The Role of Sugammadex and Quantitative Monitoring in “Fast-Track Anesthesia” During Liver Transplantation

NCT05216991

13Nov2023

Investigator Studies Program (MISP) Protocol Template

Requirements for Submitting a Full Proposal

Section #1 - MISP Protocol Identification

Study Title:	The Role of Sugammadex and Quantitative Monitoring in "Fast-Track Anesthesia" during Liver Transplantation.
Request Date:	November 13, 2023 Protocol Version 1.1
Institution Name	Mayo Clinic Florida
Investigator Contact Information: – Full address – Phone No. – Fax No. – e-mail address	J. Ross Renew, MD Assistant Professor of Anesthesiology, College of Medicine, Mayo Clinic Department of Anesthesiology 4500 San Pablo Rd S Jacksonville, FL 32224 O: (904) 953-3312 E: Renew.j@mayo.edu

Section #2- Core Protocol	
2.1 Objectives & Hypotheses	2.1 List the objectives. **Primary Objectives** • To estimate the incidence of postoperative residual weakness (train-of-four ratio < 0.9) in patients receiving sugammadex after undergoing liver transplantation with quantitative monitoring **Secondary Objectives** • To estimate the proportion of patients that never require admission to the intensive care unit after receiving 'fast track' anesthesia • To estimate the mean hospital length of stay for patients receiving 'fast track' anesthesia and compare this to national averages • To estimate the frequency of postoperative pulmonary complications in patients receiving sugammadex as part of 'fast track' anesthesia 2.1.1 List the clinical hypotheses. **Primary Study Endpoints** The primary endpoint of the study is the incidence of postoperative residual weakness in the recovery room following 'fast track anesthesia' during liver transplantation in which patients receive sugammadex and are monitored with quantitative monitoring. We believe the combination of sugammadex and quantitative monitoring represents best practice and will result in a low incidence (<5%) of residual weakness in this high risk group. **Secondary Study Endpoints** The secondary endpoints include whether a patient requires ICU admission following liver transplantation. We hypothesize that this number is low (<5%). Another secondary endpoint is hospital length of stay. We hypothesize this will be significantly less than the national average (10 days). Finally, the third endpoint is the occurrence of postoperative pulmonary complications defined as pneumonia, and respiratory failure in patients receiving 'fast track' anesthesia. We hypothesize that such complications occur rarely (<5%).
2.2 Background & Rationale, Significance of Selected Topic & Preliminary Data	Neuromuscular blocking agents (NMBAs) are a class of medications routinely used during anesthesia to facilitate endotracheal intubation (1) and improve conditions for optimal surgery (2). Routine reversal of neuromuscular blockade is very common in order to return patients' spontaneous breathing and prevent residual blockade and all the associated complications (3, 4). Sugammadex, a γ-cyclodextrin, is a unique neuromuscular reversal drug first reported by Anton Bom. It is the first in a new class of selective relaxant binding agents, and it was designed to rapidly reverse rocuronium-induced neuromuscular block (5, 6). Sugammadex-rocuronium binding reduces the amount of free muscle relaxant in the plasma, reducing the level of free NMBA at the neuromuscular junction (7). The dose of sugammadex depends on the level of blockade. While a peripheral nerve stimulator can provide some information regarding the level of blockade, quantitative neuromuscular monitoring is the only method to confirm adequate recovery prior to extubating the trachea (8). Empiric administration of sugammadex without proper monitoring reduces the incidence of postoperative residual weakness, however, this practice does not eliminate residual weakness (9). Optimal neuromuscular blockade management incorporates sugammadex and quantitative monitoring to minimize the risks associated with postoperative residual weakness. Mayo Clinic in Jacksonville, Florida is one of the busiest liver transplantation centers in the world and has

