Effectiveness of Sugammadex versus Neostigmine on neuromuscular reversal in pediatric patients undergoing laparoscopic appendectomy for acute appendicitis: A Randomized Controlled Trial

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PROTOCOL TITLE:

Effectiveness of Sugammadex versus Neostigmine on neuromuscular reversal in pediatric patients undergoing laparoscopic appendectomy for acute appendicitis: A Randomized Controlled Trial

EXTERNAL (NON-EMORY) COLLABORATORS

Children's Healthcare of Atlanta

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VERSION: **3:25SEP2024**

FUNDING SOURCE: MERCK SHARP & DOHME CORP.

REVISION HISTORY

No need to review this section if this is the first version of the protocol you are submitting to the IRB

Revision #	Version Date	Summary of Changes

Table of Contents

1. Study Summary

Project Title	Effectiveness of Sugammadex vs. Neostigmine on neuromuscular reversal in pediatric patients undergoing laparoscopic appendectomy for acute appendicitis: A randomized cotrolled trial
Project Design	This study is designed as a randomized controlled trial with patients assigned to neuromuscular reversal with either sugammadex or neostigmine/glycopyrrolate reversal. The study will not be blinded to the anesthesiologist to allow for appropriate decision making on timing and dosage of reversal. This is a single center study. They will be assigned by a computerized random number generator.
Primary Objective	To determine if the utilization of sugammadex versus neostigmine for neuromuscular reversal in pediatric patients affects efficiency as measured by time from surgery end to out of the operating room (OR)
Secondary Objective(s)	To determine the effects of sugammadex on: • Return to bowel functon • Time to tolerance of an oral diet • The association of using Sugammadex on exposure to inhalational anesthesia • Length of hospital stay • Post-Anesthsia Care Unit (PACU) length-of-stay
Research Intervention(s)/Interactions	Suggamadex or Neostigmine for reversal of neuromuscular blockade
Study Population	Patients of Children's Healthcare of Atlanta
Sample Size	120
Study Duration for individual participants	1.25 years
Study Specific Abbreviations/ Definitions	TO4 – Train of Four RSI- Rapid Sequence Induction PACU- Post Anesthesia Care Unit
Funding Source (if any)	Merck Sharpe & Dohme Corp.

2. Objectives

Primary:

To determine which of the two neuromuscular reversal agents: Sugammadex or Neostigmine among pediatric patients undergoing laparscopic appendectomy-- affects efficiency as measured by end-time of surgery until exit of operating room (OR).

Secondary:

To determine effect of Sugammadex: on return of bowel function, time to tolerance of an oral diet.

To determine if the utilization of Sugammadex affects: hospital length of stay, post-anesthesia care unit (PACU) length of stay.

To determine the association of using Sugammadex on exposure to inhalational anesthesia.

Hypothesis: We hypothesize that utilizing sugammadex in comparison to neostigmine for neuromuscular reversal in pediatric patients undergoing laparoscopic appendectomy will result in improved efficiency demonstrated by decreased time from surgery end to out of the OR.

Furthermore, we predict utilizing sugammadex in comparison to neostigmine for neuromuscular reversal will result in a quicker return to first bowel movement.

We hypothesize that utilizing sugammadex in comparison to neostigmine for neuromuscular reversal in pediatric patients undergoing laparoscopic appendectomy for acute appendicitis will result in a faster time to tolerance of an oral diet.

We also anticipate that the use of Sugammadex over Neostigmine, will be correlated with a decreased exposure to volatile anesthesia as measured by the average inspired sevoflurane concentration from surgery start to finish.

3. Background

Patients presenting to the operating room for laparoscopic appendectomy with a diagnosis of acute appendicitis require rapid sequence induction (RSI) due to significant vomiting and concern for increased gastric content. For this reason succinylcholine—accompanied by neostigmine—is predominately used in adults for RSI to prevent potential aspiration. Unfortunately, in pediatric patients there are many concerns about the use of succinylcholine, including complications such as bradycardia, hyperkalemia, dysrhythmias and cardiac arrest from undiagnosed skeletal muscle myopathy. For many anesthesiologists, these concerns prompt the decision to use a non-depolarizing muscle relaxant such as rocuronium for induction. However, if the standard RSI dose is used, it often results in residual paralysis at the end of short procedures such as laparoscopic appendectomies. It has recently been demonstrated that prolonged paralysis is prevalent even at low doses of rocuronium in pediatric patients. For these reasons, it is imperative to find a way to provide adequate and safe

