FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Informed Consent for Assisted Reproduction

In Vitro Fertilization With Optional Preimplantation Genetic Testing

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, or donor 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 that 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 stimulate the growth of multiple eggs
- Retrieval of eggs from the ovary or ovaries
- Insemination of eggs with sperm
- Culture 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 pregnancy

In most cases, these additional procedures will be employed:

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

***Note**: At various points in this document, rates are given which reflect what are believed to be U.S. national averages for those employing IVF treatments. These include items such as pregnancy rates, Cesarean delivery rates, and preterm delivery rates. These rates are not meant to indicate the rates of these outcomes within individual practices offering IVF, and are not to be understood as such. Individual practices may have higher or lower pregnancy and delivery rates than these national averages, and also higher or lower risks for certain complications. It is appropriate to ask the practice about their specific rates.*

Also note that while this information is believed to be up to date at the time of publication (2008), newer reports may not yet be incorporated into this document.

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Genetic Sources for IVF and/or ART

I/We voluntarily agree to participate in the Assisted Reproductive Technologies (ART) Program at the Fertility Center, LLC and Embryo Services, LLC (herein after referred to as the "Center" and including physicians, embryologists, members of the IVF team, associates and all supporting persons and any corporation they represent, whether participation is direct or indirect) in order to perform In-Vitro Fertilization (IVF) utilizing eggs to be fertilized to create embryos to achieve pregnancy. This consent extends from the initial period of participation in the IVF program until the cycle is completed or until the Recipient and/or Partner decide to discontinue participation in the program.

For the purposes of this IVF cycle we have chosen to use…

…eggs obtained from

☐ _____
Intended Mother

☐ _____
Known Egg Donor

☐ _____
Anonymous Egg Donor #

…sperm obtained from

☐ _____
Intended Father

☐ _____
Known Sperm Donor

☐ _____
Anonymous Sperm Donor #

or, we have elected to use the following embryos that were made available for use by another couple.

☐ _____
Anonymous Embryo Donor #

☐ _____
Known Donor Couple

I/we give consent to the Center to transfer embryos created from the eggs and sperm listed above, or pre-existing embryo(s) as listed above, into the uterus of _____.
Name (Print)

_____ _____ /_____ /_____
Patient Signature Date

_____ _____ /_____ /_____
Partner Signature Date

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Technique of IVF

Medications for IVF Treatment

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

- ***Gonadotropins, or injectable "fertility drugs"*** (Follistim®, Gonal-F®, Bravelle®, Menopur®): These natural hormones stimulate the ovary in hopes of inducing the simultaneous growth of several oocytes (eggs) over the span of 8 or more days. All injectable fertility drugs have FSH (follicle stimulating hormone), a hormone that will stimulate the growth of your ovarian follicles (which contain the eggs). Some of them also contain LH (luteinizing hormone) or LH like activity. LH is a hormone that may work with FSH to increase the production of estrogen and growth of the follicles. Luveris®, recombinant LH, can also be given as a separate injection in addition to FSH or alternatively, low-dose hCG can be used. 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 there 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 that 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 few or no eggs obtained at egg retrieval or even cancellation of the treatment cycle prior to egg retrieval.

  Some research suggested that the risk of ovarian tumors may increase in women who take any fertility drugs over a long period of time. These studies had significant flaws that 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 early reports may have falsely attributed the risk resulting from infertility to the use of medications to overcome it. In these studies, conception lowered the risk of ovarian tumors to that of fertile women. (see 2.b.2 below for further discussion)

- ***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 (U.S. Food and 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-a 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-a. GnRH-a have not been associated with any fetal malformations however you should discontinue use of the GnRH-a 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 natural 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, and in some cases, estradiol****:* Progesterone and estradiol are hormones normally produced by the ovaries after ovulation. After egg retrieval in some women, the ovaries will not produce adequate amounts of these hormones for long

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

enough to fully support a pregnancy. Accordingly, supplemental progesterone, and in some cases estradiol, are 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 reaction and if given by intra-muscular injection includes the additional risk of infection or pain at the injection site. Estradiol, if given, can be by oral, trans-dermal, intramuscular, or vaginal administration. Side effects of estradiol include nausea, irritation at the application site if given by the trans-dermal route and the risk of blood clots or stroke.

