
InVia Fertility Specialists

Informed Consent for Assisted Reproduction:

*In Vitro Fertilization,
Intracytoplasmic Sperm Injection
Assisted Hatching
Embryo Freezing*

OVERVIEW

In Vitro Fertilization (IVF) has become an established treatment for many forms of infertility. The main goal of IVF is to allow a patient the opportunity to become pregnant using her own eggs 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.

This consent reviews the IVF process from start to finish, including the risks that this treatment might pose to you and your offspring. While best efforts have been made to disclose all known risks, there may be risks of IVF which are not yet clarified or even suspected at the time of this writing.

An IVF cycle typically includes the following steps or procedures:

- Medications to grow multiple eggs
- Retrieval of eggs from the ovary or ovaries
- Insemination of eggs with sperm
- Culture (continued growth) of any resulting fertilized eggs (embryos)
- Placement ("transfer") of one or more embryo(s) into the uterus
- Support of the uterine lining with hormones to permit and sustain a pregnancy

In certain cases, these additional procedures may be employed:

- Intracytoplasmic sperm injection (ICSI) to increase the chance for fertilization
- Assisted hatching of embryos to increase the chance of embryo attachment ("implantation")
- Embryo Cryopreservation (freezing)

Outline of Consent for IVF

- A. Technique of In Vitro Fertilization
 - 1. Core elements and their risk
 - a. medications
 - b. transvaginal oocyte retrieval
 - c. in vitro fertilization and development
 - d. embryo transfer
 - e. luteal support
 - 2. Additional elements and their risk
 - a. Intracytoplasmic sperm injection
 - b. embryo hatching
 - c. embryo cryopreservation
 - d. cryopreserved embryo disposition and storage
 - B. Risks to the woman
 - 1. ovarian hyperstimulation syndrome
 - 2. risks of pregnancy
 - C. Risks to offspring
 - 1. overall risks
 - 2. birth defects
 - 3. multiple pregnancy
 - D. Ethical / religious concerns
 - E. Psychosocial effects
 - F. Legal considerations and legal counseling
 - G. Alternatives to IVF
 - H. Reporting outcomes
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Please initial each page to indicate that you have read and understood the information provided. If you do not understand the information provided, please speak with your treating physician. There are a few locations within the consent form where you are being asked to make a decision. Please initial your choice and sign where requested. Your signatures must be witnessed by either a notary or by an InVia Associate at the time of your nurse consult.

A. Technique of IVF

1. Core elements and their risk

a. Medications for IVF Treatment

- The success of IVF largely depends on growing multiple eggs at once
- Injections of the natural hormones FSH and/or LH (gonadotropins) are used for this purpose
- Additional medications are used to prevent premature ovulation
- An overly vigorous ovarian response can occur, or conversely an inadequate response

Medications may include the following (not a complete list):

Gonadotropins, or injectable "fertility drugs" (Follistim®, Gonal-F®, Repronex®, Bravelle®, Menopur®, Luveris®): These natural hormones stimulate the ovary in hopes of inducing the simultaneous growth of several oocytes (eggs) over the span of several days. These fertility drugs contain FSH (follicle stimulating hormone), LH (luteinizing hormone), or both. Some of these medications (i.e. hCG) contain LH-like activity. These hormones stimulate the growth of ovarian follicles (which contain the eggs). These medications are given by subcutaneous or intramuscular injection. Proper dosage of these drugs and the timing of egg recovery require monitoring of the ovarian response, usually by way of blood tests and ultrasound examinations during the ovarian stimulation.

As with all injectable medications, bruising, redness, swelling, or discomfort can occur at the injection site. Rarely, there can be an allergic reaction to these drugs. The intent of giving these medications is to mature multiple follicles, and many women experience some bloating and minor discomfort as the follicles grow and the ovaries become temporarily enlarged. Up to 2.0 % of women will develop Ovarian Hyperstimulation Syndrome (OHSS) [see full discussion of OHSS in the Risks to Women section which follows]. Other risks and side effects of gonadotropins include, but are not limited to, fatigue, headaches, weight gain, mood swings, nausea, and clots in blood vessels.

