Written Consent to Participate in a Research Study

Project Title: A double-blind, randomized, parallel group study to compare rocuronium reversal with Sugammadex (Bridion®) versus neostigmine/glycopyrrolate and the incidence of urinary retention after elective ambulatory posterior lumbar spine surgery.

Principal Investigator Name: Julie M Marshall, MD

Sponsor: Merck Sharp & Dohme and the Department of Anesthesiology and Perioperative Medicine

IRB Assigned Project Number: #2096001 MU

Consent Version: 6

Key Information About the Study

You are being asked to participate in a clinical trial. The purpose of the clinical trial is to determine the difference in urinary retention after administration of two commonly used drugs (Neostigmine versus Sugammadex) that reverse muscle relaxation which is necessary during spine surgery. Even if you do not participate in the study, you will be administered one of these two drugs on the discretion of your anesthesiology team.

You are being asked to participate in a clinical trial which will involve: (1) being administered one of the two drugs that reverse muscle relaxation, (2) being asked questions regarding the ability to urinate and your general wellbeing after surgery, and (3) to potentially have a bladder ultrasound performed to determine the amount of urine in your bladder after surgery.

There are no potential direct benefits for you if you participate in the study. There are potential risks with administration of any medication, including those in this study. However, both Neostigmine and Sugammadex are commonly administered worldwide in patients after surgery. There is also a limited risk for the loss or misuse of your protected health information. Despite this, medical staff are trained in the protection of this information and preventative steps are in place for to monitor the access and storage of your information as part of this study.

Please read this form carefully and take your time. You can discuss this study with your family, friends, or doctor if you want. Let us know if you have any questions before participating. The research team can explain words or information that you do not understand. Research is voluntary and you can choose not to participate. If you do not want to participate or choose to start then stop later, there will be no penalty or loss of benefits to which you are otherwise entitled.

There may be reasons why you are not allowed to take part in this study. The study doctor or staff will discuss these reasons and review with you why you may not be allowed to enter the study.

IRB Approval Date: Jul 24, 2025; Written Consent with HIPAA Authorization ID #798913; Amendment ID #459304

Purpose of the Research

You are being asked to participate in this study. The purpose of this study is to:

- Evaluate the rate of urinary retention after administration of one of the drugs studied, Sugammadex, compared to Neostigmine, in adults undergoing spine surgery.

During surgery, certain drugs (neuromuscular blocking agents such as Rocuronium) are given as part of general anesthesia to cause your muscles to be completely relaxed.

These drugs also make it easier for your anesthesiologist to place a breathing tube and to ventilate your lungs during surgery. While your muscles are completely relaxed, you will need a breathing machine to help you breathe through the breathing tube until you can breathe on your own again at the end of the surgery.

The muscle relaxing effects of drugs in spine surgery are given until the end of the surgery to help the surgeon to perform the surgery. Sugammadex or Neostigmine are used to reverse (or stop) the muscle relaxation and to help your muscles recover quickly after surgery. For example, by reversing the relaxation of muscles used for breathing, Sugammadex or Neostigmine can help you recover the ability to breathe on your own more quickly.

There two drugs (Sugammadex and neostigmine) may have different effect on your ability to empty your bladder after the surgery. This effect is not well studied and that is why we are conducting this study.

You may be able to join this study if you have a medical diagnosis requiring that you have a need for scheduled posterior (surgical incision made at the back of the spine) lumbar spine surgery that will require a neuromuscular blocking agent to relax your muscles during surgery. The scheduled surgery can be either ambulatory (does not require hospitalization) or short stay (discharge anticipated from hospital within 1 day). There are other requirements for study participation which the study staff will discuss with you.

What will happen during the study?

There will be about 118 subjects participating in this study.

This study is “blinded”, which means that you and the study team (except for research pharmacists) will not know which drug you are getting until the end of the study. This way, no one’s expectations of what will happen in the study will affect the results.

In an emergency, the study doctor can find out which drug you are getting.

There are four (4) study-related visits. It is expected that two (2) to three (3) could occur while you are still in the hospital for your surgical procedure.

If you take part in this study, you will have the following tests and procedures:

IRB Approval Date: Jul 24, 2025; Written Consent with HIPAA Authorization ID #798913; Amendment ID #459304

Before surgery:

- The study doctor or staff will explain the study to you and obtain your informed consent.
- Review your medical history.
- Review your prior and current medications.
- Review the inclusion and exclusion criteria to see if you can be in the study.
- Explain and review the forms with you that will be used to ask you study questions.

