

**Interagency Registry for Mechanically Assisted Circulatory Support**

# **Manual of Operations and Procedures**

**Sponsored by the National Heart Lung and Blood Institute**

**Data Coordinating Center:** University of Alabama at Birmingham

**Version 4.0**

**May 30, 2014**

## Table of Contents

List of Abbreviations .....	5
1 Overview .....	6
2 Registry Synopsis .....	7
3 Registry Organization and Responsibilities .....	9
3.1 NHLBI, National Institutes of Health .....	9
3.2 Investigators .....	9
3.3 Data and Clinical Coordinating Center (DCC) .....	10
3.4 Committees .....	11
3.4.1 Executive Committee .....	11
3.4.2 Operations Committee .....	11
3.4.3 Medical Event Review Committee .....	11
3.4.4 Data Access, Analysis, and Publications Committee .....	12
3.4.5 Hospital Standards Committee .....	12
3.4.6 Industry Committee .....	12
3.4.7 Quality (QoL) Subcommittee .....	13
3.4.8 Pediatrics Committee .....	13
3.4.9 Conflict of Interest Subcommittee .....	13
3.4.10 Coordinators Council Subcommittee .....	13
3.4.11 Business Advisory Committee .....	14
4 Communication .....	14
4.1 Specific Lines of Communication .....	14
4.2 INTERMACS® Website .....	15
4.3 ClinicalTrials.gov .....	15
5 Registry Design .....	15
6 Registry Procedures .....	16
6.1 Site Registration and Activation .....	16
6.2 Annual Re-certification .....	19
6.3 Screening and Eligibility .....	19
6.4 Enrollment and Assignment of Registry Identification Number .....	20
6.5 Follow-up .....	21

6.6	Transfer.....	21
6.7	Data Collection.....	22
6.7.1	Web-based Data Entry .....	22
6.7.2	Quality of Life Evaluation .....	27
6.7.3	Functional Capacity Evaluation .....	29
6.7.4	Neurocognitive Evaluation .....	32
7	Informed Consent and Release of Medical Records .....	34
7.1	Waiver of Authorization and Consent.....	35
7.2	Informed Consent Process.....	35
7.3	HIPAA and Release of Medical Records.....	37
8	Training .....	37
8.1	Privacy Awareness Training.....	37
8.2	Web-based Data Entry System (INTERMACS® Application) Training .....	38
9	Quality Assurance .....	39
9.1	Overview .....	39
9.2	Data Audits.....	40
9.3	Hospital Standards Committee Review .....	40
9.4	Medical Event Review .....	40
9.5	Observational Study Monitoring Board Oversight .....	41
10	Medical Device Reporting.....	42
10.1	Overview .....	42
10.2	INTERMACS® .....	44
10.3	pediMACS.....	46
11	Data Access .....	47
12	Standard Quality Improvement Reports .....	48

**Appendices:**

[Appendix A: Adverse Event Definitions](#)

[Appendix B: IRB Guidelines and Templates](#)

[Appendix C: Patient Information Sheets and Consent Templates](#)

[Appendix D: Site Registration Agreements](#)

[Appendix E: INTERMACS® Financial Disclosure and Conflict of Interest Form](#)

[Appendix F: Quality of Life Questionnaires](#)

- EQ-5D
- PedsQL
- VADQoL

[Appendix G: Trail Making Test \(Part B\)](#)

[Appendix H: Kansas City Cardiomyopathy Questionnaire \(KCCQ\)](#)

[Appendix I: Modified Rankin Scale](#)

[Appendix J: Data Access Request Form](#)

[Appendix K: Device Brand Lists](#)

- Adults ( $\geq$  19 years of age)
- Pediatrics ( $<$  19 years of age)

[Appendix L: INTERMACS® Rosters and Contact Information](#)

[Appendix M: INTERMACS® Users' Guide](#)

[Appendix N: pediMACS Users' Guide](#)

[Appendix O: INTERMACS® and pediMACS Profiles of Advanced Heart Failure](#)

[Appendix P: Data Collection Forms for INTERMACS®](#)

[Appendix Q: Data Collection Forms for pediMACS](#)

## List of Abbreviations

Abbreviation	Definition
6MWT	Six-minute Walk Test
CLIA	Clinical Laboratory Improvement Amendment(s)
CMS	Centers for Medicare and Medicaid Services
CPX	Cardiopulmonary Exercise
DAAP	Data Access, Analysis, and Publications Committee
DCC	Data and Clinical Coordinating Center
DT	Destination Therapy
EB	Ethics Board
EC	Executive Committee
EQ-5D	EuroQoL Questionnaire
ET	Eastern Time
FDA	United States Food and Drug Administration
FWA	Federal Wide Assurance
HHS	Health and Human Services
HICN	Health Insurance Claim Number
HIPAA	Health Insurance Portability and Accountability Act
IRB	Institutional Review Board
INTERMACS®	Interagency Registry for Mechanical Assisted Circulatory Support
KCCQ	Kansas City Cardiomyopathy Questionnaire
LVAD	Left Ventricular Assist Device
MCSD	Mechanical Circulatory Support Device
MDR	Medical Device Report
MOP	Manual of Operations and Procedures (Registry-specific)
MOPP	Manual of Policies and Procedures (Administrative)
mRS	Modified Rankin Scale
NHLBI	National Heart, Lung, and Blood Institute
NYHA	New York Heart Association (heart failure classification)
OC	Operations Committee
OPC	Objective Performance Criteria
OPTN	Organ Procurement and Transplant Network
OSMB	Observational Study Monitoring Board
pediMACS	INTERMACS® for pediatric patients
PedsQL	Pediatric Quality of Life Inventory
PHI	Protected Health Information
PI	Principal Investigator
QA	Quality Assurance
RVAD	Right Ventricular Assist Device
QoL	Quality of Life
SRE	Single Reporter Exemption
TAH	Total Artificial Heart
TVE	Time Variance Exemption
UAB	University of Alabama at Birmingham
UDI	Unique Device Identifier
UNOS	United Network for Organ Sharing
VADQoL	Ventricular Assist Device Quality of Life instrument

## 1 Overview

The Interagency Registry of Mechanically Assisted Circulatory Support (INTERMACS®) is a registry of adult and pediatric patients receiving a mechanical circulatory support device (MCSD) to treat heart failure. With data collected since 2006, INTERMACS® now serves as the national quality improvement system to assess the characteristics, treatments, and outcomes of patients receiving MCSDs approved by the United States Food and Drug Administration (FDA). The registry also includes MCSD-implanting hospitals in Canada. These activities are supported by the INTERMACS® data and clinical coordinating center (DCC) under contract to the National Heart, Lung, and Blood Institute (NHLBI).

The INTERMACS® registry for pediatric patients is also referred to as pediMACS and was launched on September 19, 2012. While INTERMACS® has always included durable devices implanted in pediatric patients, pediMACS has been developed to focus on capturing data elements unique to pediatric patients. PediMACS evaluates special issues in the pediatric population receiving MCSD therapy, differences in available devices, and the particular pediatric population for whom this therapy may be most effective. Unless otherwise noted in this document, reference to INTERMACS®, includes pediMACS.

Data reports from INTERMACS® are shared with the NHLBI, FDA and the Centers for Medicare and Medicaid Services (CMS) through a collaboration agreement. The FDA is interested in patient/device outcomes as a way to monitor safety, and CMS through the Joint Commission utilizes INTERMACS® data for site-based quality improvement assessments. Key performance measures are supplied to every participating hospital each quarter, along with a description of the benchmarking methodology used, to facilitate comparison of one institution's outcomes to aggregated national data. Following review of a request for dissemination, data may be shared with basic and clinical researchers, with consideration for privacy regulations. Analytic strategies and data analyses are conducted resulting in publications, presentations, and potentially follow-up investigations.

INTERMACS® collects information pertaining to patients, care providers, hospitals, and devices. Most of these data are collected through chart review by trained nurses and physicians at the clinical sites. Standard of care data on Quality of Life (QoL) and functional capacity are collected for adults and pediatric patients through administration of instruments and tests. Additionally, standard of care neurocognitive data are collected for adults. **No data beyond the data gathered in the course of routine care will be collected for this registry.**

INTERMACS® requires that to be a member in good standing, each participating hospital must enter complete data on consecutively implanted patients into the INTERMACS® database. To facilitate this requirement, INTERMACS® works closely with the member hospitals.

## 2 Registry Synopsis

<b>Title:</b> Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS®)	
<b>Contract Number:</b> HHSN268201100025C	
<b>Objectives:</b> <ol style="list-style-type: none"> <li>1. Collecting pertinent and standardized patient demographic, clinical and device-related data elements from participating hospitals to measure and assess the quality of care and outcomes for patients receiving MCSDs;</li> <li>2. Providing confidential periodic reports to the participating hospitals, government agencies, and industrial partners to improve the quality of care of patients receiving mechanical circulatory support and to evaluate the effectiveness and optimal utilization and performance of these devices;</li> <li>3. Fostering collaborative research based upon the data collected by means of INTERMACS®; and</li> <li>4. Serving as a scalable data infrastructure for pre and post market studies.</li> </ol>	
<b>Registry Design:</b> INTERMACS® is a registry for both adults (INTERMACS® - Adults, or INTERMACS®) and children (INTERMACS® - Pediatrics, or pediMACS) in which data are collected primarily retrospectively from existing medical records or concurrently in the normal course of treatment on patients who meet the eligibility criteria. Additional standard of care evaluations and contact with the patient outside of the index hospitalization are required at defined intervals.	
<b>Number of Subjects:</b> Any patient receiving an FDA-approved MCSD in the United States and Canada is eligible to participate.	<b>Number of Sites:</b> Any medical center in the United States and Canada that has an active MCSD program is eligible to participate.
<b>Period of Evaluation:</b> Patients are followed for the life of the FDA-approved device. If the device is explanted without transplantation, the patient will be followed for 1 year following explant for the major events of death or transplantation.	
<b>Major Endpoints:</b> Discrete <ol style="list-style-type: none"> <li>1. Death</li> <li>2. Transplant</li> <li>3. Explant for Recovery</li> </ol> Complex <ol style="list-style-type: none"> <li>1. Adverse Events</li> <li>2. Improvement Indicators</li> </ol>	

3. Quality of Life
4. Costs
5. Hospitalizations

**Statistical Considerations:**

Because this registry is observational in nature, analyses will be on-going for descriptive variables. More specific analyses for hypothesis generation will be determined as appropriate.

**Title:**

INTERMACS - Adults (INTERMACS®)

**Registry Design Following Implant:**

Post implant follow-up data are collected at 1 week, 1 month, 3 months, 6 months and every 6 months after that for up to 1 year after the device is explanted. Physical examination and functional capacity testing is a routine portion of the care for these patients; the interview consists of survey questions from the EuroQOL (EQ-5D) and Kansas City Cardiomyopathy Questionnaire (KCCQ) for quality of life assessment and the Trail Making Neurocognitive Test, Part B, for neurocognitive assessment. No data beyond the data gathered in the course of routine care will be collected for this registry.

**Criteria for Inclusion:**

All patients ≥19 years of age who receive an FDA-approved durable MCS\* implanted at an INTERMACS®-activated hospital. (NOTE: Patients implanted before the hospital activation date are not eligible for participation in INTERMACS®.)

\*Refer to [Appendix K](#) for a list of FDA-approved durable MCSDs.

**Criteria for Exclusion:**

1. Patients who receive a durable MCS, which is **not** FDA-approved.
2. Patients who are < 19 years of age.
3. Patients who are incarcerated persons (prisoners).