Even with pre-treatment attempts to assess response, and even more so with abnormal pre-treatment evaluations of ovarian reserve, the stimulation may result in very few follicles developing. The end result may be that few or no eggs are obtained at egg retrieval. Cancellation of the treatment cycle prior to egg retrieval may also occur.

Some older research suggested that the risk of ovarian tumors is increased in women who take any fertility drugs over a long period of time. These studies had significant flaws which limited the strength of the conclusions. More recent studies have not confirmed this risk. A major

risk factor for ovarian cancer is infertility per se, suggesting that the early reports may have falsely attributed the risk resulting from infertility to taking medications used to overcome it. In these studies, conception lowered the risk of ovarian tumors to that of fertile women. Put another way, women with infertility who ultimately conceived experienced no higher risk for the development of ovarian tumors than women who never experienced infertility.

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.

GnRH-agonists (Leuprolide acetate) (Lupron®): This medication is taken by injection. There are two forms of the medication: A short acting medication requiring daily injections and a long-acting preparation lasting for 1-3 months. The primary role of this medication is to prevent a premature LH surge, which could result in the release of eggs before they are ready to be retrieved. Since GnRH-agonists initially cause a release of FSH and LH from the pituitary, they can also be used to start the growth of the follicles or initiate the final stages of egg maturation. Though leuprolide acetate is an FDA (Federal Drug Administration) approved medication. It has not been approved for use in IVF, although it has routinely been used in this way for more than 20 years. Potential side effects usually experienced with long-term use include but are not limited to hot flashes, vaginal dryness, bone loss, nausea, vomiting, skin reactions at the injection site, fluid retention, muscle aches, headaches, and depression. No long term or serious side effects are known. Since GnRH-agonists are oftentimes administered after ovulation, it is possible that they will be taken early in pregnancy. The safest course of action is to use a barrier method of contraception (condoms) the month you will be starting the GnRH-agonist. If your cycle involves pretreatment with birth control pills, there is no need to use barrier contraception during the GnRH-agonist portion of the treatment. GnRH-agonists have not been associated with any fetal malformations. Nevertheless, you should discontinue use of this medication as soon as pregnancy is confirmed.

GnRH-antagonists (Ganirelix Acetate or Cetrorelix Acetate) (Antagon®, Cetrotide®): These are another class of medications used to prevent premature ovulation. They tend to be used for short periods of time in the late stages of ovarian stimulation. The potential side effects include, but are not limited to, abdominal pain, headaches, skin reaction at the injection site, and nausea.

Human chorionic gonadotropin (hCG) (Profasi®, Novarel®, Pregnyl®, Ovidrel®): hCG is a hormone used in IVF to induce the eggs to become mature and fertilizable. The timing of this medication is critical to retrieve mature eggs. Potential side effects include, but are not limited to breast tenderness, bloating, and pelvic discomfort.

Progesterone: Progesterone is a hormone normally produced by the ovaries after ovulation. After egg retrieval, the ovaries often will not produce adequate amounts of this hormone for long enough to fully support a pregnancy. Accordingly, supplemental progesterone is given to ensure adequate hormonal support of the uterine lining. Progesterone is usually given by injection or by the vaginal route (Endometrin®, Crinone®, Prochieve®, Prometrium®, or pharmacist-compounded suppositories) after egg retrieval. Progesterone is often continued for some weeks after a pregnancy has been confirmed. Progesterone has not been associated with an increase in fetal abnormalities. Side effects of progesterone include depression, sleepiness, allergic reactions and if given by intra-muscular injection include the additional risk of infection and/or pain at the injection site.

Oral contraceptive pills or the vaginal contraceptive ring: Many treatment protocols include oral contraceptive pills to be taken for 10 days or more before gonadotropin injections are started in order to suppress hormone production or to schedule a cycle. Side effects include unscheduled bleeding, headache, breast tenderness, nausea, swelling and the risk of blood clots or stroke.

