GENETICS & IVF Institute

INFORMED CONSENT: FROZEN EMBRYO TRANSFER

3015 Williams Drive | Fairfax, VA 22031 | 703-698-7355 | www.givffertility.com

INSTRUCTIONS:

- Read this consent completely before Initialing on Page 7 & signing on page 8.
- If you have any questions, please speak with your doctor. Treatment **cannot** be started until all consents are signed.
- Consents must be signed in front of a Genetics & IVF (GIVF) staff member or a Notary Public, or through a GIVF-initiated ID verified DocuSign.

INTRODUCTION:

During a Frozen Embryo Transfer (FET), embryos that have been previously frozen following in vitro fertilization (IVF) can be thawed and transferred into a patient's uterus to attempt to achieve a pregnancy. This document explains the FET treatment process and describes the risks, benefits, and alternatives.

An FET cycle includes the steps and procedures outlined below. Patients are not guaranteed success at any or all these steps. If optimal results are not achieved at any step, it may be recommended that the treatment be stopped, and the cycle cancelled.

- Maturation of the uterine lining using either a non-medicated or medicated approach
- Monitoring of uterine lining development with blood hormone tests, vaginal ultrasound exams, and/or urine pregnancy tests
- Thawing of Frozen Embryos
- Placement (transfer) of one or more embryos into the uterus of the patient or gestational carrier

PRE-TREATMENT RECOMMENDATIONS

During treatment, the patient should avoid any activity, behavior, or medications that could reduce the chance of conceiving and having a healthy baby. These recommendations should be followed:

- A prenatal vitamin with at least 0.8 mg of Folic Acid should be taken daily before beginning treatment, optimally for at least one month prior to conception to help prevent some major birth defects of the baby's brain (anencephaly) and spine (spina bifida).
- Smoking and the use of smokeless tobacco or nicotine products (e.g.: cigarettes, vaping, nicotine gum, etc.) must be avoided before and during treatment and pregnancy. Recreational drugs should not be used before or during treatment or pregnancy.
- The use of alcohol should be avoided during treatment and pregnancy.
- Aspirin or aspirin-like products (e.g., Motrin, Advil, Anaprox, Naprosyn, Aleve, etc.) should be avoided during treatment. However, in certain circumstances you may be advised to take low dose aspirin (baby aspirin, 81mg). Tylenol is safe to take before and during treatment.
- The use of all prescription and over-the-counter medications, including herbal remedies, should be discussed with your care team before starting a treatment cycle.

FROZEN EMBRYO TRANSFER TREATMENT COMPONENTS

UTERINE LINING MATURATION

- Maturation of uterine lining can happen through either a non-medicated or medicated process.
- Monitoring visits will be needed to assess the progress of the uterine lining preparation.

In FET cycles, the uterus must be prepared for implantation for several weeks prior to thawing of the embryo(s) and embryo transfer. There are several ways to prepare the uterine lining so that embryo transfer is done when it is within the window of receptivity.

Non-Medicated (or Natural) Cycle:

During a menstrual cycle, a single ovarian follicle develops that ultimately results in the ovulation of a single egg. Prior to ovulation the follicle produces estrogen which stimulates the growth of the lining of the uterine cavity (endometrium). After ovulation, the ovary then produces progesterone, which causes the maturation of the endometrium so that it is receptive for embryo implantation. With the non-medicated approach, the embryo transfer is performed withing a specific time period after ovulation as determined by hormonal blood tests or following the administration of hCG (human chorionic gonadotropin) injection to induce ovulation at the appropriate time. If the timing of the ovulation cannot be accurately determined it may be recommended to cancel the cycle and proceed with a medicated approach. Progesterone supplementation may or may not be used in these cycles. Sometimes a modified version of this cycle is used with oral medication to enhance the ovulation process. **It is important to avoid intercourse during this type of cycle as pregnancy can occur from the ovulated egg(s).**

Medicated Cycle:

The main advantage of a medicated approach is that there is more control of the uterine preparation process and therefore a lower chance of having to cancel the cycle. It is also the recommended option in patients who do not ovulate regularly or normally. Depending on the protocol prescribed, the following medications may be used in a medicated cycle to stimulate and mature the uterine lining:

- ☐ **Estrogen:** Estrogen is administered orally (Estrace®) by itself or in combination with an estrogen patch (Vivelle®) and/or injection. The estrogen is started at the beginning of the patient's menstrual period. After the estrogen has been administered for approximately two weeks, **progesterone** is begun when the uterine lining appears adequate. Estrogen is continued for a few weeks after pregnancy and does not cause birth defects.
- ☐ **Progesterone** (pills, intramuscular injections, vaginal suppositories, or gel): This is administered to mature the lining in the uterus so that it is receptive for embryo implantation. Progesterone is continued for a few weeks after pregnancy and does not cause birth defects.
- ☐ **Lupron®:** Lupron® is an injectable medication that *may* be used to suppress the ovary and limit the risk of breakthrough ovulation during a medicated cycles which can disrupt the timing and result in cycle cancelation. It initially stimulates the pituitary gland to release FSH and LH, which are the hormones that regulate ovulation. With continued administration of Lupron®, the pituitary gland is temporarily depleted of FSH and LH, which suppresses the ovaries. After the Lupron® achieves this desired effect, estrogen and progesterone are administered as described above.