**Title:**

INTERMACS - Pediatrics (pediMACS)

**Registry Design Following Implant:**

Post implant follow-up data is collected at 1 week, 1 month, 3 months, 6 months and every 6 months after that for up to 1 year after the device is explanted. Physical examination and functional capacity is a routine portion of the care for these patients; the interview will consist of survey questions from the Pediatric Quality of Life Inventory (PedsQL) and Ventricular Assist Device Quality of Life (VADQoL) instruments. Neurocognitive assessments will **not** be performed in pediMACS. No data beyond the data gathered in the course of routine care will be collected for this registry. Of note,



once a patient is entered as a pediatric patient, the patient will remain in pediatric status until the implanted device is explanted.

**Criteria for Inclusion:**

All patients <19 years of age who receive an FDA-approved durable or temporary MCS\* implanted at an INTERMACS®-activated hospital.(NOTE: Patients implanted before the hospital activation date are not eligible for participation in pediMACS.)

\*Refer to [Appendix K](#) for a list of FDA-approved durable or temporary MCSs .

**Criteria for Exclusion:**

1. Patients who receive an MCS, which is **not** FDA-approved.
2. Patients who are  $\geq$  19 years of age at time of implant (NOTE: These patients should be enrolled into INTERMACS®.)
3. Patients who are incarcerated persons (prisoners).

### 3 Registry Organization and Responsibilities

INTERMACS® represents an interagency partnership with the NHLBI, FDA, and CMS that works collaboratively with participating hospitals, and industry. INTERMACS® is currently supported through a Public-Private Partnership, which includes funding from the NHLBI and fees collected from participating hospitals and device companies manufacturing FDA-approved MCSs. These collaborations are coordinated by the Data and Clinical Coordinating Center (DCC) at the University of Alabama at Birmingham. The overall structure of INTERMACS® is described below.

#### 3.1 NHLBI, National Institutes of Health

As the primary funding agency, NHLBI, located in Bethesda, Maryland is both the major partner and regulator of the registry. In addition to its oversight role, NHLBI has been involved with many of the day-to-day activities of INTERMACS®, including the role of ensuring scientific and regulatory integrity and patient protection. NHLBI staff includes:

- Contracting Officer's Representative (COR): Marissa A. Miller, DVM, MPH;
- Alternate COR: J. Timothy Baldwin, PhD
- Clinical Trials/Regulatory Specialist: Wendy C. Taddei-Peters, PhD
- Program Analyst: Catherine Burke, MA
- Contracts Specialist: Caitlin Henning

#### 3.2 Investigators

The team of investigators, working in collaboration with the NHLBI to oversee registry activities, includes:

- Principal Investigator: James K. Kirklin, MD, University of Alabama at Birmingham (UAB)

- Director, Data Coordinating Center (DCC) UAB: David Naftel, PhD
- Study Chair: James B. Young, MD, Cleveland Clinic Lerner College of Medicine
- Co-Investigators:
  - Elizabeth D. Blume, MD, Boston Children's Hospital
  - Robert L. Kormos, MD, University of Pittsburgh
  - Francis D. Pagani, MD, PhD, University of Michigan Medical School
  - Lynne Warner Stevenson, MD, Brigham & Women's Hospital

Additional information on each of the investigators may be found in the *Administrative Manual of Operations, Policies and Procedures* (MOPP).

### **3.3 Data and Clinical Coordinating Center (DCC)**

The university-based DCC located in the Cardiac Research Group within the Department of Surgery at the University of Alabama at Birmingham (UAB) is responsible for administrative support, data management, monitoring, analysis, and reporting. The DCC is organized into multiple functional groups and headed by the Director and Executive Director who report directly to the PI.

DCC staff includes:

- Director: David Naftel, PhD
- Executive Director: S. Craig Collum, MPH
- Administrative and Fiscal Oversight
  - S. Craig Collum, MPH, Director
  - Nicole Kirklin, Assistant Director
  - Devin Koehl, Administrative Manager
  - Sharmene Smith, pediMACS Manager
- Clinical Affairs
  - Kathryn Hollifield, BSN, RN, Director
  - Gail Mertz, BS, RN, CCRC, Assistant Director
  - Tammy Davis, RN, Nurse Monitor
  - Janella Miller, BSN, RN, Nurse Monitor
- Data Management
  - David Helms, Director
  - John Pennington, Data Analyst
- Information Security & Technology
  - Robert Kasco, Director
  - Maceo Cleggett, IT Specialist
- Regulatory Affairs
  - Mary Lynne Clark, Director
  - Jeanne Anne Love, Manager
  - David Baldwin, Regulatory Support
  - Chase Lenderman, Website Administrator
  - Sherita Brown, Document Control
- Research & Analysis
  - Susan L. Myers, Database Administrator

- Grant K. Studdard, Program Manager
- Statistical Reporting
  - Ryan Cantor, Director
  - Jennifer Gunther, Data Analyst
  - John Pennington, Data Analyst
  - Maceo Cleggett, Data Analyst

The responsibilities of the DCC-UAB staff members are described in the *Administrative MOPP*. Contact information for DCC staff is found in [Appendix L](#) of this MOP.

### **3.4 Committees**

INTERMACS Committees and Subcommittees are described below. Contact information for Committee chairs is located in [Appendix L](#).

#### **3.4.1 Executive Committee**

The Executive Committee (EC), led by Study Chair James Young and comprised of the PI (J. Kirklin), DCC Director (D. Naftel) Co-Is (R. Kormos, F. Pagani, L. Warner Stevenson and E. Blume), and the NHLBI COR (M. Miller) and Alternate COR (T. Baldwin), provides direction, oversight and approval to the registry's design, architecture, refinement, policies, procedures, data collection forms and other functional components. As the driving force behind the entire registry, the EC reviews and formalizes all major decisions and initiatives of the registry. The EC convenes weekly via conference calls.

#### **3.4.2 Operations Committee**

The Operations Committee (OC), led by the Study Chair, consists of the INTERMACS® EC, representatives from the NHLBI, FDA, CMS, DCC, and chairs of the other committees. This committee addresses the expanding expectations of requests received by the DCC for INTERMACS® data and analyses. The OC provides recommendations regarding policy and procedural decisions, reviews current issues, and helps to set priorities. The OC holds monthly conference calls.

#### **3.4.3 Medical Event Review Committee**

The Medical Event Review Committee, chaired by Co-I R. Kormos, focuses on proper definitions and descriptors of major adverse events following MCS therapy, promotes consensus from industry as well as clinicians about the precise definitions of these events, and proposes data elements that will aid in differentiating the underlying causes of adverse events as device-related, patient illness, and management-related. This Committee:

- provides guidance on summarizing and evaluating the quality of the adverse event data;

- provides strategies for electronically identifying duplicate events and questionable events;
- focuses on the review and categorization of device malfunction; and
- provides guidance to the nurse monitors for auditing the correct capture of adverse events. All data identified as questionable are resolved via direct interactions between the nurse monitors and the local hospital.

The Medical Events Review Committee holds quarterly conference calls and may meet more frequently as needed.

#### **3.4.4 Data Access, Analysis, and Publications Committee**

The Data Access, Analysis, and Publications (DAAP) Committee, chaired by Co-I F. Pagani, addresses issues of: access to registry data by investigators, proposed analyses which feature INTERMACS® data, collaborations, publications, and overall prioritization of such activities. Recommendations are provided to the EC and OC about specific analyses that are most useful in addressing the objectives of the registry. The DAAP meets quarterly via conference call and may convene more frequently as needed.

#### **3.4.5 Hospital Standards Committee**

The Hospital Standards Committee, led by the Study Chair and comprised of the EC as well as representatives from the NHLBI and DCC, sets the criteria that participating hospitals must meet to become members of the INTERMACS® registry. It also establishes policies and procedures to ensure satisfactory performance from participating hospitals. Oversight is provided for staff training of participating hospitals in registry methods of data collection such that eligible hospitals can be certified to participate in the registry. This Committee reviews hospitals that fail to meet or maintain performance standards and develops remedial or educational efforts to reestablish compliance. The Hospital Standards Committee works with the DCC Clinical Affairs group to ensure efficient resolution. This Committee holds conference calls as needed, but no less than quarterly.

#### **3.4.6 Industry Committee**

The Industry Committee consists of industry representatives and is chaired by DCC Director D. Naftel. The purview of this Committee includes recommending policies to protect proprietary device information while allowing device prototype analyses; reviewing registry information to aid in the development of new devices; considering revisions of adverse event definitions in response to emerging device technology; and informing the OC of pending clinical trials. The Industry Committee meetings are held quarterly via conference calls.

### **3.4.7 Quality (QoL) Subcommittee**

The QoL Subcommittee, chaired by Kathleen L. Grady, PhD, Northwestern University Feinberg School of Medicine, assesses current QoL instruments in patients with advanced heart failure. This Committee advises the OC on the utilization of these questionnaires, is instrumental in the analysis of the data, including QoL outcomes and identification of risk factors for worsening QoL, as well as direct dissemination of results via abstracts, publications and other forms of media. The QoL Subcommittee holds quarterly conference calls.

### **3.4.8 Pediatrics Committee**

The Pediatrics Committee, chaired by Co-I E. Blume, oversees pediMACS and evaluates special issues in the pediatric population receiving MCS therapy, differences in available devices, and the particular pediatric population for whom this therapy may be most effective. They provide expertise on the unique aspects of infants, children, and teenagers receiving MCS therapy. This committee is instrumental in the analysis of pediatric data, and direct dissemination of results via abstracts, publications and other forms of media. The Pediatrics Committee Chair interacts directly with the EC, and members of the Pediatrics Committee also participate in other committees. This Committee meets via conference calls on a monthly basis.

### **3.4.9 Conflict of Interest Subcommittee**

The Conflict of Interest Subcommittee, chaired by PI J. Kirklin, is responsible for establishing and maintaining oversight of any perceived or real conflicts arising directly or indirectly from INTERMACS® members. Specific charges of this Committee include:

- Conducting an assessment of all annual Conflict of Interest Disclosures related to INTERMACS® activities;
- Reporting to the Executive Committee the nature of the conflict of interest and the action taken by the Committee;
- Approving or disapproving plans to manage perceived or real conflicts of interest, where appropriate, and recommending any corrective actions as necessary to assure that the approved management plan is followed; and
- Maintaining an awareness of financial conflict of interest policies and guidelines issues by financial sponsors such as the Public Health Service (PHS) and Food and Drug Administration (FDA).

In addition to the PI, this Committee is composed of the Study Chair J. Young, NHLBI COR M. Miller, and the DCC Director of Regulatory Affairs M.L. Clark.

### **3.4.10 Coordinators Council Subcommittee**

The Coordinators Council Subcommittee, which reports to the Operations Committee, is charged with assisting trained site staff in completing the site

enrollment process and completing all data entry. They provide guidance to the OC and EC on issues associated with data collection, data entry, and data definitions, as well as observations related to changing patient characteristics. Examples of Council activities include: Training and Participant Screening, Institutional Review Board (IRB)/Ethics Board (EB) Coordination, Questions and Answers for sites, and Participant and Site Challenges/Barriers. This subcommittee is co-chaired by Sherri Wissman, RN, BSN, CCTC, Ohio State University, and Tony Martin, APRN-BC, Newark Beth Israel Medical Center, and generally convenes quarterly via conference call.

