**UNIVERSITY OF CALIFORNIA, SAN FRANCISCO**

**Research Consent Form and Authorization To Use Your Health Information For Research Purposes**

**HOPE Registry**

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| **Sponsor / Study Title:** | | **Department of Health and Human Services / “Trio Analysis of Recurrent Pregnancy Loss Integrated Bioinformatics Genomics Study (TRIOS)”** |
| **Principal Investigator:**  **(Study Doctor)** | **Aleksandar Rajkovic, MD** | |
| **Telephone:** | **(415) 741-7213 (24 Hours)** | |
| **Address:** | **University of California, San Francisco, Department of Ob/Gyn, Center for Reproductive Health**  **499 Illinois St.**  **San Francisco, CA 94158** | |

Please check all that are applicable:

I am an adult participant in this study.

Print your name here:

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I am the parent or legal guardian granting permission for a child in this study (the use of "you" refers to "your child" or “your ward.”)

Print child’s name here:

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**KEY INFORMATION:** You are invited to participate in a research study. This research study is studying recurrent pregnancy loss, that is being conducted at Stanford University, University of California San Francisco and Oregon Health and Science University. The investigators are aiming to understand what biologic factors (genes or chromosome regions and molecular profiles) are associated with unexplained pregnancy loss. Little is understood about the genetic cause of pregnancy loss. By studying the unique genetic makeup of those affected by pregnancy loss, including their male partners, we may gain insights into the causes of pregnancy loss and in the future be able to offer better diagnostics and therapies.

This is a medical research study. Your study doctor(s)Aleksandar Rajkovic*,* PhD, M.D., from the UCSF Department of Obstetrics andGynecology, will explain this study to you.

About 500 people will take part at UCSF.

This research will include genetic analysis and possibly whole genome sequencing of fetuses lost to miscarriage and participants with recurrent pregnancy loss. Other participating family members including children may provide additional information about the genes associated with pregnancy success and pregnancy loss.

Tissue and DNA from miscarriages and pregnancy losses could potentially be obtained from past miscarriages through contacting the laboratory or hospital where your miscarriage was diagnosed and managed. If you consent, a study coordinator will assist you in obtaining tissue from past losses.

With genetic sequencing we may identify gene changes that are associated with pregnancy loss. You will be given the option to receive these types of results if found. Participation in this study should not be considered a substitute for clinically recommended testing. If you wish to learn about your results, genetic counseling will be provided at that time. It is unlikely that the results will be used to guide your current clinical care as it may take up to 1-2 years to complete our analysis. In addition, if adequate DNA cannot be obtained from prior pregnancy loss tissue, we will not be able to do our analysis. Any abnormalities found in this study will need to verify in a clinical (not research) laboratory.

**When whole genome sequencing is performed, there is a small chance (approximately 3-5%) that we might find a genetic change or a variant that may cause a future health risk or predispose you to a certain genetic condition that is unrelated to pregnancy or pregnancy loss (risk of cancer, heart disease, neurologic and other conditions). These types of results might be important for your health now or in the future.**

**We expect that only a 3-5% of people will get results like this.**

**You can decide if you want to learn about these conditions or not. If you elect to receive your results and are found to have a significant genetic change that could impact your future health, our study team will help confirm this finding in a genetic testing lab and provide you with genetic counseling and refer you for follow up.**

**If you elect to not receive these results, we will not contact you with your results. Genome sequencing may not be performed on all samples.**

The goal of this study is to find explanations of pregnancy loss and learn how we can predict future pregnancy outcomes. In order to do this, we are very interested in your future pregnancy outcomes as well as your past pregnancy outcomes. This information will be requested through periodic online surveys and telephone contact.

Participation in this study DOES NOT replace clinical care and/or recommendations. We encourage you to proceed with your clinical care and all recommended tests and treatment as part of your clinical care.

