March 28, 2014

Subject: INTERMACS® Protocol Amendment, Version 4.0

Dear Review Board Director:

Please refer to the protocol entitled, “Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS®)” sponsored by the National Heart, Lung, and Blood Institute (NHLBI) under Contract #HHSN268201100025C awarded to the University of Alabama at Birmingham (James K. Kirklin, MD, Registry Principal Investigator) to serve as the Data and Clinical Coordinating Center (DCC).

At the strong recommendation of the independent Observational Study Monitoring Board appointed by the NHLBI to request a waiver of consent, we have modified the INTERMACS® protocol to reflect this request. The justification for this request is as follows:

JUSTIFICATION FOR WAIVER OF CONSENT

The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS®) has been collecting data since July 2006 and now serves as the national quality improvement system to assess the characteristics, treatments, and outcomes of patients receiving Food and Drug Administration (FDA)-approved mechanical circulatory support devices (MCSDs). The Joint Commission currently requires as a condition of hospital certification as a destination therapy (DT) center that the hospital be an active, continuous member of INTERMACS®. INTERMACS® further requires that to be a member in good standing, each participating hospital must enter data on consecutively implanted patients into the INTERMACS® database. As a result, the procedures described in the INTERMACS® protocol are now the standard of care for MCSD-implanted patients.

INTERMACS® is utilized by the FDA for regulatory considerations, the Centers for Medicare & Medicaid Services (CMS) for reimbursement oversight, and the NHLBI for establishing best medical practices. In accordance with 21 CFR 803.19, implanting centers participating in INTERMACS® for adults are exempt from the normal requirements in 21 CFR 803.30 for adverse events reported to INTERMACS®. Instead, INTERMACS® submits the appropriate reports to both the FDA and manufacturer on behalf of the implanting centers. INTERMACS® served a critical role in CMS’s recent National Coverage Decision (CAG-00432R published October 31, 2013) by providing the data to answer questions posed by their October 1, 2003 registry requirement. In addition, INTERMACS®, through its DCC, works closely with the NHLBI, MCSD-implanting centers, device manufacturers, clinicians and researchers to enable evaluation of best medical practices for advancement of public health with respect to the use of MCSDs for the treatment of advanced heart failure.

The purposes of INTERMACS® specifically include:
1. Collecting pertinent and standardized patient data elements from participating hospitals and other health care providers that measure and assess the quality of care for patients receiving MCSDs;
2. Providing confidential periodic reports to the participating hospitals, government agencies, and device manufacturers to evaluate and improve the quality of care in these areas;

3. Serving as a tool for clinical research based upon the data collected by means of INTERMACS®, and

4. Serving as a scalable data infrastructure for pre and post market FDA studies.

Although INTERMACS® has required written informed consent since its inception, we are now requesting a waiver of consent for the following reasons:

1. The data collected for this registry are for quality improvement purposes. Any potential research studies involving the data shall use de-identified datasets only. For certain pre- and post-market studies, device manufacturers may request to use INTERMACS® data for their control arm. Under these circumstances, INTERMACS® will ensure that written informed consent is obtained from any patient whose protected health information (PHI) is included in the datasets.

2. Written consent cannot be obtained from critically ill patients (or their legally authorized representative) who undergo emergent MCSD implantation and/or die within the first 24-48 hours, thus, skewing the registry data toward healthier participants and not reflecting the true patient population.

3. This registry involves a rare patient population and within this population, important data are missing, as written consent cannot be obtained from approximately 12% of the patients for a variety of reasons, including patient is too sick to approach, patient is not asked to sign the informed consent, or patient has difficulty understanding the standard of care procedures that are required of him/her after receiving an MCSD implant. Missing consent from approximately 12% of the subjects in this rare patient population has the potential to introduce selection bias, which undermines the goals of the registry.

4. Participation in the registry is of minimal risk and will not negatively impact the welfare of the patient. Moreover, the information gained from this registry is of great value to the public as compared to the low risk faced by patients. The data obtained are critical to understanding the characteristics, treatments, and outcomes of patients receiving MCSDs.

5. This registry collects data primarily through medical record abstraction (retrospectively), and any follow-up physical examinations and interviews are now the standard of care for patients with MCSDs. All data collected concurrently through interviews or assessments is of minimal risk, and the benefits gained for this patient population at large far outweigh any risks.

6. Limited PHI (e.g., patient’s name; date of birth; last 5 digits of social security number, or in the event that a social security number is not available, the last 5 digits of the transplant wait list number; health insurance claim number; device serial number; implant date; and hospital medical record number) is collected by INTERMACS®. This information allows a patient to be linked to the United Network for Organ Sharing database should the patient undergo transplantation, to CMS databases to aid in coverage decisions, as well as for mandatory medical device safety reporting to the FDA. Because INTERMACS® complies with all national patient privacy regulations, all registry data are transmitted from the treating facility to the database through a secure website and maintained on secure servers with necessary safeguards in place. All INTERMACS® employees have passed federal HHS background
checks for Federal Government clearance. Access to the production databases containing
protected health information is highly restricted. Protected health information is not available
to any employee outside of INTERMACS®, unless required by law (e.g., to ensure the
patient’s safety). No published or unpublished report or visual or speaking presentation about
the registry will include any material that will identify a specific patient in this registry.

For the reasons discussed above, we believe that a waiver of consent is warranted.
Considering that INTERMACS® is a registry for primarily collecting data retrospectively and
providing valuable information for quality improvement purposes, it is important that data are
collected from all patients receiving MCSDs. Missing data as a result of the inability to
obtain informed consent will undermine the goals of this quality improvement registry, which
include providing data to the FDA for safety and effectiveness oversight, to CMS for
reimbursement oversight, and to the NHLBI and other key parties for assessing best medical
practices.

The protocol amendment also includes other substantial changes:
  • Because the protocol was modified to no longer require written informed consent, patient
    information summaries (one for adults and one for pediatrics) were developed and are to
    be provided to any patient/patient’s family or legally authorized representative who is
    given the MCSD implantation surgical consent for signature. This will inform the patient
    that by consenting to the surgery for MCSD implantation, they will be participating in the
    registry.

  • The protocol was removed from the Manual of Operations; a separate Manual of
    Operations and Procedures (MOP) was written to complement the protocol and elaborate
    on procedures and requirements of the protocol.

  • The protocol was made more user friendly for adult and pediatric clinicians involved with
    the registry by separating the adult portion of the protocol (INTERMACS® - Adults, or
    simply INTERMACS®) from the pediatric portion of the protocol (referred to as
    INTERMACS® - Pediatrics, or pediMACS).

The revisions to the protocol are described in the Revision Record for the protocol. We include
the following documents in this amendment:

  • Protocol Revision Record for Version 4.0, dated February 27, 2014

  • Revised Protocol, Version 4.0, dated February 27, 2014

Please contact INTERMACS if you should have any questions.

Sincerely,

[Signature]

David C. Naftel

James K. Kirklin, M.D., Principle Investigator for the INTERMACS® Registry
David C. Naftel, Ph.D., Co-Investigator, Director of the Data Coordinating Center