- ☐ **Oral contraceptive pills (birth control pills):** Many treatment protocols may include birth control pills (with or without Lupron) before starting uterine preparation to also suppress the ovaries which can help with scheduling and/or to limit the risk of breakthrough ovulation. Side effects include bleeding, headache, breast tenderness, nausea, and swelling. There is also a risk of blood clots or, very rarely, stroke.

MONITORING

Monitoring for FET cycles includes frequent blood draws and transvaginal pelvic ultrasounds to monitor the hormone levels and uterine lining. Monitoring helps determine appropriate dosing of medications and timing of the embryo transfer.

Blood drawing may be associated with mild discomfort and, possibly, bruising, bleeding, infection, or scar at the needle sites. Vaginal ultrasound examinations are usually painless and generally considered to be safe; however, the possibility of harm cannot be excluded.

THAWING OF FROZEN EMBRYOS

On the day of the scheduled embryo transfer, the frozen embryo(s) will be removed from the storage tank and thawed. After the thawing is completed, the embryos are examined to determine their viability. The chance of pregnancy following this treatment is related to the number and quality of the embryos that are transferred. It may be necessary to thaw and examine multiple embryos to reach the desired number of **viable** embryo(s) for transfer.

With newer vitrification (freezing) techniques, statistics show that over 95% of frozen embryos survive the warming process. However, it is possible that none of the embryos will survive. There is no data showing that children born from frozen and thawed embryos or frozen and thawed eggs have any more health problems than those born from fresh embryos, however, that possibility cannot be excluded.

ASSISTED HATCHING

- ➢ Assisted hatching is used to facilitate the embryo hatching and implantation process. It involves making a hole in the outer shell surrounding the embryo.
- ➢ Assisted hatching is a standard component of the Preimplantation Genetic Testing (PGT) protocol.

The cells that make up the early embryo are coated with a membrane (shell) called the zona pellucida. Normally, as an embryo grows, this shell dissolves, allowing the embryo to be released or “hatch” from the shell; hatching is required before an embryo can implant in the uterus. Assisted hatching helps encourage the embryo to hatch by making a small hole in the shell with a special laser.

Studies suggest that assisted hatching might help improve pregnancy chances for some patients, including those transferring embryos that have previously been frozen. At GIVF we perform assisted hatching on non-PGT embryos as routine protocol.

If embryos undergo Preimplantation Genetic Testing (PGT) prior to vitrification, assisted hatching is performed before the embryo biopsy. Thus, these embryos do not need assisted hatching after subsequent thawing since it has already been done.

There is a slight increased risk for identical twins in embryos that have undergone assisted hatching. Very rarely, an embryo can be damaged from the assisted hatching process.

EMBRYO TRANSFER

- The number of embryos transferred affects the pregnancy rate and risk of twins or other multiples.
- Embryos are placed into the uterine cavity using a catheter and ultrasound guidance.
- Not all embryos transferred become pregnancies.

One or more embryos are placed in the uterus using a thin tube called a catheter. Ultrasound guidance is used to help guide the catheter and confirm placement through the cervix and into the uterus. Although this is a simple process, there are some very rare risks. These risks include infection, loss of the embryo(s), or damage to the embryo(s). Not all embryos become pregnancies, and not all pregnancies are normal or lead to a healthy live birth. Some patients may experience miscarriage (which is an age-related risk) or ectopic pregnancy where the embryo implants outside the uterus (e.g., implants in the tube).