Other medications: Antibiotics may be given for a short time during the treatment cycle to reduce the risk of infection associated with egg retrieval or embryo transfer. Antibiotic use may be associated with yeast infections, nausea, vomiting, diarrhea, rashes, sensitivity to the sun, and allergic reactions. Other medications such as steroids, heparin, low molecular weight heparin or aspirin may also be included in the treatment protocol.

b. Transvaginal Oocyte Retrieval

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

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 the procedure cannot be completed. Anesthesia is generally used to reduce if not eliminate discomfort. Risks of egg retrieval include:

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% (1 in 200). Treatment of infections could require the use of oral or intravenous antibiotics. On rare occasions, severe infections may require surgery to remove the infected tissue. Infections can have a negative impact on future fertility. Prophylactic antibiotics are often administered before the egg retrieval procedure to reduce the risk of pelvic or abdominal infection. Despite the use of antibiotics, there is no way to eliminate this risk completely.

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% (1 out of every 1,000 procedures). Major bleeding may require surgical repair and possibly loss of the ovary. The need for blood transfusion is rare.

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. 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.

Failure: It is possible that the aspiration will fail to obtain any eggs or the eggs may be abnormal or of poor quality and otherwise fail to produce a viable pregnancy.

c. 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 media are designed to permit normal fertilization and early embryo development
- Embryo development in the lab helps distinguish embryos with more potential for implantation from those with less or none

After the eggs are retrieved, they are transferred to the embryology laboratory where they are kept in conditions that support their needs and growth. The embryos are placed in small dishes or tubes containing "culture medium," which is special fluid developed to support the embryos. The dishes containing the embryos are then placed into incubators, which control the temperature and atmospheric gases to which the embryos are exposed.

A few hours after the eggs are retrieved, sperm is 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. Periodically over the next few days, the dishes are inspected for fertilization and development.

It is important to note that since many eggs and embryos are abnormal, it is expected that not all eggs will fertilize and not all embryos will divide at a normal rate. The chance that a developing embryo will produce a pregnancy is related to whether its development in the lab is normal, but this correlation is not perfect. This means that not all embryos developing at the normal rate are in fact also genetically normal, and not all poorly developing embryos are genetically abnormal. Nonetheless, their visual appearance is the most common and useful guide in the selection of the best embryo(s) for transfer.

In spite of reasonable precautions, any of the following may occur in the lab that would prevent the establishment of a pregnancy:

- Fertilization of the egg(s) may fail to occur.
- One or more eggs may be fertilized abnormally. These abnormal embryos will not be transferred.
- The fertilized eggs may degenerate before dividing into embryos, or adequate embryonic development may fail to occur.
- Bacterial contamination or a laboratory accident may result in loss or damage to some or all of the eggs or embryos.
- Laboratory equipment may fail, and/or extended power losses can occur which could lead to the destruction of eggs, sperm and embryos.
- Other unforeseen circumstances may prevent any step of the procedure from being performed or prevent the establishment of a pregnancy.
- Tornadoes, floods, or other 'acts of nature' beyond InVia Fertility Specialists' control, as well as bombings or other terrorist acts beyond its control, could destroy the laboratory or its contents, including any sperm, eggs, or embryos being stored there.

d. Embryo transfer

- After a few days of development, the highest quality embryos are selected for transfer
- The number chosen influences the pregnancy rate and the multiple pregnancy rate
- A woman's age and the appearance of the developing embryos are the best predictors of pregnancy outcome
- Embryos are placed in the uterine cavity with a thin catheter
- 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 using a thin 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 both the pregnancy rate and the multiple pregnancy rate. The age of the woman and the appearance of the developing embryo have the greatest influence on pregnancy outcome and the chance for multiple pregnancy. While it is possible, it is unusual to develop more fetuses than the number of embryos transferred. On rare occasions, an embryo may split, leading to the development of identical twins. It is critical to discuss the number of embryos to be transferred before the transfer is done.

e. 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 implantation of embryos within the uterus depends in part on adequate hormonal support of the lining. Progesterone is a critical hormone required to support the uterine lining. Normally, the ovary makes sufficient amounts of progesterone to support a pregnancy. However, in IVF cycles, this support is not always adequate. Therefore, progesterone is routinely given following retrieval of the eggs. Progesterone is given by the intramuscular or vaginal route. It is generally discontinued before the end of the first trimester of pregnancy.

2. Additional elements and their risk

a. Intracytoplasmic Sperm Injection (ICSI)

ICSI is used to increase the chances of fertilization when fertilization rates may be compromised due to:

- Low sperm counts
- Decreased sperm motility
- Previously failed fertilization using natural insemination

ICSI may also be used on a portion of the eggs to decrease the possibility of failed fertilization.

