MSK PROTOCOL COVER SHEET

Pilot Trial of the Robotic Uterine Manipulator

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1.0 PROTOCOL SUMMARY AND/OR SCHEMA

The objective of this study, entitled "Pilot Trial of the Robotic Uterine Manipulator," is to evaluate the feasibility, safety and utility of a newly developed robotic uterine manipulator system. The Barakat Automated Uterine Manipulator (BAUM) was developed by Dr. Richard Barakat in collaboration with the MSK Innovation and Technology Team (ITT) and with the support of the Device Design and Development Fund (3DF). Subsequent funding for the external development by a development engineering partner with an extensive track record in developing medical devices, MPR Inc., has been provided through Dr. Barakat's discretionary funding and institutional donor funding. There will be a single robotic unit available for testing that robotically positions the clinically established and FDA approved V-Care uterine manipulator. Our hypothesis is that use of the BAUM will be feasible in nearly all patients undergoing total laparoscopic or robotic-assisted hysterectomy, will provide sufficient uterine manipulation and will have a low rate of associated intraoperative complications.

All patients undergoing total laparoscopic or robotic-assisted hysterectomy that will include the use of a uterine manipulator would be eligible for participation in this study. Annually, MSK's Gynecology Service performs approximately 500 laparoscopic and robotic-assisted hysterectomies. It is estimated that 90% of these patients would be eligible for this study. The standard protocol accrual rate is 30-35%. We estimate that this pilot study will reach the target accrual of 40 patients in one year or less.

Eligible patients will be consented for the study at the time of their surgical consultation. At the time of surgery, the BAUM prototype will be available for placement, use, and evaluation. The robotic manipulator will be affixed to the V-Care at the start of each case. The V-Care is an FDA approved uterine manipulator which will attach to the investigational BAUM. The V-Care manipulator will be used internally to move or manipulate the uterus to ensure that the surgeon's view is not blocked, so that he or she can perform the surgery effectively and safely, given the nearness of surrounding organs, such as the ureters, bladder, and colon. Historically a clinical staff member was responsible for positioning the instrument according to verbal commands from the surgeon. The BAUM will be utilized in place of a clinical staff member, attaching directly to the V-Care.

Unsuccessful mounting will be documented on the product evaluation form and the V-Care uterine manipulator of the surgeon's choice will be used manually instead. Successful docking of the robotic manipulator to the V-Care will be documented on the product evaluation form by the attending surgeon. If there are associated intraoperative complications, such as uterine perforation or cervical laceration, continued use of the robotic manipulator will be at the discretion of the attending surgeon. Product evaluation forms are required to be completed by the attending surgeon by the end of the case. Forms will be collected in the OR or immediately following surgery. Surgical videos and/or photos will be obtained for analysis of the robotic manipulator.

The goal is to have at least 8 of the 12 surgeons on the Gynecology Service use and evaluate the robotic manipulator. All responses on the product evaluation form will be

analyzed to determine utility of the device. Safety will be measured by the number of robotic uterine-manipulator-associated intraoperative complications. Patients will be followed by the study team for 25-35 days after surgery.

2.0 OBJECTIVES AND SCIENTIFIC AIMS

- **Primary Objective:** To determine the feasibility and safety of the robotic manipulator in women undergoing total laparoscopic or robotic-assisted hysterectomy at MSK. Feasibility will be determined by whether successful manipulation of the V-Care manipulator is achieved. Safety will be measured by the number of intraoperative complications attributed to the robotic manipulator.
- **Secondary Objective:** To determine the utility of the robotic manipulator in patients undergoing total laparoscopic or robotic-assisted hysterectomy at MSK. Utility will be measured by the product evaluation form provided by the Department of Perioperative Services.