The number of embryos to transfer is an important decision. A patient's age and the quality of the embryo affect both the chance for pregnancy as well as the chance for multiple embryos to implant. If multiple embryos implant, a multiple pregnancy (twins, triplets, or more) will result. In some cases, an embryo can split into two (identical twins) after transfer. To limit the multiple pregnancy rate, single embryo transfer is strongly recommended when appropriate, such as in cases where the embryo has been genetically tested or in younger patients. As a member of the Society of Assisted Reproductive Technologies (SART), GIVF is obligated to follow the American Society for Reproductive Medicine (ASRM) guidelines:

ASRM GUIDELINES ON THE MAXIMUM NUMBER OF EMBRYOS TO TRANSFER

Age	<35	35-37	38-40	41-42	>42
Cleavage-stage embryos					
Normal # chromosomes	1	1	1	1	1
From Egg Donor <35	1	1	1	1	1
Other favorable*	1	1	≤3	≤4	Not Known
All others	≤2	≤3	≤4	≤5	Not Known
Blastocyst-stage embryos					
Normal # chromosomes	1	1	1	1	1
From Egg Donor <35	1	1	1	1	1
Other favorable*	1	1	≤2	≤3	Not Known
All others	≤2	≤2	≤3	≤3	Not Known

*Other favorable = any ONE of these criteria: Fresh cycle: expectation of 1 or more high-quality embryos available for cryopreservation or previous live birth after an IVF cycle; FET cycle: availability of vitrified day-5 or day-6 blastocysts, euploid embryos, 1st FET cycle, or previous live birth after an IVF cycle.

ADDITIONAL RISKS

Assisted reproductive technologies in most cases leads to successful delivery of healthy singleton pregnancies. However, there are complications of pregnancy that may develop more frequently in those conceived using IVF and Frozen Embryo Transfers.

Birth Defects: The risk of birth defects in the general population is 2%-3% and is slightly higher among infertile patients. Most of this risk is due to delayed conception and the underlying cause of infertility. Whether or not IVF alone is responsible for birth defects remains under debate and study. When intracytoplasmic sperm injection (ICSI) is done along with IVF, there may be an increased risk of birth defects. Rare genetic syndromes called imprinting disorders may be slightly increased with IVF.

Miscarriage and ectopic pregnancy: The rate of miscarriage after IVF is similar to the rate following natural conception, with the risk going up with the mother's age. The rate of miscarriage may be as low as 15% for women in their 20s to more than 50% for women in their 40s. There is a small risk (1-2%) of an ectopic (tubal, cervical, or abdominal) pregnancy with IVF. These abnormal pregnancies outside of the uterus may need to be treated with medication or surgery. There is less than 1% risk for a heterotopic pregnancy after IVF, typically in cases where multiple embryos are transferred. This is when an embryo implants and grows in the uterus while another embryo implants in the tube or elsewhere, leading to a simultaneous ectopic pregnancy. Heterotopic pregnancies usually require surgery to remove the ectopic pregnancy. In most cases, the pregnancy in the uterus can continue to develop and grow safely after the tubal pregnancy is removed.

Risks of Multiple Pregnancy: Having a multiple pregnancy (pregnancy with more than one baby) is more likely with IVF, particularly when more than one embryo is transferred. These pregnancies carry significant risks, including:

- ☐ Preterm labor and/or delivery: premature babies (regardless of whether they were conceived naturally or with IVF) are at higher risk for health complications such as lung development problems, intestinal infections, cerebral palsy, learning disabilities, language delay, and behavior problems
- ☐ Maternal hemorrhage
- ☐ Delivery by cesarean section (C-section)
- ☐ Pregnancy-related high blood pressure
- ☐ Gestational diabetes

Early delivery accounts for most of the higher risk of complications associated with babies from multiple pregnancies. IVF twins deliver an average of three weeks earlier than IVF single babies, and they weigh about 2 pounds less than IVF single babies. Triplet (and greater) pregnancies deliver before 32 weeks (7 months) in almost half of cases. Fetal growth problems and unequal growth among the fetuses can also result in perinatal illness and death before or shortly after delivery.

Multiple fetuses that share the same placenta, such as most identical twins, have additional risks. Twin-to-twin transfusion syndrome, a condition of the placenta where the blood circulation is not equal between the fetuses, can occur in up to 20% of identical twins that share a placenta. Twins sharing the same placenta have a higher frequency of birth defects. Death of one fetus in a twin pregnancy after the first trimester is more common with a shared placenta and may cause harm to the surviving fetus.

Your doctor will transfer the minimum number of embryos necessary to provide a high likelihood of pregnancy with the lowest risk of multiple pregnancy. The more embryos that are transferred into the uterus, the greater the risk of multiple pregnancy and chances of a problem during pregnancy or delivery. Patients with twins or more may choose to continue with the pregnancy (with all the risks that have already been stated); end the pregnancy; or reduce the number of fetuses (selective reduction), as clinically appropriate and/or permitted by state law. Selective reduction can be a difficult decision to make; the main danger is losing the entire pregnancy. The odds of losing the entire pregnancy are about 1 in 100 (1%) and the odds are greater if there are more than 3 fetuses present.

OTHER CONSIDERATIONS

Psychosocial Effects Treatment: Infertility and its treatment can affect intended parent's emotions, health, finances, and relationships with others. During evaluation and treatment, patients may feel anxious, helpless, depressed, lonely, or moody. Intended parents are encouraged to consider meeting with a counselor or other mental health professional who is specially trained in infertility care. Support groups, such as RESOLVE or Path2Parenthood, are also available.

