
Carolinas Fertility Institute

Recipients of Donor Eggs

Process, Risks, Consent

Date: _____	
Partner #1 Last Name: _____	First Name: _____
ID# _____	Gender – M / F (Circle One)
Partner #2 Last Name: _____	First Name: _____
ID # _____	Gender – M / F (Circle One)
Address: _____	

Donor Egg (DE) therapy has become an established treatment for infertility due to egg problems or certain genetic issues. The main goal of DE is to allow a patient the opportunity to become pregnant using eggs from a donor and sperm from her partner or from a donor. This is an elective procedure designed to result in the patient's pregnancy when other treatments have failed or are not appropriate.

Steps in the Process

Screening of Egg Donor

Donor Screening. Egg donors have had their medical, psychological, genetic and family history recorded and screened. Part of this screening is federally mandated (by the FDA), but most is based on regularly updated guidelines issued by the American Society for Reproductive Medicine. No screening or testing regimen is perfect, so it is possible for children with major congenital malformations (birth defects) or health problems to occur despite appropriate screening. The **CENTER** does not guarantee

any characteristics of a child resulting from the egg donation process, including, but not limited to, gender, blood type, eye color, hair color, height or intellectual ability.

Infectious Disease Testing Of The Egg Donor. The donor must have federally mandated infectious disease testing within 30 days of the egg retrieval. Unless these test results are available prior to the embryo transfer, the embryo transfer cannot take place and all of the eggs or embryos must be frozen for use and/or transfer at a time when the results are available. If the anonymous donor tests positive for any of the infectious diseases as mandated by federal law, the donor is considered ineligible and the eggs or embryos must be disposed of according to American Society for Reproductive Medicine (ASRM) Ethical Guidelines. These requirements should be considered carefully when determining how many eggs to add sperm to and what should be done with extra eggs as described above.

All donors are screened and/or tested for infectious diseases including HIV (the virus responsible for AIDS), syphilis, and hepatitis (types B and C) as mandated by federal law. Even with this screening, it is possible that an infectious disease could be transmitted to a child conceived with the donated eggs or to the woman who will carry the pregnancy.

Matching and Synchronization to Donor

A suitable egg donor will need to be identified first. Depending on availability, in some cases the donor will be able to provide fresh eggs. In other cases her eggs will already be stored in an Egg Bank. All donors must pass screening before any of their eggs can be used.

Once you have selected the donor, a schedule can be developed for the embryo transfer. If the donor eggs are already in an Egg Bank, the transfer can often occur within a few weeks. If the donor needs to undergo ovarian stimulation to produce the eggs, additional time will be needed, and synchronization of the donor's cycle and the recipient's cycle is usually necessary.

Ovarian Stimulation of Donor to Obtain Eggs

- Injections of the natural hormones FSH and/or LH (gonadotropins) are used to cause a group of eggs to develop to maturity in the donor.
- Additional medications are used to prevent premature ovulation.
- An overly vigorous ovarian response can occur, or conversely an inadequate response.

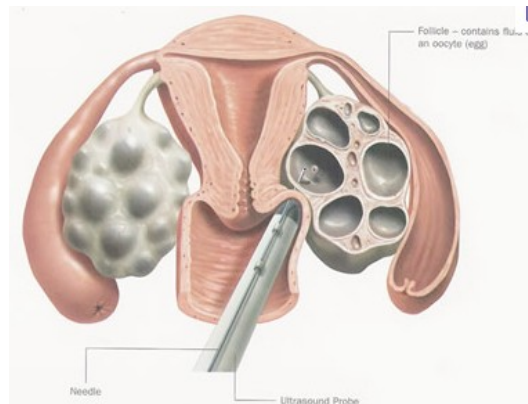
Medications are used to stimulate the ovary in hopes of inducing the simultaneous growth of several oocytes (eggs) over the span of 8 or more days. Monitoring of the donor's ovarian response by ultrasound is important. A typical pattern of office visits is shown below:



This process does not cause the donor to run out of eggs sooner in the future. The eggs that are induced to grow by these medications were already “linked” to this cycle and would have died anyway had they not been induced to grow.

Egg Retrieval from a Donor

- Eggs are removed from the ovary with a needle under ultrasound guidance.
- Anesthesia is provided to make this comfortable.
- Injury and infection are rare.



A transvaginal ultrasound probe is used to visualize the ovaries and the egg-containing follicles within the ovaries. A long needle is guided into each follicle and the contents aspirated. The aspirated material includes the egg. For the egg donor, the retrieval is the last step.

In vitro fertilization and embryo culture

- Sperm and eggs are placed together in specialized conditions (culture media, controlled temperature, humidity and light) in hopes of fertilization.
- Culture medium is designed to permit normal fertilization and early embryo development, but the content of the medium is not standardized.
- Embryo development in the lab helps distinguish embryos with more potential from those with less or none.

After eggs are retrieved, they are transferred to the embryology laboratory where they are kept in conditions that support their needs and growth. The eggs are placed in small dishes or tubes containing "culture medium," which is special fluid developed to support development of the embryos made to resemble that found in the fallopian tube or uterus. The dishes containing the embryos are then placed into incubators, which control the temperature and atmospheric gasses the eggs experience.

A few hours after eggs are retrieved, sperm are placed in the culture medium with the eggs, or individual sperm are injected into each mature egg in a technique called Intracytoplasmic Sperm Injection (ICSI) (see below). The eggs are then returned to the incubator, where they remain to develop. Periodically over the next few days, the dishes are inspected so the development of the embryos can be assessed.