RSI conditions for intubation, appropriate muscle relaxation for laparoscopic procedures and the ability to quickly reverse neuromuscular blockade in this pediatric population. Sugammadex has the potential to allow for the utilization of an appropriate RSI dose of rocuronium for intubation, as it provides the ability to reverse neuromuscular blockade earlier than the neostigmine reversal, which is currently the standard of care. Retrospective reviews have shown the use of Sugammadex in pediatric patients to be safe and effective. However, there has not been prospective data about the effect on operating room efficiency on brief pediatric procedures such as laparoscopic appendectomies—one of the most common urgent pediatric surgeries performed. There are numerous other potential benefits of using sugammadex over typical reversal including quicker return of bowel function, faster time to tolerance of an oral diet and decreased exposure to volatile anesthesia. The return of bowel function is particularly important in pediatric patients undergoing laparoscopic procedures. We hypothesize that the utilization of sugammadex in pediatrics results in a quicker return to bowel function. This has previously been demonstrated in adults, but data is lacking in the pediatric population. We also hypothesize that patients receiving sugammadex versus neostigmine reversal will have an improved time to tolerance of an oral diet, which may impact wound healing and nutrition. As anesthesiologists often under dose rocuronium in these short procedures, due to lack of quick reversal options, high levels of volatile anesthesia are utilized to compensate for inadequate muscle relaxation. With the use of sugammadex allowing for proper muscle relaxation throughout the entire case, we hypothesize that patients will have a lower total volatile anesthetic exposure during the procedure. This is exceedingly important in pediatric anesthesia, where the detrimental effects of volatile anesthetics on the developing brain have been demonstrated in numerous animal studies.

4. Study Endpoints

Improved efficiency demonstrated by decrease time from suregery end to to out-of the operating room: use of rocuronium with anticholinesterase reversal is associated with a 5-minute increase in surgery end to out of OR time relative to Neostigmine/Succinylcholine (18 minutes vs 13 minutes, respectively). We expect the Sugammadex cohort to mirror the Neostigmine/Succinylcholine group. In order to show a mean difference of 5 minutes between the two groups with standard deviation of 7.5 minutes, an alpha error of 5% and a beta error of 5%, 60 patients will be needed in each cohort to power the study appropriately.

Lower total volatile anesthetic exposure: as sevoflurane is the only volatile anesthetic administered during this procedure, a calculation of average sevoflurane at 5 minute increments multiplied by the time of exposure will be used. The total time of exposure will be determined by the presence of end tidal sevoflurane in the anesthetic record.

The primary variable of time from surgery end to out of the OR will be evaluated via the Epic computer chart after discharge from the hospital. The secondary variables, including time to first bowel movement, time to tolerance of an oral diet, total inhalational anesthesia

exposure, PACU length of stay and hospital length of stay will be evaluated via the Epic computer record after discharge from the hospital.

5. Study Intervention/Investigational Agent

Study drug provided by the sponsor will be kept and stored at the Children's Healthcare of Atlanta pharmacy. Eligible participants that have been consented will be randomized by a member of the study team. The unblinded anesthesiologist will obtain the randomized drug from the pharmacy and administer the reversal agent.

The research pharmacy at Children's Healthcare of Atlanta will be responsible for dispensing the study medication, Sugammadex. Approximately 60 patients will be randomized to receive Sugammadex. The research pharmacy will require 51 2mL vials and 9 5mL vials of sugammadex. There will be no blinding of the medication by pharmacy.

The dose administered by the anesthesiologist is determined by patient weight: 2mg/kg is recommended if spontaneous recovery has reached the reappearance of the second twitch in response to TOF stimulation; 4mg/kg is the maximum dose allowable.

We will be using Sugammadex for it's FDA approved indication, and FDA indicated age range. However, our standard of care reversal agent is Neostigmine/Glycopyrrolate. Due to the cost differential between Sugammadex and Neostigmine, our pharmacy keeps Sugammadex stored away, which requires a member of the anesthesia team to go to the pharmacy to obtain medication. Since Neostigmine is readily available in the OR, Sugammadex is used if we are concerned about the reversability of our patient. There are other large pediatric hospitals throughout the country who have changed to use Sugammadex as their standard of care for children 2-17 years of age.

6. Procedures Involved

- Participants meeting the inclusion criteria will be identified via Epic on the surgery status board.
- A member of the study team will approach a potential participant to obtain consent.
- Once consented, a study team member will randomize the patient usong the computerized RedCap database prior to their scheduled surgery.
- The patient will be randomized to 1 of 2 arms: Sugammadex (Arm 1), or Neostigmine (Arm 2).
- The research pharmacy at Children's will dispense the drug to the unblinded anesthesiologist.
- Induction of anesthesia will include the administration of Rocuronium, as the standard dosing by anesthesiologists at our institution (0.6-1.2 mg/kg), so as not to influence the normal practice.
- Neuromuscular relaxation will be checked and documented after intubation and at 15-minute intervals during the procedure utilizing qualitative TOF monitoring.
- At surgery closing, the anesthesiologist will again evaluate the qualitative TO4 measurement.

