EVMS
Eastern Virginia Medical School

February 11, 2020

Seifeldin T Sadek, MD
601 Coley Ave
Norfolk, VA 23507

RE: IRB # 19-08-FB-0189

This form provides additional information to the *Amendment Assessment by the Investigator Form* that accompanies this letter. The amendment assessment is the official document that confirms IRB review and type of approval and includes the IRB#, study title, summary of the changes, IRB stamp that includes approval and expiration dates, and an appropriate chair, vice-chair or IRB member signature.

☒ Amendment identifier: Protocol Change Consent Change

☒ IRB Study Title: Randomized Control Trial for Prophylactic Tranexamic acid in minimally invasive myomectomies

- Protocol: Randomized Control Trial for Prophylactic Tranexamic acid in minimally invasive myomectomies
  Version Date: Jan-02-2020

☒ Unsupported, no sponsor has been identified as providing funding for this study or project.

☒ Subject Consent Form: Version 2 Date: Jan-02-2020

YOUR CONSENT FORM HAS BEEN STAMPED WITH THE APPROVAL DATE AND IS ENCLOSED FOR YOUR USE UNTIL A DIFFERENT CONSENT SUPERSEDES IT.

☒ Additional Materials: Letter from Pharmacy; Article - Safety of a High-Dose Tranexamic Acid Protocol in Complex Adult Spinal Deformity: Analysis of 100 Consecutive Cases; Article - Comparison of Two Doses of Tranexamic Acid in Adults Undergoing Cardiac Surgery with Cardiopulmonary Bypass; Lexicomp Drug Information

☒ This Amendment was reviewed and approved pending changes at the **convened Board meeting December 17, 2019**. The changes were given final approval on **February 11, 2020**.

☒ **As a reminder, your protocol expiration date is September 16, 2020. Please see the attached form for the due date of the next continuing review submission.**

☒ Please remember that prompt reporting to the IRB of proposed changes in a research activity (e.g., changes to the protocol, consent form(s), advertisements, or other study-related materials) is required. This includes information related to funding sources. In addition, the changes must be reviewed and approved by the EVMS IRB ***before*** the changes can be initiated *except* when it is necessary to eliminate apparent immediate hazards to the subject.

Remember that a copy of all correspondence relating to any site visit or regulatory visit must be submitted to the IRB office within five (5) days of receipt by the EVMS site. Refer to the *2007 EVMS IRB SOPs Section 22.0* for more information.

Eastern Virginia Medical School (EVMS) has a Federalwide Assurance (FWA 00003956) from OHRP. The Institutional Review Boards (IRB 00000460 and IRB 00001345) are registered with OHRP and are in compliance with 45 CFR 46, 21 CFR 50, and 21 CFR 56.

Please reference the IRB number, principal investigator and study title in any correspondence regarding this protocol.

Thank you for your continued cooperation with the Institutional Review Board.

Sincerely,

Daniel Sullivan, PhD, CIP
IRB Assistant Director

DMS/rls

EVMS
Eastern Virginia Medical School

FWA #00003956
January 2019; v.1

AMENDMENT ASSESSMENT BY THE INVESTIGATOR
EVMS Institutional Review Board

NOTES: 1. File this form with any Protocol, Consent Form, Advertising or Other Change forwarded to the EVMS IRB

2. A copy of the last approved, stamped consent form must be attached to this submission.

3. Two hard copies of each document described on this form as being changed must be attached to this form. All changes must be highlighted on one of those two copies.

IRB Number:	19-08-FB-0189

ADMINISTRATIVE INFORMATION

Study Title:	A RANDOMIZED CONTROL TRIAL INVESTIGATING THE IMPACT OF HIGH DOSE PROPHYLACTIC TRANEXAMIC ACID ON BLOOD LOSS AT THE TIME OF MINIMALLY INVASIVE MYOMECTOMY	**Date Submitted:** ~~(IRB USE ONLY)~~ RECEIVED DEC 1 1 2019 BY:	
Principal Investigator:	Seifeldin Sadek		
PI Dept / Address	700 W Olney Rd,		
City / State / Zip	Norfolk/VA/23507		
Phone Number(s):	757.446.7979	**E-Mail:**	sadeks@evms.edu
Person Preparing This Submission			
Name:	Seifeldin Sadek	**Role:**	Principal Investigator
Address:	700 W olney Rd		
Phone Number(s):	757.446.7979	**E-Mail:**	sadeks@evms.edu

ENROLLMENT INFORMATION

Is the study still open to enrollment:	Yes	**Number of subjects enrolled to date:**	0	**Number of subjects active at this time:**	0

AMENDMENT INFORMATION

Date of the Change: 12/3/2019	**Identifier for the change:** Protocol change 1 (e.g., Amendment 1, Protocol change A2, etc.)