3.0 BACKGROUND AND RATIONALE

Hysterectomy for benign and malignant disease is one of the most common surgical procedures among women in the United States; approximately 600,000 of these procedures are performed annually.[1] Traditionally, hysterectomies have been performed using the open approach via laparotomy. However, since the introduction of laparoscopic and robotic-assisted gynecologic surgery, minimally invasive hysterectomy has become the preferred surgical method with studies showing that greater than 70% of cases are performed using these techniques.[2] At MSKCC we do approximately 500 minimally invasive hysterectomies each year. This surgical method is especially well-suited for the treatment of endometrial cancer, as laparoscopic and robotic-assisted hysterectomy are associated with fewer postoperative adverse events and shorter hospital stay without compromised oncologic outcomes.[2-5] These recent surgical options are particularly beneficial to the morbidly obese endometrial cancer population, affording these patients complete surgical staging without the need for a large laparotomy incision.[6]

Uterine manipulation is paramount to performing a successful, uncomplicated laparoscopic or robotic-assisted hysterectomy. The ability to deviate the uterus in any desired direction is essential for visualization, dissection, and safety, especially given the proximity of the ureters, bladder, and colon.

Manual manipulations of uterine positioning instruments are inefficient as they require a clinical staff member to stand and position the manipulator according to verbal commands from the surgeon. Communicating the intended anatomical location and having the assistant reliably follow these instructions is challenging as real world anatomical positional instructions are often not easy to verbalize. Furthermore, requiring a person to

hold the anatomy under positive pressure for long periods of time intraoperatively can result in anatomical drift, as well as fatigue and injury to the assisting staff member.

The BAUM system (Figure: 1) has been designed to fit easily in the space required for positive uterine positioning regardless of the minimally invasive surgery method, whether robotic assisted or laparoscopic. The system uses a proven robotic arm unit specifically sourced for its utility and form factor. A custom interface that allows the BAUM to positively attach to the V-Care has been designed and implemented. The surgical control panel (Figure: 2) from which the surgeon will control the movements of the BAUM arm, will sit alongside the Da Vinci surgeon console for robotic cases or be sterilely draped and placed near the operating surgeon. The arrows on the figure indication that the arm can move in all directions including, up, down, left, right, rotation to the left and rotation to the right.

We hypothesize that the robotic manipulator will be easy to dock to the V-Care and will not require any special setup outside of the established patient setup.

