CENTER REGULATORY COMPLIANCE: STAFFING, MHA & IRB APPROVAL

US CENTERS: INSTITUTIONAL REVIEW BOARD APPROVAL

All US transplant centers must obtain Institutional Review Board (IRB) approval to comply with federal regulations and to acquire IRB-approved informed consent from recipients, regardless of data submission level (TED or CRF). CIBMTR governs its research program under the three protocols that the IRB oversees (e.g. Research Database Protocol, PRO Data Collection Protocol, and CIBMTR Biorepository Protocol).

There are 2 options for IRB approval:

1. **Use your institution's local IRB**
   - If your center chooses to use your local IRB, your center will be responsible for all IRB submissions to your local IRB

2. **Utilize a single IRB (sIRB) through NMDP**
   - While enrolling in the sIRB takes some additional work up front, utilizing the NMDP IRB will likely reduce the time your center spends on study administration, as CIBMTR staff are responsible for most NMDP IRB submissions for this research
   - CIBMTR staff is responsible for submitting protocol amendments, consent form template updates and annual updates to the NMDP IRB

All transplant centers that are NMDP member centers must also have IRB approval for the *Protocol for a Research Sample Repository for Hematopoietic Cell Transplantation, Other Cellular Therapies and Marrow Toxic Injuries,* and *Protocol for Collection of Patient Reported Outcomes (PRO) Data* for unrelated recipients. Protocols and informed consent documents are available on the CIBMTR website for both the Research Database and the Biorepository.

- Prior to obtaining IRB approval for these consent documents, all centers must work with the CIBMTR study team to review any revisions to the study consent documents
- For any sites obtaining initial approval on the studies after January 20, 2020, reliance on the NMDP IRB through Single IRB (sIRB) is required
- Upon obtaining IRB approval, the CIBMTR study team must receive a copy of the IRB's approval letter, approved protocol and informed consent documents
- Sites will receive a renewal reminder approximately two months in advance of the local continuing review date
- Failure to have current local IRB approval can impact a center's ability to meet CPI requirements for data and sample submission




QUALITY & COMPLIANCE

CIBMTR centers partake in several quality and compliance programs to ensure accurate and timely data is being reported in FormsNet3. These programs aim to keep centers accountable and on target for their data submission in order to promote collaborative research that increases access and improves outcomes of all cellular therapies.

AUDIT* **

Ongoing data audits are performed at all CIBMTR participating transplant centers as part of the overall data quality assurance program. Auditors compare source documentation, maintained in the transplant center medical records, to data that was reported in the CIBMTR outcomes registry. These on-site or remote visits are conducted at regular intervals (at least once every 4 years) to ensure continued accuracy of submitted data. Only centers that have performed at least 20 transplants are eligible for audit, including any combination of related or unrelated allogeneic and autologous transplants. For non-US-based centers, audits are currently performed at centers whose medical records are primarily documented in English. In addition to the above listed eligibility criteria, the audit program will also identify whether the non-US center has utilized a donor or product from the US. For additional information, please visit the CIBMTR Audit Guide.

CONTINUOUS PROCESS IMPROVEMENT* **

Continuous Process Improvement (CPI) is a compliance program to ensure timely and accurate submission of data. CPI supports the ability to perform benchmarking and provide accurate population level data. Centers are required to complete a pre-determined percentage of forms within a specific timeframe, relative to the due dates of the forms. The program is based on a trimester schedule, with each trimester having a specific set of standards centers must meet to be in good standing with CIBMTR. Additionally, it requires that centers have an MHA in place and, for US centers, that their IRB approval is current. For additional information, please visit the CIBMTR Data Management Guide.

CONSECUTIVE TRANSPLANT AUDIT* **

Consecutive Transplant Audit (CTA) ensures all HCT infusions performed in the prior calendar year (January – December), at each active center, have been reported to CIBMTR. As part of the CPI program, centers will submit a CTA list to CIBMTR, resolve any data discrepancies and resolve data queries. Each of these steps aligns with the CPI trimesters. For additional information, please visit the CIBMTR Data Management Guide.