- The reversal agent, Sugammadex or Neostigmine, will be administered at the start of closure.
- If sugammadex is the randomized reversal drug, the dose will be 4mg/kg for a TOF 0-1and a post-tetanic count greater than or equal to 1, and 2mg/kg for a TOF 2 or greater.
- If Neostigmine/Glycopyrrolate is the randomized reversal drug, 0.07mg/kg of Neostigmine and 0.01mg/kg of will be administered once at least two twitches are present.
- A final qualitative TOF will be documented immediately prior to extubation.
- A Case Report Form will be used to fill out data pertinent to the study from the Anesthesia Report.
- Data from nursing documentation will be evaluated to determine return of bowel function and time to tolerance of an oral diet.
- The anesthetic record will be used to determine medications administered, evaluate hemodynamic changes and calculate volatile anesthetic exposure.
- The hospital record will be used to obtain: time from surgery end to out-of the OR, PACU length of stay and hospital length of stay.
- Study data will be evaluated by the primary investigator(s). The information will not be blinded to investigators.
- Once patient is discharged from hospital, there will be no follow-up by the study team.

7. Statistical Analysis Plan

All statistical analyses will be performed using R statistical software (version 4.1.1). Univariate associations between the outcomes and the primary exposure will be determined statistically with either Fisher's exact test or Wilcoxon rank sum test, as determined by the distributions. If differences occur in demographic, preoperative, and/or intraoperative variables between the two cohorts, multivariable regressions with those variables will be included as explanatory variables (in addition to the exposure) in order to limit confounding. A two-sided p-value of <0.05 will be considered statistically significant throughout.

Although the randomization should limit any bias from the effects of external factors, there is still a small chance of confounding that can occur randomly. In order to minimize bias, these external factors (e.g. preoperative midazolam administration, intraoperative propofol dose, intraoperative dexmedetomidine dose, and trainee vs anesthetist staff) will be collected for each patient and compared between the two cohorts. Any differences in these external factors will be controlled out using linear regression.

8. Sharing of Results with Participants

Participants of this study will be blinded to the neuromuscular reversal agent they are randomized to at the time of their procedure. Once patient is billed for anesthesia services, they will be unblinded to which neuromuscular blockade they were given. We will not be sharing study results with patients.

9. Study Timelines

- The study subject will participate for one day.
- Patient will be approached for consent after their surgery for laparoscopic appendectomy has been posted on the status board.
- During surgery, pertinent study data, including dosage of randomized drug and any adverse events, if applicable, will be notated.
- There will be no follow-up with patient from study team after the patient is discharged.
- The estimated date of study completion is: 01/01/2026.

10. Inclusion and Exclusion Criteria

Inclusion Criteria

- Patients 2-17 years of age.
- Diagnosis of acute appendicitis
- Patient undergoing laparoscopic appendectomy at Children's Healthcare of Atlanta.
- Parent or Legal Authorized Representative willing to participate, able to understand and sign informed consent

Exclusion Criteria

- Patient with an allergy to Sugammadex or Neostigmine
- History of renal dysfunction
- Parent or legal guardian unwilling or unable to understand the informed consent
- Females that are pregnant or nursing

11. Vulnerable Populations

Patients that are cognitively impaired will be approached to participate in the study, so long as the child's legal guardian displays knowledge and agrees to study consent and procedures.

12. Local Number of Participants

We predict a total of 150 patients will be screened; we will recruit 120 participants at Children's Health campus for this study. Because there is no predominance of laparascopic appendectomy among male or female, we anticipate the number of male/female subjects should be fairly equal.

13. Recruitment Methods

- Both the Principal Investigator and study staff will take initiative to search for potential study candidates on Epic.
- Potential patients will be identified on Epic via surgery status board. Patients diagnosed with acute appendicitis, who are undergoing a laparascopic appendectomy will be approached by study staff prior to their procedure.

- No flyers, advertisements or social media/online recruitment mechanisms will be used to recruit patients.

14. Withdrawal of Participants

Parents or Legal Authorized Representative may withdrawal participant from study without penalty at any given time.
A participant may be withdrawn from study if their surgery is scheduled after hours, or if they do not receive paralytic.
Principal Investigator may withdrawal subject at her discretion as deemed fit for patient safety.

15. Risk to Participants

Sugammadex

- Hypersensitivity: The most common hypersensitivity adverse reactions are nausea, pruritus and urticaria. More severe hypersensitivity reactions such as anaphylaxis are rare and in clinical studies, occurred in 0.3% of patients.
- Decreased effectiveness of hormonal contraceptives. If a hormonal contraceptive is used an additional, non-hormonal contraceptive method or back-op method of contraception for the next 7 days is recommended. (Sugammdex educational handout created by CHOA will be provided to patients taking hormonal contraceptives).
- Bradycardia. Rare instances of significant bradycardia requiring treatment with medication
- Anaphylaxis

Neostigmine/Glycopyrrolate:

- Gastrointestinal distress. The most common reactions are nausea, vomiting, diarrhea and abdominal cramps.
- Increased secretions. Neostigmine commonly increases salivation and mucus membrane production. It can also increase lacrimation.
- Bradycardia. Significant bradycardia is commonly seen following neostigmine administration, so it is regularly administered with glycopyrrolate to prevent this reaction.
- Anaphylaxis

16. Potential Benefits to Participants

If patient is randomized to Neostigmine/Glycopyrrolate, the participant will receive the standard of care; thus, no potentential benefits are anticipated.