- *Oral contraceptive pills*: Some treatment protocols include oral contraceptive pills to be taken for 2 to 4 weeks 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 causing a yeast infection, nausea, vomiting, diarrhea, rashes, sensitivity to the sun, and allergic reactions. Anti-anxiety medications or muscle relaxants may be recommended prior to the embryo transfer; the most common side effect is drowsiness. Other medications such as steroids, heparin, low molecular weight heparin or aspirin may also be included in the treatment protocol. Also, some ovarian stimulation protocols may use Clomiphene (Clomid®) or Letrozole (Femara®) as part of the course of treatment.

Transvaginal Oocyte Retrieval

If necessary, 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 transabdominal retrieval is necessary. These procedures and risks will be discussed with you by your doctor if applicable. 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%. 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. Prophylactic antibiotics are sometimes used before the egg retrieval procedure to reduce the risk of pelvic or abdominal infection in patients at higher risk of this complication. 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%. Major bleeding will frequently 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 lead 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.

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.

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Disposition of Immature Eggs and Excess Sperm

Quality control in the lab is extremely important. Sometimes immature or unfertilized eggs, sperm or abnormal embryos (abnormally fertilized eggs or embryos whose lack of development indicates they are not of sufficient quality to be transferred) that would normally be discarded can be used for quality control. You are being given the opportunity to allow the clinic to use this material for quality control purposes before being discarded in accordance with normal laboratory procedures and applicable laws. None of this material will be utilized to establish a pregnancy or a cell line unless you sign other consent forms to allow the clinic to use your eggs, sperm or embryos for research purposes. Please indicate your choice below:

☐ I / We hereby CONSENT to allow the clinic to utilize my/our immature or unfertilized eggs, left-over sperm or abnormal embryos for training and/or research purposes before they are discarded.

_____ _____ /_____ /_____
Patient Signature Date

_____ _____ /_____ /_____
Partner Signature Date

☐ I / We hereby DO NOT CONSENT to allow the clinic to utilize my/our immature or unfertilized eggs, left-over sperm or abnormal embryos for training and/or research purposes. This material will be discarded in accordance with normal laboratory procedures and applicable laws.

_____ _____ /_____ /_____
Patient Signature Date

_____ _____ /_____ /_____
Partner Signature Date

Limited or Complete Egg Fertilization

_____ / _____ It is my/our intention to fertilize the following number of available eggs: _____.
Specific Number or "All"

_____ / _____ We have clearly been advised that by limiting the number of oocytes we allow to be fertilized we are also limiting the number of potentially normal embryos and therefore also limiting the potential of achieving pregnancy.

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

In-vitro Fertilization and Embryo Culture

After 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 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 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. 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.

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 resulting in an abnormal number of chromosomes in the embryo; 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 to be performed or prevent the establishment of a pregnancy.
- Hurricanes, floods, or other 'acts of God' (including bombings or other terrorist acts) could destroy the laboratory or its contents, including any sperm, eggs, or embryos being stored there.

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Intracytoplasmic Sperm Injection (ICSI)

The use of ICSI provides an effective treatment for male factor infertility. The negative effects of abnormal semen characteristics and sperm quality on fertilization can be overcome with ICSI if viable sperm are available because the technique bypasses the shell around the egg (zona pellucida) and the egg membrane (oolemma) to deliver the sperm directly into the egg. 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 can be performed even in men with no sperm in the ejaculate if sperm can be successfully collected from the epididymis or the testis.

Reports on the risk of birth defects associated with ICSI (compared to those associated with conventional fertilization in IVF cycles) have yielded conflicting results. The most comprehensive study conducted thus far, based on data from five-year-old children, has suggested that ICSI is associated with an increased risk of certain major congenital anomalies. However, whether the association is due to the ICSI procedure itself, or to inherent sperm defects, could not be determined because the study did not distinguish between male factor conditions and other causes of infertility. Note that even if there is an increased risk of congenital malformations in children conceived with ICSI, the risk is relatively low (4.2% versus ~3% of those conceived naturally). The impact of ICSI on the intellectual and motor development of children conceived via ICSI also has been controversial. An early report suggested that development in such children lagged significantly behind that of children resulting from conventional IVF or those conceived naturally. However, more recent studies from larger groups, using standardized criteria for evaluation, have not detected any differences in the development or the abilities of children born after ICSI, conventional IVF, or natural conception.