*Denotes US Center Program **Denotes International Center Program

QUALITY & COMPLIANCE

DATA QUALITY* **

To ensure the accuracy of data submitted to CIBMTR, data quality (DQ) checks are continuously run to identify possible data discrepancies. FormsNet3 has the functionality to place a query on a form or tool when CIBMTR identifies a possible error. Centers are required to address and resolve queries in a timely manner, designated by the CPI program.

DELIVERABLES & REPORTS

CENTER PERFORMANCE ANALYTICS* **

The Center Performance Analytics (CPA) application provides centers on-demand access to the same center specific analysis data set used to prepare their annual TCSA report. The CPA application utilizes the annual, three-year Transplant Center Specific dataset and organizes relevant descriptive statistics in category-specific tabs enabling visualization of these data in a bar chart or pivot table. Predefined filters permit comparison of a center with the same aggregated data provided by other centers based on center size, patient population (pediatric, adult or both), center performance and region. The application provides center's one-year survival rate and the ability to export their entire TCSA data set to an Excel file format.

CENTER VOLUME DATA REPORT*

Center Volume Data Report (CVDR) represents the total number of transplants reported in the last 5 years using FormsNet3. Annually, as part of CIBMTR's contract with the US Health Resources and Services Administration (HRSA), CIBMTR publishes transplant center volumes data on the C.W. Bill Young Cell Transplantation Program government website. The HCT volumes and demographic data, by transplant center, are made accessible to the public and transplant community. The data reflected in the charts, found within the CIBMTR Portal application, are the latest refreshed dataset from FormsNet3. For additional information on CVDR, please visit the CIBMTR Data Management Guide.

*Denotes US Center Program **Denotes International Center Program

DELIVERABLES & REPORTS

DATA BACK TO CENTERS* **

Data Back to Centers (DBtC) provides significant enhancements with easier access to and better visualization of a center's data. DBtC provides self-service access to a limited set of both CRF- and TED-level data, including descriptive statistics and outcomes. Predefined filters permit centers to isolate and review data subsets of interest and robust visualization features provide one-click options for viewing data in a chart or table. Centers are able to export filtered data in Excel file formats. DBtC data are extracted from the CIBMTR Research Database and are validated, reviewed and refreshed monthly.

REQUEST FOR INFORMATION*

Request for Information (RFI) is a self-service tool to provide centers with the ability to access, view, reconcile, format and supplement form data submitted to CIBMTR to fulfill annual RFI obligations for payers. Data for RFI are not a report, but a data extract that centers can export into the standardized format developed by the American Society for Transplantation and Cellular Therapy (ASTCT). Centers can supplement the extract with additional data not collected by CIBMTR and update to match any discrepancies that might exist with center-based records. Centers are strongly encouraged to check their data for completeness and accuracy before submitting to payers or other organizations.

TRANSPLANT CENTER SPECIFIC ANALYSIS* **

Transplant Center Specific Analysis (TCSA), also referred to as Center-Specific Survival Analysis or Center Outcomes Analysis, is a robust analysis providing an equitable, balanced and scientific performance measurement tool that can be used by the transplant community to define and improve quality. TCSA is used to predict one-year survival of first allogeneic transplants, based on data reported to CIBMTR. This program is mandatory for US centers performing allogeneic transplants. Since centers vary considerably in the risk level of cases treated, a statistical model was developed to adjust for several risk factors known or suspected to influence transplant outcomes. This model is used to predict an "expected" 1-year (365+ days) survival post-first allogeneic transplant for a center, given the types of patients and diseases treated. The actual survival observed at a center is then compared against the "expected" survival. For additional information on TCSA, visit the CIBMTR Data Management Guide.

***International centers can apply to participate*

**Denotes US Center Program **Denotes International Center Program*

REPORTING & RESEARCH

CELL THERAPY & GENE THERAPY* **

Reporting of cell and gene therapy infusions to CIBMTR is voluntary, although reporting of commercially available cell and gene therapy product infusions is strongly encouraged. All types of cell therapy products/infusions can be captured in the registry and cell therapy data are captured on the cell therapy suite of forms while gene therapy data are captured on the HCT suite of forms. For additional information on cell therapy reporting, please visit the CIBMTR Data Management Guide.

