Neuromodulation Research Standard Operating Procedures: Medical Monitoring and Adverse Event Reporting

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Purpose: Provide comprehensive, multidisciplinary oversight for individuals with spinal cord injury participating in research. This procedure ensures proper documentation when an adverse event is discovered during a research study.

Scope: This SOP applies to the investigators, study physicians, research nurses, research physical and occupational therapists, research navigators, research staff, research medical staff, medical monitor, and all other research staff within KSCIRC.

Policy: To ensure that the process for adverse event monitoring, documenting, and reporting is standardized to provide the highest level of protection against risk for human subjects.

Study Personnel:

1. Principal Investigator (PI) – The individual who is responsible and accountable for conducting the study. Although the PI may delegate tasks to members of their research team, they retain the responsibility for the conduct of the study, including full responsibility for the evaluation of human subjects and for the integrity of the research data and results.
    - Delegation of responsibilities
    - Oversight of research team
    - Knowledge of Human Research Protection Standards
    - Evaluation of the adequacy of resources
    - Training Requirements
    - Disseminate up-to-date and necessary regulatory information to the study team and ensure these practices are carried out in all experiments and assessments.

2. Co-Investigator – Key personnel who have responsibilities like that of a PI on a research study. While the PI has ultimate responsibility for the conduct of a research project, the Co-PI/Co-I is also obligated to ensure the project is conducted in compliance with applicable laws and regulations and institutional policy.

3. Study Physician – the study physician holds a medical license and preferably specializes in spinal cord medicine. The individual who is responsible for medical oversight and ongoing clinical care, responds to adverse events, determines adverse event seriousness, severity, expectedness, and relatedness to study, collaborates and consults with physicians in other clinical specialties and supervises the research nurses. Identification of the appropriate medical personnel and immediate referral for participants. Act as treating provider for the participant when requested by the participant. Review adverse events upon receipt and follow up with study personnel as needed. Attend Research Medical meetings.

4. Participating Clinician – A study member who is performing a role or duty that would also be found in the course of their clinical job description: Physician; Physical Therapist; Occupational Therapist, Nurse

   Physician: respond to adverse events in their specialty in collaboration with the Study Physician.

   Research Physical Therapist: Maintain participant documentation, specifically Progress notes. Triage of adverse events with possible request for consult with the Study Physician. Consult on intervention sessions and assessments as indicated. Provide physical therapy evaluation and ASIA Impairment Scale (AIS) evaluation.

   Research Occupational Therapist: Maintain participant documentation. Triage of adverse events with possible request for consult with the Study Physician. Consult on intervention sessions and assessments as indicated.

   Nurse: Maintain participant documentation. Triage of adverse events with possible request for consult with the Study Physician. Consult on intervention sessions and assessments as indicated.

5. Research Nurse – Study personnel holding Registered Nurse or Licensed Practical Nurse licensure. Provide necessary medical attention to the participant. Triage of adverse events with the request for a consultation with the Study Physician as needed. Perform check-ins with the participants, report to the PI, and the study physician. Maintain participant documentation, specifically progress notes, adverse event logs, adverse event reports, and Research Medical Minutes. Review the progress notes weekly and follow up with study personnel as needed. Attend Research Medical Meetings and provide minutes.

6. Lead Activity-Based Recovery Technician (Research Navigator)– Study personnel performing tasks for which they have achieved competency that does not require clinical licensure. Attend all intervention visits and assessments for assigned research participants. Maintain documentation of each participant interaction and Progress notes and sign and date each entry. Notify Research Nurse/Physician in the instance of an adverse event. Maintain constant communication among study personnel regarding the research participant. Maintain participant documentation, including Progress notes and data collection for each participant interaction.

7. Researchers- Study personnel performing research tasks for which they have achieved competency that does not require clinical licensure.

8. Medical Monitor-Independent physicians interact with study monitors and reviews reports. Provides medical expertise for trial oversight and safety concerns. Reviews adverse events for seriousness, severity, expectedness, and relatedness to the study. Acknowledges and provides guidance when a research participant needs to be unblinded due to an adverse event. Provides medical expertise for trial oversight and safety concerns.

Monitoring and Reporting

Routine Monitoring of Research Participant:

1. No individual can participate in a study without being examined by the study physicians.

2. The assigned Research Navigator accompanies the research participant to each intervention visit and assessment and is in routine communication with the Research Nurse/Participating Clinician/PI regarding the well-being of the research participant.

3. The information from each visit/assessment/interaction is documented in StudyLINQ by the research navigator, researchers, research nurse, participating clinician and/or investigator.

4. Participants are continuously monitored for any signs of discomfort or risks during every assessment and intervention.

5. The skin integrity will be checked, and the joints will be examined for swelling or redness before and after every assessment and intervention visit. Blood pressure and heart rate will be routinely measured and verified against individual clinical limits.

6. If there are no adverse events during an assessment or intervention visit, this will be documented in StudyLINQ and signed by the research navigator, research nurse, research staff and/or investigator.

7. The Research Nurse/Participating Clinician will assess the research participant at least once a week when participating in an interventional study by reviewing the progress notes in StudyLINQ from all participant interactions.

8. All participant statuses are reviewed in the monthly Research Medical Meeting with the study physician and investigators.

Response to Adverse Event:

1. In the instance of an adverse event, the Research Navigator or research team member notifies the Research Nurse/Participating Clinician.

2. The Research Nurse/Participating Clinician assesses and triages the adverse event to ensure the participant receives the necessary medical attention. If needed, the research nurse/participating clinician will request a consultation with the Study Physician.