	been a pioneer in establishing 'fast track' anesthesia in which these patients emerge from anesthesia in the operating room, spend time in the recovery room, and are then transferred to their hospital room while bypassing the intensive care unit (11). This pioneering feature of our clinical practice allows for unique research opportunities. Last year Mayo Clinic Florida completed over 150 liver transplant patients with approximately 60% of these patients being 'fast tracked'. Like other enhanced recovery pathways, optimal neuromuscular blockade management with quantitative monitoring and antagonism with sugammadex is a cornerstone of 'fast track' anesthesia for liver transplantation at our institution. Assessing level of neuromuscular blockade during these cases is typically achieved with a peripheral nerve stimulator and/or quantitative monitoring. The purpose of this study is to determine the incidence of postoperative residual weakness (a train-of-four ratio < 0.9) in patients getting 'fast track anesthesia' following liver transplantation. Our clinical practice routinely utilizes sugammadex in this patient population and we have anecdotally observed excellent outcomes. We hypothesize that the incidence of postoperative residual weakness with sugammadex and quantitative monitoring is low (<5%) and that patients receiving fast track anesthesia have shorter hospital length of stays than the national average (12). Additionally, postoperative pulmonary complications (PPC) can occur from residual weakness. We will utilize previous definitions of PPCs (13). Specifically, postoperative pneumonia within 30 days or respiratory failure that requires unplanned non-invasive mechanical ventilation (such as bilevel positive airway pressure ventilation) or need for reintubation due to respiratory distress will be documented.
2.3 Study Design	This unblinded, single center, prospective, randomized, observational study will involve 30 patients undergoing liver transplantation that receive 'fast track anesthesia'. **Inclusion Criteria** • Age > or = 18 years old • Patients willing to participate and provide an informed consent • Patients undergoing primary liver transplantation **Exclusion Criteria** • Patients with unilateral disorders, such as stroke, carpal tunnel syndrome, broken wrist with nerve damage, Dupuytren contracture, or any similar wrist injury. • Patients with systemic neuromuscular diseases such as myasthenia gravis • Patients with a known history of cerebrovascular accident (CVA) • Patients undergoing repeat liver transplantation or concomitant pancreas/kidney transplantation at the time of liver transplantation • Patients admitted to the intensive care unit prior to liver transplantation. **Subject Recruitment, Enrollment and Screening** On an annual basis there are around 150 liver transplantations performed at Mayo Clinic in Florida that require a pulmonary artery catheter and thus no difficulties in accrual based on historical volumes are anticipated. We expect that approximately 3 participants per week will be completed for this study. The initial accrual period will last at least 4 months. Patients will be provided with a Research Participant Consent and Privacy Authorization Form describing the study protocol, inclusion and exclusion criteria, as well as risks and benefits of participation. **Method of Assigning Subjects to Study Groups** This is an open-label pilot investigation and all study participants are assigned to receive their routine standard of care intraoperatively. The randomization involves whether patients are monitored with a

quantitative monitor (TetraGraph) on their dominant or nondominant hand.

The randomization will be performed utilizing REDCap and assigned anesthesia clinical care team will be informed of patients' assignment to guide them with the selection of the appropriate monitoring option.

Data Handling and Record Keeping

Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (long term survival status that the subject is alive) at the end of their scheduled study period.

Source Documents

Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents. Examples of these original documents, and data records include: hospital records and any forms completed specifically for this study.

Case Report Forms

All data necessary for this study will be obtained from EHR or at the time devices are being used and recorded on the electronic Case Report Forms (CRFs) created in REDCap. All missing data will be explained.

Data Management

Study data to be collected and managed using EHR and study-generated source documents and transcribed into electronic CRFs in REDCap, electronic data capture software, hosted by CTSA at Mayo Clinic. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Data Processing

All study date will be stored and analyzed at Mayo Clinic in Florida using the REDCap electronic data capture tool.

Data Security and Confidentiality

All source documents including clinical findings, observations or other activities will be stored in a REDCap database that will be designed by an Investigator. Access to the REDCap database will be limited to the Principal Investigator, Investigators, Study Team members, and Statistician.

Data Quality Assurance

Once the study is completed the Principal Investigator will randomly select 3 participants and compare the data documented in the EHR with what is entered into the REDCap database. If there is any discrepancy, the Principal Investigator and/or Investigators will cross-reference all 30 patients to ensure accuracy.

Data Clarification Process

For any data query the Principal Investigator and Investigators will meet to clarify the data queried and make corrections based on consensus.

Records Retention

The sponsor-investigator will maintain records and essential documents related to the conduct of the study. These will include subject case histories and regulatory documents. Each site's Principal Investigator will maintain regulatory and essential study documents to ensure compliance with local and federal policies/guidelines.