ICSI is a procedure used to increase the likelihood of fertilization in couples presenting with male factor infertility, unexplained infertility, and/or previous failed fertilization. ICSI involves the injection of a single sperm directly into a mature egg after oocyte retrieval in an IVF cycle. While ICSI does increase the likelihood of fertilization in some cases, there is no guarantee that fertilization will occur. There is a small risk that one or more of the eggs may be damaged by the procedure.

Reports on the risk of birth defects associated with ICSI (as compared to conventional IVF) have yielded conflicting results. The most comprehensive study to date, based on data from five-year-old children, has suggested that ICSI is associated with a slightly increased risk of congenital malformations. Whether this increase in risk is due to the ICSI procedure itself, or inherent defects with the sperm, could not be determined as the study did not distinguish between male factor conditions and other causes of infertility. It should be noted that the risk in ICSI patients is still relatively low. The overall risk of birth defects in a naturally conceived pregnancy is 3%. In patients utilizing ICSI for fertilization, this incidence may rise to 4.2%.

b. Assisted Hatching

- Assisted Hatching involves thinning the outer shell (zona pellucida) that surrounds the embryo
- Hatching may make it easier for embryos to escape from the shell which 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 is made by mechanical means utilizing a laser.

For some patients, "assisted hatching" is believed to improve pregnancy success rates. To date, definitive evidence of this is lacking. Normally, embryos will "hatch" on their own between days 5 and 7 of development.

Risks that may be associated with assisted hatching include damage to the embryo resulting in loss of embryonic cells, or destruction of the embryo. Artificial manipulation of the embryo may increase the

rates of monozygotic (identical) twinning which lead to significantly more complicated pregnancies. There may be other unknown risks associated with assisted hatching.

c. Embryo cryopreservation

- Freezing of viable embryos not transferred after egg retrieval provides additional chances for pregnancy
- Frozen embryos do not always survive the process of freezing and thawing
- Ethical and legal dilemmas can arise when couples separate or divorce, such that disposition agreements are essential
- It is the responsibility of each couple with frozen embryos to remain in contact with the clinic and update the clinic regarding any change in their marital status or a change in their decisions regarding embryo disposition

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. 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). Other possible reasons for cryopreservation of embryos include freezing all embryos in the initial cycle to prevent severe ovarian hyperstimulation syndrome (OHSS), or if a couple were concerned that their future fertility potential might be reduced due to necessary medical treatment (e.g., cancer therapy or surgery).

Indications:

- To reduce the risks of multiple gestation
- To preserve fertility potential in the face of certain necessary medical procedures
- To increase the chance of having one or more pregnancies from a single cycle of ovarian stimulation
- To minimize the medical risk and cost to the patient by decreasing the number of stimulated cycles and egg retrievals
- To temporarily delay pregnancy and the risk of OHSS occurring by freezing all embryos, when this risk is high

Risks of embryo 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 embryos thawed after cryopreservation, but there can be no certainty that embryos will thaw normally, nor be viable enough to divide and eventually implant in the uterus. Cryopreservation techniques could theoretically injure 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 for 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.

CHOICE A: We agree and consent to cryopreservation and, therefore, we are obligated to choose one of the options as stated below:

AGREEMENT AND CONSENT:

- We hereby give consent for the cryopreservation of extra embryos resulting from assisted reproductive technology procedures.
- We request that these embryos be stored for subsequent transfer to the female partner's uterus or other such use as is permitted by this consent.
- We understand that embryos not claimed by us within (3) years after the date of cryopreservation may be disposed of in an ethically acceptable manner.
- We acknowledge that we are financially responsible for the freezing and storage of these embryos and, should we fail to keep this financial account current, the embryos will be disposed of in an ethically acceptable manner with prior written notice to us. We agree to disclose such information as is required to determine our financial status and ability to pay for cryopreservation.
- We understand that the fees associated with the cryopreservation of embryos and the storage of these embryos are usually not a covered benefit by most insurance companies and will therefore be our responsibility.
- We understand that delinquent accounts may be turned over to an attorney or collection agency for collection of delinquent amounts.
- We acknowledge it is our responsibility to notify InVia Fertility Specialists of any change of address.