**PROCEDURES for Participants with History of Pregnancy Loss:**

If you choose to participate,

* You will be asked to complete an online survey with questions about your medical, pregnancy, and family history and your medical record will be reviewed.
* You will be asked to provide sample (1 teaspoon of saliva or 3-4 teaspoons of blood) for DNA analysis.
* If available, you will be asked to donate tissue from your past miscarriage(s) for analysis
* If appropriate, you will be asked to refer your partner to participate and provide a sample for DNA analysis (saliva or blood sample).
* You may be contacted by the study team from one of the collaborating sites via phone call or email

**Optional Procedures for Participants with History of Pregnancy Loss:**

* You will be sent follow-up surveys every 6-12 months up to 5 years to provide updates about your pregnancy history which you can opt-out at any time.
* If you are currently having a miscarriage or have a miscarriage after enrollment, we would like to collect the tissue for our study, please let your study team know if this applies to you.
* Additional samples may include: children’s saliva for DNA testing; urine; hair; semen; placenta, Additional blood sample (3-4 teaspoons)
* You may be asked to contact family members if their DNA may help us understand the importance of genetic changes found in your analysis.

**Procedures for Family Members:**

Family members, other than you and your partner, can help us in the discovery of genes that cause pregnancy loss. If the investigative team determines that other individuals in your family may be helpful with this study, you may be asked to contact your family members.

* You will be contacted by phone, and you will be asked questions about your medical and family history
* You will be asked to donate a single blood (3-4 teaspoons) or saliva sample (1 teaspoon) for DNA extraction
* Genetic testing may include single gene changes, whole exome sequencing or whole genome sequencing
* We may contact you in the future if additional medical information is needed

Future use of Private Information and/or Specimens

Research using private information and/or specimens is an important way to try to understand human disease. You are being given this information because the investigators want to save private information and/or specimens for future research.

Your specimens will be stored with a unique study code number assigned to you. The specimens will not have your personal identifiers. The link between the study code number and your identifiers will be only accessible to the principal investigators and the study coordinator.

Identifiers might be removed from identifiable private information and/or identifiable specimens and, after such removal, the information and/or specimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you.

Any of your specimens which are used in research may result in new products, tests or discoveries. In some instances, these may have potential commercial value and may be developed and owned by the investigators, the study site and/or others. However, donors of specimens do not retain any property rights to the materials. Therefore, you would not share in any financial benefits from these products, tests or discoveries.

Will my medical information be kept confidential?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Some information from your medical records will be collected and used for this study. If you do not have a UCSF medical record, one will be created for you. Your signed and dated consent form and some of your research tests will be added to your UCSF medical record. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your medical record as a result of your participation. Study tests that are performed by research labs, and information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

* Representatives of the Sponsor [Department of Health and Human Services]
* Representatives of the University of California
* Representatives of the Food and Drug Administration (FDA)
* Advarra IRB

Genetic Testing and Future Research

As part of the analysis on your specimens, the investigators will do genetic testing. Genetic research studies genes, including gene characteristics and gene versions that are transmitted by parents to children. Genetic research may include looking at information, such as personal appearance and biochemistry, gene sequences, genetic landmarks, individual and family medical histories, reactions to medications and responses to treatment. Genetic research raises certain questions about informing you of any results.

How will my genetic information be shared?

Genetic information (also known as genotype data) and the medical record data (also known as phenotype data) may be shared broadly in a coded form for future genetic research or analysis. We may give certain medical information about you (for example, diagnosis, blood pressure, age if less than 85) to other scientists or companies not at UCSF, including to a government health research database, but we will not give them your name, address, phone number, or any other identifiable information.

Donating data may involve a loss of privacy, but information about you will be handled as confidentially as possible. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security. Genetic information that results from this study does not have medical or treatment importance at this time. However, there is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health. Taking part in a genetic study may also have a negative impact or unintended consequences on family or other relationships. It is possible that future research could one day help people of the same race, ethnicity, or sex as you. However, it is also possible through these kinds of studies that genetic traits might come to be associated with your group. In some cases, this could reinforce harmful stereotypes.