The sponsor-investigator will retain the specified records and reports:

1. As outlined in the Mayo Clinic Research Policy Manual –"Retention of and Access to Research Data Policy" [redacted]

Study Monitoring, Auditing, and Inspecting

Study Monitoring Plan

The investigator will allocate adequate time for such monitoring activities. The Investigator will also ensure that the compliance or quality assurance reviewer is given access to all the study-related documents.

Auditing and Inspecting

The investigator will permit study-related monitoring, audits, and inspections by the IRB, the sponsor, and government regulatory agencies, of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc.).

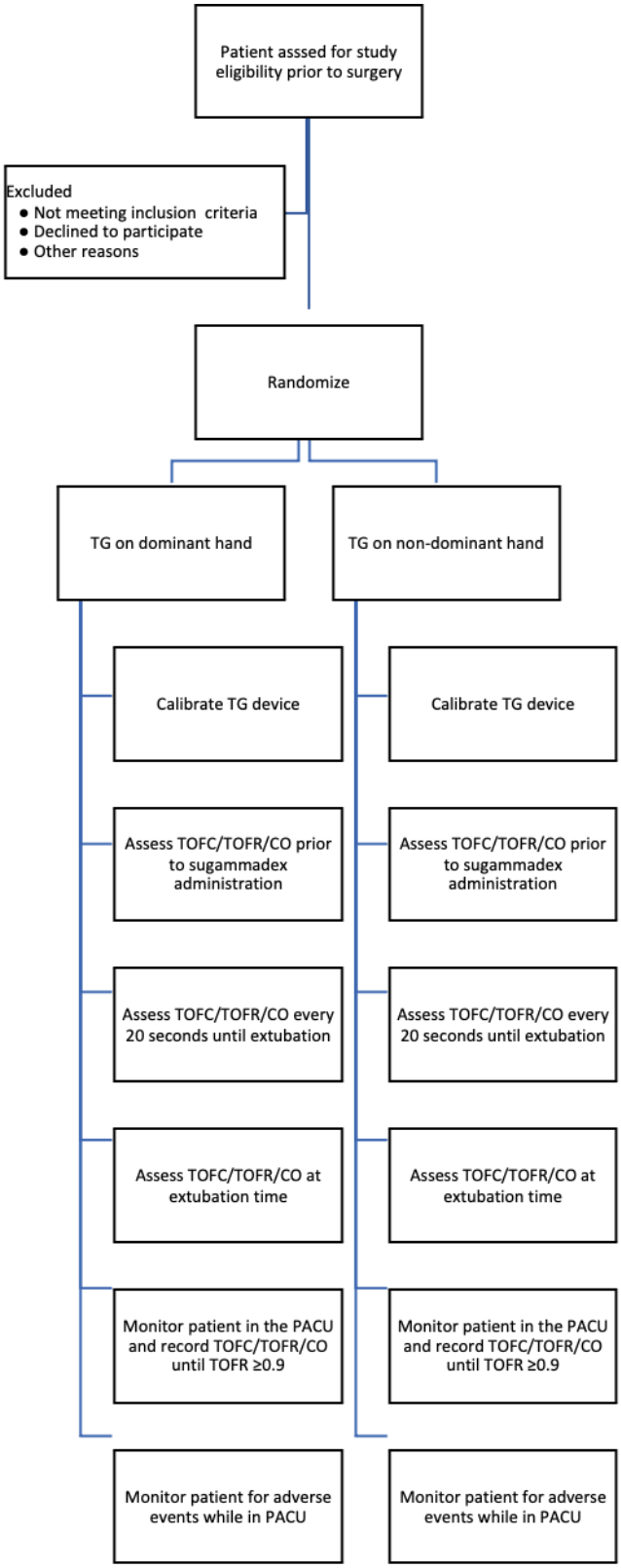
Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable compliance offices.

Ethical Considerations

This study is to be conducted according to United States and International government regulations and

	Institutional research policies and procedures. This protocol and any amendments will be submitted to a properly constituted local Institutional Review Board (IRB), in agreement with local legal prescriptions, for formal approval of the study. The decision of the IRB concerning the conduct of the study will be made in writing to the sponsor-investigator before commencement of this study. All subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. This consent form will be submitted with the protocol for review and approval by the IRB for the study. The formal consent of a subject, using the Approved IRB consent form, must be obtained before that subject undergoes any study procedure. The consent form must be signed by the subject and the individual obtaining the informed consent.
2.4 Diversity & Inclusion	We plan to enroll the 30 patients regardless of race or gender. Every patient listed on the liver transplant list will be approached and invited to participate in this study.

