

## INFORMED CONSENT FOR OOCYTE CRYOPRESERVATION

This consent reviews the process for oocyte cryopreservation, including the risks that this treatment might pose to you and your future offspring. In addition to these known risks, there may be risks with in-vitro fertilization (IVF) that have not yet been established or even suspected. This consent concerns only procedures carried out by authorized personnel at Northwestern Medical Group's Division of Fertility and Reproductive Medicine, hereafter referred to as NMG.

In order to cryopreserve oocytes (eggs), the following steps are typically followed:

1. Administration of medications to stimulate the development of multiple follicles. A follicle is a sac in the ovary that typically contains an egg and produces hormones.
2. Retrieval of oocytes from the follicles in the ovaries.
3. Cryopreservation of the retrieved oocytes.

Patients who choose to cryopreserve oocytes do so for one of the following reasons:

- You will be undergoing chemotherapy or radiation therapy treatments to treat a medical condition, such as cancer or rheumatologic diseases. Although not all chemotherapy and/or radiation treatments affect fertility (the ability to become pregnant), the treatment(s) you will receive may affect your ovaries and may cause you to become sterile, or unable to become pregnant, after the treatment is finished. Oocyte banking must take place before your treatment begins.
- You will be undergoing In-Vitro Fertilization (IVF) to treat infertility, but you are unable to consent to freezing embryos or the sperm sample required to fertilize your oocytes is not available – your partner may not be available, your partner was unable to collect a sample, or the sample that you are receiving from a cryobank did not arrive in time for your procedure.
- You plan on taking gender affirming hormones or undergo gender affirming surgery which may affect your future fertility.
- You are someone who wishes to freeze your oocytes for family planning reasons (e.g. you do not have a partner, or you and your partner would like to delay family building).

Published studies indicate that mature oocytes (eggs) can successfully be removed from the ovaries, frozen and subsequently thawed and then fertilized with sperm using a technique called in-vitro fertilization (IVF). Pregnancies have resulted from such treatments. Early results indicate that the babies resulting from these pregnancies are no more likely to have birth defects than babies conceived naturally.

If you choose to freeze your oocytes, you will undergo oocyte (egg) retrieval. Your oocytes will then be frozen and stored at a long term storage facility. The stored oocytes will be available to you at any time after the storage procedure if you wish to try to become pregnant. You may also, at any time, elect to have the oocytes discarded or donated for research purposes. Any such research will not involve fertilizing the eggs with sperm.

## **WHAT WILL FREEZING MY EGGS ENTAIL?**

**Pre-operative Assessment:** Prior to beginning fertility medications, you will be evaluated to confirm that the retrieval process will not represent an increased risk to you by virtue of your disease or general state of health. A blood test, called Anti-Mullerian Hormone, is required to confirm that your ovaries are likely to yield a sufficient number of healthy eggs to justify doing the retrieval. You will also be assessed by your oncologist (if applicable), a reproductive endocrinologist and a clinical psychologist. The purpose of this screening is to confirm that you are eligible for egg freezing and specifically, to ensure that the risk you will incur is acceptably low (particularly if you have a medical condition that will require chemotherapy and/or radiation). This will require 1-2 additional office visits, each lasting between 30-60 minutes.

**Ovarian Stimulation:** In order to permit the recovery of as many oocytes as possible, you will be treated with a series of self-administered hormone injections (gonadotropins) to stimulate your ovaries to develop a number of mature follicles simultaneously. Ordinarily, in a natural menstrual cycle, only one follicle develops which releases only one oocyte (egg). The injections are self-administered under the skin on a daily or twice daily basis for 8-13 days. Your response to the medication will be monitored by frequent blood tests and ultrasound examinations. Your daily dose of medication may change during this course of your treatment depending on how you respond and the results of your blood tests and ultrasounds. You will take an additional medication about mid-way through the treatment cycle, called a GnRH antagonist. This medication helps prevent premature ovulation and is also injected under the skin while you continue to administer the gonadotropins. When the follicles appear to be mature, you will administer a single injection of Human Chorionic Gonadotropin (hCG) to help facilitate oocyte growth for the next 36 hours.

**Oocyte Retrieval:** Oocyte retrieval is an outpatient procedure performed under conscious sedation about 36 hours after the hCG injection. The retrieval involves the intravenous administration of pain medication and relaxants – including, but not limited to, Fentanyl, Versed, Propofol and/or Diazepam. This is designed to keep you comfortable during the procedure, which usually takes 10-15 minutes. These medications will usually cause patients to fall asleep from time to time, but should not prevent communication between the patient and the medical staff performing the procedure.