During surgery:

Because we do not know which of the drugs is best for urinary retention, we will "randomize" you into one of the 2 study groups. "Randomize" means putting you into a group by chance. It is like flipping a coin or pulling a number from a hat. You will have an equal chance of being placed in either group. A computer program chooses which group you go in.

You and the study doctor cannot choose which group you go into to receive an intravenous (IV) injection of one of the following study drugs:

- Sugammadex 2 milligrams (mg) per kilogram (kg) IV, dosed by actual body weight, according to the approved product's label.
- Neostigmine and Glycopyrrolate IV, dosed according to the approved products' labels.

After surgery:

- You will be asked to remember the approximate time of the first time you go to the bathroom.
- You need to be available for a follow-up visit around 6 hours after surgery (phone call if you are discharged).
    - You will be asked questions on being able to urinate.
    - If you are still in the hospital and have not yet urinated:
        - An ultrasound bladder scan (research only procedure) will be performed.
    - Study staff will review any adverse events that have occurred.
- You need to be available for a follow-up visit at around 9 a.m. on the morning after the surgery (phone call if you are discharged).
    - If necessary, you will be asked questions on when you first urinated after surgery.
    - You will also be asked 4 simple questions for a urinary retention questionnaire (research only procedure).
    - Study staff will review any adverse events that have occurred.
- One week after your surgery, study staff will review your electronic medical records for any adverse events that have occurred, pain medications you were given in the hospital, and the time and date of your hospital discharge. After that is done, your study participation will be considered completed.

IRB Approval Date: Jul 24, 2025; Written Consent with HIPAA Authorization ID #798913; Amendment ID #459304

Will you share with me any results or health problems/issues that you learn about me while in the study?

An ultrasound bladder scan will be done as a part of the research in this study if you have both: (1) not urinated by 6 hours after surgery, and (2) not left the hospital at 6 hours after surgery. The result of the bladder scan provides the research team the amount of urine in your bladder at the time of the scan was performed. This information will not be shared with you or your clinical team since it is not normally done outside of research after lumbar spine surgery in our hospital. Ability to urinate (or not) will not keep you from being discharged from the hospital after your surgery. This is standard in our hospital. All medical decisions regarding your wellbeing or urinary retention after surgery will be made by your clinical team.

How long will I be in the study?

Your participation in the clinical trial is expected to last about 8 days, which includes the follow-up period (7 days).

While in the hospital, you will receive the study drug after surgery and participate in answering questions regarding your recovery after surgery. You will be asked questions for this study by research staff or study physicians and, if you discharge from the hospital, you will also receive 1 or 2 follow-up phone calls to answer study questions.

In-person visits (or phone calls, as applicable) will occur on the day of your surgery and 1 day after your surgery. After that, for this study, the research team will only monitor your wellbeing/recovery without direct contact with you, as we are able to review your electronic medical records until 7 days after surgery.

You will be no longer considered part of this study after 7 days following the day of your surgical procedure.

Are there benefits to taking part in the study?

There is no guarantee that taking part in this research will result in any changes in your surgery outcome or your wellbeing. You will receive one of the study drugs even if you do not participate in the study.

You may expect to benefit from taking part in this research to the extent that you are contributing to medical knowledge.

The benefit to society is that information learned from the study may help other people in the future.

IRB Approval Date: Jul 24, 2025; Written Consent with HIPAA Authorization ID #798913; Amendment ID #459304

What are the possible risks of participating in this study?

You will be put into a group by chance. The drug you receive may turn out to be less effective or have more side effects than that in the other group. It may also be less effective and have more side effects than other drug available for reversal of muscle relaxation. Should you not breathe adequately and/or remain weak after receiving the study drug, you will receive a rescue dose of Sugammadex. Should this happen, the following will occur: 1) you will be excluded from the study; 2) unblinding of the study drug you received will be done with the pharmacy; 3) you will be closely monitored for a little longer once you wake up to ensure that you don't have additional side effects; 4) we will follow up with you once you are fully awake from anesthesia and inform you of what happened; 5) we will call you (if discharged) or visit you (if inpatient) approximately 6 hours after your surgery ended to ensure that you don't have residual side effects.

There are risks expected when taking part in this study. There are some that we know about, and some we may not know about yet.

To help lower these possible risks, we will monitor you closely during and after surgery as is the standard for our institution during the delivery of anesthesia services. You will provide answers after surgery in response to additional questionnaires that will assess your wellbeing and be reviewed by your study physicians. Your study physicians and their research staff will also review your electronic medical records to evaluate your wellbeing while you are part of this study.