2.5 Study Flowchart



2.6 Study Procedures	**Visit 1 (Screening and Enrollment up to the day of surgery)** • Review of medical record • Informed Consent - Patients will be identified during their preoperative appointment and introduced to a study; they will be provided with a copy of the consent document and information about the study. The consenting will take place after additional discussion on the day of surgery. **Visit 2 (Randomization and Treatment – day of surgery)** • Anesthetic management will include rocuronium, sevoflurane, and sugammadex at the discretion of the attending anesthesiologist as per standard of care practice. • Patients will be randomized to be monitored with TetraGraph device on either the dominant or nondominant hand. NMBA administration will be at the discretion of the anesthesiologist. Reversal with sugammadex will be based on manufacturer dosing recommendations. The TetraGraph will record data throughout the operation and into the PACU stay. • TetraGraph monitor placed prior induction of anesthesia and the values will be used to guide care. The TetraGraph will record data throughout the operation and into the PACU stay. • Following recirculation of the transplanted liver, the attending anesthesiologist will declare whether the patient is a fast-track candidate or not. If the patient is not a fast-track candidate, they will be considered screen failure. If they are deemed to be a fast-track candidate, their participation continues. The attending anesthesiologist can change their mind at any time and remove 'fast-track' status as the clinical situation evolves. • At the conclusion of the operation, the patient will be reversed with sugammadex as per standard of care practice and manufacturer's dosing recommendations. • The patient's trachea will be extubated at the discretion of the attending anesthesiologist as per routine practice. • Upon arrival to the recovery room for patients in both groups, two sets of train-of-four ratio (TOFR) will be obtained. If these values are more than 20% different, a third set will be obtained. Measurements will be obtained in a similar fashion 5 minutes and 10 minutes into the recovery room stay. If any TOFR < 0.9, the attending anesthesiologist will be notified as to intervene if medically appropriate. • The patient's electronic medical record will be reviewed for up to 30 days postoperatively. Patient characteristics such as age, gender, albumin level, type of surgery, and baseline glomerular filtration rate will be recorded.

	Schedule of Events	
Study Activity	Visit 1	Visit 2
TetraGraph/Peripheral Nerve Stimulator		X
Sugammadex		X
Informed consent	X	
Review of Medical Record	X	X
Adverse event evaluation		X

2.7 Study Duration	Subject participation will be 3-6 hours, depending on duration of surgery. The entire study will be completed within 2 years based on the total number of eligible patients.
2.8 Statistical Analysis and Sample Size Justification	This is an open-label investigation. Masking and blinding procedures are not applicable. **Sample Size Determination** Assuming the incidence of postoperative weakness incidence with sugammadex without quantitative monitoring is 46% (9) and the incidence of weakness with sugammadex and a quantitative monitor is 5% (11), 28 patients would be required to be powered (80% power, $p<0.05$) to show evidence of a reduction in residual weakness with the use of quantitative monitoring to below 46%. However, we will consent up to 100 patients to account for possible dropouts and missing data to meet target accrual of 30 patients. **Statistical Methods** Continuous variables will be summarized as mean (standard deviation) or median (range) while categorical variables will be reported as frequency (percentage). For the primary aim, we will calculate the proportion of patients who have postoperative weakness, expressed as a percentage; we will perform a one-sample binomial test of the null hypothesis that the true proportion is 46%, and we will calculate an exact binomial 95% confidence interval (CI) for the true proportion of postoperative weakness for patients who are fast tracked. For the first secondary aim, we will similarly calculate the proportion of patients who go to the ICU, expressed as a percentage along with a 95% CI for the true proportion. For the second secondary aim we will calculate the sample mean length of stay of the patients in the study along with a 95% CI – due to the skewness of the distribution of length of stay we will construct a bootstrap-based CI. For the third secondary aim, we will calculate the proportion of patients who have postoperative

complications along with a 95% CI. We will also summarize the frequencies of patients with each particular complication type.