### **3.4.11 Business Advisory Committee**

The Business Advisory Committee, co-chaired by PI J. Kirklin and Study Chair James Young, provides guidance to the EC concerning the sustainability of the registry. This committee is responsible for implementing and maintaining a public-private collaboration. This Committee is further charged with ensuring that private financial support is provided on an increasing scale, thereby allowing the registry to be maintained in the future when funding by the NHLBI is reduced. The Business Advisory Committee is comprised of representatives from the DCC, NHLBI, hospitals and industry (i.e., MCSD manufacturers). This committee meets quarterly via conference calls and more frequently as needed.

## **4 Communication**

***[NOTE: The INTERMACS® protocol inadvertently refers to Section 4.4 of this MOP for a description of the Patient Transfer process. However, patient transfer from one hospital to a second hospital is described in [Section 6.6](#) of this MOP. The protocol will be corrected via the next protocol amendment.]***

UAB serves as the DCC for INTERMACS® and conducts all aspects of administrative guidance, oversight, and support. The DCC is also responsible for clinical site coordination, data collection, management, and analyses, and preparation of regulatory packages (including protocol amendments, protocol revision records, and corresponding memos and templates) in support of the registry. Communication, both method and frequency, between the entities of the DCC, Clinical Sites, Operations Committee, Executive Committee, and additional Subcommittees, as well as the government and industry collaborators are outlined below.

### **4.1 Specific Lines of Communication**

The DCC facilitates all INTERMACS® in-person meetings and teleconferences between stakeholders, which include the participating hospital clinicians and site administrators; participating MCSD manufacturers; Federal collaborators (NHLBI, FDA, and CMS); and the INTERMACS® PI and Co-investigators.

Additionally, stakeholders may contact DCC staff directly via email or telephone. For a complete listing of DCC staff with contact information, refer to [Appendix L](#). Key DCC staff may also be found on the INTERMACS® website and contacted through the general DCC email address at: [intermacs@uab.edu](mailto:intermacs@uab.edu).

## 4.2 INTERMACS® Website

In addition to specific lines of communication between the DCC and all stakeholders, a comprehensive public website has been created to enhance overall registry organization and flow. This website contains:

- Special sections designated for general information regarding registry organization, history, and activities;
- Guidance for MCSD implanting centers who wish to participate in the registry (refer to [Participation](#));
- Information for MCSD implanting center staff already participating in the registry, including the current protocol and MOP;
- Information for researchers who may wish to request data sets for analysis or collaborate with INTERMACS® investigators ([Data Requests](#));
- “[FAQ – Frequently Asked Questions](#)” that can be used as a resource for INTERMACS® clinicians;
- A listing of INTERMACS® [publications and abstracts](#);
- INTERMACS® [presentations](#) and [statistical summaries](#); and
- Links to stakeholder websites.

To access the INTERMACS® website, click on the following link:

<http://www.uab.edu/medicine/intermacs/>

## 4.3 ClinicalTrials.gov

The ClinicalTrials.gov Identifier for INTERMACS is NCT00119834. Please contact the DCC at [intermacs@uab.edu](mailto:intermacs@uab.edu) with any identified errors or updates. The posting can be accessed through the link below:

<http://clinicaltrials.gov/ct2/show/NCT00119834?term=NCT00119834&rank=1>

## 5 Registry Design

***[NOTE: The INTERMACS® protocol inadvertently refers to Section 5.2 of this MOP for a description of the Informed Consent process. However, this process is described in [Section 7](#) of this MOP. The protocol will be corrected via the next protocol amendment.]***

While INTERMACS® was intended to be primarily a prospective registry when it was first established, in actuality the data are collected retrospectively from existing medical records or concurrently in the normal course of treatment on patients who meet the eligibility criteria. Additional standard of care evaluations and contact with the patient outside of the index hospitalization are required for this registry. Specifically, post implant follow-up data are collected at 1 week, 1 month, 3 months, 6 months and every 6 months after that for up to 1 year after the device is explanted. Physical examination is a routine portion of the care for these patients. The interview consists of survey questions from the EuroQOL (EQ-5D) and Kansas City Cardiomyopathy Questionnaire (KCCQ) QoL, as well as the Trail Making Neurocognitive Test, Part B neurocognitive assessment instruments in adults (refer to **Appendices F-H, and M**). In children, the interview consists of survey questions from the Pediatric Quality of Life Inventory (PedsQL) and Ventricular Assist Device Quality of Life (VADQoL) instrument (see **Appendices F and N**). Functional capacity in adults and children is also measured (refer to **Appendices M and N**, respectively).

INTERMACS® does not require additional consent other than the routine consent that is required for the MCS D surgical procedure. This is an observational data registry. **No data beyond the data gathered in the course of routine care will be collected for this registry.**

## 6 Registry Procedures

### 6.1 Site Registration and Activation

Any medical center in the United States and Canada that has an active MCS D program is eligible to participate in INTERMACS®. The program must provide personnel and facilities to record and transmit INTERMACS®-required data into the web-based electronic database.

Registration and activation of a new center into INTERMACS® involves meeting a series of requirements, which are as follows:

1. Complete the online enrollment forms, which include the **Hospital Information** and **Personnel Contact Information** forms, located at:  
<http://www.uab.edu/medicine/intermacs/intermacs-site-enrollment> .
  - A local PI representing the hospital's MCS D program and a Site Administrator as a primary contact for the registry must be identified and their contact information entered into the INTERMACS® on-line form during the registration process.
    - The local PI will be responsible for oversight of data submissions and regulatory compliance.
    - The Site Administrator will serve as the "point person" for data related inquiries, receipt of reports, and audit coordination.



- An INTERMACS® regulatory staff member will review the information entered in the form and provide additional enrollment guidance to the Site Administrator, as needed.
  - An email notification regarding application status will be sent to the Site Administrator after the forms are submitted.
2. Download the documents needed for IRB/EB submission, which are located at <http://www.uab.edu/medicine/intermacs/>. These documents include:
    - Protocol Version 4.0
    - Protocol Record of Revisions
    - Patient Information Sheets for Adults and Pediatrics
    - Justification for Waiver of Authorization and Consent
    - Memorandum for the Transition Phase (applicable through June 1, 2014)
  3. Follow local policies regarding additional IRB/EB requirements (e.g., submission of the Users' Guides, data collection forms, and other required documents). IRB/EB Guidelines are located in [Appendix B](#). Data collection forms for INTERMACS® (patients ≥ 19 years of age) are located in [Appendix P](#) and for pediMACS (patients < 19 years of age) in [Appendix Q](#).
  4. Complete the following agreements and disclosures, which must be submitted as part of the Enrollment Package (described below in item 5):
    - The Participation Agreement is an agreement between the local hospital and INTERMACS® outlining the responsibilities of the hospital and INTERMACS®. The agreement must be signed and dated by both a hospital official and an INTERMACS® representative. The Participation Agreement template is located in [Appendix D](#).
    - The Business Associates Agreement is an agreement between the local hospital and INTERMACS® that describes the applicable Health Insurance Portability and Accountability Act (HIPAA) requirements for sharing protected health information (PHI) and allows INTERMACS® to perform quality improvement services on behalf of the local hospital. The agreement must be signed and dated by both a hospital official and an INTERMACS® representative. This template is also located in [Appendix D](#).
    - Financial Disclosure and Conflict of Interest forms must be completed for all INTERMACS® team members. This form must be updated on an annual basis. The form is located in [Appendix E](#).
  5. Submit the Enrollment Package to the INTERMACS® DCC at [intermacs@uab.edu](mailto:intermacs@uab.edu). This package includes the following documents:
    - IRB/EB approval of the protocol and waiver of authorization and informed consent.
      - In the event that your IRB/EB indicates that this Quality Improvement Registry no longer falls under their purview, then request that your IRB provide a letter stating that they have reviewed the protocol and do not

believe that it falls under their purview; therefore, they cannot grant approval.

- In the event that a waiver cannot be obtained, then the approved informed consent and patient authorization, as well as any other related correspondence must be submitted to the INTERMACS® DCC instead.
- Instructions and updated authorization and consent templates are located in [Appendix C](#).
- Follow local policies regarding additional IRB/EB requirements (e.g., submission of Users' Guides [**Appendix M-Adults and N-Pediatrics**]).
- Current Federal Wide Assurance Number (FWA);
- Current Clinical Laboratory Improvement Amendments (CLIA) Certificate;
- Documentation of Privacy Awareness Training. If local training is not available, then NIH's Security and Privacy Awareness Training may be substituted (refer to [Section 8.1](#) for further instruction).
- Signed Participation Agreement, which requires a participation fee in order to activate the site.
- Signed Business Associates Agreement; and
- Completed Financial Disclosure and Conflict of Interest forms

The submission process takes *approximately 2 months*. Sufficient time is needed for IRB/EB review, completion of agreements and disclosures, and staff training on Privacy Awareness.

6. After submission of the Enrollment Package, INTERMACS® staff will:
- Review the package to verify that all documents have been submitted in accordance with INTERMACS® requirements.
  - Provide an invoice for the participation fee, which is invoiced annually thereafter.

Verification and processing of the documents by the DCC takes approximately 2-3 weeks after receipt of the Enrollment Package.

7. Site training will occur after acceptance of the Enrollment Package and payment of the participation fee.
- The enrolling site will be contacted by INTERMACS® staff to schedule a live web-based training session to be held via conference call and Cisco Web-Ex..
  - Training sessions run approximately 2 hours. At least one team member from the site is required to receive training.
  - During this session, the trainer will review the protocol requirements, QoL and Neurocognitive assessments, and other relevant procedures. In addition, site staff will be trained on data entry.
8. The site is normally activated within 24-72 hours of training. A secure email notification with a username and password will be sent to each trained member at the activated site.

## 6.2 Annual Re-certification

Once activated, INTERMACS® requires annual submission of regulatory documents and the participation fee to continue participation in the registry. The following regulatory documents are required annually:

- Provide the annual IRB/EB approval and current FWA Number;
  - In the event that your IRB/EB indicates that this Quality Improvement Registry does not fall under their purview, then provide a letter signed by the PI stating that your IRB reviewed protocol version 4.0 (include date of review) and that they recognize this protocol does not fall under their purview; therefore, they will not grant annual approval. Additional information may be required. Decision pending.
- Provide current CLIA documentation;
- Provide an updated Conflict of Interest disclosure; and

NOTE: Provide documentation that site staff has taken Privacy Awareness refresher training per local IRB requirements or every 2 years, whichever comes first. If refresher training is not offered locally, then NIH's Security and Privacy Awareness refresher training may be substituted. Refer to [Section 8.1](#) for details.

Comply with data submission requirements outlined in the protocol and Users' Guide (Appendix M for adults and N for pediatrics).

## 6.3 Screening and Eligibility

All patients receiving MCSDs will be screened according to the inclusion and exclusion criteria provided in [Section 2](#) and in the protocol (Sections A.1.1 and B. 1.1). Procedural guidance for the two inclusion criteria are as follows:

1. The device brand lists of FDA-approved devices for adults and for pediatrics (< 19 years of age) may be found in [Appendix K](#). Of note, the adult device brand list also provides a listing of unapproved devices that are not allowed for entry into INTERMACS®.
2. Patients receiving an MCSD must be at an INTERMACS®-activated hospital. The hospital is considered to be activated once it has received local IRB approval and has gained access to the INTERMACS® database.