I understand that if this is my choice and I have embryos in excess of the number that is designated to be returned to the female patient's uterus, that these embryos will be cryopreserved. I acknowledge that I have received information regarding the approximate cost of such cryopreservation and I am aware that such costs are estimates and may increase at any time. I accept and acknowledge financial responsibility for the freezing and storage fees of any/all excess embryos.

Option #1: Have sperm added to ALL retrieved oocytes in an attempt to achieve fertilization. We agree to cryopreserve any excess embryos.

Option #2: Have sperm only added to 12 oocytes maximum in an attempt to try and avoid creating excess embryos after an embryo transfer. We agree to cryopreserve any excess embryos.

We have chosen to cryopreserve - (initial the option you both agree to):

____ Option #1: Attempt to fertilize ALL retrieved oocytes.
Female Partner

____ Option #2: Attempt to fertilize up to 12 oocytes.
Female Partner

CHOICE B: We do NOT agree or consent to cryopreservation for our own use, but would like excess embryos donated to research. Please initial the option you have chosen.

____ Option #1: Donate to research. There will be no storage or freezing fee if
Female Partner option is chosen.

CHOICE C: We do NOT agree or consent to cryopreservation and therefore we have to choose one of the options as stated below. Please initial the option you have chosen.

Female _____
Partner **Option #1:** Have sperm added to all oocytes in an attempt to achieve fertilization. If there are any excess embryos after my embryo transfer, I agree to allow InVia Fertility Specialists to discard these embryos according to InVia Fertility Specialists' guidelines in an ethical manner.

Female _____
Partner **Option #2:** Have sperm added to only 12 oocytes in an attempt to achieve fertilization. If there are any excess embryos after my embryo transfer, I agree to allow InVia Fertility Specialists to discard these embryos according to InVia Fertility Specialists' guidelines in an ethical manner.

Female _____
Partner **Option #3:** Have sperm added to _____ oocytes (MAXIMUM 6) and then transfer ALL viable embryos to the woman's uterus per InVia Fertility Specialists' guidelines

In the event a situation occurs (medical, weather, family emergency), in which a transfer cannot be performed, and we have elected not to cryopreserve excess embryos initially, we choose to:

Female _____
Partner **Option #1:** Cryopreserve ALL embryos for use in a future frozen embryo transfer cycle. In this case, the usual and customary cryopreservation costs will apply.

Female _____
Partner **Option #2:** Discard all embryos according to InVia Fertility Specialists' guidelines in an ethical manner

Female _____
Partner **Option #3:** Donate the embryos to InVia Fertility Specialists for RESEARCH according to center guidelines.

Female _____
Partner **Option #4:** Donate the embryos to InVia Fertility Specialists' anonymous Embryo Donation Program.

Because of the possibility of you and/or your partner's separation, death or incapacitation, it is important to decide on the disposition of any embryo(s), fresh or cryopreserved, that remain in the laboratory. Since this is a rapidly evolving field, both medically and legally, the clinic cannot guarantee what the available or acceptable avenues for disposition will be at any future date. At the present time, the alternatives are:

- 1) Continuing to store the cryopreserved embryo(s) in the lab.
- 2) Discarding the cryopreserved embryo(s)
- 3) Donating the cryopreserved embryo(s) for research
- 4) Donating qualified cryopreserved embryos anonymously to InVia Fertility Specialists for use by another couple. In such cases, the identity of the donating and receiving couples will not be disclosed to one another. (You will be required to undergo additional infectious disease testing and screening recommended by the FDA if you select this option. You will also be asked to complete additional paperwork.) Please

Initials: Patient _____ Partner (if applicable) _____

note that if your embryos do not qualify for anonymous donation, you will be asked to choose another option.

Embryos are understood to be your property, with rights of survivorship. No use can be made of these embryos without the consent of both partners (if applicable).