***Select international centers*

INDUSTRY, BMT CTN, & CRO STUDIES * **

CIBMTR is at the forefront of both observational and prospective research in HCT and other cellular therapies. At any given time, CIBMTR has 185+ ongoing studies and clinical trials. We provide opportunities for involvement, resources and data management, and increased visibility for transplant advancements.

Corporate studies are included under the umbrella of CIBMTR Research Database Protocol and Consent. Enrollment into these studies is completed based on product name reported on the appropriate form. To view current CIBMTR corporate studies, see the Data Management Guide.

The Blood and Marrow Transplant Clinical Trials Network (BMT CTN) conducts large, multi-institutional trials to improve outcomes of cellular therapies, such as HCT, cellular vaccines and chimeric antigen receptor T-cells (CAR-T) for patients facing life-threatening disorders. Established in 2001, the BMT CTN infrastructure facilitates the participation of a large network of centers in trials available to patients in all regions of the US.

CIBMTR Clinical Research Organization Services (CRO Services) supports trials of all phases, with specific expertise in Phase I and Phase II trials. Offering full CRO capabilities, we specialize in the design and oversight of HCT and other cellular therapy clinical trials, with a focus on collaboration with organizations for the highest-impact clinical trials.

***Select international centers*

RESOURCES

Data managers play a critical role in advancing HCT and other cellular therapies through complete, accurate and timely data submission to CIBMTR. These efforts are crucial in supporting the research that has led to increased survival and an enriched quality of life for thousands of patients. CIBMTR provides member centers with a variety of online tools and resources to communicate with us and securely exchange data.

CIBMTR.ORG

The CIBMTR website provides information about current research studies, working committees, research programs, data operations information (membership, protocols and consent, manuals, guides, communications and system applications), information about the Tandem Meetings, resources about recipient and donor data, biorepository inventories, publications, publicly available data sets, Center-Specific Survival Analysis and more.

CIBMTR PORTAL

The CIBMTR Portal provides on-demand access to CIBMTR's suite of center-facing applications including Survival Calculator, DBtC, CPA, RFI, CVDR, Audit Reporting and Training & eLearning resources. Within the training section of the Portal, centers can review job aids, the data manager discussion forum, past Tandem Meetings materials and cell & gene therapy product training resources.

FORMSNET3 & DATA AUTOMATION

FormsNet3 is a secure clinical research management system for electronic submission of outcomes data to CIBMTR, in compliance with the SCTOD. CIBMTR provides center staff with regularly updated manuals and guides to navigate the platform, instructions on how to submit data on TED and CRF data collection forms, as well as the chance to utilize supported data automation platforms (i.e. CRA, Upstream CRID).

Guides: Audit Guide, CIBMTR Reporting Application Guide, Data Management Guide, Forms Instruction Manual and FormsNet3 Training Guide

TRAINING

CIBMTR offers comprehensive information and training materials for data management professionals regarding data submission requirements of CIBMTR and field knowledge. Members of participating centers are encouraged to complete the Self-Guided Onboarding course, Introduction to Resources and FormsNet3 Functionality training and either Live-Virtual or Recorded New Data Manager Onboarding held twice a year (March and September). These trainings provide a thorough overview of several topics including CIBMTR resources, FormsNet3 functionality, TED and CRF data reporting, CIBMTR Portal, disease specific data reporting, CPI/CTA and cell therapy reporting.

NEXT STEPS

AT-A-GLANCE: BECOMING A CIBMTR CENTER

Interested in becoming a CIBMTR member? Complete the New Center Questionnaire and visit the Center Membership section of www.cibmtr.org to get started.

After the New Center Questionnaire is submitted, CIBMTR will contact the center with a prepared MHA. Centers have the opportunity to ask questions and propose edits to the MHA Agreement.

1. Explore CIBMTR Website
2. Submit a New Center Questionnaire
3. Receive Center Number (CCN) Assignment
4. Review & Sign MHA
5. Determine Local or NMDP IRB
6. CIBMTR Membership Starts
7. Create Accounts for Staff for FormsNet3 & CIBMTR Portal
8. CIBMTR Center and Data Manager Training
9. Access to FormsNet3 Data Submission

QUESTIONS?
CONTACT US.

CIBMTR® is a research collaboration between the Medical College of Wisconsin and NMDP.

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