RICHARD L. ROUDEBUSH VETERANS AFFAIRS MEDICAL CENTER
INFORMED CONSENT STATEMENT FOR RESEARCH

A Pilot Open-Label Study to Evaluate the Safety, Tolerability, and Performance of FAST PV Technology™ in Chronic Dialysis Patients with Extremely Reduced or No Kidney Function

Sponsor: FAST Biomedical Protocol #2008193898

Arjun (AJ) Sinha, M.D. – Principle Investigator

ABOUT THIS RESEARCH

You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

TAKING PART IN THIS STUDY IS VOLUNTARY

You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled, and will not affect your relationship with the Richard L. Roudebush Veterans Affairs Medical Center **(**Roudebush VAMC).

Study Summary

We are asking you to take part in a research study. The purpose of this research is to study the safety and performance of the FAST PV Technology™ in chronic dialysis patients with extremely reduced or no kidney function. The study consists of 4 in person visits and 1 follow-up phone call. Your participation in the study will be up to 59 days from the screening day to the final phone call (Visit 5 - last visit). All visits are to occur at the Dialysis Clinic at the Roudebush VAMC. This research study may help develop a new test which will help doctors more rapidly and accurately and determine the amount of fluid in your body. The new technology, the Visible Fluorescent Injectate (VFI) is an investigational product and has not yet been approved by the U.S. Food and Drug Administration (FDA). People who enter into the study will have the VFI injected into their vein and will have a series of blood samples drawn in order to determine the amount of fluid in their body. If you take part you will have both the VFI and iohexol injected once both before and again after a single standard dialysis treatment. VFI is a fluorescent tracer and iohexol is an FDA approved iodine based dye that will also help to measure your body fluid amount. Your treatment will not change as a result of participating in this study. The FAST PV (plasma volume) Technology device used to calculate the volume of fluid in your body is also investigational, though this device will be in a laboratory and you will have no contact with this device.

Please review the rest of this document for more details about this study and the things you should know before making a decision about whether to participate in this study.

WHY IS THIS STUDY BEING DONE?

This research study may help develop a new test which will help doctors more rapidly and accurately and determine the volume of fluid in your body. The new technology, the Visible Fluorescent Injectate (VFI) is an investigational product and has not yet been approved by the U.S. Food and Drug Administration (FDA). Understanding the amount of fluid in a person's body may be helpful in determining the dose and frequency of dialysis treatments for patients in the future. The FAST PV (plasma volume) Technology device used to calculate the volume of fluid in your body is also investigational, though this device will be in a laboratory and you will have no contact with this device.

Four clinical trials with a total of 139 people have been completed investigating the VFI. This has included healthy people, people with kidney dysfunction, and individuals with heart failure. During these studies, different doses of VFI were assessed, including doses up to three times higher than the dose being used in this study. The study risks are described in the risk and discomfort section of this consent on page 5.

You were selected as a possible participant because you are on long term hemodialysis and you meet the other requirements for participating in this research.

The study is being conducted by Arjun (AJ) Sinha, MD and the Roudebush Veterans Affairs Medical Center (Roudebush VAMC). It is funded by FAST BioMedical, the company that has developed the VFI and the FAST PV Technology.

HOW MANY PEOPLE WILL TAKE PART?

If you agree to participate, you will be one of 10 participants taking part in this research and all 10 subjects will receive 2 injections of the VFI. The Roudebush VAMC is the only site participating in this study.

WHAT WILL HAPPEN DURING THE STUDY?

If you agree to be in the study, you will do the following things:

The study consists of 4 in person visits and 1 follow-up phone call. Your participation in the study will be up to 59 days from the screening day to the final phone call (Visit 5 - last visit). All visits are to occur at the Dialysis Clinic at the Roudebush VAMC and they will last between 1 and 2 hours each, except Visit 2 that is longer.