For patients who do not meet the eligibility criteria, the following information will be recorded on the screening log:

- gender,
- race,
- age decade,
- brand of the implanted device (left or right side of the heart),
- date of implant,

- whether the patient is in an MCSD clinical trial, and
- death should it occur within 2 days of implant

Refer to Section 1.2 of the Users' Guide-**Appendix M** for adults and **Appendix N** for pediatrics. This basic information is necessary to assess completeness of patient capture and possible bias in the registry. No further information will be collected on patients who do not meet the eligibility criteria.

For patients who meet the eligibility criteria, additional data are requested for those individuals with congenital diagnoses. For adult (non-congenital) patients, these data elements are not visible.

#### 6.4 Enrollment and Assignment of Registry Identification Number

During the time that the patient is being consented for implant of their MCSD or as soon as possible after implant in emergent cases, consider providing each patient with a copy of the patient information summary. **The information sheet is provided as a courtesy and is not a requirement of INTERMACS®.** These attachments, Patient information sheets, one specific for adult and another specific for pediatric patients are provided in [Appendix C](#).

For those sites where a Waiver of Authorization and Consent has not been granted, patients will be required to sign an IRB/EB-approved informed consent and HIPAA authorization. Refer to [Appendix C](#) for instructions and templates.

All data will be entered electronically through the INTERMACS® web-based data entry system (INTERMACS® application). In order to begin entering patient data, click on the secure data entry login at the following link:

<https://intermacs.uab.edu/InterMACs/WBDE/Account/LogOn?ReturnUrl=%2fInterMACs%2fWBDE> and enter your user name and password. Once logged into the INTERMACS® application, select either INTERMACS® (patients ≥ 19 years of age) or pediMACS (patients < 19 years of age) for entering patient data. The instructions for data entry beginning with the Screening Log are located in the Users' Guide-[Appendix M](#) for adults and [Appendix N](#) for pediatrics Sections 1.2 and 2.1).

The Screening Log records the results of the inclusion/exclusion criteria and must be completed at the time of patient enrollment. Once the patient has met the eligibility criteria listed on the screening log, you will automatically be directed to the INTERMACS® or pediMACS data entry system.

A registry identification number, which is generated by the INTERMACS® application, will be assigned to each patient at the time of initial data entry into INTERMACS®. This identification number will be used as the primary patient identifier between the site, INTERMACS®, MCSD manufacturers, and government agencies.

## 6.5 Follow-up

For all patients entered into the registry, follow-up will occur at select time points (i.e., 1 week, 1 month, 3 months, 6 months and every 6 months thereafter) for as long as an MCSd is in place, or for up to 1 year, if a patient has an MCSd removed and is not transplanted. Vital status, including transplantation and survival, will be determined during this 1-year follow-up period. If a patient has an MCSd removed and is transplanted, then the patient is no longer followed in INTERMACS®. At that time, the patient becomes part of the Organ Procurement and Transplant and Network (OPTN) transplant database and will be followed by that database. A patient undergoing transplantation more than 1 year after VAD explantation will be included in INTERMACS® for the first year after explant, and then will be followed through the OPTN at the time of transplantation.

## 6.6 Transfer

If a patient transfers his/her care to another hospital, the patient is deactivated at the implanting hospital at the time of transfer. The patient is re-activated at the new center, provided the new center is an INTERMACS®-participating center.

The following steps must be completed for a patient transfer:

1. The original (implanting) hospital must complete any required event forms before the official date of transfer.
2. The original (implanting) hospital must complete the **Patient Registry Status Form** in the INTERMACS® application indicating that the patient is no longer receiving care.
3. The new hospital must have the patient complete the **Patient Authorization for INTERMACS® to Release Information Form**. In the event that the IRB/EB did not grant a waiver of consent at the new hospital, then the patient must also sign the local IRB/EB-approved Informed Consent Form.
4. The new hospital must provide the DCC with the patient's date of birth, gender, race and implant date ***before the patient can be transferred to the new site***.
5. If a patient is transferred to a site that uses a unique identifier in place of the patient's name or partial social security number, the following steps must be taken:
  - Ask the original (implanting) center to edit the name and partial social security number by using a code appropriate for the new (receiving) hospital. (The original center may require IRB approval prior to revising the identifiers.)
  - If a patient is transferred to a center that does not collect the partial social security number, then replace the number with "99999" as shown in the example below for patient "John Doe".

Example:

Old Identifiers:	Name - John Doe Partial SS# - 56789
New Code:	Name - Jo Do SS# Code - 99999

The registry-assigned ID number will remain the same.

6. The DCC will re-activate the patient once all submitted documentation has been verified as complete and accurate.

Once the transfer has been completed, the original (implanting) hospital will have “read only” access to pre-transfer INTERMACS® data and will no longer be able to review or make any changes to patient records after the transfer date. The new (receiving) hospital will have “read only” access to all forms prior to and up to the transfer date. Once the transfer has been completed, any follow-up entries automatically generated past the transfer, will be completed by the new hospital.

*[Note: Since the transfer process involves participant Protected Health Information (PHI), only send PHI through secure e-mail. Access to the INTERMACS® secure e-mail is available by contacting INTERMACS® at [intermacs@uab.edu](mailto:intermacs@uab.edu).]*

## 6.7 Data Collection

### 6.7.1 Web-based Data Entry

The INTERMACS® Application, which is a web-based data entry system, is comprised of a series of forms. The data to be collected are divided into forms that correspond to the clinical time course of the patient. It is critical that each site stay current with INTERMACS® data entry. Data that are submitted late will have an adverse effect on many of the internal INTERMACS® calculations, including survival estimates, incidence of adverse events, and rates of transplant. Forms should generally be completed within 10 days of an event, but always within 30 days. Forms entered beyond the 30-day window will be flagged as late and used as a criterion for site compliance as described in [Section 9.1](#).

Instructions for entering data along with the Data Dictionary for these forms are located in the Users' Guide ([Appendix M](#) for adults and [Appendix N](#) for pediatrics, Sections 1.0 and 2.0). Listed below are the clinical data forms requiring data entry along with the timing of data entry, if applicable, for each form. Specific instructions are located in the INTERMACS® and pediMACS Users' Guides in the specific sections listed next to each data entry form below.

### Demographics (Section 2.2 of Users' Guides)

- To be completed prior to implant and as close to implant as possible
- Collects the following data:

Name	Gender	Employment status - adults only
Medical record #	Ethnicity	Work level (e.g., full-time, part-time, disability) - adults only
Last 5 digits of SSN	Race	Participation in VAD study
Health Insurance Claim Number (HICN) - adults only	Marital status - adults only	
Date of birth	Education level - adults only	

### Pre-implant (Section 2.3 of Users' Guides)

- To be collected at the time of implant or closest to the implant date and within 30 days of pre-implant, but not to be collected in the operating room
- Collects the following information:

Height	Known cardiac biopsy - adults	Concurrent ICD or CRT
Weight	Prior cardiac surgeries	Metallozone/thiazide therapy - adults
Blood type	Admitting diagnosis	Phosphodiesterase inhibitors - adults
Device strategy	Hospital clinical events & interventions pre-implant	Laboratory values
Co-morbidities	Inotrope therapy	Medical condition – NYHA Class for patients $\geq$ 2 years, Ross Class for patients < 2 years
Time since first cardiac diagnosis	INTERMACS® profile at time of primary implant	Functional capacity (exercise function)
# of cardiac hospitalizations in last 12 months	Primary & secondary reasons for implant - pediatrics	QOL
Primary cardiac diagnosis	Hemodynamic parameters pre-implant	Neurocognitive function – adults
Secondary cardiac diagnosis – adults	Concurrent medications - adults	

### Implant (Section 2.4 of Users' Guides)

- To be completed within 1 week of post implant
- Collects information on:

Additional indication for VAD	LVAD inflow cannula parameters	RVAD pump size - pediatrics
Device type	LVAD outflow cannula parameters	Total artificial heart (TAH) UDI
Device brand	LVAD pump size - pediatrics	Associated findings (surgical observations or intraoperative TEE)
Implant date	RVAD UDI	Concomitant surgery
LVAD unique device identifier (UDI)	RVAD inflow cannula parameters	Total cardiopulmonary bypass and cross clamp times
Surgical approach	RVAD outflow cannula parameters	Total surgery time

### 1 Week and 1 Month Follow-up (Section 2.5 of Users' Guides)

- To be collected 1 week  $\pm$  3 days **and** 1 month  $\pm$  7 days post-implant date
- Collects information on:

Hemodynamic parameters	Transfusion - pediatrics	Functional capacity and Excursions - pediatrics
Concurrent medications	Laboratory values	Zones (hemolysis and right heart failure zones)
Pump change	Medical condition - NYHA Class patients $\geq$ 2 years, Ross Class for patients < 2 years	Adverse events

### 3 Month and 6 Month Follow-Up (Section 2.6 of Users' Guides)

- To be collected 3 months  $\pm$  30 days, 6 months  $\pm$  60 days, and every 6  $\pm$  60 days post-implant perpetually
- Collects information on:

Hemodynamic parameters	Device parameters	
Concurrent medications	Device inspection	Zones (hemolysis and right heart failure zones)
Pump change	Functional capacity (exercise function)	Neurologic status (adults)
Transfusion - pediatrics	Medical condition - NYHA Class patients $\geq$ 2 years, Ross Class for patients < 2	QoL



	years	
Laboratory values	Patient status	Neurocognitive function – adults
Device function	Functional capacity and excursions - pediatrics	Major outcomes & adverse events

### **Implant Discharge (Section 2.7 of Users' Guides)**

- Collects information about a patient from the device implant to one of the following occurrences during the implant hospitalization:
  - Patient is discharged from the hospital with a device in place;
  - Patient receives a transplant during the implant hospitalization (date of transplant is considered the date of discharge);
  - Patient dies during the implant hospitalization (date of death is considered to be the date of discharge); or
  - Patient has the device(s) explanted due to recovery (date of device(s) explant is considered to be the date of discharge).
- Information collected includes functional capacity, transfusions, pump change, major outcomes and adverse events.

### **Listing Date for Transplant (Section 2.8 of Users' Guides)**

- If the patient was NOT listed for transplant at the time of implant, then the list date for transplant, if applicable to patient, is collected on this form.

### **Re-hospitalization (Section 2.9 of Users' Guides)**

- To be collected within 1 week from re-hospitalization discharge and is intended to collect information about a patient from the date of re-hospitalization to one of the following occurrences:
  - Patient is discharged from the hospital with a device in place;
  - Patient receives a transplant during the re-hospitalization;
  - Patient dies during the re-hospitalization;
  - Patient has the device(s) explanted due to recovery during the re-hospitalization.

### **Adverse Events (Section 2.10 of Users' Guides)**

- Four forms are associated with the 4 major adverse events that are to be collected at the time of the event; they include: Major Infection, Neurological Dysfunction, Device Malfunction/Failure and/or Pump Thrombus, and Major Bleeding.
- For patients who experience a neurologic event post-implant, the modified Rankin Scale (mRS) scale must be administered and recorded at the time of the event and at follow-up visits as part of the patient's routine care (Refer to [Section 6.7.4 and Appendix I](#)). Event reminders for all other adverse events (Tier 2 Events) listed in [Appendix A](#), are asked during each follow-up and re-hospitalization.