The following day, after eggs have been inseminated or injected with a single sperm (ICSI), they are examined for signs that the process of fertilization is underway. At this stage, normal development is evident by the still single cell having 2 nuclei; this stage is called a zygote or a 2PN embryo. Two days after insemination or ICSI, normal embryos have divided into about 4 cells. Three days after insemination or ICSI, normally developing embryos contain about 8 cells. Five days after insemination

or ICSI, normally developing embryos have developed to the blastocyst stage, which is typified by an embryo that now has 80 or more cells, an inner fluid-filled cavity, and a small cluster of cells called the inner cell mass.

Certain decisions regarding this phase will need to be made beforehand, including:

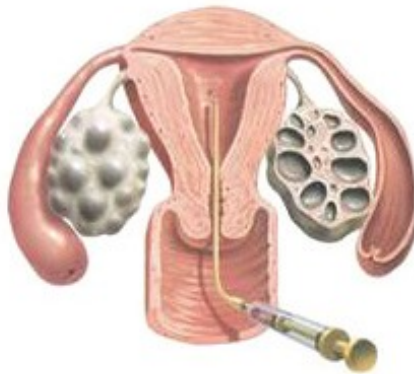
- The manner of fertilization
 - ICSI involves the direct injection of a single sperm into the interior of an egg using an extremely thin glass needle. ICSI allows couples with male factor infertility to achieve fertilization and live birth rates close to those achieved with in vitro fertilization (IVF) using conventional methods of fertilization in men with normal sperm counts. ICSI may also be used to maximize the rate of fertilization of previously cryopreserved (frozen) eggs or eggs that are shared with other recipients.
- The number of eggs to inseminate
 - If many mature eggs are available, you might choose to inseminate only some of them, and freeze the rest as eggs.
- What to do with extra eggs and/or embryos
 - Freezing (or “cryopreservation”) of embryos is a common procedure. Since multiple eggs (oocytes) are often produced during ovarian stimulation, on occasion there are more embryos available than are considered appropriate for transfer to the uterus. These embryos, if viable, can be frozen for future use. This saves the expense and inconvenience of stimulation to obtain additional eggs in the future.

Embryo Transfer into Recipient or Carrier

- After a few days of development, the best appearing embryos are selected for transfer.
- The number chosen influences the pregnancy rate and the multiple pregnancy rate.
- Embryos are placed in the uterine cavity with a thin tube.
- Excess embryos of sufficient quality that are not transferred can be frozen.

After a few days of development, one or more embryos are selected for transfer to the uterine cavity. Embryos are placed in the uterine cavity with a thin tube (catheter). Ultrasound guidance may be used to help guide the catheter or confirm placement through the cervix and into the uterine cavity. Although the possibility of a complication from the embryo transfer is very rare, risks include infection and loss of, or damage to, the embryos.

The number of embryos transferred influences the pregnancy rate and the multiple pregnancy rate. The age of the woman who provided the eggs, and the appearance of the developing embryo, have the greatest influence on pregnancy outcome and the chance for multiple pregnancy.



Hormonal support of the uterine lining

- Successful attachment of embryo(s) to the uterine lining depends on adequate hormonal support.
- Progesterone, given by the intramuscular or vaginal route, is routinely given for this purpose.

Successful attachment of embryos to the uterine lining (endometrium) depends on adequate hormonal support of the lining. The critical hormones in this support are progesterone and estradiol. Normally, the ovary makes sufficient amounts of both hormones. However, in IVF cycles, this support is not always adequate. Therefore, progesterone is routinely given, and some clinics also prescribe estradiol. Progesterone is given by the intramuscular or vaginal route. Estradiol is given by the oral, vaginal, transdermal or intramuscular route. The duration of this support is from 2 to 10 weeks.

Special Issues with the Use of Donor Eggs

Donor Identity. If our donor is anonymous, we pledge that we will never seek her identity, except as allowed below or if a court orders otherwise. We (I) also understand that the **CENTER** will protect our (my) identity and will not reveal it to the donor except as allowed below, as required by law, or if a court orders otherwise. However, we (I) understand that if a child born from this donation has a medical or psychological need that might be met by the donor, then we may contact the **CENTER** and ask that our request be relayed to the donor. Such requests may be for a medical need such as a bone marrow transplant, or, once any child or children born from this donation are legal adults, a request may be made by the child or children for the identity of the donor to be revealed. The donor is under no obligation to consent to any request.

Information on all cycles of Assisted Reproductive Technology treatment, along with data identifying recipients and women who undergo ART with their own eggs, is currently collected into a national database under the 1992 Fertility Clinic Success Rate and Certification Act. As part of this process, the Society for Assisted Reproductive Technology plans to begin to collect identifying information on all egg donors. As with recipient cycles and cycles for women using their own eggs, this information may be used to track outcomes. For this purpose, certain donor identifying information such as name, date of birth, and social security number may be reported to a Registry by SART member clinics for data aggregation purposes. ASRM guidelines currently require permanent records be kept for all egg donation cycles. Efforts to collect this information are intended to respect donation confidentiality and not to disclose confidential identifying information to recipients, donors, or offspring. Control of such information in the future may, however, depend on applicable law.

Parental Rights and Responsibilities. We (I) understand and accept our (my) responsibilities for the care of any child resulting from the egg donation process, and it is our (my) intent to be the legal parent(s) of any child that results from the egg donation process, with all the rights and responsibilities that come with parenting. Under no conditions will we (I) seek financial aid from the donor or **CENTER**. We (I) understand that neither the **CENTER** nor the donor will assume any financial responsibility for the upbringing of any child resulting from the egg donation process under any circumstances except as provided by law. We (I) assume responsibility for all costs associated with the use of donor eggs.