For Visit 2, you should come to the Dialysis Clinic fasting for at least 9 hours. You may drink water during the fasting period. We will provide breakfast after the blood tests are done.

Study Visits:

- Visit 1 or Screening
- Visit 2: At most 28 days after screening. This is the dosing and testing visit (all day clinic stay)
- Visit 3: Follow-up at the next scheduled dialysis appointment (2-3 days after Visit 2 dosing and testing visit)
- Visit 4: A 2nd follow-up will occur during the second scheduled dialysis appointment after the Visit 2, the dosing and testing visit. This will occur approximately 1 week after the dosing and testing visit.
- Visit 5: The final follow-up event will be a phone call sometime between 30 and 32 days after Visit 2, the dosing and testing visit

Visit 1 or Screening:

This is the first study visit will be conducted at the Roudebush VAMC and is intended to evaluate your health and to determine if you can be in the study. This visit is expected to take 1 to 2 hours. The study team will collect information about you from your medical records and use it for this study. If you meet the study requirements you will be asked to review and sign this informed consent form once all your questions about the study are answered and you will be scheduled for the next study visit within 28 days.

This screening visit includes:

- Measuring your height and weight and calculating body mass index (BMI), which is a calculation to estimate whether you are underweight or overweight
- Questions about medications you are taking
- Questions about demographics (including sex, age, race, and ethnicity) and medical history
- Complete physical examination by Dr. Sinha or other investigators (if applicable) taking part in the study
- Checking vital signs: heart rate, blood pressure and oximetry (to measure the amount of oxygen your blood is carrying)
- Reviewing your medical record for results from routine blood for kidney function, blood cell counts, enzymes, electrolytes
- Pregnancy test (nonmenopausal females only)
- *No genetic testing is included in this study*

Visit 2 or testing visit:

This visit should occur no more than 28 days after the screening on a scheduled dialysis day. It is the longest visit. The visit starts at around 6AM to 7AM and will last approximately 11 hours. The study does not require an overnight stay, and you will be able to return home after all Visit 2 activities have been completed.

- At the VA Dialysis Clinic, you will be provided with a TV and meals. The nurse will bring your meals including breakfast, lunch and an afternoon snack.
- Twenty-four (24) hours before you arrive at the VA Dialysis Clinic, you will be asked not to drink any alcoholic beverages.
- The night before you arrive at the VA Dialysis Clinic, you will be asked to not eat or drink anything except water after midnight.
- Vigorous physical exercise is not allowed 72 hours prior to Visit 2 and during Visit 2.

- On arrival at the VA Dialysis Clinic you will receive a bottle containing 1.5 liters of water to drink and you should drink when you are thirsty.
- The investigator and nurse will repeat many of the procedures from Visit 1 in order to ensure that you still meet the criteria for participating in the study.
- You will have one small tube or intravenous (IV) catheter inserted into your dialysis access (fistula or graft).
- You will have 6 milliliters or slightly less than ½ a tablespoon of blood drawn from the catheter no more than 30 minutes before receiving the VFI and Iohexol doses.
- The IV catheter will be used to draw blood tests and to inject 3 mL or slightly more than ½ a teaspoon (or slightly more if you weigh more than 220 pounds) of VFI as well as 5 mL or roughly 1 a teaspoon of Iohexol through the same catheter. Iohexol is an FDA approved iodine-based dye which will help better understand your blood volume. The Iohexol and VFI will be given once (at roughly the same time) through the small tubes or IV catheters placed in the vein in your arm.
- You will receive 1 dose of VFI and 1 dose of Iohexol approximately 4 hours prior to undergoing your standard dialysis treatment followed by a second dose of VFI and second dose of Iohexol approximately 1 hour after completing dialysis.
- During and after these injections the nurse will collect blood specimens several times for special analysis to determine your blood volume. The total amount of blood that will be taken for blood volume testing is slightly less than than 5 1/2 tablespoons. Each blood draw will be taken from the small tube already inserted in the arteriovenous fistula or graft.
- Upon receiving the VFI and Iohexol, the catheter used for the injection may be removed and you will remain under observation at the VA Dialysis Clinic until you are released after collecting the final blood sample on the testing visit.
- You will be given the telephone number to report any adverse events (side effects or changes in how you are feeling) or concerns