3. The Study Physician identifies the appropriate medical treatment and provides immediate care and/or referral. (If a physiatrist's expertise is required, the Study Physician can offer to be the medical treating clinician. The research participant has the choice to seek care from any physician of their choice.

4. The research nurse/participating clinician documents the adverse event in the research participant's Adverse Event Log in StudyLINQ. The Research Nurse/Participating Clinician identifies any pertinent information from the Adverse Event Log that constitutes an event that should be reviewed by the study physician and completes the Adverse Event Report in StudyLINQ. This documentation is available to the Study Physician, Principal Investigator, Research Nurse/Participating Clinician, and Research Navigator.

5. The study physician determines adverse event seriousness, severity, expectedness, and relatedness to study.

6. The study physician provides adverse event documentation to the medical monitor for review.

7. The research nurse/participating clinician and study physician inform the principal investigator of the event for reporting purposes and if the adverse event is a study-related adverse event, the study physician notifies the PI of any study restrictions as a result. The PI is responsible for reporting the event to regulatory authorities per policy and updating study documents as needed to reflect protocol changes or risk changes.

8. The study physician and research nurse/participating clinician ensure the research participant is being followed up medically, and the adverse event is documented and resolved. If a physician outside the study team treats the research participant, the study physician will follow the event to assess the following:
    a. The medical condition affecting their medical eligibility for research
    b. Determination on causality of the event
    c. The event's effect on research assessments or interventions

9. Research medical team documents ongoing status in research participant's Progress Notes, Adverse Event Log, and Adverse Event form in StudyLINQ.

10. The research medical team documents the ongoing status in the research participant's Progress Notes, Adverse Event Log, and the Adverse Event form in STUDYLINQ. The Study physician reviews the Adverse Events log and follows up with the principal investigator and research team members as needed.

11. All conclusions reached by the study physician will be communicated to the PI. The PI is responsible for reporting the event to regulatory authorities per policy and updating study documents as needed to reflect protocol

changes or risk changes. When the medical event is determined to be medically expected and unrelated to the study it will be reported.

Response to Emergent Adverse Event:

In an emergency, the individual is taken immediately to the emergency room, or the hospital emergency procedures are followed. Follow up will be conducted as indicated above.

Adverse Event Documentation (STUDYLINQ):

1. The Research Nurse/Participating Clinician reviews all progress notes from the current week to identify any adverse events. Any events reported to the Research Nurse/Participating Clinician directly from the participant or staff members will also be documented in the progress notes.

2. The Research Nurse/Participating Clinician will elevate any adverse events from the progress notes to the Adverse Event Log.

3. The Study Physician will determine the seriousness, severity, relatedness, and expectedness of each event. The study physician signs the reports after review and submits them to the medical monitor. The study physician will update the adverse event report with any recommendations from the medical monitor.

4. If the adverse event is determined as non-study related, it remains on the Adverse Event Log and is reported at the continuation review.

5. The research nurse/participating clinician will keep in contact with the study physician on any adverse events that require follow up. This will be documented on the Adverse Event Log and Study-Related Adverse Event Form when needed.

6. The research nurse will Inform project PIs and PI designees of ongoing adverse events and report them in the Research Medical Meeting.

7. Follow-up logs and reports are written as new information is available by the research nurse.

8. When an adverse event has been resolved, the documentation is finalized on the Adverse Event form clearly indicating the event “Resolved” and submitted by the PI to all regulatory authorities per policy.

9. Documentation Considerations

    a. The “Event” title must contain the medical event that is being described; this does not mean the procedure during which it happened; and CATCAE terms.
    b. Each event must be documented in the adverse event log and Study-Related Adverse Event Form until it is resolved.
    c. Events reached the Research Nurse and/or Physician level, or that significantly affect study timeline(s), must be reported in the Adverse Event Report Form.
    d. Regarding severity, relatedness, and expectedness of each event, if deciding between levels, always choose the most conservative.
    e. If there are no new medical events during the week, enter “No new medical events” in the “Event” title for that week.

Reporting an Adverse Event:

1. Principal Investigator determines reporting requirements to regulatory entities (DSMB, IRB, FDA).
2. Serious Adverse Events need to be reported to the IRB within 48 hours.
3. If the Adverse Event meets the requirements for expedited reporting, the Medical Monitor reviews the adverse event and provides reporting, participation in research, and/or medical recommendations to the study physician.

4. Research Nurse documents initial details of Adverse Event in daily medical log and starts an adverse event form in STUDYLINQ.

5. Study Physician determines seriousness and study relatedness.

6. Medical Monitor reviews adverse events and provides recommendations to the study physician.

7. Principal Investigator determines reporting requirements to regulatory entities.

8. Principle Investigator determines if Adverse Event needs to be reported to the DSMB within 48 hours.
   Events need to be reported to the DSMB within 48 hours if they meet any of the following criteria:

   - Non-bladder infections requiring antibiotics
   - Hospitalization
   - Any Emergency Department visit
   - Fracture
   - Neurologic Changes (such as seizure, worsening motor/sensory function, stroke, etc)
   - Autonomic dysreflexia requiring pharmacologic treatment beyond normal for the participant/change from baseline.
   - New implant or replacement of existing device.

9. The nurse continues to document the event in STUDYLINQ until it has resolved.

10. Study Physician and Principal Investigator Reviews the Adverse Event report generated in STUDYLINQ when resolved.

11. Study Physician signs the Adverse Event, when required the medical monitor then signs the Adverse Event Report and lastly, the Principal Investigator signs the adverse event.

12. The Adverse Event is filed in Research Medical Records by research medical staff and provides to designated research staff for regulatory documentation.

13. Adverse events reporting for Continuing Review must include all study related or non-study related that were not previously submitted since the last Continuing Review.