We (I) are/am aware that while there are may be laws in my state governing the legitimacy and legal status of children born following the use of donor eggs or sperm, there are no such laws related to the use of donor embryos or gestational carriers. Furthermore, such laws only protect children that are

actually born in my state. We (I) understand that that the laws governing egg/embryo/sperm donation regarding who the legal parents are vary from state to state. In some cases, the intended parents may obtain a pre-birth Court order establishing their parental rights, and in some states they will need to formally adopt the child (or children). The **CENTER** does not offer legal advice on these matters and we (I) acknowledge and agree that we (I) must consult an attorney with expertise in family law related to assisted reproductive technologies in the state where the child will be delivered concerning these matters.

Confidentiality. We (I) understand and agree that, if we have an identified donor, aspects of our (my) medical care and conditions and that of the donor may be revealed and/or discerned as part of the treatment process.

We (I) understand the confidentiality of medical records, including any photographs, X-rays or recordings, will be maintained in accordance with applicable state and federal laws. We (I) may request our records be released to other physicians. Data from the ART procedure will also be provided to the Centers for Disease Control and Prevention (CDC), and to the Society for Assisted Reproductive Technologies (SART) of the America Society for Reproductive Medicine (ASRM) if my/our clinic is a member of this organization. The 1992 Fertility Clinic Success Rate and Certification Act requires that CDC collect data on all assisted reproductive technology cycles performed in the United States annually and report success rates using these data. Because sensitive information will be collected on you, CDC applied for and received an “assurance of confidentiality” for this project under the provisions of the Public Health Service Act, Section 308(d). This means that any information that CDC has that identifies you will not be disclosed to anyone else without your consent.

Limits to the Success of the Process

There are a number of reasons IVF using donated eggs may be unsuccessful:

- Inadequate egg development in the egg donor may result in cancellation of the cycle prior to egg retrieval. We (I) understand that we (I) are financially responsible for all charges resulting from a cancelled egg donation cycle, including fees for services for the donor, recipient and partner, up to and including the day of cancellation.
- The egg donor may respond too vigorously to the medications and be at risk of ovarian hyperstimulation syndrome (OHSS) and this may necessitate cancellation of the cycle prior to egg retrieval. We (I) understand that we (I) are financially responsible for all charges resulting from a cancelled egg donation cycle, including fees for services for the donor, recipient and partner, up to and including the day of cancellation.
- Ovulation may occur spontaneously before the donor eggs can be retrieved.
- The egg donor may not be able to complete the cycle for medical, personal or logistical reasons and may withdraw from the treatment cycle before the egg retrieval.
- In rare cases, no donor eggs may be retrieved.
- The donor eggs may not be normal.
- A fresh semen sample may not be able to be produced the day of the procedure; a frozen specimen (if previously provided) will then be utilized, however, this may result in fewer eggs being fertilized.
- The frozen sample of sperm or tissue may be unusable or non-viable.
- Fertilization may not occur, or may occur abnormally, e.g. an egg may be fertilized by more than one sperm (polyspermia) and could develop abnormally. Fertilization may not occur or abnormal fertilization may occur, even with the use of intracytoplasmic sperm injection. Such embryos will not be transferred.
- Intracytoplasmic sperm injection may result in damage, destruction or loss of one or more eggs (oocytes) or sperm.
- Cleavage or cell division of fertilized eggs may not occur.

- The embryos may not develop normally.
- Selective assisted hatching may lead to damage or loss of one or more embryos.
- The embryo transfer may be difficult or may not be possible.
- An anonymous egg donor's infectious disease testing results (performed within 30 days of the egg retrieval) may be unavailable making it necessary to freeze all the eggs or embryos for use at a later time.
- An anonymous egg donor's infectious disease testing results (performed within 30 days of the egg retrieval) may be positive making it necessary to discard the eggs or embryos. If the eggs or embryos need to be discarded (no embryo transfer takes place), we (I) understand that we (I) are financially responsible for all charges resulting from our egg donation cycle, including fees for the donor, recipient and partner, up to and including the day the eggs or embryos are discarded.
- Implantation of the embryos into the wall of the uterus may not occur, even with the use of selective assisted hatching.

Laboratory. An event may occur in the laboratory resulting in loss or damage to some or all of the eggs or embryos. We (I) understand that assisted reproductive technologies involve the use of mechanical and/or electrical equipment. The Center will take reasonable measures to maintain and monitor this equipment. However, despite their best efforts, equipment failure may result in the damage or loss of one or more of our (my) sperm, eggs or embryos. We (I) understand and agree that The Center shall be responsible only for acts of negligence on its part and the part of its employees, contractors, and consultants. The program will account honestly for all gametes and embryos.

Pregnancy Loss. Although pregnancy may be successfully established, there is still the possibility of miscarriage, ectopic pregnancy, stillbirth and/or congenital abnormalities (birth defects). Conceptions resulting from IVF/ET) have been associated with a slightly higher risk of birth defects than pregnancies resulting from a natural conception. However, it is still unclear whether the risk is related to patients, medications, or laboratory procedures. It is possible that infertile couples differ from the general population, and it is not the technology that leads to the higher risk.