This visit also includes:

- Pregnancy test (if applicable)
- Collection of all urine during the visit
- Collect routine blood labs
- Questions about medication you are taking (past week)
- Questions about medical history since screening (past week)
- Complete physical examination by Dr. Sinha or, if applicable, other investigators participating in this research
- Checking vital signs: heart rate, blood pressure and oximetry (several times)
- Questions about adverse events during procedures. In case of adverse events, Dr. Sinha might decide to repeat a clinical examination and/or order additional laboratory test(s)

Blood will be analyzed at FAST BioMedical's laboratory to determine the amount of VFI in the blood samples. Blood samples will also be analyzed at the Advanced Diagnostics and Research Laboratory at the University of Minnesota to determine the amount of Iohexol in the blood and to double check the amount of VFI in the blood. All specimens that leave the Roudebush VA will not have any information included that may identify you.

Unless otherwise required by the U.S. Food and Drug Administration or other laws or regulations, samples will be stored for a maximum of 18 months after collection and then destroyed. Samples will be

labeled with a unique code study identifier, the collection date, and collection time. The samples will not have information that could identify you.

You can go home after completion of the last blood draw and after Dr. Sinha or the clinical staff have confirmed that it is safe for you to leave the VA Dialysis Center.

Visit 3 and 4 or follow-up clinic visits:

Visits 3 and 4 will occur during the next two regularly scheduled dialysis appointments after Visit 2, and Visits 3 and 4 will occur at the VA Dialysis Clinic. During these visits the following activities will take place:

- Collecting routine blood for kidney function, blood cell counts, enzymes, electrolytes, coagulation. This will require roughly 1 teaspoon of blood.
- Evaluation, if applicable, of any adverse events or serious adverse events you may have experienced since the dosing of the VFI and Iohexol

Visit 5 or final follow-up phone call:

You will receive a phone call between 30 and 32 days after the Visit 2 dosing and testing day. During this phone call you will be asked if you have experienced any adverse events or serious adverse events that have not previously been reported to Dr. Sinha. If no additional follow up is required, your participation in this study will end after this phone call.

Please note that you must not participate in any other clinical trial or donate blood or plasma while participating in this clinical trial.

WHAT ARE THE RISKS OF TAKING PART IN THE STUDY?

While participating in the study, the risks, side effects, and/or discomforts are detailed below. These risks, side effects, and/or discomforts were developed based on previous animal studies and human clinical studies. All discomforts were of mild to moderate intensity.

The main risks are the following:

- **Blood draws and injections:** the risks include pain, bleeding or swelling around the injection site. Risks of intravenous (IV) catheter use include infiltration (fluid leak into surrounding tissues), hematoma (bruising), air embolism (air bubble in a vein), and phlebitis (inflammation of a vein). Other rare risks include extravasation (when a potentially harmful drug leaks outside the vein or onto the skin) which can result in severe tissue damage. To reduce these risks the IV catheter will be placed in your dialysis access by trained dialysis nurses. All blood draws and IV injections will be done by trained dialysis nurses only.
- **VFI injection:** The main risks are headache, nausea, diarrhea, itching, muscle enzyme changes, and liver enzyme changes. Other risks include allergic reaction to the study drug. Symptoms of an allergic reaction are rash, hives, nasal congestion, breathing difficulty, a tight feeling in the chest and swelling in the face, tongue or skin; wheezing or labored breathing. Allergic reactions can vary from minor to life threatening and the start of symptoms is seconds or minutes after exposure. To

address these risks you will be monitored for 3-4 hours after each VFI injection to watch for drug reactions in the hospital setting, where allergic reactions can be treated with medicines such as Benadryl or steroids. To protect against changes in muscle and liver enzymes you will have blood drawn twice on dialysis in the week after you receive the VFI doses to check your muscle and liver enzyme levels.