Once sedation has been established, your ovaries will be visualized using an ultrasound probe inserted into the vagina. Under ultrasound guidance, a needle will be passed into the ovaries and the follicles. Each follicle containing an oocyte will be emptied one by one with the needle. Once all of the follicles have been emptied, the procedure will be terminated. The effects of the sedation should be gone by the following day, but you will need a trusted adult to drive you home from the procedure, as you will not be allowed to drive while recovering from sedation.

## **OOCYTE CRYOPRESERVATION AND STORAGE**

**IF YOU ARE A CANCER OR TRANSGENDER PATIENT SEEKING FERTILITY PRESERVATION OR A PATIENT PURSUING OOCYTE CRYOPRESERVATION FOR PLANNED FAMILY BUILDING PURPOSES:**

Your oocytes will be passed directly into the IVF laboratory, where they will undergo the cryopreservation (freezing) process. Your recovered oocytes will be stored for your future use at an accredited, long term storage facility, Reprotech, LTD (RTL), located in St. Paul, MN. You will be asked to sign a separate storage agreement with Reprotech that addresses the ownership, storage, shipping

and future disposition of your samples. You and/or your insurance carrier will be responsible for costs associated with the shipping (approximately \$195) and storage (approximately \$275 per year) of your oocytes. There is no limit as to how long your samples may be stored at Reprotech, provided your storage fees are paid annually. Reprotech has financial assistance program in place for those who qualify. When you are ready to use your oocytes, your oocytes will be transferred by Reprotech to the facility of your choice, at your request, and at your expense. All stored oocytes will be considered your property and will not be made available to anyone other than you without your approval. Your oocytes will be stored at an NMG laboratory for a short period of time prior to transfer to Reprotech and the storage agreement that you sign with Reprotech will determine the disposition of your oocytes if something were to happen to you.

**IF YOU ARE AN IVF PATIENT WHOSE PARTNER IS UNABLE TO PROVIDE A SEMEN SAMPLE ON THE DAY OF EGG RETRIEVAL:**

Your oocytes will be passed directly into the IVF laboratory, where they will undergo the cryopreservation (freezing) process. Your oocytes will be stored for you at Northwestern Medical Group (NMG) for a period of up to two years (from the date of freezing), provided your applicable annual storage fees are paid. You will have access to your oocytes for the purpose of initiating a pregnancy at any point in time following their initial storage, provided your applicable annual storage fees are paid. You will also have the option of having your oocytes discarded or donated for any appropriate research studies at any point. If you choose to donate your oocytes for research studies, no such studies will involve a fertilization step.

**ABANDONMENT OF OOCYTES IN STORAGE:**

There are fees associated with keeping oocytes in storage. You must remain in contact with NMG on at least an annual basis in order to inform NMG of your wishes in regard to these oocytes and to pay fees associated with the storage of these oocytes. In situations where there is no contact with NMG for a period of two (2) years or annual fees associated with oocyte storage have not been paid for a period of two (2) years and NMG is unable to contact you after reasonable efforts have been made, the oocytes will be considered to be abandoned and may be destroyed by NMG in accordance with normal laboratory procedures and applicable law. Reasonable efforts may include phone calls and registered mail to the most recent phone numbers/address in your medical chart. At the end of two years, if you do not notify us of what you wish to do with your oocytes on an ongoing basis (utilizing the oocytes, disposing of them, or transferring them to a long term storage facility at your expense) they will be discarded. If your oocytes are sent to Reprotech for storage, the separate storage agreement that you sign with Reprotech describes the disposition of your oocytes if you fail to pay your storage fees, abandon the oocytes, or die while they are in storage.

**INFECTIOUS DISEASE TESTING:**

Banking and subsequent use of your eggs is regulated by the Food and Drug Administration (FDA). In order to comply with current tissue banking regulations and to be prepared for any future changes in regulations while your oocytes are in storage, you may be tested and screened for a number of infectious diseases prior to banking your oocytes – particularly if you are a patient who is banking oocytes for medical reasons (such as before chemotherapy, radiation, hysterectomy, or oophorectomy) where carrying a pregnancy in the future is not possible or safe. These tests will include, but are not limited to, HIV, Hepatitis B and Hepatitis C, based on current federal regulations. Some screenings and tests that will be performed are the same that would be performed on an anonymous reproductive tissue donor and will include a physical examination and questions about possible high risk behaviors, as

well as blood tests. In this way, the oocytes could potentially be used by you or would be suitable for use in another individual, such as a gestational carrier or surrogate, in the future if this is necessary. Your oocytes will be stored with oocytes of the same infectious disease status – for example, eggs that have been retrieved from a healthy patient with no communicable diseases will be stored with eggs from other healthy patients with no communicable diseases. This blood work must be drawn within 30 days of your oocyte retrieval.