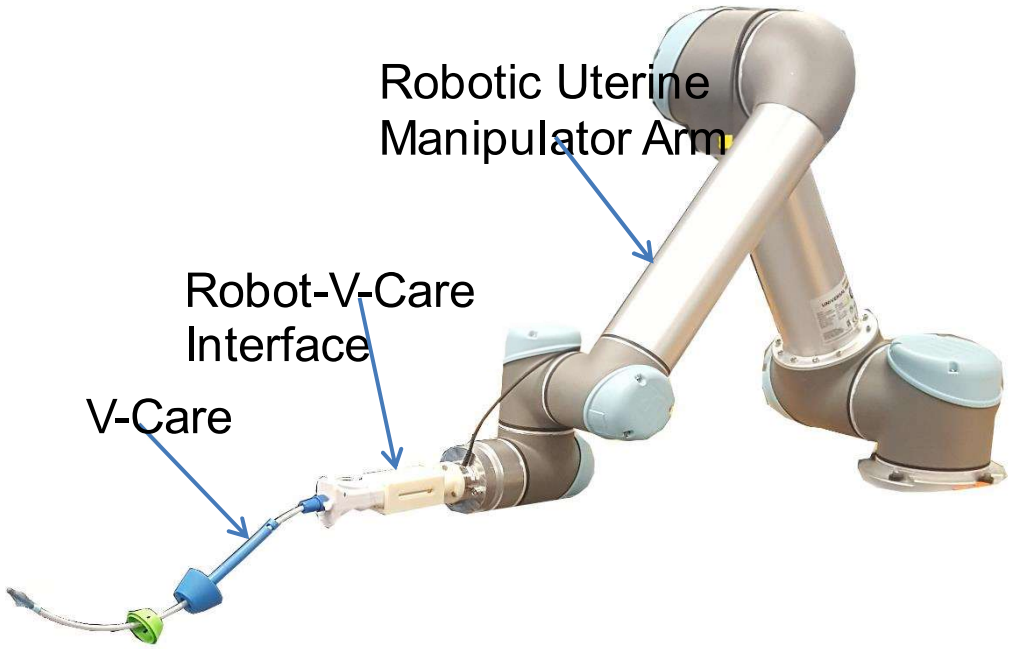

Figure: 1

Figure: 2

MSK is poised to be a leader in innovation and technology development, presenting a unique opportunity for the Department of Surgery to become more involved in planning, operationalizing, and commercializing technological advances. The ITT program seeks to increase recognition of surgeon-driven ideas, increase intellectual property protection and increase support for the development of new and evolving technologies. Within this framework, the ITT program has distributed and funded requests for applications aimed at encouraging surgeon-inventors to put ideas forward. The first of these is the Device Design and Development Fund (3DF). The development and creation of several prototypes of the robotic uterine manipulator has been funded by the 3DF grant. Analysis of the device on a clinical trial is the next step in development; tests of its utility and safety will spur design improvements and modifications prior to production. The robotic manipulator could replace existing uterine manipulators in use at MSK. Ultimately, the device has the potential to decrease OR time, decrease OR costs, and increase patient safety.

4.0 OVERVIEW OF STUDY DESIGN/INTERVENTION

4.1 Design

This feasibility study will aim to accrue 40 patients in one year or less. All patients who are consented for a total laparoscopic or robotic-assisted hysterectomy will be eligible for the trial, unless the surgeon does not plan to use a uterine manipulator. On average, the GYN Disease Management Team performs about 500 robotic and laparoscopic hysterectomies per year.

Dr. Leitao and Paul Booth will provide an educational training session to all GYN surgeons and fellows at an attending's meeting and/or a GYN Treatment Planning Conference prior

to protocol activation. All surgeons that will use the device will be provided with this training.

Dr. Barakat will receive composite results to provide consulting guidance regarding the device and any further manufacturing. There will not be any PHI included in the information provided to him.

Contingent on successful completion of this trial, an application for FDA approval may be filed for this device.

4.2 Intervention

The robotic manipulator will be placed at the start of each case. The manipulator will be cleaned and sanitized using the same process as other reusable OR devices. Feasibility will be determined by the rate of successful robotic manipulator docking and if the manipulation of the uterus was successful for the duration of the procedure. Placement of a BAUM will be noted on the operative note. In addition, we have included a question on the product evaluation form (Appendix A). Safety will be measured by the number of intraoperative complications reported during surgery. Of 554 minimally invasive hysterectomies performed from July 2014 through Jun 2015, only 2 intraoperative complications were reported. Patients would also be assessed for complications immediately after surgery. Utility and ease of use will be assessed by the product evaluation form provided by the Department of Perioperative Services. The form will be completed by all GYN Surgeons who use the robotic manipulator. The goal is to have at least 8 of the 12 surgeons use the robotic manipulator and evaluate the product. A surgeon will have to complete one docking with the BAUM and one clinical manipulation of the uterus to participate. The responses from all surgeons and cases will be analyzed to determine the utility of the manipulator. Surgical videos and/or photos will be obtained for analysis of the robotic manipulator. After surgery, patients will be followed by the study team for 25-35 days to record any postoperative complications that may be related to the robotic device. If the standard-of-care post-operative visit is outside of the 25-35 day window, a clinician will call the patient during the 25-35 day window and document any post-operative complications. The complications will be tracked in the study database. There are no anticipated additional risks above what can be experienced during the scheduled surgery performed without the BAUM. If a complication occurs, Dr. Leitao and/or the treating physician will review to determine if it is attributable to the use of the BAUM. Attribution determination will be made based on the type of complication and whether it is a medical or anesthetic complication of surgery, for example surgery complications may include bleeding or infection. Participants will be monitored for all complications for 25-35 days post surgery.

5.0 CRITERIA FOR SUBJECT ELIGIBILITY

Describe the characteristics of the subject population.