- **Iohexol injection:** side effects in order from less severe to more severe include flushing or a sensation of heat, pain at the injection site, nausea, vomiting, headache, dizziness, itching, pale skin color, sweating, metallic taste, weakness, visual disturbances; lower or high blood pressure, fast or slow heart rate. Allergic reaction is another risk, identical to the VFI above. To address these risks you will be monitored for 3-4 hours after each iohexol injection to watch for drug reactions in the hospital setting, where allergic reactions can be treated with medicines such as Benadryl or steroids.
- **Interviews:** You may feel uncomfortable answering questions. There is a potential risk of loss of confidentiality. To reduce your discomfort we will ask only questions necessary for the research and for safety. To protect your confidentiality, we keep your electronic information on a secure computer and paper copies in a locked cabinet in a locked room.
- **There also may be other side effects that we cannot predict.**

INFORMATION FOR WOMEN OF CHILDBEARING POTENTIAL AND/OR MEN CAPABLE OF FATHERING A CHILD

We do not know if the study drug will affect mother's milk or an unborn fetus. Therefore, breast-feeding and pregnant women are not allowed to take part in the study. If you are pregnant or become pregnant, there may be risks to the embryo or fetus that are unknown at this time. Women who can become pregnant must take a pregnancy test before the start of the study.

You should not father a child while on this study as the treatment may affect an unborn child. If you are sexually active and are at risk of causing a pregnancy, you and your female partner(s) must use a method of birth control to avoid pregnancy that works well or you must not have sex.

Females must be 1 year postmenopausal, surgically sterile (hysterectomy, bilateral oophorectomy, or tubal ligation with documentation), or be using a medically acceptable method of birth control from screening until 30 days after last dose.

Males who are sexually active with females of child-bearing potential must agree to abstinence or use condoms from screening through 90 days after last dose, and their partners must be willing to use a medically acceptable method of contraception (barrier method, IUD, hormonal contraception) from screening through 90 days after last dose. Males must also agree to not donate sperm for 90 days after last dose.

Pregnancy tests will be performed (if applicable) during the study.

If you are female and become pregnant after enrolling in the study, you must inform the study doctor. If you are male and your partner becomes pregnant from the time of dosing until the end of the study, you must inform the study doctor.

WHAT ARE THE POTENTIAL BENEFITS OF TAKING PART IN THE STUDY?

We don't expect you to receive any medical benefit from taking part in this study, but we hope to learn things which will help scientists in the future.

WILL I RECEIVE MY RESULTS?

If you participate in this study, we may learn things about you from the study activities that could be important or interesting to you. We will share some of that information with you. Depending on the information, you might need to meet with professionals with expertise to help you learn more about next steps. The study team/study will not cover the costs of any follow-up consultations or actions. We will share the following information with you:

- Results from laboratory tests performed specifically for the purpose of the research that may be important to your health.
- You will not receive results related to your blood volume, the VFI or the investigational technology used in this research.

HOW WILL MY INFORMATION BE PROTECTED?

Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. No information which could identify you will be shared in publications about this study. Research records will be maintained by the investigator in accordance with the VHA Records Control Schedule.

Specimens collected during the study will be sent to the sponsor FAST BioMedical and to the Advanced Research & Diagnostic Laboratory at the University of Minnesota for analysis. The specimens will not have any information that can identify you.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the investigator and his/her research associates, the study sponsor, the Indiana University Institutional Review Board or its designees, the VA Research and Development Committee's designees, and federal agencies, including but not limited to the Office for Human Research Protections (OHRP), the Office of Research Oversight (ORO), VA Office of the Inspector General (OIG), and the Food and Drug Administration (FDA) which may choose to inspect research records that include the subject's individual medical records.