In the event of divorce, and embryos remain in storage, we elect the following option (please initial):

- | | | | |
|--------|---------|-------------------|---|
| _____ | _____ | Option #1: | Embryos will become the property of the female partner. She will have sole custody and make all decisions regarding embryo disposition. |
| Female | Partner | | |
| _____ | _____ | Option #2: | Embryos will become property of the female's partner. He will have sole custody and make all decisions regarding embryo disposition. |
| Female | Partner | | |
| _____ | _____ | Option #3: | Disposal of all existing embryos according to InVia Fertility Specialists' center guidelines. |
| Female | Partner | | |
| _____ | _____ | Option #4: | Embryos are to be donated to InVia Fertility Specialists for research according to the center guidelines. |
| Female | Partner | | |

In the event that one of us dies, and embryos remain in storage, we elect the following option (please initial):

- | | | | |
|--------|---------|-------------------|--|
| _____ | _____ | Option #1: | Embryos will become property of the surviving partner. The surviving partner will have sole custody and make all decisions regarding the disposition of embryos. |
| Female | Partner | | |
| _____ | _____ | Option #2: | Disposal of existing embryos according to InVia Fertility Specialists' center guidelines. |
| Female | Partner | | |
| _____ | _____ | Option #3: | Embryos are to be donated to InVia Fertility Specialists for research according to the center guidelines. |
| Female | Partner | | |

In the event that both of us die, and embryos remain in storage, we elect the following option (please initial):

- | | | | |
|--------|---------|-------------------|---|
| _____ | _____ | Option #1: | Disposal of existing embryos according to InVia Fertility Specialists center guidelines. |
| Female | Partner | | |
| _____ | _____ | Option #2: | Donation of the embryos to InVia Fertility Specialists for research according to the center guidelines. |
| Female | Partner | | |

d. Cryopreserved embryo storage

The Clinic will only maintain cryopreserved embryos for a period of 3 years. After that time, any cryopreserved embryos must be:

- 1) thawed and transferred
- 2) donated to another couple
- 3) donated to research
- 4) discarded or
- 5) transferred to another storage facility

If continued storage of the embryos is desired beyond the initial 3 year period, this consent form must be updated and resigned.

Additionally, maintaining embryo(s) in a frozen state is labor intensive and expensive. There are fees associated with freezing and maintaining cryopreserved embryo(s). Patients/couples who have frozen embryo(s) must remain in contact with the clinic on a regular basis in order to inform the clinic of their wishes as well as to pay fees associated with the storage of their embryo(s). In situations where there is no contact with the clinic for a period of 1 year or fees associated with embryo storage have not been paid for a period of 1 year and the clinic is unable to contact the patient after reasonable efforts have been made, the embryo(s) will be considered to be abandoned and may be discarded by the clinic in accordance with normal laboratory procedures and applicable law.

In certain situations, donating embryo(s) for research or to another couple may not be possible or may be restricted by law. While efforts will be made to abide by your wishes, no guarantees can be given that embryo(s) will be used for research or donated to another couple. In these instances, if after 3 years no recipient or research project can be found, or your embryos are not eligible, your embryo(s) will be discarded by the lab in accordance with laboratory procedures and applicable laws.

B. Risks to the Woman

1. Ovarian Hyperstimulation Syndrome

To increase the number of eggs that develop, a series of hormone shots are given. The hormones used in this regimen are known to have, or are suspected of having, a variety of side effects, some minor and some potentially major.

The most serious side effect of ovarian stimulation is ovarian hyperstimulation syndrome (OHSS). 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, and/or death. The severe cases affect only a very small percentage of women who undergo in vitro fertilization—0.2 percent (2 in 1,000 patients) or less of all treatment cycles—and the very severe are an even smaller percentage. Only about 1.4 in 100,000 cycles have lead to kidney failure. OHSS occurs in 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 produced by the embryo during pregnancy). 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 chance that this will occur. In these cases, all viable embryos would be frozen for future use.

2. Risks of Pregnancy

Pregnancies that occur with IVF are associated with increased risks of certain conditions. 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. There may be additional risks related to the IVF procedure per se, but it is difficult to determine their relative contributions.

Currently, more than 30% of IVF cycles result in a pregnancy involving twins or higher-order multiple gestations (triplets or greater). Identical twinning occurs in 1.5% to 4.5% of IVF pregnancies. IVF twins deliver on average three weeks earlier and weigh 1,000 gm less than IVF singletons. Of note, IVF twins do as well as spontaneously conceived twins. Triplet (and greater) pregnancies deliver before 32 weeks (7 months) in almost half of cases.