- The occurrence of the following events are considered “trigger events”, which are triggered based on the relevant data collected at follow-up and re-hospitalization:
  - hemolysis
  - hypertension
  - right heart failure

**Death (Section 2.11 of Users’ Guides)**

- To be collected at the time of death
- Collects data related to the patient’s death, including date, time, place, cause, whether device was functioning normally, if expected or unexpected

**Explant for Device Exchange, Recovery or Transplant (Section 2.12 of Users’ Guides)**

- To be collected at the time of explant; this includes devices that are “turned off” AND left in place
- Collects data related to the explant, including device type, explant date, and reason for explant

**1 Year Post Device Recovery and/or Device Turned Off (Section 2.12b of Users’ Guides)**

- To be collected 1 year after one of the following events:
  - Ventricular recovery – device removed
  - Ventricular recovery – device not removed but turned off
  - Device removed (or turned off) for reasons other than recovery, transplant, or death
- Collects outcome data, including date of form completion, patient status, and date of outcome (e.g., transplant or death)

**Patient Registry Status (Section 2.13 of Users’ Guides)**

- To be completed when a patient transfers their care to another hospital as discussed in [Section 6.6](#);
- If the receiving hospital is not an INTERMACS® hospital, then patient records are ‘stopped’ at time of transfer.

**Quality of Life (Section 2.14 of Users’ Guides)**

- QOL questionnaires are to be administered pre-implant and post-implant (3 months, 6 months, and every 6 months thereafter) as part of the patient’s routine care; if these questionnaires are not considered standard of care at your site, INTERMACS® does not require the data.
- All adult patients should complete the EuroQoL (EQ-5D) and Kansas City Cardiomyopathy Questionnaire (KCCQ), which are located in [Appendix F](#) and [Appendix H](#), respectively, and discussed below in [Section 6.7.2](#).
- All pediatric patients should complete the Pediatric Quality of Life Inventory (PedsQL) and Ventricular Assist Device Quality of Life

(VADQoL) instruments, which are located in [Appendix F](#) and discussed below in [Section 6.7.2](#).

### **Neurocognitive Function Test (Section 2.15 INTERMACS® Users' Guide only)**

- The Trail Making B test is to be administered pre-implant and post-implant (3 months, 6 months and every 6 months thereafter) as part of the patient's routine care; if this assessment is not considered standard of care at your site, INTERMACS® does not require the data.
- All adult patients should complete the Trail-Making Part B test, which is located in [Appendix G](#) and discussed below in [Section 6.7.4](#).

## **6.7.2 Quality of Life Evaluation**

### **Adult Patients**

QoL will be measured by the EQ-5D and the KCCQ instruments in adult patients as part of the patient's routine care. If these assessments are not considered standard of care at your site, INTERMACS does not require the data to be entered into the web-based electronic database. The EQ-5D and KCCQ are located in [Appendix F](#) and [Appendix H](#), respectively.

The EQ-5D and KCCQ may be printed for the patient to complete. The EQ-5D and the KCCQ are available in English. It is anticipated that completing these instruments will take the patient 20 minutes per instrument. Administering the instrument and entering the data into the registry will require approximately 30 minutes of clinical staff time. The QoL instruments are completed pre-implant and post-implant (3 months, 6 months, and every 6 months thereafter for the life of the device).

The EQ-5D and KCCQ are provided to patients by trained clinical staff as designated by each participating medical center. The patient is to complete both instruments via self-report independently. If the patient is unable to complete these instruments, the trained clinician or a family member is to read the questions to the patient and complete both questionnaires documenting the patient's responses. Indicate on the instruments that the EQ-5D and KCCQ were self-administered or administered verbally by another. NOTE: There should be no coaching regarding responses.

The patient is to complete the EQ-5D and KCCQ *before MCS D implant and at the return clinic visits closest to the appropriate data collection time points* (assuming the patient has been discharged prior to the data collection time points). Otherwise, the questionnaires are to be administered during hospitalization at the appropriate data collection time points. **Pre-implant assessment of quality of life is essential in evaluating MCS D therapy.** Every effort should be made to obtain this information at each time point as part of the patient's routine care.

The EQ-5D and KCCQ are to be reviewed for missing or unclear data at the time of instrument completion. Corrections must be made with the patient at that time. Enter the patient's answers from the paper form into the database through [www.intermacs.org](http://www.intermacs.org).

For patients who do not complete the EQ-5D or KCCQ, enter reason as to why these questionnaires were not completed.

Refer to the Users' Guide ([Appendix M](#)) for additional data entry instructions.

### **Pediatric Patients**

In pediatric patients, QoL will be measured by the PedsQL and VADQoL instruments as part of the patient's routine care. If these assessments are not considered standard of care at your site, INTERMACS does not require the data to be entered into the web-based electronic database. The PedsQL and VADQoL may be printed for the patient/parent to complete.

The following PedsQL instruments are located in [Appendix F](#) in English, Spanish, and French:

- Parent Report for Toddlers (Ages 2-4 years)
- Young Child Report (Ages 5-7 years)
- Parent Report for Young Children (Ages 5-7 years)
- Child Report (Ages 8-12 years)
- Parent Report for Children (Ages 8-12 years)
- Teen Report (Ages 13-18 years)
- Parent Report for Teens (13-18 years)

The following VADQoL instruments are also located in [Appendix F](#) in English only:

- Parent Report for Children Ages < 2 years
- Parent Report for Children Ages ≥ 2 years
- Child Report for Children Ages > 8 years

It is anticipated that completing these instruments will take the patient/parent 20 minutes per instrument. Administering the instrument and entering the data into the registry will require approximately 30 minutes of clinical staff time. The QoL instruments will be completed pre-implant and post-implant (3 months, 6 months, and every 6 months thereafter for the life of the device) as part of the patient's routine care.

The PedsQL and VADQoL are provided to patients/parents by trained clinical staff as designated by each participating medical center. The patient/parent is to complete the PedsQL and VADQoL instruments via self-report independently. If the patient/parent is unable to complete the instruments, the trained clinician or a

family member is to read the questions to the patient/parent and complete the instruments documenting the patient's/parent's responses. Indicate on the instruments that the PedsQL and VADQoL were self-administered or administered verbally by another. NOTE: There should be no coaching regarding responses.

The patient/parent is to complete the PedsQL and VADQoL *before MCS D implant and at the return clinic visits closest to the appropriate data collection time points* (assuming the patient has been discharged prior to the data collection time points). Otherwise, the questionnaires are to be administered during hospitalization at the appropriate data collection time points. **Pre-implant assessment of quality of life is essential in evaluating MCS D therapy.** Every effort should be made to obtain this information at each time point as part of the patient's routine care.

The PedsQL and VADQoL are to be reviewed for missing or unclear data at the time of instrument completion. Corrections must be made with the patient/parent at that time. Enter the patient's/parent's answers from the paper form into the database through [www.intermacs.org](http://www.intermacs.org).

For patients who do not complete the PedsQL and VADQoL, enter reason as to why these instruments were not completed.

Refer to the Users' Guide ([Appendix N](#)) for additional data entry instructions.

### 6.7.3 Functional Capacity Evaluation

#### Adult Patients

Functional capacity measures are collected pre-implantation and within follow-up intervals post implant at 3 months, 6 months, and every 6 months thereafter. Included in these functional capacity measures are: 6 minute walk test (6MWT), gait speed, and cardiopulmonary exercise indices.

All patients should be encouraged to attempt to complete these functional capacity measurements especially for those patients classified as INTERMACS® patient profile levels 4-7:

- 6MWT: The 6MWT should be performed along a long, straight, quiet 30-meter corridor. The turnaround points can be marked with tape or a cone (such as a bright orange traffic cone). The subject's usual medications should be continued. Subjects should not have exercised vigorously for at least 2 hours prior to the walk test. Exercise can be done after a light meal.

The patient should sit in a chair near the start line for at least 5 minutes before the test starts. Resting heart rate and blood pressure should be checked to ensure that the patient is not too ill to undergo the test (e.g.,

patients with unstable angina, a heart rate >120 bpm, or systolic BP < 80 mm Hg should not undergo the walk test). The patient should then stand at the starting line.

Set the lap counter to zero and stopwatch to 6 minutes.

The following script may be used to instruct the patient:

"The object of the test is to walk as far as possible in 6 minutes. You will walk back and forth in this hallway to the designated markers. You will be exerting yourself and you may get exhausted or short of breath. You are permitted to slow down and stop if you need to rest. You may lean against the wall while resting but should resume walking as soon as you are able. You should make sharp turns around the markers and continue back and forth without hesitation. I will use a counter to keep track of your laps and click it each time you reach the starting line.

REMEMBER THE OBJECT OF THE TEST IS TO WALK AS FAR AS POSSIBLE IN 6 MINUTES BUT DON'T RUN OR JOG.

During the test I will tell you how much time has elapsed. I will let you know when there is only 15 seconds remaining. At the end of 6 minutes, I will tell you to stop. Please stay where you are and I will come to you.

Let me know when you are ready to start."

The staff member performing the test should not walk with the patient but should stand *behind* the patient to avoid undue influence on pace. He/she should use an even tone of voice and standard phrases of encouragement. He/she should not tell or signal to the patient to speed up or hurry. The staff member should report the time remaining to the patient. Use phrases like – "Keep up the good work. You have x minutes remaining." "Good job, you're halfway through." "You are doing well, x minutes remain."

All efforts should be made to perform the 6MWT for any patient able to walk more than a few steps. A distance as short as 3 feet may be recorded. If the test is not done, the reason must be indicated as "not done: too sick" or "not done: other", for which an example might be a patient needing to remain supine after a groin puncture for routine catheterization. Any musculoskeletal limitation to walking should be recorded as "not done: too sick".

- Gait Speed (First 15-foot walk): Record the time in seconds required for the patient to walk 15 feet. The "starting" line and the 15-foot line should be clearly marked. Record the time from the first footfall at 0 feet to the first footfall at 15 feet in the nearest 0.1 seconds with a stopwatch. NOTE: You may use the time from the first 15 feet of the 6MWT for the Gait Speed test.

All efforts should be made to perform the Gait Speed test for any patient able to walk more than a few steps. If the test is not done, the reason must be indicated as “not done: too sick”, “not done: other” or “none”.

- Maximum volume of oxygen the body can consume during exercise (Peak VO<sub>2</sub> Max) is measured in mL/kg/min: Peak VO<sub>2</sub> Max is measured during symptom-limited cardiopulmonary exercise (CPX) either on a bicycle or treadmill. The values recorded during bicycle CPX are usually 1-2 mL/min lower than for the treadmill; however, it is assumed that most institutions will use only one instrument. If both are available, the bicycle is preferable as the mode easiest to standardize. If CPX is not done, the reason must be indicated as “not done: too sick”, “not done: other” or “none”.
- R Value at Peak: R Value at Peak is the respiratory quotient of carbon dioxide production divided by oxygen consumption and is used as an index of how vigorously the patient exercised. A value above 1.05 is generally considered to represent an adequate effort. If CPX is not done, the reason must be indicated as “not done: too sick”, “not done: other” or “none”.

Refer to the Users' Guide ([Appendix M](#)) for additional data entry instructions.

### **Pediatric Patients**

Functional capacity measures for pediatric patients ages  $\geq 10$  years are collected pre-implantation and within follow-up intervals post implant at 3 months, 6 months, and every 6 months thereafter. Included in these functional capacity measures are: 6MWT, gait speed, and cardiopulmonary exercise indices as described above for adults. All patients  $\geq 10$  years of age at the time of implant should be encouraged to attempt to complete these functional capacity measurements especially for those patients classified as pediMACS patient profile levels 4-7:

- 6MWT: If the test is not done, the reason must be indicated as “not done: too sick”, “not done: other”, or “not done: age inappropriate”.
- Gait Speed test: If the test is not done, the reason must be indicated as “not done: too sick”, “not done: other”, or “not done: age inappropriate”.
- Peak VO<sub>2</sub> Max: If CPX is not done, the reason must be indicated as “not done: too sick”, “not done: other”, or “not done: age inappropriate”.
- R Value at Peak: If CPX is not done, the reason must be indicated as “not done: too sick”, “not done: other”, or “not done: age inappropriate”.

