INFORMED CONSENT DOCUMENT

Project Title: **Balancing Comfort and Success: Post-retrieval Ketorolac in Fresh Embryo Transfers**

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This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you are undergoing an in vitro fertilization (IVF) cycle with a planned **fresh embryo transfer**.

The purpose of this study is to test whether findings from prior studies showing that a medication called **ketorolac,** given following egg-retrieval, improves pain control without impacting IVF outcomes. Administration of this medication may decrease the need for narcotic pain medications following egg-retrieval.
Before you decide to join this study, please take time to read the following information carefully. Ask any questions you may have.

Ketorolac is an FDA approved drug for short-term management of moderate to severe pain. However, ketorolac is not typically used for the purpose for which it will be used in this study because, historically, there has been concern about its impact on implantation. Nonetheless, retrospective studies have demonstrated that ketorolac is safe and associated with a low risk of affecting implantation.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 200 people will take part in this study conducted by investigators at the University of Iowa.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for up to 45 weeks (until the resolution of your pregnancy)**. The active study time is as follows:**

- On the day of your egg retrieval you will: Sign the consent and be **randomly assigned** to one of two groups (usual care plus ketorolac OR usual care without ketorolac).
- At the end of the retrieval procedure while you are still under sedation, the anesthesiology team will administer either usual care plus ketorolac OR usual care without ketorolac through your pre-existing IV line.
- Your IVF care will otherwise remain the same as planned.
- No additional visits, tests, or procedures will be required as part of this study. However, we will continue to review and collect data from your medical records for up to 45 weeks.

WHAT WILL HAPPEN DURING THIS STUDY?If you consent to participate:

1. You will be randomly assigned to receive one of the **2** study treatments, either usual care plus ketorolac OR usual care without ketorolac**.** This means that whichever study treatment you receive will be determined purely by chance, like flipping a coin. You will have a **50/50** chance of receiving any one of the study treatments. Neither you nor the research team will know which study treatment you are receiving, but we will be able to get this information quickly if we need it to ensure your safety. **Regardless of which arm you are randomized to, your post-procedure pain will be monitored and treated using standard of care pain medications as needed.**
2. You will undergo egg retrieval as part of your standard IVF care under monitored anesthesia care administered by a certified nurse anesthetist in the IVF procedure suite.
3. At the end of the retrieval procedure (which typically can take between 5 to 30 minutes), while you are still under sedation, the anesthesiology team will administer either ketorolac (30 mg) through your pre-existing IV line or no ketorolac according to your randomized group assignment.
4. Following the procedure, you will be monitored in the recovery area as per standard protocol.
5. This process does not add any additional time to the standard care provided during IVF retrieval and recovery.
6. Embryo transfer will proceed on day 5 post-retrieval according to the clinic's usual IVF process.
7. No additional procedures or contact points outside of standard clinical follow-up will be required for study participation. Outside of your physical participation while in our procedure suite or clinic, our team will be collecting some information regarding your health information. We will collect pre-specified information from your medical record and put it in a de-identified database for analysis. We will collect information from your medical record and put it in a database for analysis. Clinical information that we collect include demographic and medical information, including, but not limited to:
    - age, medical diagnosis, physical exam findings such as height and weight, laboratory testing, and ultrasound results

- reproductive history including how long you have been trying to conceive, infertility diagnoses, outcomes of past pregnancies, outcomes of prior infertility evaluation and treatments
- the types and doses of medications used, types of infertility treatments used, and information about your treatment cycles. Treatment cycle information will include, but is not limited to:
  - how you respond to ovarian stimulation,
  - sperm count,
  - embryo development and quality,
  - any post-retrieval evaluations for pain and/or bleeding, and
  - whether or not a pregnancy resulted.
  - narcotic use during recovery, and time to discharge
- Outcomes from the fresh embryo transfer following your retrieval. If you conceive a pregnancy, then we will follow your pregnancy through the resolution of your pregnancy. We will collect information about your:
  - pregnancy hormone levels,
  - confirmation or pregnancy ultrasound findings,
  - information on implantation, clinical pregnancy, miscarriage, and live births.

