UNIVERSITY of MARYLAND BALTIMORE

# RESEARCH CONSENT FORM AND HIPAA AUTHORIZATION

**Protocol Title:** ENRICH-PLUS – A Non-Randomized Controlled Trial to Examine the Safety and Suitability of Supplementing Early Minimally Invasive Parafascicular Surgery (MIPS) for Clot Evacuation of Basal Ganglia Intracerebral Hemorrhage (ICH) with Pioglitazone

**Study No.:** HP-00102344

**Principal Investigator:** J. Marc Simard, MD, PhD
410-328-0850

**Grant Support:** NICO Corporation

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You are being asked to take part in a research study. Taking part is voluntary. You can ask questions at any time about this research study. This consent form contains information about the study that will help you decide if you want to take part. Please read this form carefully before making your choice. If you agree to be in the study, we will ask you to sign this consent form. You will be given a copy of the form to take home with you. If you are consenting for someone else who is unable to provide consent themselves, then the word "you" refers to that person.

Below is a list of words used in this consent form.

**Intracerebral Hemorrhage (ICH):** A type of stroke. ICH is caused by bleeding into the brain because of a ruptured blood vessel. With ICH, part of the brain does not get the oxygen and nutrients needed to survive.
**Minimally Invasive Parafascicular Surgery (MIPS):** A minimally invasive surgery to remove the extra blood from the brain.
**Computed Tomography (CT):** Images of the brain/body using a small amount of radiation.



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**CONCISE SUMMARY:**

- You are being asked to take part in this research study because you have a type of bleed called an intracerebral hemorrhage (ICH). ICH caused a clot of blood deep in your brain.
- This study will assess the safety and efficacy of combining a minimally invasive surgical procedure (MIPS) to remove the clot from the brain, with a drug called pioglitazone.
- The drug will be given 3 times daily for up to 3 weeks. You will receive the drug by mouth or through a tube that carries food and medicine through the nose to your stomach.
- You will have a screening to see if you are eligible to take part in this study. During this screening, as well as at study specific time points, you will have tests, exams, and procedures done that are part of your standard care and for study purposes. These study procedures will be explained in this document.
- The study will take about 6 months.
- There are potential benefits and risks linked to this study. These will be explained in this document.
- Your decision to take part in the study is voluntary. Refusing to take part in this research study will not keep you from pursuing other medical treatments for your condition with your doctor. If you are interested in learning more about this study, please keep reading below.

**PURPOSE OF STUDY**

A research study is a study to find out how a new drug or treatment works in patients. Taking part in a research study is different from getting regular medical care. The aim of regular care is to improve your health. The aim of a research study is to collect and analyze information which may help many patients to get better care in the future.

The purpose of this research study is to compare early Minimally Invasive Parafascicular Surgery (MIPS) plus the drug pioglitazone to MIPS alone for the treatment of Intracerebral Hemorrhage (ICH). The goal of the study is to show improved outcomes in patients who have both MIPS and pioglitazone.

MIPS is already offered at the University of Maryland Medical Center (UMMC) as a standard medical practice. Pioglitazone is approved by the U.S. Food and Drug Administration (FDA) for the treatment of Type II diabetes in adults. Pioglitazone is *not* approved for use in the treatment of ICH. Our research is an investigational, off-label use of this medication in ICH patients.

You are being asked to take part in this study because you or a loved one has been diagnosed with a type of bleeding stroke called an ICH. Your doctor believes MIPS is the best medical treatment



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based on UMMC's experience. There is no placebo or randomization in this study. If you choose to take part in this study and you are eligible, you will receive pioglitazone in addition to MIPS.

This research is only being done here at the University of Maryland, Baltimore. We plan to enroll up to 20 subjects over 2 years. Taking part in the study will last about 6 months.

**PROCEDURES**

As part of both the study and your routine medical care, you will have certain medical procedures and tests done. Those that are required for the study are listed below. Some may already have been done, or will be done, as part of routine medical care.

Screening assessments

To take part in this study, you must meet certain requirements. If you agree to take part in the study, the research team will check to see if you qualify. During this period:

- Your medical history, vital signs, level of ability and independence, and demographic data (sex, age, etc.) will be collected and recorded.
- Information from your routine medical care will be collected and recorded. The research team will review a CT scan of your head, laboratory results from blood tests, and results from an assessment called the NIH Stroke Scale.
- If you have not had these tests they will be done in order for you to be considered for this study.