5.1 Subject Inclusion Criteria

- Female participant must be scheduled for a total laparoscopic or robotic-assisted hysterectomy for a gynecologic condition
- Female participants must be 18 years of age or older

5.2 Subject Exclusion Criteria

- Female participant is not eligible if the surgeon does not plan to use a uterine manipulator

6.0 RECRUITMENT PLAN

Potential research subjects will be identified by a member of the patient's treatment team, the principal investigator, or a member of the research team. If the treatment team member is an investigator on the research study, s/he will screen their patients' medical records for suitable research study participants and contact those patients to discuss the study and the potential for enrolling in the study. If the treating physician is not a study investigator and identifies potential subjects, the patients will be contacted by their treating physician and will be referred to the investigator/research staff of the study.

Potential study participants who meet our basic inclusion/exclusion criteria will be approached by their physicians to volunteer for this study. If the patient indicates a willingness to participate, an investigator will explain the study in detail. The goal is to obtain 40 patients undergoing surgery from at least 8 of the 12 GYN surgeons. The Research Study Assistant (RSA) will maintain a sign-up sheet to track the surgeries scheduled to use the robotic manipulator, as only one device is available. The maximum number of robotic uses per surgeon will be 8. This will allow us to obtain a representable sample of responses regarding the robotic manipulator and its utility.

7.0 ASSESSMENT/EVALUATION PLAN

After obtaining informed consent, data regarding the patient's treatment and disease status will be abstracted from the medical record for the purpose of characterizing the sample. Data will be collected regarding the disease stage, surgical characteristics, and patient demographics.

During the surgery, the surgeon will note any intraoperative complications. These are recorded on the operative report. The operative report is synoptic. Nomenclature and severity of grading for intraoperative complications is standardized. The surgeon or fellow will also note the feasibility of docking the V-Care uterine manipulator. If the robot cannot be docked with the V-Care and does not stay securely in place, the reason will be recorded.

After surgery, the surgeon will complete the product evaluation form and deliver it to the RSA. The evaluation form asks questions to determine ease of use, specifically, whether manipulation with the BAUM was successful, whether the device was successfully docked, the occurrence of any complications, and how easy it was to use. Patients will be followed by the study team for 25-35 days after surgery to track any postoperative complications

related to the robotic device. The complications will be tracked in the study database. There are no anticipated additional risks above what can be experienced during the scheduled surgery performed without the BAUM. If a complication occurs, Dr. Leitao and/or the treating physician will review to determine if it is attributable to the use of the BAUM. Attribution determination will be made based on the type of complication and whether it is a medical or anesthetic complication of surgery, for example surgery complications may include bleeding or infection. Participants will be monitored for all complications for 25-35 days post surgery. If the standard-of-care post-operative visit is outside of the 25-35 day window, a clinician will call the patient during the 25-35 day window and document any post-operative complications.

8.0 TOXICITIES/SIDE EFFECTS

There are no anticipated additional toxicities associated with study participation other than the standard risks of utilizing a uterine manipulator. Those include uterine perforation and vaginal laceration.

9.0 PRIMARY OUTCOMES

The primary outcomes for this study are feasibility, safety, and utility of the BAUM device. Feasibility will be determined by whether successful docking of the BAUM is achieved and if the manipulation of the uterus was successful for the duration of the procedure. Safety will be measured by the number of intraoperative complications attributed to the robotic device during surgeries using this manipulator. Utility will be measured by the product evaluation form provided by the Department of Perioperative Services.

All outcomes will be assessed by the attending surgeon during the total laparoscopic or robotic-assisted hysterectomy. Successful or unsuccessful docking of the robotic manipulator with the V-Care, and any intraoperative complications related to the robotic manipulator will be recorded on the product evaluation form. Utility will be assessed using an 8-item questionnaire on the product evaluation form. This form must be completed by the attending surgeon upon completion of the case.