### **WHAT ARE SOME OF THE RISKS ASSOCIATED WITH PATIENTS WHO FREEZE OOCYTES?**

**OVARIAN STIMULATION:** The ovarian stimulation step often cause a sense of fullness or bloating, which usually goes away within a few days after retrieval. About 1% of the time, patients will develop ovarian hyperstimulation syndrome (OHSS) which is a serious complication resulting in the accumulation of fluid in the abdominal cavity. This complication is self-limited, but severe cases may require several days of hospitalization for fluid management.

**OOCYTE RETRIEVAL:** This is the removal of eggs from the ovaries. It is usually performed by inserting an ultrasound probe into the vagina. By means of the ultrasound, the ovaries and the follicles containing the oocytes are visualized. The ultrasound probe contains a long needle that can be seen on ultrasound. The needle is guided into each follicle and the contents are aspirated (drawn into a test tube). This procedure is performed on each ovary. During the procedure, the patient is provided with sedation and pain medication which is administered intravenously. Some patients may experience some discomfort during the procedure. The aspirated material usually includes follicular fluid, oocytes, and granulosa (egg-supporting) cells. Rarely, the ovaries cannot be reached by the vaginal route (transvaginally). In that situation, the oocyte retrieval will have to be performed through the abdominal wall (transabdominal). If transabdominal retrieval is necessary, your doctor will discuss the procedure and its risks with you. Risks of oocyte retrieval include, but are not limited to:

- ❖ **INFECTION:** Bacteria normally present in the vagina may be unknowingly transferred into the abdominal cavity by the needle. This bacteria may cause an infection of the uterus, fallopian tubes, ovaries or other abdominal organs. The estimated incidence of infection after oocyte retrieval is less than 0.5%. Treatment of infections could require the use of oral or intravenous antibiotics. Severe infections occasionally require surgery to remove infected tissue. Infections can have a negative impact on future fertility. Rarely, infection may become severe enough to require a hysterectomy and/or the removal of one or both ovaries. Oral antibiotics are used before and after the oocyte retrieval procedure to reduce the risk of pelvic or abdominal infection. Although the use of antibiotics reduces the potential incidence of infection, there is no way to eliminate this risk completely.
- ❖ **BLEEDING:** The needle must pass through the vaginal wall and into the ovary to obtain the oocytes. Both of these structures contain blood vessels. In addition, there are other blood vessels nearby. The needle may pierce a blood vessel. Small amounts of blood loss are common during oocyte retrievals. The incidence of major bleeding problems has been estimated to be less than 0.1%. Major bleeding may require surgical repair and possible loss of the ovary. The need for blood transfusion is rare. Although very rare, review of the world literature with IVF indicates that unrecognized bleeding has led to death.

- ❖ **TRAUMA:** Although the procedure is directed by the use of ultrasound guidance, it is possible to damage other nearby organs during the oocyte retrieval. Reports in the medical literature have described damage to the bowel, appendix, bladder, ureters, uterus, and ovary. Some patients may develop adhesions (internal scarring). Damage to internal organs may result in the need for additional treatment such as surgery for repair or removal of the damaged organ. However, the estimated risk of such trauma is less than 0.1 %.
- ❖ **ANESTHESIA:** The use of anesthesia during the oocyte retrieval can produce unintended complications such as allergic reaction, low blood pressure, nausea or vomiting and, in rare cases, death.
- ❖ **PROCEDURE FAILURE:** It is possible that the retrieval will fail to obtain oocytes. It is also possible that retrieved oocytes may be abnormal or of poor quality and, thus, unable to produce a normal pregnancy.

**CRYOPRESERVATION (FREEZING):** Although care will be taken, damage to your oocytes may occur during any part of the cryopreservation (freezing) and storage process. The long term effects of cryopreservation and storage on the human oocytes are not known and possible damage to the oocyte may occur. The risk of birth defect(s) and/or genetic damage to any child who may be born following such a procedure is also unknown. Oocytes are frozen using a method called vitrification. This is the process of freezing using high concentrations of cryoprotectant and ultra-rapid cooling to solidify the cell into a glass-like state without the formation of ice. Cryopreservation protocols usually involve removing cumulus cells from oocytes in order to assess oocytes maturity. Because removing cumulus cells may reduce fertilization following standard insemination and because zona pellucida (the outer shell of an oocyte) hardening has been reported after thawing cryopreserved oocytes, intracytoplasmic sperm injection (ICSI) is generally used for fertilizing previously cryopreserved oocytes. You will sign an additional consent form when you are ready to thaw and fertilize your cryopreserved oocytes.