Surgery and pioglitazone administration

To take part in this study, your doctor must recommend Minimally Invasive Parafascicular Surgery (MIPS) as a treatment. You must consent to this procedure. After you consent to be in the study and the screening assessments are done, the following events will take place:

- You will be given pioglitazone either within 24 hours before your surgery or within 3 hours after the surgery is over. You will continue to get pioglitazone 3 times per day by mouth or through a tube from your nose to your stomach for 3 weeks.
- About 30 minutes before each dose of pioglitazone, you will be given a glucose fingerstick to check your blood sugar levels. This will continue for at least 3 days. If your blood sugar levels have stayed within normal limits after 3 days, you will no longer be given fingersticks.
- If low blood sugar levels are found, the next dose of pioglitazone will be skipped. You will instead have the standard treatment for low blood sugar based on hospital guidelines. The next pioglitazone dose will be given once you have normal blood sugar levels again.



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Hospital course and follow ups

Data on the other medications and therapies you have as routine medical treatment will be recorded. You will also have additional assessments and exams for the study.

- About 7 days after your surgery, you will have a study-specific CT scan of your head. This is the only extra CT scan that you will have that is not part of your routine medical care.
- When you leave the hospital, information on your length of stay and discharge information will be recorded.
- About 30 days after your surgery, you will be contacted by a member of the research team to see if you have had any adverse events, additional medications, or treatments.
- About 90, 120, and180 days after your surgery, you will be contacted again, with more questions about your functional status and quality of life.

**OPTIONAL BIOMARKER BLOOD SAMPLES**

In this study, staff are collecting 3 additional blood samples to learn more about specific biomarkers (signals in the blood) that may help predict disease outcomes. These additional blood samples are voluntary. If you decline these additional samples, it will not affect your eligibility for the study. Volunteering to provide these additional samples will not provide any direct benefit to you.

If you volunteer for these additional samples, approximately 1 teaspoon of blood will be taken prior to receiving the first dose of pioglitazone, 3-5 days from the first dose, and 10 days from the first dose for a total of 3 additional teaspoons of blood.

☐ Yes, I consent to provide these additional, research-specific blood samples

☐ No, I do NOT consent to provide these additional, research-specific blood samples.

All samples will be labeled and stored using a unique study number, in which only the PI and research staff will be able to link you to your samples.

If you decide to consent to collection, samples will be collected as part of the research and, even if identifiers are removed, will not be distributed for future research studies. These specimens will not be used to generate cell lines for genetic testing or genome sequencing.

**WHAT ARE MY RESPONSIBILITIES IF I TAKE PART IN THIS RESEARCH?**

If you take part in this research, you will be responsible following your doctor's plan of care to the best of your ability. You are also responsible for staying in contact with the research team.



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They will see you during your stay in the hospital and contact you for the 30, 90, 120, and 180 day follow ups.

**POTENTIAL RISKS/DISCOMFORTS:**
There are risks involved with your medical treatment. Taking part in this research study may expose you to other risks or discomforts. Please read these potential study-specific risks carefully.

Risks associated with pioglitazone
The study drug, pioglitazone, may have side effects. Side effects are much more common in diabetic patients, patients who get insulin, and patients who take pioglitazone for a long time. Side effects may be different in patients with ICH or who take pioglitazone for a short time. Very serious side effects in diabetic patients after treatment with pioglitazone are:

- a risk of congestive heart failure (the heart has difficulty pumping blood) - 6%,
- edema (swelling) - 27%,
- hypoglycemia (low blood sugar) – 16%
- new or worsening macular edema (swelling of the eye) – 1.15%
- and, rarely, liver toxicity – 0.26%

Other possible risks include:

- weight gain – 26%
- increased risk of broken bones, particularly in women – 5%

To lessen these risks, we will not enroll patients with a known history of heart/kidney/liver failure or type 2 diabetes managed with insulin. To reduce the risk of low blood sugar, we give the drug as 3 doses per day and check blood sugar levels before each dose. You may have a slight discomfort with the fingersticks used to measure blood sugar levels.

Contact your healthcare provider immediately if any of the following symptoms develop while taking pioglitazone: rapid weight gain, swelling, unusual fatigue, trouble breathing, shortness of breath, unexplained nausea, vomiting, abdominal pain, anorexia, dark urine, yellowing of skin or whites of eyes, discomfort when urinating, urinary urgency, or changes in vision.

Risk of radiation dose
You will have an additional CT scan of your head if you take part in this study. This will expose you to additional radiation. This is not essential for your routine medical care. This extra dose of radiation in the study has been approved by UMB's Radiation Safety Committee because it follows the committee's safety guidelines for research subjects. This risk is lessened by institutional practices to reduce the amount of radiation necessary to do these types of scans.