Handling of Missing Data

This is a prospective study and therefore we do not anticipate any missing data. In the event of any unexpected missing data, no attempt to impute this missing data will be made; missing data will simply be treated as missing in the statistical analysis, and replacement participants will be enrolled to achieve the target accrual of n=30 participants.

Subject Population for Analysis

Each participant who undergoes surgery and completes neuromuscular monitoring will be included in the primary analysis regardless of study withdrawal for any reason. In the event of any study withdrawals, in secondary analysis we will examine the sensitivity of our results to the exclusion of patients who withdrew.

Intraoperative Data

Study ID:					
Examiner Initials:			Date (dd / mm / yyyy):		
Dominant side: Hand with TetraGraph on	L / R L / R		Age (yrs)		
Weight (kg):		Height (cm):		BMI:	
Muscle relaxant name:					
Muscle relaxant total dose (mg):					
Time of last muscle relaxant dose (mm : hh):	: am / pm				
Reversal agent name:					
Reversal agent dose (mg):					
Time of reversal agent administration (mm : hh):	: am / pm				

	Cardiac output at time of reversal administration:
	Time of extubation: : am / pm

TOFC and TOFR (if TOFC = 4) prior to extubation			
TOFC and TOFR (if TOFC = 4) at time of extubation			
TOFC and TOFR (if TOFC = 4) on arrival to PACU			
TOFC and TOFR (if TOFC = 4) 5 min after PACU arrival			
TOFC and TOFR (if TOFC = 4) 10 min after PACU arrival			

2.9 Specific Drug Supply Requirements

All drugs used in the course of providing medical care for the 30 patients will be supplied by the participating institution in this protocol.

2.10 Adverse Experience Reporting

Safety and Adverse Events

Definitions

Unanticipated Problems Involving Risk to Subjects or Others (UPIRTSO)

Any unanticipated problem or adverse event that meets the following three criteria:

- Serious: Serious problems or events that results in significant harm, (which may be physical, psychological, financial, social, economic, or legal) or increased risk for the subject or others (including individuals who are not research subjects). These include: (1) death; (2) life threatening adverse experience; (3) hospitalization - inpatient, new, or prolonged; (4) disability/incapacity - persistent or significant; (5) birth defect/anomaly; (6) breach of confidentiality and (7) other problems, events, or new information (i.e. publications, DSMB reports, interim findings, product labeling change) that in the opinion of the local investigator may adversely affect the rights, safety, or welfare of the subjects or others, or substantially compromise the research data, **AND**
- Unanticipated: (i.e. unexpected) problems or events are those that are not already described as potential risks in the protocol, consent document, or not part of an underlying disease. A problem or event is "unanticipated" when it was unforeseeable at the time of its occurrence. A problem or event is "unanticipated" when it occurs at an increased frequency or at an increased severity than expected, AND
- Related: A problem or event is "related" if it is possibly related to the research procedures.

Adverse Event

An untoward or undesirable experience associated with the use of a medical product (i.e. drug, device,

biologic) in a patient or research subject.

Serious Adverse Event

Adverse events are classified as serious or non-serious. Serious problems/events can be well defined and include;

- death
- life threatening adverse experience
- hospitalization
- inpatient, new, or prolonged; disability/incapacity
- persistent or significant disability or incapacity
- birth defect/anomaly

and/or per protocol may be problems/events that in the opinion of the sponsor-investigator may have adversely affected the rights, safety, or welfare of the subjects or others, or substantially compromised the research data.

All adverse events that do not meet any of the criteria for serious, should be regarded as **non-serious adverse events**.

Adverse Event Reporting Period

For this study, the follow-up period is defined as up to 10 minutes after arrival to PACU or TOFR is ≥ 0.9 (whichever occurs first).

Preexisting Condition

A preexisting condition is one that is present at the start of the study. A preexisting condition should be recorded as an adverse event if the frequency, intensity, or the character of the condition worsens during the study period.

Post-study Adverse Event

All unresolved adverse events should be followed by the sponsor-investigator until the events are resolved, the subject is lost to follow-up, or the adverse event is otherwise explained. At the last scheduled visit, the sponsor-investigator should instruct each subject to report, to the sponsor-investigator, any subsequent event(s) that the subject, or the subject's personal physician, believes might reasonably be related to participation in this study.