10.0 CRITERIA FOR REMOVAL FROM STUDY

Patients will be removed from the study for any of the following reasons and they will be replaced:

- If at any time the patient is found to be ineligible for the protocol as designated in the section on Criteria for Patient/Subject Eligibility (e.g., a change in diagnosis that necessitates an open hysterectomy), she will be removed from the study.
- If the patient decides to withdraw consent or discontinue participation in the study, she will be removed from the study.
- If the use of the BAUM device is abandoned for any reason prior to surgery, the patient will be removed from the study.

If the surgeon is unable to dock the robotic manipulator or if it fails to operate properly during the procedure for any reason, the patient will not be replaced and this reason will be recorded. These patients will be considered as failures for the primary endpoint.

11.0 BIOSTATISTICS

The primary aim of the study is to show that the docking of the BAUM is feasible and subsequent uterine positioning is feasible. The BAUM will be considered successfully docked when the V-Care is inserted into the uterus and secured in place to the robotic arm to hold for the duration of the procedure. Interim data will be reviewed and presented.

We expect a very high percentage (90-95%) of patients to achieve successful docking and that the device will be held securely in place for the duration of the procedure. With 40 patients, the 95% confidence interval around a hypothetical 50% success rate is (35%, 65%); if the hypothetical success rate is 90% then the confidence interval is (81%, 99%), assuming binomial proportions. If the number of successes is less than 35 we will warrant re-design of the device and reassessment of its feasibility. The table below provides the probability of observing at least 35 successes (>=35) out of 40 patients under true hypothetical rates of success from 0.5 to 0. 9..

Obs	n	m	p	Prob of seeing >=35	Probability of seeing <35
1	40	35	0.5	0.00000	1.00000
2	40	35	0.6	0.00014	0.99986
3	40	35	0.7	0.00862	0.99138
4	40	35	0.8	0.16133	0.83867
5	40	35	0.9	0.79373	0.20627

Safety will be assessed by reporting all intraoperative complications during the surgery. Complications might include vaginal tear or uterine perforation. The number and type of complications will be reported. Among 554 patients who underwent laparoscopic or robotic-assisted hysterectomy at MSK from 7/1/14-6/30/15, there were 2 patients who experienced 2 true intraoperative complications. There are no expected postoperative complications, as the manipulator is removed following surgery so patients participating in the study will undergo routine follow-up. The study will stop for safety if we observe 2 intra-operative complications out of 40 patients. The table below provides the probability of observing at least 2 complications (>=2) out of 40 patients under true hypothetical rates ranging from 0.05 to 0.2. We expect the complication rate to be much smaller than 0.05.

Obs	n	m	p	Prob of seeing 2 or more	Probability of seeing 1 or less
1	40	2	0.05	0.60094	0.39906
2	40	2	0.10	0.91953	0.08047
3	40	2	0.15	0.98789	0.01211
4	40	2	0.20	0.99854	0.00146

The utility of the BAUM will be assessed by data collected from surgeons using the standard MSK OR new product evaluation form (see Appendix). All data will be reported descriptively. Surgeons will rate the robotic manipulator on different patients. In addition to using the cutoff of 3 or above (acceptable or better), the percentage of robotic uses for which surgeons rated each item as acceptable or better (score of 3, 4, or 5) will be reported for each item separately. Question 8 asks for the surgeon's recommendation for future use of the robotic manipulator. The maximum number of robotic manipulator uses per surgeon will be 8. This will allow us to obtain a representative sample of responses regarding the robotic device and its utility. If there are issues with utility, we will re-evaluate the design of the device to address the concerns.

12.0 RESEARCH PARTICIPANT REGISTRATION AND RANDOMIZATION PROCEDURES

12.1 Research Participant Registration

Confirm eligibility as defined in the section entitled Inclusion/Exclusion Criteria. Obtain informed consent, by following procedures defined in section entitled Informed Consent Procedures. During the registration process registering individuals will be required to complete a protocol specific Eligibility Checklist. The individual signing the Eligibility Checklist is confirming whether or not the participant is eligible to enroll in the study. Study staff are responsible for ensuring that all institutional requirements necessary to enroll a participant to the study have been completed. See related Clinical Research Policy and Procedure #401 (Protocol Participant Registration).