Write a **BRIEF SUMMARY** of the change(s). DO NOT cut-and-paste large sections of text from the protocol. *(500 characters max)*

We would like to use a higher dose of tranexamcic acid to help reduce blood loss in minimially invasive myomectomeies. After further review of the literature. there is a significant benefit of using higher doses of tranexamic acid, with no increase in reported side effects. We hope to show that at higher doses tranexamic acid can reduce blood loss.

IMPORTANT: *Two hard copies of each revised document must be included with this form. For example, if you are making consent changes, then a revised consent, one with the changes highlighted and one clean, must be provided.*

IF ADDING INVESTIGATORS AND/OR RESEARCH TEAM MEMBERS PLEASE COMPLETE THE FOLLOWING FOR EACH:

Name	Department and Address	Role
		-- Choose One --
		-- Choose One --
		-- Choose One --
		-- Choose One --

IF ADDING INVESTIGATORS AND/OR RESEARCH TEAM MEMBERS PLEASE COMPLETE THE FOLLOWING FOR EACH:		
		-- Choose One --

CONFLICT OF INTEREST POLICY

If your project is sponsored you must meet the EVMS COI Policy requirements before a final approval for this Amendment can be issued. **You also must notify the IRB of any COI determination(s).**

Refer to the Office of Research *Policy on Conflicts of Interest in Research and Sponsored Projects* (COI).

For questions regarding the COI Policy and COI submissions contact the Office of Research at 446-8480.

CHOOSE ONE	In the Principal Investigator's opinion, how does this amendment change the risk experienced by subjects	Please explain the nature of the change(s).
☐	Increase the risk	
☒	Decrease the risk	We believe the higher dose of tranexamic acid will further decrease the risk of bleeding in comparison to the 1000mg standard dose, with no reported increase in side effects.
☐	Reduce the benefit experienced by subjects	
☐	No change in the risk experienced by subjects	

PRINCIPAL INVESTIGATOR SIGNATURE	DATE OF SIGNATURE
	12 / 4 / 19

THIS SECTION FOR IRB USE ONLY

FINAL DISPOSITION:

REVIEW CATEGORY	ACTION	IS RE-CONSENT NEEDED?	CONTINUING REVIEW DEADLINE
☐ Not Human **or** ☐ Not Research	☒ Approved	☒ No ☐ Yes ☐ N/A	
☐ Exempt	☐ Disapproved	If yes, note any conditions/stipulations:	07/01/20
☒ Expedited	☐ Withdrawn		
☒ Full (Convened) Board			

dm SK

IRB SIGNATURE:		DATE:	2 / 11 / 20
SIGNED BY:	☒ IRB CHAIR ☐ IRB VICE CHAIR ☐ IRB MEMBER		

EVMS IRB #: 19-08-FB-0189
IRB APPROVAL DATE: 12/17/19
EXPIRATION DATE: 09/16/20

Subject Consent Form

Eastern Virginia Medical School (EVMS) Institutional Review Board

STUDY TITLE

A Randomized Control Trial Investigating the impact of High dose Prophylactic Tranexamic acid on blood loss at the time of minimally invasive myomectomy

Key Summary of Information

We are inviting you to take part in a research study to compare the volume of blood loss in patients undergoing minimal invasive myomectomies who receive prophylactic high dose tranexamic acid vs placebo. This page is intended to provide you with key information to help you decide whether to participate. The detailed consent form follows this page. Please ask the research team questions. If you have questions later, the contact information for the principal investigator in charge of this study is below.

WHAT IS THE PURPOSE, WHAT ARE THE PROCEDURES, AND WHAT IS THE DURATION OF THIS STUDY?

This study is attempting to assess the effectiveness of tranexamic acid to decrease blood loss in gynecological surgeries. You will be randomized to one of two groups, one group will receive the medication, the other will not. We will then measure the amount of blood loss during the procedure. The duration of the study will be 6 weeks, which is standard of care for any patient undergoing minimally invasive myomectomies.