For pediatric patients  $< 10$  years of age, general functional capacity data is collected pre-implant, implant discharge, and at follow-up intervals (i.e., 3 and 6 months and every 6 months thereafter for as long as the MCS is in place).



These data include the child's functional capacity (e.g., sedated, paralyzed, intubated, ambulating), primary nutrition, and if the patient has had non-medically required excursions off the unit (collected at 1 week and 1 month post implant and at implant discharge).

Refer to the Users' Guide ([Appendix N](#)) for additional data entry instructions.

#### 6.7.4 Neurocognitive Evaluation

##### Trail Making Neurocognitive Test, Part B

Neurocognitive function will be measured by the Trail Making Neurocognitive Test, Part B in adults only as part of routine care. If this assessment is not considered standard of care at your site, INTERMACS® does not require the data to be entered into the web-based electronic database. The test is located in [Appendix G](#) and must be printed for the patient to complete. This test of general cognitive function also specifically assesses working memory, visual processing, visuospatial skills, selective and divided attention, and psychomotor coordination. It is anticipated that completing this assessment will take less than 5 minutes of the patient's time.

The Trail Making Test, Part B, requires the patient to draw in ascending order and alternating sequentially between circled numbers (1-13) and alphabet letters (A-L) without lifting the pencil. The test is timed (measured in seconds), with the faster times (seconds) being better. Lifting the pencil and wrong direction with the examiner prompting constitutes errors.

The test is to be administered **pre-implant** and **post-implant** (at 3 months, 6 months, and every 6 months thereafter) as part of the patient's routine care.

After the subject completes Part B, take the test sheet and record the time in seconds. Errors contribute to the evaluation of the performance principally by increasing the total performance time. If the patient completes the test, but the test is considered invalid, select "completed but invalid (score not entered)". ***Do not allow patient to retake the test.***

Steps in administering the test are as follows:

1. Let the patient practice with the Trail Making Sample B. The following script may be used to instruct the patient (refer to italicized text):

*"On this page are some numbers and letters. Begin at 1 (point to the number 1) and draw a line from 1 to A" (point to A) "A to 2," (point to 2), "2 to B" (point to B), "B to 3" (point to 3), "3 to C" (point to C), "and so on, in order, until you reach the end" (point to the circle marked "end").*



*“Remember, first you have a number” (point to 1), “then a letter” (point to A), “then a number” (point to 2), “then a letter” (point to B), “and so on. Draw the lines as fast as you can. Ready--- Begin!”*

If the subject completes the sample B correctly say: *“Good! Let’s try the next one.”* Proceed immediately to the test as described in step 2 below.

**If the subject makes a mistake on sample B, point out the error and explain why it is incorrect.** The following explanations of mistakes serve as illustrations:

*“You started with the wrong circle. This is where you start (point to 2). “You skipped this circle” (point to the circle the subject omitted). “You should go from 1” (point to 1) “to A” (point to A), “A to 2” (point to 2), “2 to B” (point to B), “B to 3” (point to 3), “and so on until you reach the circle marked end” (point to the circle marked “end”).*

**If the subject cannot complete Sample B,** take his/her hand and guide the pencil, using the eraser end, through the circles. Then say:

*“Now you try it. Remember, you begin at number 1” (point to the number 1), “and draw a line from 1 to A” (point to A), “A to 2” (point to 2), “2 to B” (point to B), “B to 3” (point to 3), “and so on until you reach the circle marked ‘end’.” (point to this word), “Ready --- Begin!”*

2. Ask patient to complete the actual Trail Making Test, Part B.

After the subject has correctly completed the sample, turn the paper over to Part B and say:

*“On this page, there are both numbers and letters. Do this the same way. Begin at number 1” (point to 1), “and draw a line from 1 to A” (point to A), “A to 2” (point to 2), “2 to B” (point to B), “B to 3” (point to 3), “3 to C” (point to C), “and so on, in order, until you reach the end” (point to the circle marked “end”). “Remember, first you have a number” (point to 1), “then a letter” (point to A), “then a number” (point to 2), “then a letter” (point to B), “and so on. Do not skip around, but go from one circle to the next in the proper order. Draw the lines as fast as you can. Ready ---Begin!”*

Using a stopwatch, start timing as soon as the subject is told to begin. Remember to be alert for mistakes. If the subject makes an error, DO NOT STOP TIMING. Point it out immediately, return the subject to the last correct circle and say, *“Now, are you looking for a number or a letter?”* Continue the test from that point. DO NOT STOP TIMING.

After the subject completes Part B, take the test sheet and record the time in seconds. Errors contribute to the evaluation of the performance principally by increasing the total performance time. If the patient completes the test, but the test is considered invalid, select “**Other, specify**” and, specify the reason you are not entering a score. ***Do not allow patient to retake the test.***

Refer to the Users’ Guide ([Appendix M](#)) to enter the Trail Making Data results. Status (e.g., completed, completed but invalid, attempted but not completed, not attempted) and the time it required to complete the test (in seconds) must be entered.

### **Modified Rankin Scale (mRS) Score**

For patients who experience a neurological event post-implant, the mRS score ([Appendix I](#)) must be recorded. The mRS is a scale commonly used for measuring the degree of disability or dependence in the daily activities of individuals who have suffered a stroke. The mRS is administered at the time of the event and at follow-up visits after the event. The assessment requires approximately 5 minutes to complete.

The scale runs from 0-6, running from perfect health without symptoms to [death](#):

- 0 - No symptoms
- 1 - No significant disability despite symptoms; able to carry out all usual duties and activities.
- 2 - Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance.
- 3 - Moderate disability; requires some help, but able to walk unassisted.
- 4 - Moderately severe disability; unable to walk unassisted and unable to attend to own bodily needs without assistance.
- 5 - Severe disability; bedridden, incontinent, and requiring constant nursing care and attention.
- 6 - Dead

Only clinical staff trained to administer the test may do so. Training may be obtained at the following website:

<http://www.rankinscale.org/>.

## **7 Informed Consent and Release of Medical Records**

***[NOTE: The INTERMACS® protocol inadvertently refers to Section 7.3 of this MOP for a description of the medical device reporting process. However, this process is described in [Section 10](#) of this MOP. The protocol will be corrected via the next protocol amendment.]***

INTERMACS® does not require additional consent other than the routine consent that is required for the MCSD surgical procedure because this is a quality improvement registry. In general, information will be retrieved from existing medical records. Minimal testing and contact with the patient outside of the index hospitalization is required for follow-up interviews and physical examination. Physical examination, functional capacity testing, and interviews are considered standard of care for these patients. **No data beyond the data gathered in the course of routine care will be collected for this registry.**

## 7.1 Waiver of Authorization and Consent

For sites who have been granted a Waiver of Authorization and Consent, consider providing patients (or their parents) with a written summary describing INTERMACS® at the time that the patient/parent is completing the routine MCSD surgical consent form. Patient Information Sheets, one for adult patients and one for pediatric patients, may be provided as a courtesy but are not a requirement of INTERMACS®. These sheets are located in [Appendix C](#).

**NOTE: Before providing the Patient Information Sheet to the patient/parent, insert the name of your institution in the first paragraph and the appropriate contact information at the bottom of the page to ensure that all patients have access to qualified staff for any questions they may have regarding INTERMACS®.**

## 7.2 Informed Consent Process

In the event that Waiver of Consent is not granted by the IRB/EB, then participating sites should follow their local IRB/EB policies in regard to obtaining informed consent. Informed consent templates for adult and pediatric patients are located in [Appendix C](#), with instructions for use.

- **Adult Templates Available**
  - Informed Consent for Participation in INTERMACS®
  - Patient Authorization for INTERMACS® to Release Information (for patient transfers)
  - Revoke Authorization (for patient withdrawal)
- **Pediatric Templates Available**
  - Informed Consent for Participation in pediMACS
  - Patient Authorization for pediMACS to Release Information (for patient transfers)
  - Revoke Authorization (for patient withdrawal)

Customize the templates that are specifically required by your IRB/EB before submitting to your IRB/EB. For any questions during the submission process, contact the DCC at [intermacs@uab.edu](mailto:intermacs@uab.edu).

In some cases, the local IRB/EB may grant a waiver of authorization and consent for the overall registry but require written consent for a particular evaluation (e.g., Trail Making Test, Part B). Each site should work with their local IRB/EB to develop consent forms for specific evaluations as required. The DCC is available to provide assistance as needed. [Note: INTERMACS® does not require any evaluations that are not considered standard of care at your institution.]

### **Consent Process**

Obtaining informed consent and timing for the informed consent process must be consistent with the clinical center's institutional IRB/EB and privacy policies. The investigator or a designated individual will provide a thorough explanation of the objective, patient responsibilities, risks and benefits of the registry, and will fully address concerns raised by the patient and/or family. The consent process (and its documentation) must begin prior to all data collection and protocol procedures. This is to ensure that all potential study participants are given adequate time to review the informed consent document and consider participation in the trial.

A patient should be encouraged to have family or other support available during the informed consent process. They should be assured that declining to sign an informed consent document will in no way compromise their care, and that should they consent to participate in the study, they may revoke that consent at any time.

A signed copy of the consent form must be given to the study participant. All signed consent forms, including the initial consent and any re-consents must be available for audits (e.g., by INTERMACS® and/or local IRB/EB).

The consent process must be documented in the study participant's record according to the institutional requirements. The investigator or his/her designee must:

- Document any questions addressed with the patient and/or family during the informed consent process in the medical chart;
- Confirm that all signatures on the informed consent are complete and dated;
- File the original signed informed consent with study participant's research documents.

### **Non-English Speakers or Hearing Impaired**

Clinical sites must abide by local institutional guidelines when approaching a non-English speaker or patient with a hearing impairment during the informed consent process. Local IRBs will have guidelines in place that must be followed. For all consented non-English speaking or hearing impaired participants, the clinical site must document the information noted in the above paragraph but also specify such information as:

- A brief description of local policy on consenting a non-English speaker or patient with a hearing impairment;
- A brief description of how the policy was followed in the consent process for these patients;

- The name of the translator and/or anyone else present at the time of consent; and
- A statement that the patient was given the opportunity to ask questions and to receive answers about the study in his/her native/sign language.

### **Visually Impaired or Low Literacy Level**

Clinical sites must abide by local institutional guidelines in the informed consent process for visually impaired or patients with a low literacy level. As with consenting non-English speakers and hearing impaired patients, the clinical sites must specify additional information on the consenting process including:

- A brief description of the local policy on consenting patients with visual impairments or literacy challenges;
- A brief description of how this policy was followed in the consent process for this patient;
- The name of the person reading the consent form to the patient and/or anyone else present at the time of the consent; and
- A statement that the patient was given the opportunity to ask questions and to receive answers about the informed consent document as it was read to him/her.

## **7.3 HIPAA and Release of Medical Records**

In the event that Waiver of Authorization is not granted, each site is required to follow their institutional policy for HIPAA Authorization and Release of Medical Information. Consent to authorize release of medical records to the trial investigators, monitors, government agencies (NHLBI, FDA, CMS), device manufacturers, and the DCC must be obtained for registry participation. Sample (adult and pediatric) HIPAA Authorization templates are provided in [Appendix C](#). Customize these templates per local institutional policy before submitting to your IRB/EB. For any questions during the submission process, contact the DCC at [intermacs@uab.edu](mailto:intermacs@uab.edu).