We will tell you about any new important information we learn that may affect your decision to continue to participate in this study. Here, we include information on the potential side effects that accompany the drugs used in this study.

For Sugammadex

Sugammadex (also known as Bridion®) is a study medicine given by injection into a vein to speed up the recovery of your muscles after an operation.

Sugammadex is used to stop the muscle relaxation and to help your muscles recover quickly after surgery – for example, at the end of the operation, Sugammadex is used to help you breathe more quickly on your own. Sugammadex is approved in more than 80 countries (including by the FDA in the U.S.) and marketed in more than 50 countries worldwide. Since it was first approved in 2008, more than 30 million patients have been administered Sugammadex.

What side effects could the study drug cause?

In patients undergoing surgery, Sugammadex may occasionally cause:

- Allergic reactions, although rare, can sometimes be serious or life-threatening. These reactions can occur in persons who have not been previously treated with Sugammadex. Symptoms reported in studies or general use of Sugammadex have included: rash, hives,

IRB Approval Date: Jul 24, 2025; Written Consent with HIPAA Authorization ID #798913; Amendment ID #459304

redness of the skin; swelling of the tongue and throat that may cause difficulty breathing or swallowing; fast heartbeat, and low blood pressure.

- Shortness of breath due to muscle cramps of the airways (bronchospasm).
- Slower-than-expected recovery of muscle movement after surgery (your muscles may stay relaxed longer) or return of muscle weakness after surgery.

The most common side effects in patients undergoing surgery are:

- Cough
- Airway difficulties.
- Unwanted muscle movement or coughing during surgery.
- Change in heart rate or blood pressure due to the operation.

In rare cases, the following was seen in patients undergoing surgery: Marked slowing of the heart within minutes after giving Sugammadex for reversing the effect of relaxing the muscles for surgery. You will be carefully checked for changes in heart rate and blood pressure before and after receiving Sugammadex. Appropriate medical care will be administered in serious cases of slowed heart rate.

Other information you should know:

We will not give you the study medicine if you have had an allergic reaction to Sugammadex.

If you have lung or breathing problems, you may have an increased risk for shortness of breath due to muscle cramps of the airways (wheezing or bronchospasm).

If you have a known clotting disorder or bleeding disorder, routine clinical monitoring and practice should be conducted.

For Neostigmine

What is known about this study drug?

Neostigmine is a study medicine given by injection into a vein to help your muscles recover more quickly than they normally would after surgery and reverse the effects of the muscle relaxant. It has been approved and used worldwide for many years.

What side effects could this study drug cause?

The following side effects are thought to be caused by Neostigmine:

IRB Approval Date: Jul 24, 2025; Written Consent with HIPAA Authorization ID #798913; Amendment ID #459304

- Low blood pressure
- Slowed heart rate.
- Increased heart rate
- Abnormal heart rhythm
- Difficulty breathing that can sometimes be serious or life threatening.
- Increased mucous in the respiratory system.
- Reduction of oxygen supply to a tissue
- Difficulty speaking
- Changes in the ability to see.
- Headache
- Dizziness
- Fainting
- Inability to sleep.
- Dry mouth or increased saliva
- Nausea and vomiting after the procedure.
- Joint pain
- Itchiness, rash or redness
- Pain at the site of surgery; pain in the throat
- Muscle cramps or spasms
- Slower than expected recovery of muscle movement after surgery (your muscles may stay relaxed longer)
- Loss of bladder control
- Increased urine frequency
- Increased gas and increased bodily functions.
- Abnormal heart rhythms or increase or slowing of the heart rate that can sometimes be serious or life-threatening. You may have increased risk if you have certain heart problems.
- Wheezing or contraction of the muscles of the airway (bronchospasm). This may be worse if you have asthma.

IRB Approval Date: Jul 24, 2025; Written Consent with HIPAA Authorization ID #798913; Amendment ID #459304

- Allergic reaction that can sometimes be serious or life-threatening. Reported symptoms have included swelling of the throat that may cause difficulty breathing or swallowing, convulsions, drowsiness, difficulty in speech, involuntary muscle twitches, loss of consciousness, blurred vision, and changes in vision.

For Glycopyrrolate

What is known about this study drug?

If you are given a certain study medicine (Neostigmine) to help your muscles recover quickly after surgery, you will also receive Glycopyrrolate.