The radiation you receive from the head CT scans are considered part of research. The three organs receiving the highest amount of radiation dose are your eye (7 Rem), brain (6.2 Rem), and thyroid (4.4 Rem). Using the standard way of describing radiation dose, you will receive (.466 Rem) of total body effective radiation dose. The UMB HUSC of the Radiation Safety



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Committee, a group of experts on radiation matters, has reviewed the use of radiation in this research study and has approved this use as being within the UMB Radiation Safety Guidelines for research subjects of 3 Rem to any tissue in a 13 week period and 5 Rem in one year. The radiation dose you will receive is in the range of .300 to 5 Rem (or 5000 mRem), which is equivalent to the exposure limit of 5,000 mrem or 5 Rem per year that is established for radiation workers such as physicians and X-ray technologists who work with radiation and this level of exposure has never been associated with any definite adverse effects.

Please be aware that this radiation exposure is necessary for this research study only and is not essential for your medical care.

Risk of loss/breach of confidentiality
We make every effort to protect your privacy. There is always a risk that some of your information could be seen. We will reduce this risk by storing study data securely on password-protected computers and behind locked doors.

Unknown risks
There may be additional risks or discomforts in this study which are not yet known. We will make every effort to reduce these risks by monitoring you closely.

**POTENTIAL BENEFITS**
You may or may not benefit by taking part in this study. There is no guarantee that your condition will improve with this treatment. Possible benefits include more complete recovery from the ICH and improved quality of life. Information gained from this study may also help others in the future.

**ALTERNATIVES TO PARTICIPATION**
This research study is voluntary. You do not have to take part. If you choose not to take part, there are other options available to you. You may choose to have MIPS or another surgical intervention alone based on best medical practice. There may be other non-surgical treatment options available to you. If you choose not to take part in this study, it will not affect your treatment. You may also choose not to have any treatment.

**COSTS TO PARTICIPANTS**
There will be no fee to enroll in the study. However, you or your insurance will be billed for costs of medical care that you would have needed or received if you were not in the study.

In this study, there may be tests and procedures you will have that are standard of care (SOC) to treat your condition or disease. SOC tests and procedures would be done whether or not you take part in the study. These SOC tests and procedures will be billed to you or your insurance.

The study drug, pioglitazone, will be provided at no cost. You or your insurance will not be charged for the drug.



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**PAYMENT TO PARTICIPANTS**
You will not be paid for taking part in this study.

**STUDY RELATED INJURY**
If you have an injury, promptly seek medical care from any healthcare provider. If you have an emergency, call 911 or go to the nearest emergency room. You should tell the healthcare provider that you have participated in a research study.

If you believe the injury is related to the study, notify the study doctor. UMB, if requested, will assist you to get medical care or referrals.

UMB and/or its affiliated healthcare facilities or healthcare providers will not provide any financial compensation or reimbursement to you for the cost of medical care or other expenses arising from an injury.

In such cases, you or your insurance may be billed for the costs of medical care.

**CONFIDENTIALITY AND ACCESS TO RECORDS**
The data from the study may be published. You will not be identified by name. Your personal information will not be given out unless required by law. Everyone using study information will work to keep your personal information confidential. Your study records or data may be seen by the following groups:

- Study staff
- The Institutional Review Board (IRB)
- Any relevant governmental agency, such as the U.S. Food and Drug Administration (FDA).

By law, these groups cannot share any identifiable information, unless they are required to do so by law.

Efforts will be made to limit your personal information, including research study and medical records, to people who need to view this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this organization. The monitors, auditors, the IRB, the FDA, and other regulatory agencies will have access to your medical records to verify the research procedures and date. By signing this document, you authorize this access.

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.



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**RIGHT TO WITHDRAW**
Taking part in this study is voluntary. You do not have to take part in this research. You are free to withdraw your consent at any time. If you refuse to take part or stop taking part in the study there will be no penalty or loss of benefits to you. If you decide to stop taking part, or if you have questions, concerns, or complaints, or if you need to report a medical injury related to the research, please contact the investigator, Dr. Simard at 410-328-0850.

There will be no negative consequences if you choose to withdraw from the study. If you do choose to withdraw, please send a written request to the research team at the address listed on this form.

If you withdraw from this study, already collected data may not be removed from the study database. You will be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

**CAN I BE REMOVED FROM THE RESEARCH?**
The person in charge of the research study, or University of Maryland, Baltimore (UMB) can remove you from the research study without your approval. Possible reasons for removal include:

- failure to follow instructions of the research staff,
- or if the person in charge decides that the research study is no longer in your best interest

The study doctor will tell you about this and you will have the chance to ask questions if this happens.



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## UNIVERSITY STATEMENT

The University of Maryland, Baltimore (UMB) is committed to providing participants in its research studies all rights due to them under State and federal law. You give up none of your legal rights by signing this consent form or by participating in this study. This study has been reviewed and approved by an Institutional Review Board (IRB). The IRB is a group of scientists, physicians, experts, and community representatives. The IRB's membership includes persons who are not affiliated with UMB and persons who do not conduct research studies.