## **8 Training**

### **8.1 Privacy Awareness Training**

Site staff who will have access to the INTERMACS® Application must complete Privacy Awareness Training offered either locally or by the NIH. The NIH training modules can be accessed via the following link: <http://irtsectraining.nih.gov/>.

Follow the steps below to access the Privacy Awareness Training module:

1. Click on “Public Access to NIH Courses Enter Here” (bottom left hand corner)
2. Click on “Enter Training”
3. Click on “Entire Privacy Awareness Course”
4. Upon completion of the course print or save the certificate of training completion.
5. Submit the “Privacy Awareness Course” certificate of completion to the DCC as part of the enrollment package.

Once activated, INTERMACS® requires evidence of current training to remain a Member in Good Standing. Site staff who have access to the INTERMACS® Application must complete refresher training in accordance with local IRB policy or every 2 years, whichever comes first, and submit the certificate of refresher training to the DCC. If local training is not available, then the NIH Privacy Refresher Course can be accessed at: <http://irtsectraining.nih.gov/>.

Follow the steps below to access the refresher training module:

1. Click on “Public Access to NIH Courses Enter Here” (bottom left hand corner)
2. Click on “Enter Training”
3. Click on “[*Current Year*] NIH Annual Privacy Refresher”
4. Upon completion of the course print or save the certificate of completion.
5. Submit the “Privacy Refresher” certificate of completion to the DCC as part of the re-certification package (as outlined in [Section 6.2](#)).

## **8.2 Web-based Data Entry System (INTERMACS® Application) Training**

Training for participating clinical centers on the INTERMACS® Application will occur immediately prior to site activation as stated in [Section 6.1](#). Additional training occurs periodically after major changes are made to the system (e.g., with a protocol amendment) and on an as needed basis (e.g., for new site staff or staff having a specific issue with the system).

Web-based interactive software is used to conduct training. This is a secure, subscription-based service that allows for meetings and their related documents to be conducted in a virtual electronic environment. Participants are allowed to view the trainer’s desktop. Attendees follow along as the trainer shows step-by-step instructions and are able to ask questions and receive answers during the training.

In addition to training, a comprehensive **INTERMACS® Site User’s Guide** provides step-by-step instructions for entering data into the INTERMACS® Application and will include definitions for all fields collected in the system. The Users’ Guide will also identify main processes in the application and explain standard procedures for data collection. Refer to **Appendix M and N**, respectively, for adult and pediatric patients.

The DCC is available to provide assistance with data collection and entry, regulatory questions, data requests and analyses, and technical support. Refer to [Appendix L](#) for a complete list of DCC contacts.

## 9 Quality Assurance

### 9.1 Overview

Site performance as it pertains to the data entry process into INTERMACS® will be closely and regularly monitored for compliance, completeness, and accuracy by the DCC. The focus of monitoring is on:

- completeness of the data entered into the INTERMACS® Application during the index hospitalization, re-hospitalizations, and follow-up evaluations; and
- identification of impossible or improbable combinations of variables utilizing edit checks.

#### Data Completeness

As stated in [Section 6.7.1](#), forms should generally be completed within 10 days of an event, but always within 30 days. Forms entered beyond the 30-day window will be flagged as late. On a quarterly basis, the proportion of late forms will be calculated and used as a criterion for site compliance. This approach will also allow evaluation of follow-up forms that are not completed.

Summary screens as well as reports of patients and devices entered, current patient status, most recently reported event(s), and other data will be available to the member institutions to assist the institution in assessing the completeness of data entry. When missing data are identified by either the DCC or clinical center, the DCC will work with the center to either obtain the missing data or determine that the data cannot be obtained because evaluations could not be done. The latter information must be noted in the INTERMACS Application (e.g., not done: too sick).

#### Data Accuracy

At the end of each quarter, data submitted by the sites are checked for internal consistency by the DCC. For example, heights and weights will be compared to identify patients with improbable or impossible combinations. These checks will result in lists of possible errors that will be sent to the sites. Sites with a high proportion of impossible data will be flagged. In addition to quarterly data checks for internal consistency, site staff are required to provide INTERMACS® with a list of MCSDs that were implanted during the previous quarter at their institution, but were not entered into INTERMACS®. This list will only include the type of device, brand of device, implant date, and reason for not entering into INTERMACS®. As a check on the total implants at an institution, MCSD manufacturers will provide a tally of all implants at each institution by calendar periods.

All questionable data points entered into the INTERMACS® Application will be verified with the site. Depending on the types of discrepancies identified, the DCC will contact participating centers to resolve these issues. Resolution may be accomplished via telephone contact, e-mail, and/or hard copy mailings. Participating centers will be able to review and modify previously submitted data at any time. Resolution of the noted discrepancies and deficiencies will be tracked by the DCC.

## **9.2 Data Audits**

In addition to the remote monitoring performed by the DCC as described in the previous Section, INTERMACS® monitors conduct data audits to ensure the highest possible quality of the data. The audit process for all participating INTERMACS® sites involves interactions in the form of an on-site visit or a review of the documents submitted to the DCC and discussion with site staff via telephone and/or WebEx (remote review). Sites are notified up to 60 days prior to a routine on-site audit. Audited data include key data fields, as determined by INTERMACS®.

The INTERMACS® monitor contacts the site by phone for a pre-audit review approximately 2 weeks before the scheduled audit. During the call, the monitor reviews site specific summaries for duplicated events, unknown sources of bleeding, unknown causes of death, device explant inconsistencies and any other noted discrepancies. The sites are requested to make corrections and to provide redacted source documentation (as needed for remote review), prior to the actual audit.

During the audit, monitors will review data accuracy of web-based data submissions and information contained in source documents as well as participant performance and progress. The audit process helps to identify member institutions that perform poorly in data submission compliance.

## **9.3 Hospital Standards Committee Review**

To assist the Hospital Standards Committee in overseeing site compliance, the DCC maintains score cards for each participating center based on several measures such as meeting IRB requirements, timely submission of regulatory documents to the DCC (e.g., Conflict of Interest Disclosure, training certificates, IRB approvals where applicable), accounting for all MCSDs, timely submission of complete data, and quality of submitted data. The score card serves as the primary tool to evaluate site performance.

Periodically, the Hospital Standards Committee, which reviews hospital performance and recommends actions to reestablish compliance, will objectively review these score cards. For sites performing below acceptable metrics, the Committee will require “for cause” audits to be conducted by the INTERMACS® monitors. All audit results will be reported to both the Hospital Standards and Executive Committees. The INTERMACS® monitors, in collaboration with the Hospital Standards Committee, will work with underperforming sites to identify reasons for low rates of data collection and/or tardy data submission. These institutions will be retrained on proper data collection methods with the goal of identifying and overcoming obstacles to submission.

## **9.4 Medical Event Review**

Medical event review is an important component of the INTERMACS® quality assurance program and is a function of both the DCC and the Medical Event Review Committee. The Committee will:



- provide guidance on summarizing and evaluating the quality of the adverse event data;
- provide strategies for electronically identifying duplicate events and questionable events;
- focus on the review and categorization of device malfunction; and
- provide guidance to the nurse monitors for auditing the correct capture of adverse events. All data identified as questionable are resolved via direct interactions between the nurse monitors and the local hospital.

## **9.5 Observational Study Monitoring Board Oversight**

To further evaluate INTERMACS® and provide an independent expert perspective, an NHLBI-appointed (independent) Observational Study Monitoring Board (OSMB) was established in 2006 and meets, at a minimum, annually.

The principal role of the OSMB is to regularly monitor the data from the registry, review and assess the performance of its operations, assure patient safety, and make recommendations, as appropriate, to the NHLBI and INTERMACS® co-investigators with respect to:

- the performance of individual centers (including possible recommendation on actions to be taken regarding any centers that perform unsatisfactorily);
- issues related to maintenance of patient confidentiality;
- adequacy of registry processes in terms of:
  - the number of patients enrolled into INTERMACS® and the number of MCSDs that were implanted
  - quality control
  - data completeness
  - data analysis, and
  - publications
- issues pertaining to patient burden;
- impact of proposed ancillary studies and sub-studies on patient burden and overall achievement on the main registry goals;
- possible modifications in the registry protocol; and
- overall scientific direction of the registry

The OSMB is composed of a Chair and members with expertise in biostatistics, clinical trials, bioethics, heart failure, cardiac surgery, bioengineering and device complications. Ad hoc members may be added to the OSMB to have greater representation of expertise in a relevant biomedical field. All standing members of an OSMB may vote. Ad hoc members have the same voting rights as standing members when reviewing the protocol.

The DCC will prepare and distribute data reports at least 10 working days prior to an OSMB meeting/conference call. The basic format for the presentation of ongoing data and the need to provide these data within a certain time frame was established at the initial OSMB meeting.

During the meeting, the OSMB discusses the registry's overall performance, data quality, and subject burden. The DCC, in consultation with the Executive Committee, is responsible for preparing the meeting materials. Meeting materials are distributed by the DCC to the Board members approximately 10 days prior to the meeting. The NHLBI Executive Secretary facilitates the meetings in conjunction with the Chair and prepares minutes for approval by the Chair and NHLBI Office of the Director.

The NHLBI policy on its Monitoring Boards is located at:  
<http://www.nhlbi.nih.gov/funding/policies/dsmpolicy.htm>.

## 10 Medical Device Reporting

### 10.1 Overview

Medical device reporting (refer to [21 CFR Part 803](#)) establishes the reporting requirements for device user facilities, manufacturers and importers and serves as a mechanism for the FDA and manufacturers to identify and monitor significant adverse events involving marketed medical devices. The types of events that must be reported to the FDA are as follows:

- If the device may have “**caused or contributed**” to a death or serious injury.
- Certain device malfunctions.

“**Caused or contributed**” in this case means:

- Death or *serious injury* was or may have been attributed to a medical device;  
**or**
- A medical device was or may have been a factor in a death or *serious injury*, including events resulting from:
  - Failure
  - Malfunction
  - Improper or inadequate design
  - Manufacturing (problems)
  - Labeling (problems)
  - Use error

**A reportable serious injury is defined as:** An injury or illness that is

- Life-threatening  
**or**
- Results in permanent impairment or damage to a body function or structure,  
**or**
- Requires medical or surgical intervention to preclude permanent impairment or damage to a body function or structure

**A device malfunction is reportable when:**

- The device fails to meet its performance specifications or otherwise perform as intended
- **and**
- The device is “**likely to**” cause or contribute to a death or serious injury if the malfunction were to recur

Considerations for “**likely to**” include:

- Has there been a previous device-related death or serious injury?
- Has there been a previous “near miss” event?
- Is the device used in a setting that includes alarms and close monitoring?
- Is the device used on critical patients who would face life-threatening consequences?
- Can the source of the problem be identified?
- Are all reports of this malfunction investigated to verify that reported malfunctions have not led or contributed to death or serious injury?

[21 CFR Part 803](#) additional requirements include:

- The device manufacturer must conduct a complete investigation of each event (as per [21 CFR Part 820.198](#));
- All information required in [21 CFR Part 803.52](#);
- Develop and implement written Medical Device Reporting Procedures ([21 CFR Part 803.17](#));
- Establish and maintain Medical Device Report (MDR) event files; and
- Have a system in place that ensures access to information that facilitates timely follow-up/inspection by the FDA.