Glycopyrrolate is one of the possible study medicines given together with Neostigmine by injection into a vein. It helps to prevent some of the side effects of Neostigmine such as slowing of heart rate. Glycopyrrolate is approved for use in combination with Neostigmine and has been used in many countries for many years.

What side effects could the study drug cause?

Side effects of Glycopyrrolate may include:

- Abnormal heart rhythms, slow or fast heart rate and palpitations that can sometimes be serious or life threatening. You may be at increased risk if you have heart problems.
- Nausea, vomiting, bloated feeling
- Constipation
- Difficulty urinating
- Difficulty breathing that can sometimes be severe or life threatening.
- Blurry vision, large pupils, eye discomfort in bright light
- Dry mouth and skin
- Increased body temperature that can sometimes be serious or life threatening
- Headache
- Mental confusion
- Feeling nervous or restless
- Inability to sleep.
- Dizziness

IRB Approval Date: Jul 24, 2025; Written Consent with HIPAA Authorization ID #798913; Amendment ID #459304

- Feeling drowsy
- Muscle weakness
- Increased pressure in the eye (glaucoma). You may be at increased risk if you already have glaucoma.
- Loss of sense of taste
- Impotence (erectile dysfunction)
- Severe allergic reactions that may be life threatening
- Hives, itching.
- Decreased sweating
- Seizures
- Low or high blood pressure

Are there any other risks?

Other less common side effects have been reported with the use of the drugs in this study. The study doctor or staff can discuss these with you.

There may be other side effects or risks that are not known at this time.

As with all medications, the side effects or risks described may occur more often or be more severe than has been seen before.

What effects could the tests have on me?

You may feel discomfort during some of these tests or may experience some inconveniences.

Some may also have risks, which may include:

- Bladder Ultrasound: Use of bladder ultrasound does not have any known risks. This will be research only procedure.

Reproduction Risks

It is not known if the study drug(s) may affect an unborn or nursing baby. If you are pregnant, trying to become pregnant or breast-feeding, you may not be in the study.

As part of your standard medical examinations before surgery, your doctors will perform a urine pregnancy test and, if necessary, perform a blood pregnancy test, if you are able to have a baby.

IRB Approval Date: Jul 24, 2025; Written Consent with HIPAA Authorization ID #798913; Amendment ID #459304

Females

If you are able to have a baby, you must use a reliable birth control method during the study and for a period of 7 days after your last dose of study drug. The following birth control methods are allowed during the study:

- abstinence (no sex)
- condoms (male or female) with a spermicidal agent
- diaphragm or cervical cap with spermicide
- medically prescribed intrauterine device (IUD)
- inert or copper-containing IUD
- surgical sterilization (e.g., hysterectomy or tubal ligation)

If you become pregnant during the study, you must notify the study doctor right away.

What other choices do I have if I don't want to be in this study?

You are not required to be in this study. You can simply choose not to participate.

You do not have to be in this study to receive the medications that are in this study including Sugammadex, Neostigmine, or Glycopyrrolate. If you should decide not to participate in, or if you withdraw from this study, your clinical team will decide which of these drugs will be used for muscle relaxation reversal in your anesthesia care.

Will I receive compensation for taking part in this study?

You will not be compensated for taking part in this study.

Are there any costs for participating in this study?

You should not expect any additional costs by participating in this study.

The study will pay for all research tests and procedures. You and/or your health plan/insurance will not be billed for tests and procedures that are done for research only.

Research only procedures in this study include:

- The study drug(s)
- Administration of the study drug(s)
- Urinary retention questionnaire
- Ultrasound bladder scanner

IRB Approval Date: Jul 24, 2025; Written Consent with HIPAA Authorization ID #798913; Amendment ID #459304

You and/or your health plan/insurance will be billed for everything that is considered standard of care. This includes tests and procedures you would receive without being in this study. Some health plans/insurance companies will not pay for these costs for people who are in research studies. Check with your plan/company to find out what they will pay for.

Other costs to you from being in this study may include testing or treatment for existing or new health conditions, insurance co-payments for doctor visits, transportation, parking, childcare, and/or time off work.

A social worker and financial counselor are available to discuss concerns with you. Please let the research staff know if you would like to visit with them and an appointment will be made.

You should discuss any questions about costs with the researchers before agreeing to participate.

Will information about me be kept private?

The research team is committed to respecting your privacy and keeping your personal information confidential, including health information. We will make every effort to protect your information to the extent allowed by law. Your records will be given a code number and will not contain your name or other information that could identify you. The code number that connects your name to your information will be kept in a separate, secure location.