However, if the participant is randomized to Sugammadex, we anticipate the patient will:

- Have quicker return to bowel function
- Have faster time to tolerance of an oral diet
- Have decreased exposure to volatile anesthesia

- Have a shorter PACU length-of-stay
- Have a decreased hospital length-of-stay

17. Compensation to Participants

Participants will not be reimbursed for their involvement in the study.

18. Data Management and Confidentiality

Data regarding the administration of neuromuscular blocking agents, reversal method, time spent in PACU will be collected. Demographic and procedural data will also be collected for each study participant including: age, weight, sex. All data will be entered into a secure RedCAP database. Data will be stored on a secure server that is password protected with access to study personnel only.

If a participant declines to participate in the study, the participant will not be assigned a study ID number and the study coordinators will not collect any data on the participant. If the participant agrees to participate in the study, the participant will be assigned a study ID number and the study coordinators will collect data points pertinent to the study. These procedures will help prevent unauthorized inclusion of the patient's data in the RedCap database.

19. Data Monitoring and Participants Safety

Monitoring of Adverse Events (AEs) and Serious Adverse Events (SAEs) will be performed on a case-by-case basis. Standard operating procedures and safety measures will apply in the operating room during procedure and administration of neuromuscular reversal agent. Following procedure, the principal investigator or research coordinator will review medical record and communicate with PACU post-operatively to follow-up with patient care and recovery status of the patient. A Case Report Form will be completed by a study member to assess post-operative recovery parameters and data points. The principal investigator will determine the seriousness of adverse events and whether the event was related to the study. Serious adverse events (life-threatening, requiring intervention) will be reported to the sponsor and IRB according to sponsor/IRB standards.

Emory's self-monitoring tool will be used to ensure all requirements are met throughout the duration of the study.

DSMP Requirement	How this Requirement is Met	Frequency	Responsible Party(ies)
Real-time review of participant data during initial data collection.	Completion of Case Report Form	*Expectation is that this happens every time you obtain information.*	Principal Investigator; Research Coordinator
Site Monitoring at pre-determined intervals: The Principal Investigator has a responsibility to	Sponsor will perform Monitoring visits at their discretion	at least every six months while participants are	Research Coordinator will use Self-Monitoring Tool to ensure study is

ensure that the study is following all aspects of the protocol.	Monitoring visits will be reported to IRB	receiving intervention annually while participants are in follow-up	compliant with IRB standards. Principal Investigator will review and sign.
100% review of regulatory files	ensuring regulatory documentation requirements are met by the IRB at study start-up and close-out	Initial and close-out visits	Research coordinator
100% review of consent forms	Documentation of ICF in Epic via research note	Each time consent is obtained	Principal Investigator; Research Coordinator
Review of credentials, training records, the delegation of responsibility logs (if applicable)	All training certificates, delegation logs, etc. will be filed and kept up to date in regulatory binder.	Periodically, as needed	Research Coordinator
Comparison of case report forms (CRF) to source documentation for accuracy and completion	Review medical record and compare to Case Report Form, communicate with PACU to obtain additional necessary data points	Following participant procedure	Principal Investigator; Research Coordinator
Review of documentation of all adverse events	Identification of adverse events via medical record and CRF.	A Note to File will be created and signed by PI after an adverse event is identified. Required IRB/sponsor reporting will apply.	Principal Investigator, Research coordinator
Monitoring of critical data points (eligibility, study endpoints, etc.)	Collection of data points will be logged on Case Report Form, eligibility will be assessed by PI after a patient has met inclusion criteria.	CRF to be completed after each procedure; eligibility status will be marked on Enrollment Log	Principal Investigator; Research Coordinator
Laboratory review of processing and storage of specimens	No labs will be collected, N/A	*N/A*	N/A

Assessment of laboratory specimens stored locally	N/A	*N/A*	N/A
Test article accountability review	The sponsor/manufacturer of Sugammadex (Merck) will provide the study drug. The study drug will be stored properly and dispensed by CHOA IDS.	Lot numbers will be recorded in CRF after drug is dispensed	Merck, CHOA research pharmacy
Accountability logs, dispensing records, and other participant records	Dispensing records/ Lot# of study drug will be kept in Subject/Enrollment binder	Study drug/ lot numbers will be filed after each procedure for enrolled patient.	Research Coordinator
For FDA regulated studies, the following requirements apply:		Timing, frequency, and intensity of monitoring	
Monitoring methods (may include centralized, on-site, and self-assessment)	On-Site monitoring visits will be performed by sponsor. Self-Monitoring Assessment will be performed annually	Sponsor on-site visits (at their discretion) Annual (Self-Monitoring)	Sponsor (On-Site) PI/ Research Coordinator (Self-Assessment)
*For international studies, you are required to engage a CRO that is working in the site country and/or to consult with Emory's legal counsel regarding compliance with the country's clinical research regulations.			