WHAT ARE SOME REASONS YOU MIGHT CHOOSE TO PARTICIPATE IN THIS STUDY?

If you agree to take part in this study, there is a chance that this medication will help decreased you bleeding intraoperatively based on previous similar studies. There is no guarantee that you will personally benefit from taking part in this study. We hope the information learned from this study will benefit other people with intraoperative hemorrhage in the future.

WHAT ARE SOME REASONS YOU MIGHT CHOOSE NOT TO PARTICIPATE IN THIS STUDY?

There are very few known risks to you, beyond what we would normally expect from the side effects of Tranexamic Acid (see pages 3 and 4 of this document). Many side effects go away shortly after the tranexamic acid is given. Another risk is a breach in confidentiality, or release of personal information. We will strive to protect your records so that your personal information (like name, address, social security number and phone number) will remain private. There also may be other side effects that are unknown, and we cannot predict. For more information about risks and side effects, ask the investigator or contact 757-446-7900

DO YOU HAVE TO TAKE PART IN THIS STUDY?

If you decide to take part in the study, it should be because you really want to volunteer for it. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer. You are free to withdraw from the study at any time. You may also receive tranexamic acid even if you do not take part in the study. The use of tranexamic acid for minimizing blood loss during surgery is an off-label use, even though commonly used for surgical procedures in multiple specialties. Tranexamic acid is FDA approved for minimizing cyclical blood loss during menstruation in oral form.

WHAT IF YOU HAVE QUESTIONS OR CONCERNS?

For questions about the study, contact the investigator, Dr. Seifeldin Sadek, at (757)-446-7900
For questions about your rights as a research participant, contact a member of the Institutional Review Board through the Institutional Review Board office at (757) 446-8423.

Please continue to the next page for detailed information about the study.

Study Title

A Randomized Control Trial for Prophylactic Tranexamic acid in minimally invasive myomectomies

INVESTIGATORS

Seifeldin Sadek MD, Institute: Eastern Virginia Medical School
Hadi Ramadan MD, Institute: Eastern Virginia Medical School
Reem Sabouni, MD, Institute: Eastern Virginia Medical School
Tamar Matitashvili MD, Institute: Eastern Virginia Medical School
Laurel Stadtmauer, MD, PhD, Institute: Eastern Virginia Medical School
Joseph Hudgens, MD, Institute: Eastern Virginia Medical School
Traci Ito MD, Institute: Eastern Virginia Medical School

Sponsor

No sponsors for this study. The cost of tranexamic acid will be covered as part of the surgical management of fibroids.

WHY IS THIS STUDY BEING DONE?

In minimal invasive gynecologic surgeries, operative blood loss is a common complication that affects postoperative morbidity and recovery. Tranexamic acid is a medication used in obstetrics and gynecology, and many surgical specialties to reduce blood loss in surgery. We are performing this study specifically to assess its effectiveness in minimally invasive gynecology surgeries i.e. laparoscopic procedures.

WHY ARE YOU BEING ASKED TO TAKE PART?

You have been diagnosed with menorrhagia or abnormal uterine bleeding due uterine fibroids, and have chosen to undergo surgical management of these uterine fibroids. A normal risk of this surgery is blood loss. We believe tranexamic acid might help reduce blood loss during surgery
This is a research study. This study includes only people who choose to take part. Please take your time to make your decision and feel free to ask any questions you might have.

WHAT ARE SOME IMPORTANT DETAILS ABOUT THIS STUDY?

At this local site about 100 people will take part in this study. A total of about 100 people are expected to take part in this study at 1 site throughout the United States. We will need you to be in the study for the duration of your procedure, and your post-operative visits.
You will be receiving a higher dose of tranexamic acid to try and reduce blood loss during your surgery
We believe this higher dose does not increase your risk of side effects
Clinically relevant research results such as blood loss and blood products given will be disclosed to participants, including any that might apply individually. However, if tranexamic acid is given, it will not be disclosed to the patient

WHEN SHOULD YOU NOT TAKE PART?