Risks

Risks to Egg Donor

Transvaginal Oocyte Maory

Oocyte retrieval is the removal of eggs from the ovary. A transvaginal ultrasound probe is used to visualize the ovaries and the egg-containing follicles within the ovaries. A long needle, which can be seen on ultrasound, can be guided into each follicle and the contents aspirated. The aspirated material includes follicular fluid, oocytes (eggs) and granulosa (egg-supporting) cells. Rarely, the ovaries are not accessible by the transvaginal route and laparoscopy or trans-abdominal retrieval is necessary. **Infection:** Bacteria normally present in the vagina may be inadvertently transferred into the abdominal cavity by the needle. These bacteria may cause an infection of the uterus, fallopian tubes, ovaries or other intra-abdominal organs. The estimated incidence of infection after egg 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. **Bleeding:** The needle passes through the vaginal wall and into the ovary to obtain the eggs. Both of these structures contain blood vessels. In addition, there are other blood vessels nearby. Small amounts of blood loss are common during egg retrievals. The

incidence of major bleeding problems has been estimated to be less than 0.1%. Major bleeding may require surgical repair and possibly loss of the ovary. The need for blood transfusion is rare. (Although very rare, review of the world experience with IVF indicates that unrecognized bleeding has led to death.) **Trauma:** Despite the use of ultrasound guidance, it is possible to damage other intra-abdominal organs during the egg retrieval. Previous reports in the medical literature have noted damage to the bowel, appendix, bladder, ureters, and ovary. 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 risk of such trauma is low. **Anesthesia:** The use of anesthesia during the egg retrieval can produce unintended complications such as an allergic reaction, low blood pressure, nausea or vomiting and in rare cases death.

Ovarian Hyperstimulation Syndrome (OHSS)

OHSS is an occasional outcome of ovarian stimulation. Its symptoms can include increased ovarian size, nausea and vomiting, accumulation of fluid in the abdomen, breathing difficulties, an increased concentration of red blood cells, kidney and liver problems, and in the most severe cases, blood clots, kidney failure, or death. The severe cases affect only a very small percentage of women who undergo in vitro fertilization—0.2 percent or less of all treatment cycles—and the very severe are an even smaller percentage. Only about 1.4 in 100,000 cycles has led to kidney failure, for example. OHSS occurs at two stages: early, 1 to 5 days after egg retrieval (as a result of the hCG trigger); and late, 10 to 15 days after retrieval (as a result of the hCG if pregnancy occurs). The risk of severe complications is about 4 to 12 times higher if pregnancy occurs which is why sometimes no embryo transfer is performed to reduce the possibility of this occurring.

Cancer

Many have worried that the use of fertility drugs could lead to an increased risk of cancer—in particular, breast, ovarian, and uterine (including endometrial) cancers. One must be careful in interpreting epidemiological studies of women taking fertility drugs, because all of these cancers are more common in women with infertility, so merely comparing women taking fertility drugs with women in the general population inevitably shows an increased incidence of cancer. When the analysis takes into account the increased cancer risk due to infertility per se, the evidence does not support a relationship between fertility drugs and an increased prevalence of breast or ovarian cancer. More research is required to examine what the long-term impact of fertility drugs may be on breast and ovarian cancer prevalence rates. For uterine cancer, the numbers are too small to achieve statistical significance, but it is at least possible that use of fertility drugs may indeed cause some increased risk of uterine cancer.

Risks to Egg Recipient

In vitro fertilization and embryo culture

- Sperm and eggs are placed together in specialized conditions (culture media, controlled temperature, humidity and light) to achieve fertilization.
- Culture medium is designed to permit normal fertilization and early embryo development, but the content of the medium is not standardized.
- Embryo development in the lab helps distinguish embryos with more potential from those with less or none.

After eggs are retrieved, they are transferred to the embryology laboratory where they are kept in conditions that support their needs and growth. The eggs are placed in small dishes or tubes containing "culture medium," which is special fluid developed to support development of the eggs and embryos made to resemble that found in the fallopian tube or uterus. The dishes containing the eggs are then placed into incubators, which control the temperature and atmospheric gasses the eggs and embryos experience.

A few hours after eggs are retrieved, sperm are placed in the culture medium with the eggs, or individual sperm are injected into each mature egg in a technique called Intracytoplasmic Sperm Injection (ICSI) (see below). The eggs are then returned to the incubator, where they remain to develop. Periodically, over the next few days, the dishes are inspected so the development of the embryos can be assessed.

The following day after eggs have been inseminated or injected with a single sperm (ICSI), they are examined for signs that the process of fertilization is underway. At this stage, normal development is evident by the still single cell having 2 nuclei; this stage is called a zygote or a 2PN embryo. Two days after insemination or ICSI, normal embryos have divided into about 4 cells. Three days after insemination or ICSI, normally developing embryos contain about 8 cells. Five days after insemination or ICSI, normally developing embryos have developed to the blastocyst stage, which is typified by an embryo that now has 80 or more cells, an inner fluid-filled cavity, and a small cluster of cells called the inner cell mass.

Embryo transfer

- After a few days of development, the best appearing embryos are selected for transfer.
- The number chosen influences the pregnancy rate and the multiple pregnancy rate.
- Embryos are placed in the uterine cavity with a thin tube.
- Excess embryos of sufficient quality that are not transferred can be frozen.

After a few days of development, one or more embryos are selected for transfer to the uterine cavity. Embryos are placed in the uterine cavity with a thin tube (catheter). Ultrasound guidance may be used to help guide the catheter or confirm placement through the cervix and into the uterine cavity. Although the possibility of a complication from the embryo transfer is very rare, risks include infection and loss of, or damage to, the embryos.

The number of embryos transferred influences the pregnancy rate and the multiple pregnancy rate. The age of the woman who provided the eggs, and the appearance of the developing embryo, have the greatest influence on pregnancy outcome and the chance for multiple pregnancy.

Hormonal support of the uterine lining

- Successful attachment of embryo(s) to the uterine lining depends on adequate hormonal support.
- Progesterone, given by the intramuscular or vaginal route, is routinely given for this purpose.

Successful attachment of embryos to the uterine lining (endometrium) depends on adequate hormonal support of the lining. The critical hormones in this support are progesterone and estradiol. Normally, the ovary makes sufficient amounts of both hormones. However, in IVF cycles, this support is not always adequate. Therefore, progesterone is routinely given, and in some cases, estradiol is also prescribed. Progesterone is given by the intramuscular or vaginal route. Estradiol is given by the oral, vaginal, trans-dermal or intramuscular route. The duration of this support is from 2 to 10 weeks.