20. Provisions to Protect the Privacy Interest of Participants

Potential participants will be approached for consent in a private area/room to discuss study procedures. Participants will have ample time to ask any questions during consent process; they will be reminded that their participation in the study is voluntary, and they will not be penalized if they choose not to participate in the study. Participant discussion and data will be limited to study personnel only.

Emory's self-monitoring tool will be used to ensure all regulatory requirements are met throughout the duration of the study.

21. Economic Burden to Participants

Participants will not incur any additional charges related to the study. If a patient is randomized to Arm 1: Sugammadex, the study drug, will be provided by the sponsor. For patients randomized to Arm 2, the standard of care will apply and Neostigmine will be billed to the patient's insurance.

22. Informed Consent

- Prospective participants will be approached once their surgery for laparascopic appendectomy is posted on surgery status board.
- Assent will be obtained from participants 6-17 years of age.
- If a participant has a cognitive disability, assent will not be required; the participants' parent or legal guardian will consent on behalf of the child.
- Consent will be obtained in a private area, with only patient, legal guardian and member(s) of study staff present.
- For this study, informed consent will be obtained one time on the day of-- or within 24 hours of surgery.
- Informed consent will be obtained by a parent or legal aurthorized representative after discussion with a study member.
- We will allow ample time time discuss informed consent and answer any questions the partiipant/legal guardian may have.
- Legal guardian and patients of age to assent, will be informed that their decision to participate is completely voluntary.
- Informed consent will be obtained by both parents if present.
- If only one parent is present, consent will be obtained-- even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

Non-English-Speaking Participants

- Spanish-speaking patients and their legal guardian will be approached for this study, either by a Spanish-speaking member of the study team or an interpreter.
- A short-form consent will be used to obtain Informed Consent.
- Informed consent will be obtained by both parents if present.
- If only one parent is present, consent will be obtained-- even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

23. Setting

- The research team will identify patients at Children's Healthcare of Atlanta, that meet the inclusion criteria via Epic by viewing surgery status board.
- The CHOA pharmacy will prepare study drug provided by the sponsor after patient is ramdomized.
- The study drug will be administered in the operating room, the patient will be followed in the PACU for collection of study data points.
- Once the patient has been discharged from the hospital, there will be no follow-up by the study team and no additional data will be collected.

24. Resources Available

Laparascopic appendectomies are posted almost daily on the surgery status board. The inclusion criteria is fairly broad, which will present more opportunities for patient recruitment. Since laparascopic appendectomies are one of the most common urgent pediatric procedures, we plan to recruit 120 patients by the anticipated study end date.

All study staff have completed the required CITI training and understand their duties and role in the study. Knowledge of the protocol and study procedures will be reviewed with study members prior to patient recruitment; this will ensure patients are screened, consented, and monitored appropriately.

25. References

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26. Protocol Checklist

Please note that protocol sections with an asterisk (*) should always be included in the protocol; if the section does not have an asterisk, and you have not included the section in the protocol, the IRB will consider it your attestation that the section does not apply to your study.

Protocol Section	Added to the protocol?
External Collaborators- if applicable, add each external collaborator information and indicate whether that institution's IRB will review (or has already reviewed) that individual's engagement in human participants research activities)	☐ **Yes** **n/a**
Funding Source*: Include the information for the funding entity for this study. Please explain if this study is covered by a sub-award or other pertinent information. Say "department" if you do not have any other funding.	☒ **Yes**
Objectives*: Describe the purpose, specific aims, or objectives and state the hypotheses to be tested	☒ **Yes**
Background*: Describe the relevant prior experience and gaps in current knowledge. Describe any relevant preliminary data. Provide the scientific or scholarly background for, the rationale for, and significance of the research based on the existing literature and how will it add to existing knowledge	☒ **Yes**
Study Endpoints*: Describe the primary and secondary study endpoints. Describe any primary or secondary safety endpoints.	☒ **Yes**
Study Intervention/Investigational Agent*: Describe the study intervention and/or investigational agent (e.g., drug, device) that is being evaluated.	☒ **Yes**
Drug/Device Handling: If the research involves drugs or devices, describe your plans to store, handle, and administer those drugs or devices so that they will be used only on participants and be used only by authorized investigators. If using a drug, explain if the control of the drug is managed by IDS (or VA/Grady/CHOA research pharmacies). If not, provide IDS exemption document. If a device, explain how the device is being stored and managed.	☒ **Yes**
If the drug is under an FDA REMS, plan to complete the REMS checklist found here, on the IRB website.	☒ **Yes**
If the drug is considered a controlled substance, make sure you have filled out this form.	☐ **Yes** **n/a**