If you have any of the following conditions or are taking any of the medications listed below, you should not take part in this study:

- Severe existing medical complications involving the heart, liver, or kidney
- Moderate to severe kidney impairment
- Blood clotting abnormalities
- Age <18
- Known Allergies to tranexamic acid
- Known Contraindications to Minimally invasive myomectomies
- If you are pregnant
- History of a prior blood clot in the lung arm or leg, known as pulmonary embolism or deep vein thrombosis
- History of a stroke or mini-strokes
- History of seizures
- Concurrent oral contraceptive use
- Contraindications to receiving Tranexamic acid
    i. In patients with acquired defective color vision, since this prohibits measuring one endpoint that should be followed as a measure of toxicity
    ii. In patients with subarachnoid hemorrhage. Anecdotal experience indicates that cerebral edema and cerebral infarction may be caused by tranexamic acid in such patients.
    iii. In patients with active intravascular clotting.
    iv. In patients with hypersensitivity to tranexamic acid or any of the ingredients
    v. Moderate to severe kidney impairment

WHAT IS INVOLVED IN THE STUDY?

Since you meet criteria to participate in this study, you will be randomized to one of two groups, one group will receive the medication, the other will not. You will undergo a minimally invasive myomectomy by your surgeon at either Sentara Norfolk general, Sentara Leigh, or Sentara Princess Anne base on your surgeon's preference. The medication will be given to you 15 minutes prior to the surgery intravenously, otherwise the surgery will be completed normally as it would otherwise.
We will then measure the amount of blood loss during the procedure and will collect lab tests as we would normally do outside the study. You will then return for your post-operative visit at 2 weeks and 6 weeks. A survey will be given to you during the 2-week post-operative visit to assess for side effects of the medication.
The total duration of the study will be 6 weeks, which is also standard of care for any patient undergoing a minimally invasive myomectomy at EVMS

WHAT ARE THE RISKS OF THE STUDY?

Your surgeon will disuss the potential risks of having a momectomy. There are very few known risks to you, beyond what we would normally expect from the side effects of Tranexamic Acid.

Since this study uses a single dose of tranexamic acid, we do not anticipate the same degree of side effects that are reported for long term medication use, but there are risks associated with tranexamic acid and they include:

>10%:

- Headache
- Abdominal pain
- Nausea/vomiting
- Back pain
- musculoskeletal pain
- Nasal congestion

1% to 10%:

- Fatigue
- Anemia
- Joint pain
- Muscle cramps
- Muscle spasm
- Stroke
- Severe allergic reaction
- Upper urinary tract obstruction due to blood clot
- Blood clot in artery or veins
- Blood clot in the lungs
- Retinal artery and central retinal vein blood clot

There also may be other risks that are unknown, and we cannot predict. While on the study, you are at risk for these side effects. You should discuss these with the investigator and/or your regular doctor or healthcare provider. Many side effects go away shortly after the tranexamic acid is given.

A risk associated with allowing your data to be saved is the release of personal information from your study record. We will strive to protect your records so that your personal information (like name, address, social security number and phone number) will remain private.
There also may be other side effects that are unknown, and we cannot predict.
For more information about risks and side effects, ask the investigator or contact 757-446-7900

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. There is no guarantee that you will personally benefit from taking part in this study. We hope the information learned from this study will benefit other people undergoing minimally invasive myomectomies in the future.

WHAT OTHER OPTIONS DO YOU HAVE?

You may choose not to participate in this research study.

You may also receive tranexamic acid even if you do not take part in the study, but it will be at the regular dose
The use of tranexamic acid for minimizing blood loss during surgery is an off-label use but is still routinely used in many gynecologic procedures. The Oral version Tranexamic acid is FDA approved for minimizing cyclical blood loss during menstruation, and the IV is FDA approved for minimizing blood loss during dental procedures for patients with hemophilia
Please talk to your regular doctor or health care provider about these and other options.

WHAT ABOUT CONFIDENTIALITY?

In conducting this research study, it will not be necessary for the research team to send information about you and your health to persons in other organizations. However, the research team will need to access to information related to the study that is considered "protected health information (PHI)," which includes personal information about you. Access to your PHI will be performed through a secure PC only available to the investigators of the study on both Allscripts and EPIC electronic medical records. Your information will then be deidentified and stored in the same PC. It will be shared with others only as described below:

Description of Your PHI to Be Disclosed	Organization and Person (or their title) Disclosing Your PHI	Organization and Person (or their title) Receiving Your PHI	Purpose of Disclosure
Name, DOB, etc.	EVMS Medical group Sentara	EVMS research team associated with this study.	For research purposes only.