- We will collect the above information from your medical record and put it in a database for analysis, including information about **any outcomes from the fresh embryo transfer following your retrieval**.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Less Likely / Less Common (10% - 35%)

Mild

- Nausea or gastrointestinal discomfort
- Headache or dizziness

Rare (less than 10%)

Serious

- Increased risk of bleeding due to its effect on platelet function
- There is a potential for a loss of confidentiality by participating in this study. Measures to minimize this risks are described in the confidentiality section.

Mild

- Theoretical negative impact on implantation (though this has not been observed in retrospective studies).

WHAT ARE THE BENEFITS OF THIS STUDY?

We do not know if you will benefit from being in this study.
However, we hope that, in the future, **the information gained may help improve care for future IVF patients. We hope that other people undergoing IVF might benefit from this study because of the information and outcomes collected in this study.** Because of information about pain relief after egg retrieval collected during this study we hope future patients may need less opioid pain medications for egg retrieval procedures.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You may have **additional costs** for being in this research study if administration of pain medications following egg-retrieval exceed the usual standard of care costs. If you have insurance coverage for infertility treatment, you will be charged for IV ketorolac and administration of the medication from your insurance company. If you do not have insurance coverage for infertility treatment, then you will not be charged anything additional to your bundled payment.

You and/or your medical/hospital insurance carrier will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You will not be paid for being in this research study.

WHO IS FUNDING THIS STUDY?

The University and the research team are receiving no payments from other agencies, organizations, or companies to conduct this research study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- The University of Iowa does not plan to provide free medical care or payment for treatment of any illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.
- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

WHAT ABOUT CONFIDENTIALITY?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- federal government regulatory agencies,
- auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

To help protect your confidentiality, we will assign you a study ID number, and your name will be removed from study data. A secure, password-protected file will link your name to your study ID. Only authorized research team members will have access. Paper documents will be stored in a locked cabinet in a secure area. A small number of trained team members will extract relevant data from your medical record and collected in our database in RedCap.

If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

The University of Iowa Hospitals and Clinics generally requires that we document your participation in research occurring in a University of Iowa Health Care facility. This documentation will be in either your medical record or a database maintained on behalf of the institution reflecting that you are participating in this study. The information included will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. A copy of the informed consent document will be available on this website. 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.

A version of the informed consent document will be available on the website, Regulations.gov (Docket ID: HHS-OPHS-2018-0021), as required by U.S. Law. The informed consent document will not include information that can identify you. You can search this website at any time.

WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires **University of Iowa Health Care** to obtain your permission for the research team to access or create "protected health information" about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study. Once **University of Iowa Health Care** has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under "Confidentiality."

We may share your health information related to this study with other parties including federal government regulatory agencies, the University of Iowa Institutional Review Boards and support staff, the University of Iowa auditing departments.

You cannot participate in this study unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any non-research

alternatives available to you. Your decision will not affect your right to medical care that is not research-related. Your signature on this Consent Document authorizes **University of Iowa Health Care** to give us permission to use or create health information about you.

Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to **Dr. Jessica Kresowik, 1360 N Dodge Street Iowa City, IA 52245.** However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I Decide to Drop Out of the Study?

You may withdraw your permission at any time by contacting Aya Iwamoto at IVF-Study@uiowa.edu. If you withdraw, we will no longer collect new information, but may still use data gathered before your withdrawal. Your authorization does not have an expiration date.

If you decide to leave the study early, we will ask you to send a letter or email to Dr. Kresowik and Dr. Iwamoto at 1360 N Dodge Street Iowa City, IA 52245.

Will I Receive New Information About the Study while Participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can Someone Else End my Participation in this Study?

Under certain circumstances, the researchers might decide to end your participation in this research study earlier than planned.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Aya Iwamoto, (319) 356-1767 or IVF-Study@uiowa.edu. If you experience a research-related injury, please contact: our research team at IVF-Study@uiowa.edu.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Rd, The University of Iowa, Iowa City, IA 52242-1098, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, http://hso.research.uiowa.edu/. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed): _____

_____ _____
(Signature of Subject) (Date)

Statement of Person Who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)
the entry.)