If applicable, identify the holder of the IND/IDE/Abbreviated IDE. An Emory investigator who holds an IND or IDE is considered to be a Sponsor-Investigator (S-I). If the study is under an S-I, review this section of our website for additional requirements.	☒ **Yes**
Procedures involved*: Describe and explain the study design and include a study schema. Describe all research procedures being performed and when they are performed, including procedures being performed to monitor participants for safety or minimize risks	☒ **Yes**
Procedures-Minimizing risk*: describe the procedures performed to lessen the probability or magnitude of risks.	☒ **Yes**
Procedures- Drug/Device Use: describe all drugs and devices used in the research and the purpose of their use and their regulatory approval status	☒ **Yes**
Procedures-Source Records*: describe source records that will be used to collect data about participants. Attach all surveys, scripts, and data collection forms to the submission.	☒ **Yes**
Procedures-Data collection*: describe what data will be collected during the study and how that data will be obtained	☒ **Yes**
Procedures- Long Term Follow Up*: once all research-related procedures are complete, what data will be collected during this period. If no data is collected after procedures are completed, please state in the submission.	☒ **Yes**
Data and Specimen Banking: describe where the specimens will be stored, how long they will be stored, how the specimens will be accessed, and who will have access to the specimens. Depending on the volume and nature of the collection, this may require a separate repository-specific IRB submission. The VA Data Repository SOP is required if the study is creating a data repository at the Atlanta VA. List the data to be stored or associated with each specimen. Describe the procedures to release data or specimens, including the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.	☐ **Yes** **n/a**
Sharing of Results with Participants*: Describe whether results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with participants or others (e.g., the participant's primary care physicians) and if so, describe how the results will be shared If applicable (e.g. for studies involving scans and/or panels of exploratory testing on specimens)	☒ **Yes**

Plan for managing the types of findings that might arise. This should include any secondary findings that are being sought actively, findings that might be anticipatable, and findings that might be un-anticipatable. Plan for recognizing, analyzing, and handling incidental findings and how incidental findings will be communicated to participants during the consent process. If the plan is not to disclose any findings, then this should be included. This plan might include the option for participants to opt-out of receiving incidental findings. Description of the research team's responsibilities following disclosure of a finding. This should detail educational information about the nature of the finding, how to seek care from a clinician or specialist, obtaining health insurance to secure treatment, and/or referral to a clinical specialist, if one is required. Reminder to include language in the consent form to let the participants know your plans for this – see Modular Language for Informed Consent Forms on IRB website)	
Study timelines*: describe the duration of an individual participant's participation in the study; anticipated time to enroll all study participants and the estimated date for the investigators to complete this study (complete primary analyses)	☒ **Yes**
Inclusion and Exclusion Criteria*: describe how individuals will be screened for eligibility and the criteria that define who will be included or excluded in your final study sample	☒ **Yes**
Population*: describe the study popualation and indicate specifically whether you will include or exclude each of the following special populations: • Adults unable to consent • Individuals who are not yet adults (infants, children, teenagers) • Pregnant women • Prisoners Note: you cannot exclude people with limited English proficiency unless you can demonstrate the scientific need for such exclusion. Community Participation: For studies aimed at addressing issues that affect a certain community or group: How, if at all, will this study involve people from the target community in the design of the study? Conduct of the study? How will the results of the research be shared with the participants and/or the target community/ies? **If studying Race or Ethnicity, have you defined these terms, and explained their proposed mechanism of action if these characteristics will be used in an explanatory model?**	☒ **Yes**

Research with pregnant women, fetuses, or neonates: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☐ **Yes** **n/a**
Research with neonates of uncertain viability: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☐ **Yes** **n/a**
Research involving prisoners: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☐ **Yes** **n/a**
Research involving children: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☒ **Yes**
Research involving cognitively impaired adults: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☐ **Yes** **n/a**
Research involving economically or educationally disadvantaged persons: describe the additional safeguards that have been included in the study to protect the rights and welfare of these subjects	☐ **Yes** **n/a**
Local Number of Participants*: Indicate the total number of participants to be accrued locally. If applicable, distinguish between the number of participants who are expected to be enrolled and screened, and the number of participants needed to complete the research procedures (i.e., numbers of participants excluding screen failures.) Provide your projected enrolling goals, including the percentage of participants according to sex and race.	☒ **Yes**
Recruitment Methods*: Describe when, where, and how potential participants will be recruited. Describe the source of participants. Describe the methods that will be used to identify potential participants. Describe materials that will be used to recruit participants. Attach copies of these documents with the application. If including advertisements, attach the final copy of them. When advertisements are taped for broadcast*, attach the final* audio/videotape. You may submit the wording of the advertisement before taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/videotape. Describe the amount and timing of any payments to participants. Reimbursement for expenses/travel? If using contests or raffles as incentive, you must offer entry to all potential participants, not just those who enroll in the study/complete study-related procedures, per Georgia State Law.	☒ **Yes**