There will be no direct benefit to you from allowing your data to be kept and used for future research. However, we hope we will learn something that will contribute to the advancement of science and understanding of health and disease. If the data or any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits. If you decide later that you do not want your information to be used for future research, you can notify the investigator in writing at the address listed on the first page of this form, and any remaining data will be destroyed. However, we cannot retract any data that has been shared with other researchers.

Research results: There may be times when researchers using your information and/or specimens may learn new information. The researchers may or may not share these results with you, depending on a number of factors.

**Possible risks of knowing results include:**

Anxiety; other psychological distress; and the possibility of insurance and job discrimination. These risks can change depending on the results of the research and whether there is a treatment or cure for a particular disease.

Sometimes participants have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information Nondiscrimination Act of 2008 (GINA), generally makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information.

All health insurance companies and group health plans and all employers with 15 or more people must follow this law.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance or long-term care insurance.

**RISKS AND BENEFITS:** The risks associated with this study a potential discomfort, bruising or very rarely infection from the blood drawandthe unlikely but potential chance of loss of confidentiality.For some people, genetic testing or receiving test results may cause frustration, anxiety, depression, anger or fear. If you experience any of these or have questions, we can arrange for you to speak with a genetic counselor or mental health specialist. We cannot and do not guarantee or promise that you will receive any benefits from this study. Your decision whether or not to participate in this study will not affect your medical care.

Potential benefits include possibly discovering a cause for your miscarriage if you choose to learn the results of your genetic analysis. Even if you receive no direct benefit, your participation may help doctors and scientists improve our knowledge of pregnancy loss and other related conditions.

You might have discomforts that are not listed in this form. Tell the study doctor or study staff right away if you have any problems.

**TIME INVOLVEMENT:** Your participation in this experiment will take approximately 60-120 minutes, depending on which surveys you are asked to complete. You may receive an email with a link to a 10 minute survey every 6 months for up to 5 years.

**PAYMENTS/REIMBURSEMENTS:**

HOPE Registry/ Genetic Sequencing cohorts: $10 gift card for every long-term follow-up survey completed (up to $50).

Not all activities will have financial incentives. However, participants choosing to participate in long-term follow up will be offered a $10 gift card for each completed survey (up to $50).

You will be paid following each completed visit or at the end of your participation in the research, whichever you prefer.

**ARE THERE ANY COSTS TO ME FOR TAKING PART IN THIS STUDY?** No. The sponsor has agreed to pay for all items associated with this research study; you or your insurer will not be billed.

**ALTERNATIVES TO PARTICIPATION:** This study is for research purposes only. The only alternative is to not participate in this study.

**NEW FINDINGS:** Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you.

**TREATMENT AND COMPENSATION FOR INJURY:** It is important that you tell your study doctor if you feel that you have been injured because of taking part in this study. You can tell the study doctor in person or call the telephone number listed on the first page of the consent form.

If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs or covered by the University of California or the study sponsor [Department of Health and Human Services], depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415- 476-1814.

**PARTICIPANT’S RIGHTS:** If you have read this form and have decided to participate in this study, please understand your participation is voluntary and you have the right to withdraw your consent or discontinue participation in any part of this study at any time without penalty or loss of benefits to which you are otherwise entitled. The results of this research study may be presented at scientific or professional meetings or published in scientific journals. However, your identity will not be disclosed**.** You have the right to refuse to answer particular questions in the survey or discontinue follow up surveys.

**CERTIFICATE OF CONFIDENTIALITY:** This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research participants.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institute of Child Health and Development which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).  You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of child abuse and neglect, or harm to self or others.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document including information in the medical record or surveys.