When the results of this research are shared, we will remove all identifying information so it will not be known who provided the information. Your information will be kept as secure as possible to prevent your identity from being disclosed.

We will scan a copy of this consent form into your medical record.

What we collected from you as part of this research will not be used or shared for future research studies. It will only be used for purposes of this study.

The FDA may inspect the records since the study is FDA regulated.

Permission to Use your Protected Health Information:

State and federal privacy laws (HIPAA) protect the use and release of your health information. If you decide to take part in this study, you also give us your permission to use your private health information, including the health information in your medical records and information that can identify you.

You have the right to refuse to give us your permission for us to use your health information. However, doing so would mean that you could not take part in this study.

IRB Approval Date: Jul 24, 2025; Written Consent with HIPAA Authorization ID #798913; Amendment ID #459304

Some identifiers about you will be obtained from your health records and are necessary for this research. The identifiers will include your name, address, dates related to you, phone numbers, email addresses, medical record number, account numbers, health plan beneficiary number, photos, and other characteristics that could identify you.

We may share any of this information with the following:

- Authorized members and staff of the University of Missouri Institutional Review Board (IRB).
- Laboratories and other individuals and organizations that may need to see your health information in connection with this study.
- Study monitors and auditors who make sure that the study is being done properly.
- Dr. Julie M Marshall and the Curators of the University of Missouri who are sponsoring the study, and their contractors and partners.
- Government agencies and public health authorities, such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS), and the Office for Human Research Protections (OHRP)

Any research information shared with outside entities will not contain your name, address, telephone or social security number, or any other personal identifier unless it is necessary for review or required by law.

The people who get your health information may not be required by Federal privacy laws (such as the HIPAA Privacy Rule) to protect it. Some of those people may be able to share your information with others without your separate permission.

Your permission for us to use and/or release your information will not expire unless you cancel your permission in writing.

<u>You can cancel your permission at any time by writing to</u>:
Investigator's Name: Dr. Julie M Marshall
Institution: University of Missouri School of Medicine
Department: Department of Anesthesiology & Perioperative Medicine
Address: 1 Hospital Dr., DC005.00, Columbia, Missouri, 65212

The information we have already collected may still be used for this research study, but we will not collect anymore information after we receive your letter.

You have the right to access your protected health information that is obtained or created during your clinical care. You will not be allowed to access your protected health information that is obtained or created for research-only purposes during this in research project until the end of the study.

If you have not already received a copy of the University of Missouri Health Care Privacy Notice, you may request one. If you have any questions or concerns about your privacy rights, you may contact the Privacy Officer at 573-882-9054.

IRB Approval Date: Jul 24, 2025; Written Consent with HIPAA Authorization ID #798913; Amendment ID #459304

What if I am injured during the study?

It is not the policy of the University of Missouri to compensate human subjects in the event the research results in injury.

The University of Missouri, in fulfilling its public responsibility, has provided medical, professional and general liability insurance coverage for any injury in the event such injury is caused by the negligence of the University of Missouri, its faculty and staff. The University of Missouri also will provide, within the limitations of the laws of the State of Missouri, facilities and medical attention to subjects who suffer injuries while participating in the research projects of the University of Missouri.

In the event you have suffered injury as the result of participation in this research program, you are to contact the Risk Management Officer, telephone number (573) 882-1181, at the Health Sciences Center, who can review the matter and provide further information. This statement is not to be construed as an admission of liability.

Where can I get more information about this clinical trial?

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Who do I contact if I have questions or concerns?

If you have questions about this study or experience a research-related injury, you can contact the University of Missouri researcher who leads and oversees the conduct of this study, Dr. Julie M Marshall at 573-882-2568 or marshalljm@health.missouri.edu.

If you have questions about your rights as a research participant, or have problems or complaints, please contact the University of Missouri Institutional Review Board (IRB) at 573-882-3181 or muresearchirb@missouri.edu. The IRB is a group of people who review research studies to make sure the rights and welfare of participants are protected.

If you want to talk privately about any concerns or issues related to your participation, you may contact the Research Participant Advocacy at 888-280-5002 (a free call) or email muresearchrpa@missouri.edu.

Do I get a copy of this consent?

You will receive a copy of this consent for your records.

We appreciate your consideration to participate in this study.

Consent to Participate – Signatures

IRB Approval Date: Jul 24, 2025; Written Consent with HIPAA Authorization ID #798913; Amendment ID #459304

Subject's Signature	**Date**

Investigator Authorized to Obtain Consent	**Date**