Intracytoplasmic Sperm Injection (ICSI)

ICSI is associated with a slightly higher risk of birth defects. Whether any association is due to the ICSI procedure itself or to inherent sperm defects, however, has not been determined. The impact of ICSI on the intellectual and motor development of children has also been controversial, but recent studies have not detected any differences in the development of children born after ICSI, conventional IVF, or natural conception.

Certain genetic abnormalities have been shown to increase in IVF offspring. The prevalence of sex chromosome (X and Y) abnormalities in children conceived via ICSI is higher than observed in the general IVF population, but the difference between the two groups is small (0.8% to 1.0% in ICSI offspring vs. 0.2% in the general IVF population). Translocations (a re-arrangement of chromosomes that can cause miscarriage) may be more common in ICSI offspring (0.36%) than in the general population (0.07%). Although these differences might result from the ICSI procedure itself, men with abnormal semen analyses are more likely themselves to have chromosome abnormalities and may produce sperm with abnormal chromosomes. These abnormalities could be passed to their offspring.

Some men with extremely low or absent sperm counts have small deletions on their Y chromosome. When viable sperm can be obtained to fertilize eggs with ICSI, sperm containing a Y chromosomal microdeletion may result in male offspring who also carry the microdeletion and may be infertile.

Blastocyst culture

In some cases, one or more of the embryos may cease their development prior to reaching the blastocyst stage. This may result in fewer embryos for transfer and, in some cases, no embryo transfer at all. Higher rates of identical twinning are reported.

Assisted hatching

- Assisted Hatching involves making a hole in the outer shell (zona pellucida) that surrounds the embryo.
- Hatching may make it easier for embryos to escape from the shell that surrounds them.

The cells that make up the early embryo are enclosed within a flexible membrane (shell) called the zona pellucida. During normal development, a portion of this membrane dissolves, allowing the embryonic cells to escape or “hatch” out of the shell. Only upon hatching can the embryonic cells implant within the wall of the uterus to form a pregnancy.

Assisted hatching is the laboratory technique in which an embryologist makes an artificial opening in the shell of the embryo. The hatching is usually performed on the day of transfer, prior to loading the embryo into the transfer catheter. The opening can be made by mechanical means (slicing with a needle or burning the shell with a laser) or chemical means by dissolving a small hole in the shell with a dilute acid solution.

Some programs have incorporated artificial or “assisted hatching” into their treatment protocols because they believe it improves implantation rates, and ultimately, live birth rates although definitive evidence of this is lacking.

Risks that may be associated with assisted hatching include damage to the embryo resulting in loss of embryonic cells, or destruction or death of the embryo. Artificial manipulation of the zygote may increase the rates of monozygotic (identical) twinning which are significantly more complicated pregnancies. There may be other risks not yet known.

Cryopreservation

- Freezing of eggs and embryos can provide additional chances for pregnancy.
- Frozen eggs and embryos do not always survive the process of freezing and thawing.
- Ethical and legal dilemmas can arise when couples separate or divorce, especially for embryos. Disposition agreements are essential.
- It is the responsibility of each couple with frozen eggs and/or embryos to remain in contact with the clinic on an annual basis.

Freezing (or “cryopreservation”) of eggs or embryos is a common procedure. Since multiple eggs (oocytes) are produced during ovarian stimulation for egg donation, there are often more embryos available than are considered appropriate for transfer to the uterus. Such embryos can be frozen

for future use. Alternatively, some eggs can be frozen before being exposed to sperm. Both strategies save the expense and inconvenience of stimulation to obtain additional eggs in the future. Furthermore, the availability of cryopreservation permits patients to transfer fewer embryos during a fresh cycle, reducing the risk of high-order multiple gestations (triplets or greater). The pregnancy success rates for cryopreserved embryos transferred into the human uterus can vary from practice to practice. Overall pregnancy rates at the national level with frozen embryos are lower than with fresh embryos. This, at least in part, results from the routine selection of the best-looking embryos for fresh transfer, reserving the “second-best” for freezing. There is some evidence that pregnancy rates are similar when there is no such selection.

Indications:

- To reduce the risks of multiple gestation
- To increase the chance of having one or more pregnancies from a single cycle of egg donation

Risks of cryopreservation: There are several techniques for embryo cryopreservation, and research is ongoing. Traditional methods include “slow,” graduated freezing in a computerized setting, and “rapid” freezing methods, called “vitrification.” Current techniques deliver a high percentage of viable eggs and embryos thawed after cryopreservation, but there can be no certainty that eggs and embryos will thaw normally, nor be viable enough to divide and eventually implant in the uterus. Cryopreservation techniques could theoretically be injurious to the embryo. Extensive animal data (through several generations), and limited human data, do not indicate any likelihood that children born of embryos that have been cryopreserved and thawed will experience a greater risk of abnormalities than those born of fresh embryos. However, until very large numbers of children have been born following freezing and thawing of embryos, it is not possible to be certain that the rate of abnormalities is no different from the normal rate.

If you choose to freeze eggs or embryos, you MUST complete and notarize the Disposition for Eggs or Disposition for Embryos statement before freezing. This statement outlines the choices you have with regard to the disposition of embryos in a variety of situations that may arise. You are free to submit a statement at a later time indicating different choices, provided you both agree in writing. It is also incumbent upon you to remain in touch with the clinic regarding your residence, and to pay for storage charges as they come due.