**WITHDRAWAL FROM STUDY:** The investigator may also withdraw you from the study without your consent for one or more of the following reasons:

* + Failure to follow the instructions of the investigator and study staff.
  + The investigator decides that continuing your participation could be harmful to you.
  + You need treatment not allowed in the study.
  + The study is cancelled.
  + Other administrative reasons.
  + Unanticipated circumstances.

**WHOM TO Contact ABOUT THIS STUDY:** During the study, if you have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

* By mail:

Study Subject Adviser

Advarra IRB

6100 Merriweather Dr., Suite 600

Columbia, MD 21044

* or call **toll free**: 877-992-4724
* or by **email**: [adviser@advarra.com](mailto:adviser@advarra.com)

Please reference the following number when contacting the Study Subject Adviser: Pro00054839.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the office of the Institutional Review Board at 415-476-1814.

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.

**EXPERIMENTAL SUBJECTS BILL OF RIGHTS:** As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

* Be informed of the nature and purpose of the experiment;
* Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
* Be given a description of any attendant discomforts and risks reasonably to be expected;
* Be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
* Be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
* Be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
* Be given an opportunity to ask questions concerning the experiment or the procedures involved;
* Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
* Be given a copy of the signed and dated consent form; and
* Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

May we contact you to give you information about future studies? *Please indicate your choice by initialing on the line.*

\_\_\_\_ Yes

\_\_\_\_ No

I would like to donate optional samples (Pregnancy or Miscarriage tissue; hair sample, children’s saliva; saliva; Semen; OR Blood (3-4 teaspoons) and I would like to talk to a study coordinator about which samples I can provide. If you agree you will be able to decide which samples. *Please indicate your choice by initialing on the line.*

\_\_\_\_Yes

\_\_\_\_No

If found, would you like to receive results of genetic changes that could explain your pregnancy losses? *Please indicate your choice by initialing on the line.*

\_\_\_\_Yes

\_\_\_\_No

If genome sequencing is performed on your specimen, would you like to receive results of genetic changes that are associated an increased risk of medical conditions that could impact your future health? *Please indicate your choice by initialing on the line.*

\_\_\_\_Yes

\_\_\_\_No

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign and date a separate form authorizing access, use, creation, or disclosure of health information about you.

If you wish to participate in this study, you should sign and date below.

Date Participant's Signature for Consent

Date Parent or Legal Guardian Signature for Consent

**Attestation Statement**

I confirm that the research study was thoroughly explained to the subject. I reviewed the consent form with the subject and answered the subject’s questions. The subject appeared to have understood the information and was able to answer the following questions correctly:

1. What is the purpose of this study?
2. If you decide to be in the study, what will you be asked to do?
3. What is the possible benefit of participating in this study?
4. What are the possible risks of participating in this study?
5. If you decide not to participate in this study, what options do you have?
6. Will participating in this study cost you anything? If so, what will you have to pay for?
7. Do you have to be in this study?
8. If you decide to be in the study, can you leave the study when you want to?

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Printed Name of Person Conducting the Position

Informed Consent Discussion

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Signature of Person Conducting the Date

Informed Consent Discussion

*The following witness line is to be signed only if the consent is provided as a summary form and accompanied by a short form foreign language consent.*

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Signature of Witness Date

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Print Name of Witness (for example, study staff, translator/interpreter, family member)

*• Translated short form must be signed and dated by both the participant (or their* *parent/legal guardian) AND the witness.*

*• The English consent form ("summary form"):*

*Must be signed and dated by the witness AND the Person Obtaining Consent (POC).*

*The non-English speaking participant/parent/legal guardian does not sign and date the English consent.*

*The non-English speaking participant/parent/legal guardian should not sign and date the HIPAA participant line*

*if the participant or the parent/legal guardian is non-English speaking, the Person Obtaining Consent (POC) must ensure that 1) the legal guardian's Description of Authority is completed and 2) that any questions or options presented by the consent form are documented and initialed by the POC on the Summary Form, per the participant's wishes, as they are understood during the consent process.*