12.2 Randomization

Not Applicable

13.0 DATA MANAGEMENT ISSUES

An RSA will be assigned to the study. The responsibilities of the RSA include project compliance, data collection, abstraction and entry, data reporting, regulatory monitoring,

problem resolution and prioritization, and coordination of the activities of the protocol study team.

The data collected for this study will be entered into a study specific database. Source documentation will be available to support the computerized patient record.

All efforts will be made to ensure maintenance of patient confidentiality and HIPAA compliance. All data will be maintained in a study specific database and the Protocol Management System. All data collected will be stored on a secure server at MSK and access will be password protected. This server will only be accessible by trained study investigators.

OR videos and/or photos from each case will be accessible to study staff on VaultStream EasyView with permission from the case surgeon.

13.1 Quality Assurance

Registration reports will be generated to monitor patient accruals and completeness of registration data. Routine data quality reports will be generated to assess missing data and inconsistencies. Accrual rates and extent and accuracy of evaluations and follow-up will be monitored periodically throughout the study period and potential problems will be brought to the attention of the study team for discussion and action.

Research staff will verify eligibility, informed consent, and accuracy of the demographic data collected for all patients whenever a patient is enrolled onto the study. This will ensure the quality of the data collected and verify the presence of all pertinent study data and documents.

13.2 Data and Safety Monitoring

The Data and Safety Monitoring (DSM) Plans at Memorial Sloan Kettering Cancer Center were approved by the National Cancer Institute in September 2001. The plans address the new policies set forth by the NCI in the document entitled “Policy of the National Cancer Institute for Data and Safety Monitoring of Clinical Trials,” which can be found at: http://cancertrials.nci.nih.gov/researchers/dsm/index.html. The DSM Plans at MSK were established and are monitored by the Office of Clinical Research. The MSK Data and Safety Monitoring Plans can be found on the MSK Intranet at: https://one.mskcc.org/sites/pub/clinresearch/Documents/MSKCC%20Data%20and%20Safety%20Monitoring%20Plans.pdf.

There are several different mechanisms by which clinical trials are monitored for data, safety, and quality. There are institutional processes in place for quality assurance (e.g., protocol monitoring, compliance and data verification audits, therapeutic response, and staff education on clinical research QA) and departmental procedures for quality control. In addition, there are two institutional committees that are responsible for monitoring the activities of our clinical trials programs: the *Data and Safety Monitoring Committee* (DSMC) for Phase I and Phase II clinical trials, and the *Data and Safety Monitoring Board*

(DSMB) for Phase III clinical trials. These committees report to the Center's Research Council and Institutional Review Board. This pilot trial will be reviewed by the DSMC.

Patients will be tracked for complications for 25-35 days post-surgery to record any postoperative complications that may be related to the robotic device. Any complications identified will be tracked in the study database. Dr. Leitao and/or the treating physician will review to determine if it is attributable to the use of the BAUM. Once the first three patients complete their surgery and follow up, the IRB will be informed of how they have fared.

14.0 PROTECTION OF HUMAN SUBJECTS

Every effort will be made to ensure the safety of our patients and the confidentiality of their medical information. During the enrollment and consent process, all risks, benefits, side effects, and alternatives will be discussed. Also, it will be stressed that this is a voluntary study and that the patient can withdraw without prejudice at any time.

Benefits and Risks: The potential benefit of this study is the determination of whether the BAUM is easy to apply and provides adequate uterine manipulation in a reusable form.

The risks of participation include the standard risks associated with use of a uterine manipulator such as uterine perforation and vaginal lacerations.

Alternatives: The current standard treatment option for patients eligible for this study would be surgery with the use of existing uterine manipulators. A patient's decision on whether or not to participate in this study will not affect the availability of standard, supportive, or other investigational treatment at MSK.

Costs: There will be no additional cost incurred by the patients who participate in the study.

Voluntary Nature of the Study: Participation in this study is entirely voluntary.

Inclusion of Children in Research: This protocol/project does not include children because the number of children who require surgical intervention for gynecologic malignancies is low. This statement is based on exclusion 4a of the NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects.