I acknowledge that I have received a pamphlet with detailed information regarding the risks specifically associated with multifetal pregnancies.

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

C. Risks to Offspring

- IVF babies may have a slightly increased risk of birth defects
- The risk for a multiple (twins or more) pregnancy is significantly higher for patients undergoing IVF, even when only one embryo is transferred
- Multiple pregnancies pose the greatest risk to children resulting from IVF
- Some risk may also stem from the underlying infertile state, and/or from the IVF techniques themselves

1. Overall risks.

Since the first birth of an IVF baby in 1978, more than 3 million children have been born worldwide following IVF treatments. Numerous studies have been conducted to assess the overall health of IVF children. The majority of studies on the safety of IVF have been reassuring. As more time has passed and the dataset has enlarged, some studies have raised doubts about the equivalence of risks for IVF babies as compared to naturally conceived babies.

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.

Singletons conceived with IVF tend to be born slightly earlier than naturally conceived babies (39.1 weeks as compared to 39.5 weeks). IVF twins are not born earlier or later than naturally conceived

twins. The risk of a singleton IVF conceived baby being born with a birth weight under 5 pounds nine ounces (2500 grams) is 12.5% vs. 7% in naturally conceived singletons.

2. 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%. The difference is seen predominately in singleton males. Studies to date have not been large enough to prove a link between IVF treatment and specific types of birth defects.

Infant Development. In general, studies of long-term developmental outcomes have been reassuring; most children are doing well. It is well known that multiple pregnancies (twins or more) carry a higher risk of adverse outcomes to the fetuses. These risks include cerebral palsy and developmental delay. The most effective way to decrease these risks is by transferring fewer embryos, thereby minimizing the risk of a multiple pregnancy.

3. Risks of a Multiple Pregnancy

Among the most serious maternal complications associated with multiple gestations are preterm labor and delivery, pre-eclampsia, and gestational diabetes. Others include gall bladder problems, skin problems, excess weight gain, anemia, excessive nausea and vomiting, and exacerbation of pregnancy-associated gastrointestinal symptoms including reflux and constipation. Chronic back pain, intermittent heartburn, postpartum laxity of the abdominal wall, and umbilical hernias may also occur. Triplets and above increase the risk to the mother of more significant complications, including post-partum hemorrhage (severe bleeding) and transfusion.

Prematurity accounts for most of the excess perinatal morbidity and mortality associated with multiple gestations. Moreover, IVF pregnancies are associated with an increased risk of prematurity, independent of maternal age and fetal numbers. Fetal growth problems and discordant growth among the fetuses also result in perinatal morbidity and mortality. Multifetal pregnancy reduction decreases, but does not eliminate, the risk of these complications.

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. The death of one or more fetuses in a multiple gestation (vanishing twin) is more common in the first trimester and may be observed in up to 25% of pregnancies after IVF. Loss of a fetus in the first trimester is unlikely to adversely affect the surviving fetus or mother. No excess perinatal or maternal morbidity has been described resulting from a "vanishing" embryo.

Demise of a single fetus in a twin pregnancy after the first trimester is more common when they share a placenta, ranging in incidence from 0.5% to 6.8%, and may cause harm to the remaining fetus.

The Option of Multifetal Reduction: Pregnancies that have more than 2 fetuses are considered an adverse outcome of infertility treatment. The greater the number of fetuses within the uterus, the greater the risk for adverse perinatal and maternal outcomes. Patients pregnant with triplets or higher are faced with the options of continuing the pregnancy with all of the previously described risks, terminating the entire pregnancy, or reducing the number of fetuses in an effort to decrease the risk of maternal and perinatal morbidity and mortality. Multifetal pregnancy reduction (MFPR) decreases risks associated with preterm delivery, but often creates profound ethical dilemmas. Pregnancy loss is the main risk of MFPR. However, current data suggest that such complications have decreased as experience with the procedure has grown. The risk of loss of the entire pregnancy after MFPR is approximately 1%.