Risks of pregnancy

Pregnancies that occur with IVF are associated with increased risks of certain conditions (see Table below from the Executive Summary of a National Institute of Child Health and Human Development Workshop held in September 2005, as reported in the *Journal of Obstetrics & Gynecology*, volume 109, number 4, pages 967 to 977 in 2007). Some of these risks stem from the higher average age of women pregnant by IVF and the fact that the underlying cause of infertility may be the cause of the increased risk of pregnancy complications. This was demonstrated in an Australian study that reviewed adverse obstetric and perinatal outcomes of sub-fertile women conceiving without ART (see same Table below). There may be additional risks related to the IVF procedure per se, but it is difficult to assign the relative contributions.

All of these studies have assessed the risk from autologous IVF, that is, in women using their own eggs, rather than donor eggs to conceive. It is unknown if these risks are reduced with the use of donor eggs. Importantly, the risk of miscarriage and birth defects like Down Syndrome or Turner Syndrome are related to the age of the egg donor and will be lower for most patients using donor eggs.

Multiple gestations, which account for 30% of IVF pregnancies, increase the risk of pregnancy complications. The most important maternal complications associated with multiple gestations are preterm labor and delivery, high blood pressure (pre-eclampsia or toxemia), and gestational diabetes.

Although embryos are transferred directly into the uterus with IVF, ectopic (tubal, cervical and abdominal) pregnancies have occurred either alone or concurrently with a normal intra-uterine pregnancy.

Potential Risks in Singleton IVF-conceived Pregnancies

	Absolute Risk (%) in IVF-conceived Pregnancies	Relative Risk (vs. non IVF-conceived Pregnancies in a control population)	Relative Risk of Non-IVF Infertile Patients (vs. control population)
Pre-eclampsia	10.3%	1.6 (1.2--2.0)	1.29 (1.02-1.61)
Placenta previa	2.4%	2.9 (1.5--5.4)	
Placental abruption	2.2%	2.4 (1.1--5.2)	
Gestational diabetes	6.8%	2.0 (1.4--3.0)	1.25 (0.96-1.63)
Cesarean delivery *	26.7%	2.1 (1.7--2.6)	1.56 (1.37-1.77)

In this table, the Absolute risk is the percent of IVF pregnancies in which the risk occurred. The Relative Risk is the risk in IVF versus the risk in non-IVF, non-infertile pregnancies. For example, a relative risk of 2.0 indicates that twice as many IVF pregnancies experience this risk as compared to non-IVF pregnancies. However, the third column indicates the increased risk of adverse outcome in infertile women conceiving without ART suggesting that being infertile increases the risk of adverse outcomes unrelated to ART/IVF. The numbers in parentheses (called the "Confidence Interval") indicate the range in which the actual Relative Risk lies.

* Please note that most experts believe the rate of Cesarean delivery to be well above the 26.7% rate quoted here.

Multiple gestations, which account for 30% of IVF pregnancies, increase the risk of pregnancy complications. The most important maternal complications associated with multiple gestations are preterm labor and delivery, pre-eclampsia, and gestational diabetes. Placenta previa (placenta extends over the cervical opening), vasa previa (one or more of the blood vessels extends over the cervical opening), and placental abruption (premature separation of the placenta) are also more common in multiple gestations. Postpartum hemorrhage may complicate 12% of multifetal deliveries. Having triplets or more increases the risk of more significant complications including post-partum hemorrhage and transfusion. Other complications of multiple gestations include gall bladder problems, skin problems, excess weight gain, anemia, excessive nausea and vomiting, and exacerbation of pregnancy-associated gastrointestinal symptoms.

Although embryos are transferred directly into the uterus with IVF, ectopic (tubal, cervical and abdominal) pregnancies have occurred either alone or concurrently with a normal intra-uterine pregnancy. These abnormal pregnancies oftentimes require medical treatments with methotrexate (a weak chemotherapy drug) or surgery to treat the abnormal pregnancy.

Age-related risk to recipient / carrier

Certain risks of pregnancy increase with age. Most common are high blood pressure, diabetes, bleeding while pregnant, and growth problems for the baby. Above 44 years of age, it is prudent to have a consultation and full medical evaluation before becoming pregnant. This may involve both an internist and a high-risk obstetrician.

Risks to Offspring

- IVF babies seem to be at a slight increased risk for birth defects.

- The risk for a multiple pregnancy is significantly higher for patients undergoing IVF, even when only one embryo is transferred.
- Multiple pregnancies are the greatest risk for babies following IVF.
- Some risk may also stem from the underlying infertile state, or from the IVF techniques, or both.

Overall risks

Since the first birth of an IVF baby in 1978, more than 4 million children have been born worldwide following IVF treatments. Numerous studies have been conducted to assess the overall health of IVF children and the majority of studies on the safety of IVF have been reassuring. A major problem in interpreting the data arises from the fact that comparing a group of infertile couples to a group of normally fertile couples is not the proper comparison to make if one wants to assess the risk that IVF technology engenders. Infertile couples, by definition, do not have normal reproductive function and might be expected to have babies with more abnormalities than a group of normally fertile couples. This said, even if the studies suggesting an increased risk to babies born after IVF prove to be true, the absolute risk of any abnormal outcome appears to be small.

Birth defects

The risk of birth defects in the normal population is 2-3 %. In IVF babies the birth defect rate may be 2.6-3.9%, an increase of about 30%. Some of this risk is due to delayed conception, and some may be due to the underlying infertility issues. The risk is largely confined to singleton births. Studies to date have not been large enough to prove a link between IVF treatment and specific types of birth defects.

Childhood cancers. Most studies have not reported an increased risk with the exception of a retinoblastoma, a rare eye tumor.

Infant Development. In general, studies of long-term developmental outcomes have been reassuring so far; most children are doing well. However, these studies are difficult to do and suffer from limitations. A more recent study with better methodology reports an increased risk of cerebral palsy (3.7 fold) and developmental delay (4 fold), but most of this stemmed from the prematurity and low birth weight that was a consequence of multiple pregnancy.