Hospitalization, Prolonged Hospitalization or Surgery

Any adverse event that results in hospitalization or prolonged hospitalization should be documented and reported as a serious adverse event unless specifically instructed otherwise in this protocol. Any condition responsible for surgery should be documented as an adverse event if the condition meets the criteria for an adverse event.

Neither the condition, hospitalization, prolonged hospitalization, nor surgery are reported as an adverse event in the following circumstances:

- Hospitalization or prolonged hospitalization for therapy of the target disease of the study, unless it is a worsening or increase in frequency of hospital admissions as judged by the clinical investigator.

Recording of Adverse Events

At each contact with the subject, the study team must seek information on adverse events by specific questioning and, as appropriate, by examination. Information on all adverse events should be recorded immediately in the source document, and also in the appropriate adverse event section of the electronic case report form (CRF). All clearly related signs, symptoms, and abnormal diagnostic, laboratory or procedure results should recorded in the source document.

All adverse events occurring during the study period must be recorded. The clinical course of each event should be followed until resolution, stabilization, or until it has been ultimately determined that the study treatment or participation is not the probable cause. Serious adverse events that are still ongoing at the end of the study period must be followed up, to determine the final outcome. Any serious adverse event that occurs during the Adverse Event Reporting Period and is considered to be at least possibly related to the study treatment or study participation should be recorded and reported immediately.

Reporting of Serious Adverse Events and Unanticipated Problems

When an adverse event has been identified, the study team will take appropriated action necessary to protect the study participant and then complete the Study Adverse Event Worksheet and log. The sponsor-investigator will evaluate the event and determine the necessary follow-up and reporting required.

Sponsor-Investigator reporting: notifying the Mayo IRB

The sponsor-investigator will report to the Mayo IRB any UPIRTSOs and Non-UPIRTSOs according to the Mayo IRB Policy and Procedures. Each participating site will report SAEs to their respective IRB or Ethics Committee with copy of submission and review provided to the leading site. Should there be any SAEs at any of the participating sites; the study team at that site will notify the primary site (Mayo Clinic in Florida) within 24 hours of learning of the event.

Any serious adverse event (SAE) which the Principal Investigator has determined to be a UPIRTSO will be reported to the Mayo IRB as soon as possible but no later than 5 working days after the investigator first learns of the problem/event.

The following information will be collected on the adverse event worksheet (and entered in the research database):

- Study ID
- Disease
- The date the adverse event occurred
- Description of the adverse event
- Relationship of the adverse event to the research device*****
- Determination if the adverse event was expected
- The severity of the adverse event (severity scale described below******)
- If any intervention was necessary
- Resolution (was the incident resolved spontaneously, or after discontinuing treatment)
- Date of Resolution

The sponsor-investigator will review all adverse event reports to determine if specific reports need to be made to the IRB. The sponsor-investigator will sign and date the adverse event report when it is reviewed. For this protocol, only directly related SAEs/UPIRTSOs will be reported to the IRB.