**STORAGE:** Limited data exist regarding the effect of duration of storage on oocytes cryopreservation survival and pregnancy. One study was identified in a literature search that assessed oocyte cryopreservation efficacy with duration of storage. In this study, no difference in survival, fertilization, cleavage, embryo quality, implantation or live birth rates were observed in oocytes cryopreserved with slow-freeze and thawed after up to 48 months, compared to earlier thaws. The oocytes removed may not survive the freezing and thawing process, or pregnancy may not result when the oocytes are ultimately used. If you have reached menopause at the time you use these oocytes and they do not produce a pregnancy – you will not be able to have a child that is biologically your own.

It is possible that medications you have taken may have some damaging effect on your oocyte quality. There are many medications whose effects on the ovary or oocyte quality are not yet known or have not yet been determined. All patients should keep in mind that pregnancy rates with both frozen oocytes and frozen embryos decrease with the age of the patient at the time of freezing. Oocytes could be lost or made unusable due to equipment failure, or unforeseeable natural disasters beyond the control of this program.

### **ADDITIONAL INFORMATION**

While there are a limited number of established pregnancies and deliveries derived from cryopreserved oocytes, perinatal outcome data are reassuring. Despite concerns regarding spindle abnormalities in cryopreserved oocytes, the incidence of chromosomal abnormalities in human embryos obtained from cryopreserved oocytes is not different from that of control embryos as determined by fluorescence in-situ hybridization. A recent review of over 900 live births derived from cryopreserved oocytes, principally using a

slow-freeze technique, suggests that there is no increased risk of congenital anomalies compared to the general US population. While short term data appear reassuring, long term data on developmental outcomes and safety data in diverse (older) populations will be ongoing.

Oocyte freezing has resulted in the births of thousands of babies worldwide. The American Society of Reproductive Medicine (ASRM) recently removed the experimental label from egg freezing due to the success rates seen at numerous clinics across the United States.

### **WHAT OTHER PROCEDURES OR COURSES OF TREATMENTS MIGHT BE AVAILABLE TO ME?**

**If you are a patient undergoing medical treatments for cancer**, you may receive chemotherapy or radiation therapy without undergoing retrieval and storage of your oocytes. However, in addition to freezing and storing oocytes, you have the alternative of undergoing therapy with a type of medication called GnRH agonist, a protein which suppresses hormonal stimulation of your ovaries, prior to your cancer treatment. There is some evidence that such treatment reduces the risk of damage to the ovaries by either chemotherapy or radiation therapy. This treatment is still considered experimental and is not approved for this use at this time. You also have the option of undergoing ovarian tissue cryopreservation which is also an experimental procedure.

**If you have a partner**, you have the option of undergoing treatment with In-Vitro Fertilization (IVF) in order to cryopreserve (freeze) embryos for future use.

**If you are undergoing IVF**, have had oocytes retrieved but the sperm sample needed to fertilize your oocytes is not available, your oocytes can be discarded.

**If you are freezing oocytes for planned family building reasons**, you can decide not to do that.

**INSTRUCTIONS FOR DISPOSITION OF CRYOPRESERVED OOCYTES**

In the event of death or incapacity while my oocytes are in storage at Northwestern Medical Group (NMG), I instruct NMG and NMG's authorized personnel to dispose of my oocytes as follows: *Please **check and initial** the option you choose:*

**Initials**

Discard all oocytes \_\_\_\_\_

Donate all oocytes for an IRB approved research project that does not include adding sperm to them (fertilization). I understand that if no such study can be found at that time, the oocytes (eggs) will be discarded. \_\_\_\_\_

The individual named below can use these oocytes for the purpose of producing a pregnancy in themselves or their partner, but may not assign them to other individuals. \_\_\_\_\_

Name: \_\_\_\_\_

Address: \_\_\_\_\_

Phone Number: \_\_\_\_\_

**OOCYTE CRYOPRESERVATION CONSENT**

**I have read the Oocyte Cryopreservation Information Package and this consent form. The procedure, its risks and alternative options have been explained to me in detail. I have been given the opportunity to ask questions and they have been answered to my satisfaction. By signing below, I agree to have my oocytes cryopreserved.**

PATIENT NAME – PLEASE PRINT

PATIENT SIGNATURE

DATE OF BIRTH

DATE