Risks of a multiple pregnancy

Currently more than 30% of IVF pregnancies are twins or higher-order multiple gestations (triplets or greater), and about half of all IVF babies are a result of multiple gestations. Identical twinning occurs in 1.5% to 4.5% of IVF pregnancies.

Premature delivery accounts for most of the risk. Twins deliver on average three weeks earlier and weigh 1,000 gm less than singletons. Triplet (and greater) pregnancies deliver before 32 weeks (7 months) in almost half of cases. Fetal death rates for singleton, twin, and triplet pregnancies are 4.3 per 1,000, 15.5 per 1,000, and 21 per 1,000, respectively.

Long-term consequences of prematurity can include cerebral palsy, vision problems, and lung disease. At mid-childhood, prematurely born offspring from multiple gestations have lower IQ scores, and multiple birth children have an increase in behavioral problems compared with singletons. It is not clear to what extent these risks are affected by IVF per se.

The Option of Multifetal Pregnancy Reduction: The greater the number of fetuses within the uterus, the greater is the risk for adverse perinatal and maternal outcomes. Patients with more than twins are faced with the options of continuing the pregnancy with all risks previously described, terminating the entire pregnancy, or undergoing a procedure called multifetal pregnancy reduction. By reducing the number of fetuses, multifetal pregnancy reduction decreases some of these risks.

Risks to Intended Parents

Ethical and religious considerations in infertility treatment

Infertility treatment can raise concerns and questions of an ethical or religious nature for some patients. The technique of in vitro fertilization (IVF) involves the creation of human embryos outside the body, and can involve the production of excess embryos and/or “high-order” multiple pregnancy (triplets or more). We encourage patients and their spouses or partners who so desire to consult with trusted members of their religious or ethics community for guidance on their infertility treatment.

Psychosocial effects of infertility treatment

A diagnosis of infertility can be a devastating and life-altering event that impacts many aspects of a patient’s life. Infertility and its treatment can affect a patient and her spouse or partner medically, financially, socially, emotionally and psychologically. Feelings of anxiousness, depression, isolation, and helplessness are not uncommon among patients undergoing infertility treatment. Strained and stressful relations with spouses, partners, and other loved ones are not uncommon as treatment gets underway and progresses.

Our health care team is available to address the emotional, as well as physical symptoms that can accompany infertility. In addition to working with our health care team to minimize the emotional impacts of infertility treatments, patients may also consider working with mental health professionals who are specially trained in the area of infertility care.

While it is normal to experience emotional ups and downs when pursuing infertility treatment, it is important to recognize when these feelings are of a severe nature. If you experience any of the following symptoms over a prolonged period of time, you may benefit from working with a mental health professional:

- Loss of interest in usual activities
- Depression that doesn't lift
- Strained interpersonal relationships (with partner, family, friends and/or colleagues)
- Difficulty thinking of anything other than your infertility
- High levels of anxiety
- Diminished ability to accomplish tasks
- Difficulty with concentration
- Change in your sleep patterns (difficulty falling asleep or staying asleep, early morning awakening, sleeping more than usual for you)
- Change in your appetite or weight (increase or decrease)
- Increased use of drugs or alcohol
- Thoughts about death or suicide
- Social isolation
- Persistent feelings of pessimism, guilt, or worthlessness
- Persistent feelings of bitterness or anger

Our health care team can assist you in locating a qualified mental health professional who is familiar with the emotional experience of infertility, or you can contact a national support group such as RESOLVE, (www.resolve.org, Tel. 1-888-623-0744) or The American Fertility Association (AFA), (www.theafa.org, Tel: 1-888-917-3777).

Insurance coverage for any or all of the above procedures may not be available and we (I) will be personally responsible for all expenses of this treatment that are not covered by insurance.

Further Information

General IVF overviews

<http://www.sart.org/>

<http://www.cdc.gov/art/>

<http://www.resolve.org/site/PageServer>

Number of embryos to transfer

Guidelines on number of embryos transferred. The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology. *Fertil Steril* 2006; 86 (suppl 4): S51-S52.

Culturing embryos to the blastocyst stage

Blastocyst culture and transfer in clinical-assisted reproduction. The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology. *Fertil Steril* 2006; 86 (suppl 4): S89-S92.

Intracytoplasmic sperm injection

Genetic considerations related to intracytoplasmic sperm injection (ICSI). The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology. *Fertil Steril* 2006; 86 (suppl 4): S103-S105.

Embryo hatching

The role of assisted hatching in in vitro fertilization: a review of the literature. A Committee opinion. The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology. *Fertil Steril* 2006; 86 (suppl. 4): S124-S126.

Ovarian hyperstimulation

Ovarian hyperstimulation syndrome. The Practice Committee of the American Society for Reproductive Medicine. *Fertil Steril* 2006; 86 (suppl 4): S178-S183.

Risks of pregnancy

Infertility, assisted reproductive technology, and adverse pregnancy outcomes. Executive Summary of a National Institute of Child Health and Human Development Workshop. Reddy UM, Wapner RJ, Rebar RW, Tasca RJ. *Obstet Gynecol* 2007; 109(4):967-77.

Risks to offspring

Infertility, assisted reproductive technology, and adverse pregnancy outcomes. Executive Summary of a National Institute of Child Health and Human Development Workshop. Reddy UM, Wapner RJ, Rebar RW, Tasca RJ. *Obstet Gynecol* 2007; 109(4):967-77.

Multiple pregnancy associated with infertility therapy. The Practice Committee of the American Society for Reproductive Medicine *Fertil Steril* 2006; 86 (suppl 4): S106-S110.