Ethical And Religious Considerations: Infertility treatment can raise ethical or religious concerns for some; patients who have concerns should speak with their clinical care team, counselor, or someone else they trust.

Legal Considerations and Legal Counsel: The laws regarding embryo cryopreservation, subsequent thaw and use, and parent-child status of any resulting child(ren) is, or may be, unsettled in the state in which either the patient, spouse, partner, or any donor lives, or the state in which the ART program is located. GIVF will not provide legal advice. Intended parents are encouraged to consult a lawyer who is experienced in the areas of reproductive law if there are any questions or concerns about the present or future status of their eggs/embryos, individual or joint access to them, individual or joint parental status as to any resulting child, or any other aspect of this consent and agreement.

Alternatives To IVF: Additional alternatives to IVF treatment include intrauterine insemination, adoption, or not pursuing treatment.

Reporting Outcomes: The 1992 Fertility Clinic Success Rate and Certification Act requires the Centers for Disease Control and Prevention (CDC) to gather cycle-specific data and pregnancy outcomes on all assisted reproductive technology cycles performed in the U.S. This information is used to calculate and report annual success rates by IVF clinic. GIVF reports the required information from all procedures to the CDC, and to SART/ASRM. The information reported may also be used for research or quality assessment. All uses and disclosures will be de-identified and done in accordance with HIPPA guidelines.

Required Acknowledgements & Signature page to follow

REQUIRED ACKNOWLEDGEMENTS *Initial each of the sections below*

TERM IN EFFECT

I/We understand this Informed Consent for Frozen Embryo Transfer, including the procedures and disposition instructions set forth above, will remain in effect until one of the following events occurs:

i. one (1) calendar year has passed from the date of signature,

ii. death of patient or patient's partner,

iii. dissolution of the patient's marriage or partnership,

iv. patient's successful pregnancy which results in a live birth, or

v. written notice to GIVF of withdrawal of consent by the patient and/or the patient's partner, if applicable.

I/we acknowledge and agree that in the event of the dissolution of the patient's marriage or partnership or a live birth, GIVF will require the patient and the patient's partner, if applicable, to execute a new consent form prior to any additional procedures.

_____ / _____
Patient / Partner (if applicable)

CRYOPRESERVED EMBRYO DISPOSITION DECLARATIONS & ACKNOWLEDGEMENTS

☐ I/We have previously completed the Embryo Disposition and Storage Instructions section in CON-500B (Informed Consent for In Vitro Fertilization Signature Packet), or in FOR-518 (Cryopreserved Embryo Disposition Declarations), and **I/we reaffirm those selections with no changes**

OR

☐ I/We have not previously completed an Embryo Disposition and Storage Instructions document at the Institute. *(Requires FOR-518: Cryopreserved Embryo Disposition Declarations to be completed and signed)*

_____ / _____
Patient / Partner (if applicable)

Required Signature page to follow

ACKNOWLEDGEMENT OF INFORMED CONSENT & AUTHORIZATIONS

By signing this document, I/we acknowledge that I/we have been fully advised of the purpose, risks, and benefits of the treatment procedures, and have been informed of the available alternatives and risks and benefits of such alternatives. I/We have read the Frozen Embryo Transfer document in its entirety and this information has been supplemented by my/our consultation with my/our medical team. I/We have had the opportunity to ask questions and all my/our questions have been answered to my/our satisfaction.

I/We are voluntarily seeking treatment in order to achieve a child and have had ample time to reach my/our decision, free from pressure and coercion, and agree to proceed with my/our participation in Assisted Reproduction services as stated above

PATIENT

Signature: _____

Printed Name: _____

Date: _____

PARTNER ☐ N/A

Signature: _____

Printed Name: _____

Date: _____

Type of Picture Identification viewed:

☐ Driver's License ☐ Passport

☐ Other: _____

GIVF Witness Name: _____

Title: _____

Or notarized below:

PATIENT:

City/County of_____

State/Commonwealth of _____

The foregoing instrument was acknowledged before me this _____ day of _____, 20 _____

by _____
(Name of person seeking acknowledgment)

Notary Public's Signature: _____

Registration #: _____

My commission expires: _____

Type of Picture Identification viewed:

☐ Driver's License ☐ Passport

☐ Other: _____

Signature: _____

Date: _____

PARTNER: ☐ N/A

City/County of_____

State/Commonwealth of _____

The foregoing instrument was acknowledged before me this _____ day of _____, 20 _____

by _____
(Name of person seeking acknowledgment)

Notary Public's Signature: _____

Registration #: _____

My commission expires: _____