*** Relationship Index**

	The relationship of an AE to the Investigational Device is a clinical decision by the sponsor-investigator (PI) based on all available information at the time of the completion of the eCRF and is graded as follows: 1. Not related: a reaction for which sufficient information exists to indicate that the etiology is unrelated to the use and proper application of study device. 2. Unlikely: a clinical event, including laboratory test abnormality, with a temporal relationship to use of the study device which makes a causal relationship improbable and in which use of other devices, chemicals, or underlying disease provide plausible explanations. 3. Possible: a clinical event, including laboratory test abnormality, with a reasonable time sequence to use of the study device but which could also be explained by concurrent disease or use of other devices or chemicals. 4. Probable: a clinical event including laboratory test abnormality, with a reasonable time sequence to use of the study device, unlikely to be attributed to concurrent disease or use of other devices or chemicals. 5. Definite: a reaction that follows a reasonable temporal sequence from the use of the study device. **** Severity Scale** The maximum intensity of an AE during a day should be graded according to the definitions below and recorded in details as indicated on the CRF. If the intensity of an AE changes over a number of days, then separate entries should be made having distinct onset dates. 1. Mild: AEs are usually transient, requiring no special treatment, and do not interfere with patient's daily activities. 2. Moderate: AEs typically introduce a low level of inconvenience or concern to the patient and may interfere with daily activities, but are usually ameliorated by simple therapeutic measures. 3. Severe: AEs interrupt a patient's usual daily activity and traditionally require systemic drug therapy or other treatment.
2.11 Itemized Study Budget	A preliminary study budget must be provided with the initial proposal submitted to give guidance to the MISP Review Committee as to the expected study costs. A refined itemized budget detailing the costs associated with the study should be provided with the final protocol or included in the study agreement as Exhibit B.
2.12 References	1. Lieutaud T, Billard V, Khalaf H, Debaene B. Muscle relaxation and increasing doses of propofol improve intubating conditions. Canadian journal of anaesthesia = Journal canadien d'anesthesie. 2003;50(2):121-6. 2. Blobner M, Frick CG, Stäuble RB, Feussner H, Schaller SJ, Unterbuchner C, et al. Neuromuscular blockade improves surgical conditions (NISCO). Surgical Endoscopy. 2015;29(3):627-36. 3. Murphy GS, Brull SJ. Residual neuromuscular block: lessons unlearned. Part I: definitions, incidence, and adverse physiologic effects of residual neuromuscular block. Anesth Analg. 2010;111(1):120-8. Page 21 of 24 J. Ross Renew, MD CONFIDENTIAL 4. Brull SJ, Murphy GS. Residual neuromuscular block: lessons unlearned. Part II: methods to reduce the risk of residual weakness. Anesth Analg. 2010;111(1):129-40. 5. Puhringer FK, Rex C, Sielenkamper AW, Claudius C, Larsen PB, Prins ME, et al. Reversal of profound, high-dose rocuronium-induced neuromuscular blockade by sugammadex at two different time points: an international, multicenter, randomized, dose-finding, safety assessor-blinded, phase II trial. Anesthesiology. 2008;109(2):188-97. 6. Lee C, Jahr JS, Candiotti KA, Warriner B, Zornow MH, Naguib M. Reversal of profound neuromuscular

	block by sugammadex administered three minutes after rocuronium: a comparison with spontaneous recovery from succinylcholine. Anesthesiology. 2009;110(5):1020-5. 7. Epemolu O, Bom A, Hope F, Mason R. Reversal of neuromuscular blockade and simultaneous increase in plasma rocuronium concentration after the intravenous infusion of the novel reversal agent Org 25969. Anesthesiology. 2003;99(3):632-7; discussion 6A. 8.Naguib M, Brull SJ, Kopman AF, et al. Consensus Statement on Perioperative Use of Neuromuscular Monitoring. Anesth Analg. 2018 Jul;127(1):71-80. doi:Kotake Y, Ochiai R, Suzuki T. et al. Reversal with sugammadex in the absence of monitoring did not preclude residual neuromuscular block. Anesth Analg. 2013 Aug;117(2):345-51 10 Aniskevich S, Pai SL. Fast track anesthesia for liver transplantation: Review of the current practice. World J Hepatol. 2015 Sep 18;7(20):2303-8. 11. Renew JR, Hernandez-Torres V, Logvinov I, Nemes R, Nagy G, Li Z, Watt L, Murphy GS. Comparison of the TetraGraph and TOFscan for monitoring recovery from neuromuscular blockade in the Post Anesthesia Care Unit. J Clin Anesth. 2021 12. https://www.srtr.org/reports/program-specific-reports/ 13. Kheterpal S, Vaughn MT, Dubovoy TZ, Shah NJ, Bash LD, Colquhoun DA, Shanks AM, Mathis MR, Soto RG, Bardia A, Bartels K, McCormick PJ, Schonberger RB, Saager L. Sugammadex versus Neostigmine for Reversal of Neuromuscular Blockade and Postoperative Pulmonary Complications (STRONGER): A Multicenter Matched Cohort Analysis. Anesthesiology. 2020 Jun;132(6):1371-1381.
2.13 Publication Plan	We plan to present the study results at one of the major international anesthesia meetings (ASA Annual Meeting, IARS Annual Meeting, NY PGA Meeting), followed by publication in Anesthesiology or Anesthesia & Analgesia journals. We anticipate there will be at least one abstract and one full manuscript.
2.14 Curriculum Vitae	J.Ross Renew, MD - CV attached
2.15 Protocol Submission for Investigator-Initiated Studies	U.S. protocols should be submitted by US investigators directly to Visiontracker at [redacted] Non U.S. protocols should be submitted to the MSD office by the investigators.