A description of this clinical trial will be available on **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.

WILL MY INFORMATION BE USED FOR RESEARCH IN THE FUTURE?

Information or specimens collected from you for this study may be used for future research studies or shared with other researchers for future research. If this happens, information which could identify you will be removed before any information or specimens are shared. Since identifying information will be removed, we will not ask for your additional consent.

Specimens collected from you for this research may be used to develop products which could be sold in the future. The investigator does not plan to share any profits or losses from the sale of those products with you.

We will not use the specimens collected as a part of this study for whole genome sequencing, which involves mapping all of your DNA.

WILL I BE PAID FOR PARTICIPATION?

You will receive payment for taking part in this study. If you complete the entire study, you will receive a total of $300 as compensation for participating. If you do not complete the study, you will be paid for the visits you complete. See the schedule below for the payment amounts. Payments will be made by check from the Indiana Institute for Medical Research (IIMR) and sent to you in the USA mail to the address you provide us.

Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
$50	$150	$25	$25	$50

In order to receive payment, you may be required to provide your Social Security number or tax identification number. You may receive a 1099 tax form the following January and will need to report this payment as income on your federal and state tax returns. You are responsible for paying any state or federal taxes. If you have questions regarding how this impacts your tax return, please contact a tax professional to assist you.

WILL IT COST ME ANYTHING TO PARTICIPATE?

There will be no costs to you for any of the testing done specifically for this research study. Eligibility for medical care at a VA Medical Center is based upon the usual VA eligibility policy and is not guaranteed by participation in a research study.

You will not be required to pay for medical care or services received as a subject in a VA research project except as follows:

Some veterans are required to pay co-payments for medical care and services provided by the VA. These co-payment requirements will continue to apply to medical care and services provided by VA that are **not** part of this study.

WHO WILL PAY FOR MY TREATMENT IF I AM INJURED?

The VA medical facilities shall provide necessary medical treatment to a research subject injured as a result of participation in a research project approved by a VA Research and Development Committee and conducted under the supervision of one or more VA employees in accordance with applicable federal regulations. This does not apply to (1) treatment for injuries due to noncompliance by a subject with study procedures; or (2) research conducted for VA under a contract with an individual or a non-VA institution.

Financial compensation for research-related injuries is not available. However, by signing this form, you do not give up your legal rights to seek such compensation through the courts.

RESEARCH SUBJECT'S RIGHTS:

Participation in this study is entirely voluntary. You may refuse to participate. Refusal to participate will involve no penalty or loss of rights to which individuals are entitled. You may withdraw from this study at any time without penalty or loss of VA or other benefits. You will receive a copy of this signed consent form.

In case there are medical problems or questions, Dr. Sinha can be called at 317-988-4004 during the day and the on-call kidney doctor can be reached by calling the hospital operator at 317-554-0000 and asking to page the kidney fellow after hours. If any medical problems occur in connection with this study, the VA will provide emergency care.

Please direct questions about the consent process and the rights of research subjects to the VA Customer Service Office at (317) 988-2602. For questions about your rights as a research subject or complaints about a research study, contact the Indiana University Human Subjects Office at 317-274-8289 or 800-696-2949 or at irb@iu.edu. If you have any questions about the research study or want to check the validity, discuss problems, concerns or obtain information or offer input, please call the VA Research Personnel Office at 317-988-3032.

The study has been explained to me and all of my questions have been answered. The risks or discomforts and possible benefits of the study have been described. Other choices of available treatment have been explained.

PARTICIPANT'S CONSENT

In consideration of all of the above, I give my consent to participate in this research study. I will be given a copy of this informed consent document to keep for my records. I agree to take part in this study.

Participant's Printed Name:_____

Participant's Signature:_____ **Date**:_____

Printed Name of Person Obtaining Consent:_____

Signature of Person Obtaining Consent:_____ **Date**:_____