If you have questions, concerns, complaints, or believe you have been harmed through participation in this study as a result of researcher negligence, you can contact members of the IRB or the Human Research Protections Office (HRPO) to ask questions, discuss problems or concerns, obtain information, or offer input about your rights as a research participant. The contact information for the IRB and the HRPO is:

**University of Maryland, Baltimore**
**Institutional Review Board**
**Human Research Protections Office**
620 W. Lexington Street, Second Floor
Baltimore, MD 21201
410-706-5037



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Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

If you agree to participate in this study, please sign your name below.

| | |
|---|---|
| _____ | _____ |
| Participant's Name Printed | Printed Name of Legally Authorized Representative |
| _____ | _____ |
| Participant's Signature | Signature of Legally Authorized Representative<br>*(When applicable)* |
| Date:_____ | Relationship:_____ |
| | Date:_____ |

_____
Investigator or Designee Obtaining Consent Signature

Date:_____



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**Health Insurance Portability and Accountability Act (HIPAA)**
**AUTHORIZATION TO OBTAIN, USE AND DISCLOSE PROTECTED HEALTH INFORMATION FOR RESEARCH**

**Name of Study Participant: _____**

**Date of Birth**: _____ **Medical Record Number: _____**

**NAME OF THIS RESEARCH STUDY:** ENRICH-PLUS A Non-Randomized Controlled Trial to Examine the Safety and Suitability of Supplementing Early Minimally Invasive Parafascicular Surgery (MIPS) for Clot Evacuation of Basal Ganglia Intracerebral Hemorrhage (ICH) with Pioglitazone

**UMB IRB APPROVAL NUMBER:** HP-00102344

**RESEARCHER'S NAME:** J. MARC SIMARD, MD, PHD

**RESEARCHER'S CONTACT INFORMATION:**

*Department of Neurosurgery*
***University of Maryland School of Medicine (UMSOM)***
*22 S. Greene Street, Baltimore, MD 21201*
*410-328-0850*

**This research study will use health information that identifies you/your relative. If you agree to participate, this researcher will use just the health information listed below.**

**THE SPECIFIC HEALTH INFORMATION TO BE USED OR SHARED:**

- Past and present medical records, including personal information, such as your gender, telephone number, date of birth, and medical record number.
- Records about your study visits
- Information obtained during this research about laboratory test results
- Results from diagnostic and medical procedures
- Billing records

Also, should you experience a bad outcome or "adverse event," the Researchers may need to review other records relating to your medical history.

Federal laws require this researcher to protect the privacy of this health information. He/she will share it only with the people and groups described here.

**PEOPLE AND ORGANIZATIONS WHO WILL USE OR SHARE THIS INFORMATION:**

- Dr. Simard and his research team.
- The sponsor of the study, or its agents, such as data repositories or contract research organizations
- Organization that will coordinate health care billing or compliance such as offices within UMSOM; the University of Maryland, Baltimore (UMB); University of Maryland Faculty



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Physicians, Inc. (FPI) and the faculty practices of the UMB; University of Maryland Medical System (UMMS)
- Your health insurer to pay for covered treatments

**THIS AUTHORIZATION WILL NOT EXPIRE. BUT YOU CAN REVOKE IT AT ANY TIME.**
To revoke this Authorization, send a letter to this researcher stating your decision. He/she will stop collecting health information about you/your relative. This researcher might not allow you/your relative to continue in this study. He/she can use or share health information already gathered.

**ADDITIONAL INFORMATION:**

- You can refuse to sign this form. If you do not sign it, you cannot participate in this study. This will not affect the care you/your relative receive at:
    - University of Maryland Faculty Physicians, Inc. (FPI)
    - University of Maryland Medical System (UMMS)

  It will not cause any loss of benefits to which you/your relative are otherwise entitled.
- Sometimes, government agencies such as the Food and Drug Administration or the Department of Social Services request copies of health information. The law may require this researcher, the UMSOM, FPI, or UMMS to give it to them.
- This researcher will take reasonable steps to protect your/your relative health information. However, federal protection laws may not apply to people or groups outside the UMSOM, UMB, FPI, UMMS or
- Except for certain special cases, you/your relative have the right to a copy of your/your relative's health information created during this research study. You may have to wait until the study ends. Ask this research how to get a copy of this information from him/her.

My signature indicates that I authorize the use and sharing of my/my relative protected health information for the purposes described above. I also permit my doctors and other health care providers to share my/my relative's protected health information with this researcher for the purposes described above.

Signature: _____Date: _____

Name (printed) _____

Privacy Questions? Call the UMSOM Privacy Official (410-706-0337) with questions about your/your relative's rights and protections under privacy rules.

Other Questions? Call the researcher named on this form with any other questions.



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