- If you refuse to give your approval for your personal information to be shared as described in this consent form, you will not be able to be in this study. However, your choice will not affect any medical benefits to which you are entitled.
- By signing this consent form to participate in the study, you are allowing the research team to share PHI, as described in this consent form.
- You have the right to cancel your approval for the sharing of PHI. If you cancel your approval, you will have to leave the study. All information collected about you before the date you cancelled will not be used. To cancel your approval, you must notify Dr. Sadek in writing at 601 Colley Avenue, The Jones Institute 23507, Norfolk Virginia

- Your approval for the sharing of personal information about you for this study expires at the end of the study.
- You also have the right to review your research records, or someone you designate may review your research records on your behalf, once the study has ended unless prohibited by law.
- Any research information in your medical record will become a permanent part of that document.

Your study records may be reviewed and/or copied in order to meet state and/or federal regulations. Reviewers may include, for example, an Eastern Virginia Medical School Institutional Review Board U.S. Food and Drug Administration (FDA)
Information learned from this research may be used in reports, presentations and publications. None of these will personally identify you.

What Will Participation in the Study Cost or Pay?

There are no additional costs to you associated with taking part in this study. Predicted costs of this study will not go and beyond those of the surgery. Medications that are used to decrease blood loss during surgery such as tranexamic acid are commonly used during myomectomies and are covered by your insurance for this study.
You are still eligible to receive tranexamic acid to decrease blood loss even if you do not participate in this study.

What If You Get Injured?

In the case of injury or illness resulting from this study, emergency medical treatment is available and will be provided by Sentara Norfolk General Hospital and paid for by your own health insurance. Further medical care and/or hospitalization resulting from this injury or illness will be charged to your own health insurance

Eastern Virginia Medical School does not provide free medical care for any sickness or injury resulting from being in this study. Financial compensation for a research related injury or illness, lost wages, disability, or discomfort is not available. However, you do not waive any legal rights by signing this consent form.

What About the Collection of Data/Tissue/Specimens?

You are in a study where identifiable data and lab results are collected as part of your participation in the research study. Right now, there are no plans to use the data and lab results for another research study. However, the identifiers might be removed, and, after such removal, the data and lab results could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

What Are Your Rights as a Participant?

Taking part in this study is your choice. If you decide not to take part, your choice will not affect any medical benefits to which you are entitled. You may choose to leave the study at any time. If you do leave the study, discuss it with the investigator who will help you do so in the safest way. If you leave, the study it will not result in any penalty or loss of benefits to you.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

Virginia law says that if you or anyone associated with the study is exposed to the other person's body fluids that might transmit the virus that causes AIDS or the Hepatitis B or C virus:

- The person whose body fluids were involved is deemed to have consented to testing for those viruses so that no further consent is necessary to test the person for these diseases; and,
- Those test results will be released to the person who was exposed and to the health department as required by Virginia law.

Whom Do You Call if You Have Questions or Problems?

For questions about the study, contact the investigator, Dr. Seifeldin Sadek, at 757-446-7900

For questions about your rights as a research participant, contact a member of the Institutional Review Board through the Institutional Review Board office at (757) 446-8423.

If you believe you have suffered an injury as a result of your participation in this study, you should contact the principal investigator, Seifeldin Sadek at 757-446-7900
You may also contact Betsy Conner, director, EVMS Human Subjects Protection Program and IRB office at Eastern Virginia Medical School, at (757) 446-5854.

FDA Clinical Trial Registration

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

SIGNATURE

You will get a copy of this signed form. You may also request information from the investigator. By signing your name on the line below, you agree to take part in this study and accept the risks.

_____	_____	_____	___/___/___
Signature of Participant	Typed or Printed Name	Relationship to Subject	MM/ DD/ YY

STATEMENT OF THE INVESTIGATOR OR APPROVED DESIGNEE

I certify that I have explained to the above individual the nature and purpose of the study, potential benefits, and possible risks associated with participation in this study. I have answered any questions that have been raised and have witnessed the above signature. I have explained the above to the volunteer on the date stated on this consent form.

_____	_____ / _____ / _____
Signature of Investigator or Approved Designee	MM/ DD/ YY

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