The FDA allows for exemptions, variances, and alternative forms of adverse event reporting for medical devices through [21 CFR 803.19](#). Exemptions, variances, and alternative forms of reporting can only be granted by the FDA, and exemption orders cannot be modified. Rather, they are rescinded and re-established by the FDA.

There are six types of 21 CFR 803.19 Exemptions granted today, of which two types pertain to INTERMACS® stakeholders (*i.e., INTERMACS® participating hospitals and device manufacturers*):

- **Single Reporter Exemption (SRE)**
  - *Allows one party to report on behalf of another party. The reporting party assumes ALL of the reporting obligations of the other party, unless otherwise ordered.*
  - *SREs are granted to help facilitate better reporting from hospitals and manufacturers. This serves to feed manufacturers “enriched” reports, which would result in more useful reports to FDA’s medical device reporting program.*

- **Time Variance Exemption (TVE)**
  - Grants a modification to the normal reporting timeframe from that listed in [21 CFR 803.10](#), on a per need basis, at the discretion of FDA.
  - TVEs are granted to device manufacturers to allow them additional time to investigate these “enriched” reports to ensure the completeness and accuracy of the manufacturer’s report to the FDA.

By granting SREs and TVEs, the FDA expects to obtain:

- Enriched reports on all reportable events from user facilities
- Better quality investigation from manufacturers
- Measurable impact of “Enriched” user facility reports

## 10.2 INTERMACS®

In accordance with [21 CFR 803.19](#), sites participating in INTERMACS® (which the FDA refers to as “user facilities”) are exempt from the normal requirements in [21 CFR 803.30](#) for adverse events reported to INTERMACS®. Instead, INTERMACS® will make the appropriate reports to both the manufacturer and FDA on behalf of the site. Refer to **Figure 1** for a copy of the letter provided by the FDA to describe the SRE.

### Figure 1. Single Report Exemption (User Facility)

*“Dear User Facility:*

*FDA has been informed that your facility is participating in the INTERMACS registry, to collect information regarding mechanical circulation support devices. Because of your participation in the INTERMACS registry, you are exempt from the normal requirements in 21 CFR 803.30 for adverse events reported to INTERMACS. On your behalf, the INTERMACS registry will make the appropriate reports to both the manufacturer and FDA.*

*This exemption is specific to the mechanical circulation support devices in the INTERMACS registry. All other adverse events, not covered by your participation in the INTERMACS registry, will to [sic] be subject to the normal user facility reporting requirements in 21 CFR 803.30.”*

**NOTES:** 1. INTERMACS agrees to reporting to both manufacturer and FDA.  
2. PEDIMACS is not covered by this exemption.

Also in accordance with 21 CFR 803.19, device manufacturers participating in INTERMACS® are exempt from the 30 calendar day reporting requirement in [21 CFR 803.50](#). Instead, any adverse event reported to or received from INTERMACS®, which meets the threshold for reporting in accordance with the MDR Regulation (21 CFR 803.50) is due to FDA no later than 90 calendar days after the device manufacturer becomes aware of the event. All other FDA requirements concerning adverse event or complaint handling, investigation, retention, etc. remain unchanged. Refer to **Figure 2** for a copy of the letter that device manufacturers receive from FDA.

## Figure 2. Time Variance Exemption (Manufacturers)

*“Dear Manufacturer:*

*FDA has been informed that your facility is participating in the INTERMACS registry, to collect information regarding mechanical circulation support devices. Because of your participation in the INTERMACS registry, FDA is granting your firm an exemption from the 30 calendar day reporting requirement in 21 CFR 803.50.*

*Any adverse event reported to or received from the INTERMACS registry which meets the threshold for reporting in accordance with the Medical Device Reporting (MDR) Regulation (21 CFR 803.50) is due to FDA no later than 90 calendar days after your firm becomes aware of the event. FDA is granting this additional time so that your firm can do a thorough and complete analysis of the event and include your findings in the MDR report. All other FDA requirements concerning adverse event or complaint handling, investigation, retention, etc. remain unchanged. The manufacturer must follow normal procedures used for non-INTERMACS related events. The manufacturer must submit any reportable events on the mandatory FDA Form 3500A. Reportable events are further clarified in the MDR Regulation in 21 CFR 803.”*

Because of the exemptions granted to INTERMACS® participating sites, ***it is important to report all deaths and serious injuries that your site PI considers MCSD-related to INTERMACS® at the time that you learn of the event.*** The DCC may follow-up with questions so that they can complete their reports to the FDA and device manufacturer, respectively. You will receive a summary of all reports submitted to the FDA and device manufacturer as part of your quarterly site report.

The device manufacturer will follow-up with you as needed to complete their investigation and report to the FDA per regulations. As stated in the letter to manufacturers (Figure 3), FDA is granting a TVE so that the manufacturer can do a thorough and complete analysis of the event, which is critical to post-market monitoring and also supports premarket decision making. For example, MDRs are:

- used to monitor a manufacturer's compliance and behavior in investigating adverse events under 21CFR 820.198;
- used as evidence in recalls, seizure, injunction, Office of Criminal Investigation, and Department of Justice cases;
- provide information on how a device or a family/class of devices performs;
- used to collect information on long-term performance of devices;
- used to identify and monitor the severity of patient, device, and use-related problems).

INTERMACS® (on behalf of participating sites/user facilities) and manufacturer reporting requirements as summarized in the table below.

**Summary of MDR Reporting Requirements For INTERMACS® Only**

REPORTER	WHAT TO REPORT	WHERE	WHEN
<b>Manufacturer*</b>	Deaths, Serious Injuries, Malfunction	FDA	Within <i>90 calendar days</i> of becoming aware
	Events that require remedial action to prevent an unreasonable risk of substantial harm	FDA	Within 5 working days of becoming aware
<b>INTERMACS®</b> (on behalf of User Facility)*	Deaths	FDA and Manufacturer	Within 10 working days
	Serious Injury	Manufacturer	Within 10 working days
<b>Voluntary</b>	Any type of event	FDA	Any time

\*Per 21 CFR 803.19, SRE and TVE granted by the FDA.

### 10.3 pediMACS

As stated above, the FDA requires “user facilities” to report all serious injuries or deaths associated with a medical device to them within 10 working days of occurrence through an MDR. ***The MDR Exemptions granted to INTERMACS® by the FDA do not apply to pediMACS.*** Therefore, all sites participating in pediMACS are required to report serious injuries and deaths where the device may have caused or contributed to the event according to [21 CFR 803.10](#).

To assist participating pediatric implanting centers in meeting their post-market reporting requirements, the DCC will provide them with:

- Deaths: completed MDRs to submit to the FDA and the device manufacturer(s)
- Serious Injuries: reports to submit to the device manufacturer(s)

Therefore, ***it is important to report all deaths and serious injuries that your site PI considers MCS-related to pediMACS at the time that you learn of the event.*** The device manufacturer will follow-up with you as needed to complete their investigation and report to the FDA per MDR regulations.

User facility and manufacturer reporting requirements for pediMACS are summarized in the table below.

***Summary of MDR Reporting Requirement 21 CFR 803.10***

<b>REPORTER</b>	<b>WHAT TO REPORT</b>	<b>WHERE</b>	<b>WHEN</b>
<b>Manufacturer</b>	Deaths, Serious Injuries, Malfunction	FDA	Within 30 calendar days of becoming aware
	Events that require remedial action to prevent an unreasonable risk of substantial harm	FDA	Within 5 working days of becoming aware
<b>User Facility</b>	Deaths	FDA and Manufacturer	Within <b>10 working days</b>
	Serious Injury	Manufacturer	Within <b>10 working days</b>
<b>Importer</b>	Deaths and Serious Injuries	FDA and Manufacturer	Within 30 calendar days
	Malfunctions	Manufacturer	Within 30 calendar days
<b>Voluntary</b>	Any type of event	FDA	Any time

## **11 Data Access**

All INTERMACS® stakeholders have the ability to request raw data and/or submit proposals for DCC data analysis. For example, INTERMACS® participating sites may request their own data for quality improvement purposes required outside of the standard reports provided by INTERMACS® (discussed in [Section 12](#)). INTERMACS® also maintains open communication channels with its federal partners (NIH, FDA, and

CMS). Additionally, device manufacturers have access to data specific to their devices. The types of data that INTERMACS® releases are dependent on the specific request, which can include:

- Raw de-identified data sets (currently provided in Statistical Analysis System (SAS) format);
- Device manufacturer-specific data sets with limited PHI, as required by law, for safety purposes (requested by the device manufacturer and/or FDA);
- Analyzed data sets; or
- Select items in Excel format to participating centers (after June 1, 2014).

The policy for data access and/or analysis is located in the Administrative MOPP. Request forms are located in [Appendix J](#).

INTERMACS® also makes data and analytical resources available to the MCSD community for research purposes, in order to fulfill its goal of disseminating rigorously analyzed scientific information to the large community of physicians and other professionals interested in MCSDs for advanced heart failure. Publications originate from four general sources: (a) governmental initiatives, (b) investigator initiatives from within the Executive Committee and the Operations Committee, (c) investigator initiatives from participating INTERMACS® hospitals, and (d) investigator initiatives from the medical and scientific community. The INTERMACS® Publication Policy is located in the Administrative MOPP, and guidelines are located at:

<http://www.uab.edu/medicine/intermacs/data-request>.

## 12 Standard Quality Improvement Reports

The DCC prepares standard reports for its stakeholders at specific points during the year. These reports include:

- Public Reports (also referred to as Federal Partners Reports):  
On a quarterly basis, INTERMACS® produces a cumulative statistical report that is available to the public. This report is intended to give a current status of the Registry and contains de-identified data analyses so that no participating site can be identified nor can a specific device. Public reports may be accessed at: <http://www.uab.edu/medicine/intermacs/research/statistical-summaries>.
- Site-specific Reports:  
On a quarterly basis, reports containing site-specific information are sent individually to each participating hospital via secure email. The information contained in these reports includes:
  - a quality assurance component that compares the results of the individual hospital with the entire INTERMACS® registry;
  - a patient-specific component that focuses on patient-specific data and the quality of data at the site. Clinical summaries for each patient are



- provided and contain a chronological history of the major implant-related events; and
- MDRs that have been submitted to the FDA on behalf of the site are also included in this report.
- **Manufacturer-specific Reports:**  
On a quarterly basis, reports containing the following information are sent via secure email to the appropriate manufacturer:
  - Statistical summaries of patient demographics and clinical characteristics at the time of implant are provided to the individual manufacturers of MCSDs that are entered into INTERMACS®. Additionally, adverse event rates, including death and explant, are calculated. Of note, a specific manufacturer will not receive identifiable information about any MCSDs from other manufacturers.
  - Manufacturers also receive redacted source documentation for adjudication of serious adverse events, as required by law. The INTERMACS®-assigned identification number is used as the primary patient identifier between the site, INTERMACS®, and the MCSD manufacturer on all source documentation.
- **OSMB Reports:** On at least an annual basis, the OSMB receives a comprehensive report that includes:
  - Responses to previous OSMB recommendations and comments;
  - Registry progress updates on site activity, site monitoring and compliance, serious adverse events, reports to stakeholders, requested analyses and reports, publications, protocol amendments, etc.;
  - Additional activities such as updates on Annual Investigator Meetings, other registries under the OSMB's purview, and regular teleconference calls with stakeholders; and
  - Copies of standard reports sent to stakeholders

The OSMB meets within 30 days of receiving this report to review with INTERMACS investigators and provide recommendations. Refer to [Section 9.5](#) for additional details on OSMB oversight.