Patients will be informed of the extent of the risks, benefits, toxicities/side effects, alternatives/options for treatment, financial costs/burdens, and the voluntary nature of the study. The study will seek in every way to protect the rights of human subjects. No patient will be required to participate in the study, and participation or lack of participation will not affect the patient's subsequent care or treatment.

The patient will not incur any financial cost as a result of participation in the study. Participation will be entirely voluntary and subjects will not be reimbursed for participation in the study. The responsible investigator will ensure that this study is conducted in agreement with the Declaration of Helsinki. Throughout the study, patient confidentiality

will be maintained. No results of the study will be presented or discussed in a fashion that will allow identification of a particular patient in the study. Adverse events will be disclosed to the IRB as required by MSK IRB SOPs.

14.1 Privacy

MSK's Privacy Office may allow the use and disclosure of protected health information pursuant to a completed and signed Research Authorization form. The use and disclosure of protected health information will be limited to the individuals described in the Research Authorization form. A Research Authorization form must be completed by the Principal Investigator and approved by the IRB and Privacy Board (IRB/PB).

14.2 Serious Adverse Event (SAE) Reporting

An adverse event is considered serious if it results in ANY of the following outcomes:

- Death
- A life-threatening adverse event
- An adverse event that results in inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- A congenital anomaly/birth defect
- Important Medical Events (IME) that may not result in death, be life threatening, or require hospitalization may be considered serious when, based upon medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition

Note: Hospital admission for a planned procedure/disease treatment is not considered an SAE.

SAE reporting is required as soon as the participant signs consent. SAE reporting is required for 30-days after the participant's last investigational treatment or intervention. Any events that occur after the 30-day period and that are at least possibly related to protocol treatment must be reported.

If an SAE requires submission to the IRB office per IRB SOP RR-408 'Reporting of Serious Adverse Events', the SAE report must be sent to the IRB within 5 calendar days of the event. The IRB requires a Clinical Research Database (CRDB) SAE report be submitted electronically to the SAE Office as follows:

The report should contain the following information:

Fields populated from CRDB:

- Subject's initials
- Medical record number
- Disease/histology (if applicable)
- Protocol number and title

Data needing to be entered:

- The date the adverse event occurred
- The adverse event
- The grade of the event
- Relationship of the adverse event to the treatment (drug, device, or intervention)
- If the AE was expected
- The severity of the AE
- The intervention
- Detailed text that includes the following
    - A explanation of how the AE was handled
    - A description of the subject's condition
    - Indication if the subject remains on the study
- If an amendment will need to be made to the protocol and/or consent form
- If the SAE is an Unanticipated Problem

The PI's signature and the date it was signed are required on the completed report.

15.0 INFORMED CONSENT PROCEDURES

Before protocol-specified procedures are carried out, consenting professionals will explain full details of the protocol and study procedures as well as the risks involved to participants prior to their inclusion in the study. Participants will also be informed that they are free to withdraw from the study at any time. All participants must sign an IRB/PB-approved consent form indicating their consent to participate. This consent form meets the requirements of the Code of Federal Regulations and the Institutional Review Board/Privacy Board of this Center. The consent form will include the following:

1. The nature and objectives, potential risks and benefits of the intended study.
2. The length of study and the likely follow-up required.
3. Alternatives to the proposed study. (This will include available standard and investigational therapies. In addition, patients will be offered an option of supportive care for therapeutic studies.)
4. The name of the investigator(s) responsible for the protocol.
5. The right of the participant to accept or refuse study interventions/interactions and to withdraw from participation at any time.

Before any protocol-specific procedures can be carried out, the consenting professional will fully explain the aspects of patient privacy concerning research specific information. In addition to signing the IRB Informed Consent, all patients must agree to the Research Authorization component of the informed consent form.

Each participant and consenting professional will sign the consent form. The participant must receive a copy of the signed informed consent form.

16.0 REFERENCES

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17.0 APPENDICES

Appendix A: Product Evaluation Form