All research recruitment through social media needs to follow this guidance, which does not allow the use of personal social media accounts for some recruitment activities.	
Withdrawal of Participants*: Describe anticipated circumstances under which participants will be withdrawn from the research without their consent. Describe any procedures for orderly termination. Describe procedures that will be followed when participants withdraw from the research, including partial withdrawal from procedures with continued data collection.	☒ **Yes**
Risk to Participants*: List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the participants related to the participant's participation in the research. Include as may be useful for the IRB's consideration, a description of the probability, magnitude, duration, and reversibility of the risks. Consider physical, psychological, social, legal, and economic risks. If applicable, indicate which procedures may have risks to the participants that are currently unforeseeable. If applicable, indicate which procedures may have risks to an embryo or fetus should the subject be or become pregnant. If applicable, describe risks to others who are not participants.	☒ **Yes**
Potential Benefits to Participants*: Describe the potential benefits that individual participants may experience from taking part in the research. Include as may be useful for the IRB's consideration, the probability, magnitude, and duration of the potential benefits. Indicate if there is no direct benefit. Do not include benefits to society or others.	☒ **Yes**
Compensation to Participants*: Describe if/how subjects will be compensated for participation in this study. Indicate what method compensation will be delivered (e.g. cash, gift card, school credit). Describe the amount and timing of any payments to participants. How much? What kind? Is tax information required? (if so, must be reflected in the informed consent form). Will payments be pro-rated if a participant withdraws early?	☒ **Yes**
Data Management and Confidentiality*: Describe the data analysis plan, including any statistical procedures or power analysis. Describe the steps that will be taken to secure the data (e.g., training, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, and separation of identifiers and data) during storage, use, and transmission. Describe any procedures that will be used for the quality control of collected data.	☒ **Yes**
Describe how data or specimens will be handled study-wide*: What information will be included in that data or associated with the specimens?	☒ **Yes**

• Where and how data or specimens will be stored? • How long the data or specimens will be stored? • Who will have access to the data or specimens? • Who is responsible for receipt or transmission of the data or specimens? • How data or specimens will be transported?	
Data Monitoring and Participants Safety (if this study is more than minimal risk, this section is required):	**☒ Yes**
Ensure that you review our Data and Safety Monitoring plan guidance for specific details about this section, and examples of what the IRB will be requiring according to the level of risk. If a DSMB is needed, please describe the composition of the board (if not already detailed in the protocol). Review this guidance for more information. If the sponsor protocol does not contain all required information, please in this section. Describe the plan to periodically monitor the data at the site level according to risk level. Include the appropriate completed monitoring table, if applicable. Description of the plan for notifying the IRB of reportable events, whether the sponsor requires reporting above and beyond the Emory IRB reporting requirements, and if so, a description of the requirements and plan for meeting them. Please address the specific details below. If deemed not applicable, please provide rationale: Subject safety: • Specific subject safety parameters • Frequency of subject safety observations • Individual responsible for safety monitoring • Subject stopping rules – under what conditions will a subject be removed from study participation and who will make the decision? • Study stopping rules - under what conditions will the study be modified or stopped and who will make the decision? • Reporting mechanisms (i.e. Deviations, adverse events, UPs) Data Integrity: • Specific data elements to be reviewed • Frequency of monitoring data, points in time, or after a specific number of participants • Individual responsible for data monitoring	

Additional considerations for FDA regulated trials Depending on the procedures affecting risks to participants, the site monitoring plan should specify: • Categorization of activities done centrally and those on-site if applicable • Monitoring methods (may include centralized/remote, on-site, and self-monitoring) • Reference to any tools used (i.e. checklists) • Identification of events that may trigger changes • Identification of deviations or failures that would be critical to study integrity	
Provisions to Protect the Privacy Interests of Participants*: • Describe the steps that will be taken to protect participants' privacy interests. "Privacy interest" refers to a person's desire to place limits on whom they interact with or whom they provide personal information. • Describe what steps you will take to make the participants feel at ease with the research situation in terms of the questions being asked and the procedures being performed. "At ease" does not refer to physical discomfort, but the sense of intrusiveness a participant might experience in response to questions, examinations, and procedures. • Indicate how the research team is permitted to access any sources of information about the participants.	☒ **Yes**
Economic Burden to Participants*: Describe any costs that participants may be responsible for because of participation in the research.	☒ **Yes**
Consent Process*: Describe where the consent process will take place, any waiting period available between informing the prospective subject and obtaining the consent; and the process to ensure ongoing consent. Describe the role of the individuals listed in the application as being involved in the consent process; the time that will be devoted to the consent discussion; steps that will be taken to minimize the possibility of coercion or undue influence; and steps that will be taken to ensure the participants' understanding. **Note**: If you are planning to obtain consent via electronic signature, please review this document. Additional guidance on consent documentation and process can be found on our website, under the consent toolkit.	☒ **Yes**
Consent Process-Non-English-Speaking Participants*: Indicate what language(s) other than English are understood by prospective participants or representatives.	☒ **Yes**