D. 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 a 'high-order' multiple pregnancy (triplets or more). We encourage patients and their partners to consult with trusted members of their religious or ethics community for guidance on their infertility treatment.

E. 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 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 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 impact 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 sleep patterns (difficulty falling asleep or staying asleep, early morning awakening, sleeping more than usual)
- change in 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).

F. Legal Considerations

The law 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 currently or in the future lives, or the state in which the fertility center is located. We acknowledge that InVia Fertility Specialists has not given us legal advice, that we are not relying on the ART Program to give us any legal advice, and that we have been informed that we may wish to consult a lawyer who is experienced in the areas of reproductive law and embryo cryopreservation and disposition if we have any questions or concerns about the present or future status of our embryos, our individual or joint access to them, our individual or joint parental status as to any resulting child, or about any other aspect of this consent and agreement.

G. Alternatives to IVF

There are alternatives to IVF treatment including gamete Intrafallopian transfer (GIFT), zygote intrafallopian transfer (ZIFT) or tubal embryo transfer (TET) where eggs and sperm, fertilized eggs or developing embryos, respectively, are placed into the fallopian tube(s). Using donor sperm, donor eggs, adoption or not pursuing treatment are also options. Gametes (sperm and/or eggs), instead of embryos may be frozen for future attempts at pregnancy in an effort to avoid potential future legal issues relating to disposition of any cryopreserved embryos. Sperm freezing, but not egg freezing, has been an established procedure for many decades. Egg freezing is considered an experimental procedure at this time.

H. Reporting Outcomes

The 1992 Fertility Clinic Success Rate and Certification Act requires the Centers for Disease Control and Prevention (CDC) to collect cycle-specific data as well as pregnancy outcomes on all assisted reproductive technology cycles performed in the United States each year and requires them to report success rates using these data. Consequently, data from my/our IVF procedure will be provided to the CDC, and to the Society of Assisted Reproductive Technologies (SART) of the American Society of Reproductive Medicine (ASRM). The CDC may request additional information from the treatment center. Additionally, my/our information may be used and disclosed in accordance with HIPAA guidelines in order to perform research or quality control. All information regarding me/us and our cycle(s) will be de-identified prior to publication. De-identification is a process intended to prevent the data associated with my/our treatment being used to identify me/us as individuals.

Please sign below to indicate which components of IVF treatment you agree to undertake in your upcoming treatment cycle.

Chosen Elements of Treatment:

Signatures

_____	_____	_____	In Vitro Fertilization (including egg retrieval and embryo transfer)
Patient's signature	Partner's signature	Date	

_____	_____	_____	Intracytoplasmic Sperm Injection(ICSI)
Patient's signature	Partner's signature	Date	

_____	_____	_____	Assisted Hatching
Patient's signature	Partner's signature	Date	

_____	_____	_____	Embryo Cryopreservation
Patient's signature	Partner's signature	Date	

Patient's printed name: _____

Partner's printed name: _____

Patient's Witness	_____	_____	_____
	Signature	Printed name	Date

Partner's Witness	_____	_____	_____
	Signature	Printed name	Date

References:

General IVF overviews available on the internet

<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 Committees 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 Committees of the American Society for Reproductive Medicine Fertil Steril 2006; 86 (suppl 4): S106-S110.

NOTE: If you or your partner are unable to sign this consent at INVIA FERTILITY SPECIALISTS, you have the option of signing it in the presence of a notary.

State of _____, County of _____, I, the undersigned, a Notary Public in and for the said County in the State aforesaid; DO HEREBY CERTIFY that

Signature

personally known to me as the same person whose name is subscribed to the foregoing document (Informed Consent for Assisted Reproduction), appeared before me this day in person, and acknowledged that she signed, sealed, and delivered the said document as her free and voluntary act, for the use and purposes therein set forth.

Given under my hand and official seal this ____ day of _____, 20 ____.
Commission expires on: _____, 20____.

(Notary Public)

NOTE: If you or your partner are unable to sign this consent at INVIA FERTILITY SPECIALISTS, you have the option of signing it in the presence of a notary.

State of _____, County of _____, I, the undersigned, a Notary Public in and for the said County in the State aforesaid; DO HEREBY CERTIFY that

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Commission expires on: _____, 20_____.

(Notary Public)