Imprinting diseases and IVF: A Danish national IVF cohort study. Lidegaard O, Pinborg A and Anderson AN. Human Reproduction 2005; 20(4):950-954.

Infertility, infertility treatment, and congenital malformations: Danish national birth cohort. Zhu JL, Basso O, Obel C, Bille C, Olsen. BMJ, doi:10.1136/bmj.38919.495718.AE(published 7 August 2006).

Bergh C, Wennerholm U-B. Obstetric outcome and long-term follow up of children conceived through assisted reproduction. Best Practice & Research Clinical Obstetrics and Gynaecology (2012), doi:10.1016/j.bpobgyn.2012.05.001.

Davies MJ, Moore VM, Willson KJ, Van Essen P, Priest K, Scott H, Haan EA, Chan A. Reproductive Technologies and the risk of birth defects. N Engl J Med 2012;366:1803-13. Doi:10.1056/NEJMoa1008095).

We (I), expect this procedure to be performed with not less than the customary standard of care. We (I) understand the risks and benefits as outlined.

We (I) have had the opportunity to review this treatment and ask questions of our (my) physician concerning the alternative options to utilization of donated eggs, including adoption and no treatment. The full egg donation process has been explained to us (me), together with the known risks. We (I) understand the explanation that has been given to us. We (I) have had the opportunity to ask any questions we (I) might have and those questions have been answered to our (my) satisfaction. Any further questions may be addressed to the **CENTER** staff or **Dr. tamer Yalcinkaya at (336) 448-9100**. We (I) acknowledge that utilization of donated eggs is being performed at our (my) request and with our (my) consent.

We (I), the undersigned, request, authorize and consent to the **utilization of donated eggs** by the **CENTER**, and as appropriate, its employees, contractors, and consultants and authorized agents for the purpose of achieving a pregnancy.

We (I) understand that there are other options available to us to help us have a child. These may include adoption or treatments including such techniques as surgery, ovulation induction, in vitro fertilization and sperm donation. We (I) have had the opportunity to discuss these options, as well as others with our (my) physician. In an attempt to have a child, we (I) now elect to utilize donated eggs donated at (or transferred to) the **CENTER**.

<p>X _____ Patient Signature</p> <p>_____</p> <p>Patient Name</p>	<p>_____</p> <p>Date</p> <p>_____</p> <p>Date of Birth</p>	
<p>Notary Public Sworn and subscribed before me on this ____ day of _____, _____.</p>		
<p>_____</p> <p>Notary Signature</p>	<p>_____</p> <p>Date</p>	
<p>X _____</p> <p>Spouse / Partner Signature (if applicable)</p> <p>_____</p> <p>Spouse / Partner Name</p>		<p>_____</p> <p>Date</p> <p>_____</p> <p>Date of Birth</p>
<p>Notary Public Sworn and subscribed before me on this ____ day of _____, _____.</p>		
<p>_____</p> <p>Notary Signature</p>	<p>_____</p> <p>Date</p>	

Egg Recipient Treatment Plan

Patient name: _____

Spouse / partner name: _____

Provider of Eggs.

We (I) plan to use eggs from:

- Anonymous Egg Donor:** The Donor # _____ has been screened and determined to be eligible as a donor by ACRM. We (I) have reviewed the Donor’s profile and accept her as our (my) donor. Her identity will remain anonymous.

- Known Egg Donor:** We (I) only accept eggs donated by the woman listed below:
Donor Name: _____

Provider of Sperm.

We (I) plan to use sperm from:

- Spouse / partner
- Donor (specify name or number): _____
- Other (specify arrangement): _____

Initials: _____ / _____

Initials: _____ / _____

Carrier of embryos.

We (I) plan to transfer the embryos into:

- Me, the intended parent
- A Gestational Carrier
 ----if known, her name: _____

Initials: _____ / _____

Method of Insemination.

We (I) acknowledge that we (I) have discussed the possibility of the need for ICSI with our (my)

physician and understand, agree and consent that:

Regarding the number of eggs to expose to sperm, we (I) choose:

- ICSI **will be** used.
 Inseminate ALL Mature Eggs
- ICSI **will not** be used.
 Inseminate SOME Mature Eggs
- ICSI **will not** be used, unless the semen at time of egg retrieval is sub-optimal based on the best medical judgment of ACRM staff, or if the initial fertilization is poor. In these cases, ICSI may be used.
 Factor of number of eggs to be inseminated: _____

We (I) understand that we (I) will be notified if ICSI is performed.

Limit on Number Inseminated?

Initials: _____ / _____

Plan for Eggs NOT Inseminated (if applicable).

Regarding the eggs not exposed to sperm for fertilization, we (I) choose:

- Freeze for my later use (requires Disposition Declaration)
- Donate to:
- Research
 - Another person or couple
- Discard. This disposal will follow ASRM Ethical Guidelines. These extra eggs will no longer be available for attempting a pregnancy.

Initials: _____ / _____

Plan for Embryos NOT Transferred.

Regarding the disposition of embryos not transferred, we (I) elect the following option:

- Freeze Excess Embryos** (requires Disposition Declaration)

- Donate Excess Embryos to:**
 - Research
 - Another person or couple

- Discard Excess Embryos.** This disposal will follow ASRM Ethical Guidelines. These extra embryos will no longer be available for attempting a pregnancy.

Initials: _____ / _____

Plan for Preimplantation Genetic Testing / Screening.

We (I) choose:

- No genetic testing / screening of embryos**
- Genetic testing of all blastocysts no matter how few are available**
- Genetic testing of all blastocysts if enough are available to test** (in consultation with embryology lab staff staff).

Patient signature: _____ **Date:** _____

Partner / spouse signature: _____ **Date:** _____

CFI Staff signature: _____