If participants who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those participants will be in that language. Indicate the language that will be used by those obtaining consent. If you checked N/A, please provide reasoning of why subjects with limited English proficiency are excluded. **Note**: if you stated that subjects with LEP will be enrolled, you are approved for the use of the Emory IRB short forms. Please read the guidance about the use of short forms here.	
Consent Process-Children: After determining if the subject is a child per GA law (or if enrolled outside GA, per state/country law), please describe whether parental permission will be obtained from: • Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. • One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child. Describe whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission. Describe the process used to determine these individuals' authority to consent to each child's general medical care. When assent of children is obtained describe whether and how it will be documented per Emory Policies and Procedures	☒ **Yes**
Consent Process-Cognitively Impaired Adults: describe the process to determine whether an individual is capable of consent. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require children to sign assent documents.	☐ **Yes** **n/a**
Consent Process-Adults Unable to Consent: List the individuals from whom permission will be obtained in the order of priority. (E.g., durable power of attorney for health care, a court-appointed guardian for health care decisions, spouse, and adult child.) For research conducted in the state, review "46 LEGALLY AUTHORIZED REPRESENTATIVES AND SURROGATE CONSENT" to be aware of which individuals in the state meet the definition of "legally authorized representative." For research conducted outside of the state, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the procedure(s) involved in this research. Describe the process for the assent of the participants. Indicate whether:	☐ **Yes** **n/a**

• Assent will be required of all, some, or none of the participants. If some, indicated, which participants will be required to assent and which will not. • If assent will not be obtained from some or all participants, an explanation of why not. Describe whether the assent of the participants will be documented and the process to document assent. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require participants to sign assent documents	
Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception) Review the Emory IRB waiver document to ensure you have provided sufficient information for the IRB to make these determinations. If the research involves a waiver of the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations.	☐ **Yes** **n/a**
Setting*: Describe the sites or locations where your research team will conduct the research including where the subject will be identified and recruited, where the research procedures will be performed, and if you will involve a community advisory board. For research conducted outside the organization and its affiliates describe the site-specific regulations or customs affecting the research outside the organization and the local scientific and ethical review structure outside the organization.	☒ **Yes**
Resources Available*: Describe the resources available to conduct the research such us the feasibility of recruiting the required number of suitable participants within the agreed recruitment period; describe the time that you will devote to conducting and completing the research; describe the availability of medical or psychological resources that participants might need as a result of an anticipated consequences of the human research; describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.	☒ **Yes**
Multi-Site Research when Emory is the Lead Site: Study -Wide Number of Participants: indicate the total number of participants to be accrued across all sites. Study-Wide Recruitment Methods: If this is a multicenter study and participants will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) describe those methods. Describe when, where, and how potential participants will be recruited. Describe the methods that will be used to identify potential participants. Describe materials that will be used to recruit participants.	☐ **Yes** **n/a**

Describe the processes to ensure communication among sites. See "WORKSHEET: Communication and Responsibilities (HRP-830)." All sites have the most current version of the protocol, consent document, and HIPAA authorization. All required approvals (initial, continuing review and modifications) have been obtained at each site (including approval by the site's IRB of record). All modifications have been communicated to sites and approved (including approval by the site's IRB of record) before the modification is implemented. All engaged participating sites will safeguard data, including secure transmission of data, as required by local information security policies. All local site investigators conduct the study in accordance with applicable federal regulations and local laws. All non-compliance with the study protocol or applicable requirements will reported in accordance with local policy Describe the method for communicating to engaged participating sites (see "WORKSHEET: Communication and Responsibilities (HRP-830)"):	
• Problems (inclusive of reportable events). • Interim results. • The closure of a study	
If this is a multicenter study where you are a participating site/investigator, describe the local procedures for maintenance of confidentiality. (See "WORKSHEET: Communication and Responsibilities (HRP-830).")	
• Where and how data or specimens will be stored locally? • How long the data or specimens will be stored locally? • Who will have access to the data or specimens locally? • Who is responsible for receipt or transmission of the data or specimens locally? • How data and specimens will be transported locally?	