The prevalence of sex chromosome abnormalities in children conceived via ICSI is higher than observed in the general IVF population, but the absolute difference between the two groups is small (0.8% to 1.0% in ICSI offspring vs. 0.2% in the general IVF population). The reason for the increased prevalence of chromosomal anomalies observed in ICSI offspring is not clear. Whereas it may result from the ICSI procedure itself, it might also reflect a direct paternal effect. Men with sperm problems (low count, poor motility, and/or abnormal shape) are more likely themselves to have genetic abnormalities and often produce sperm with abnormal chromosomes; the sex chromosomes (X and Y) in the sperm of men with abnormal semen parameters appear especially prone to abnormalities. If sperm with abnormal chromosomes produce pregnancies, these pregnancies will likely carry these same defects. The prevalence of translocations (a re-arrangement of chromosomes that increases the risk of abnormal chromosomes in egg or sperm and can cause miscarriage) of paternal origin and of de novo balanced translocations in ICSI offspring (0.36%) also appears higher than in the general population (0.07%).

Some men are infertile because the tubes connecting the testes to the penis did not form correctly. This condition, called congenital bilateral absence of the vas deferens (CBAVD), can be bypassed by aspirating sperm directly from the testicles or epididymis, and using them in IVF with ICSI to achieve fertilization. However, men with CBAVD are affected with a mild form of cystic fibrosis (CF), and this gene will be passed on to their offspring. All men with CVABD, as well as their partners, should

be tested for CF gene mutations prior to treatment, so that the risk of their offspring having CF can be estimated and appropriate testing performed. It is important to understand that there may be CF gene mutations that are not detectable by current testing and parents who test negative for CF mutations can still have children affected with CF.

Some men have no sperm in their ejaculate because their testes do not produce adequate quantities (non-obstructive azoospermia). This can be due to a number of reasons such as prior radiation, chemotherapy or undescended testicles. In some men, small deletions on their Y chromosome lead to extremely low or absent sperm counts. Testicular biopsy and successful retrieval of viable sperm can be used to fertilize eggs with ICSI. However, any sperm containing a Y chromosomal microdeletion will be transmitted to the offspring. Thus the risk that male offspring might later manifest disorders including infertility is very real. However, men without a detectable deletion by blood testing can generate offspring having a Y chromosome microdeletion, because the chromosomes in the sperm may not be the same as those seen when tested by a blood test.

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Embryo/Oocyte Cryopreservation & Thawing

Freezing (or "cryopreservation") of embryos/oocytes 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/oocytes, if viable, can be frozen for future use. This saves 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). Other possible reasons for cryopreservation of embryos/oocytes include freezing all embryos/oocytes 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). 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 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 decrease the risks of hyperstimulation (OHSS- see below) by freezing all embryos, when this risk is high.

Risks of embryo cryopreservation: There are several techniques for embryo/oocyte 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/oocytes thawed after cryopreservation, but there can be no certainty that embryos/oocytes will thaw normally, nor be viable enough to divide and eventually implant in the uterus. Cryopreservation techniques could theoretically be injurious to the embryos/oocytes. 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 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.

Assisted Hatching

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.

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Hormonal Support of the Uterine Lining

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, trans-dermal or intramuscular route. The duration of this support is from 2 to 10 weeks.

Embryo Transfer

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 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. It is critical to discuss with your doctor the number to be transferred before the transfer is done.

In an effort to help curtail the problem of multiple pregnancies (see multiple pregnancies), national guidelines published in 2006 recommend limits on the number of embryos to transfer (see Tables below). These limits should not be viewed as a recommendation on the number of embryos to transfer. These limits differ depending on the developmental stage of the embryos and the quality of the embryos and take into account the patient's personal history.

In some cases, there will be additional embryos remaining in the lab after the transfer is completed. Depending on their developmental normalcy, it may be possible to freeze them for later use.

It is my/our intention to transfer _____(number) embryo(s) in an effort to produce pregnancy. By transferring more than one embryo to the uterus, we understand that there is a potential for multiple pregnancies and we understand and accept the risks inherent to this decision.

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Preimplantation Genetic Testing

Description & Purpose

The physicians and scientists at Fertility Center, LLC, invite your consent to undergo a procedure which evaluates the chromosomal contents of your eggs or embryos which result from your in-vitro fertilization procedure. Genetic errors, such as changes in chromosome numbers, or aneuploidy, and changes in chromosome configuration will be examined. Aneuploidy embryos are those with either a missing chromosome (monosomy) or an extra chromosome (trisomy). Aneuploidy occurs more frequently in eggs and embryos in women over 34 years of age. The study doctors and scientists at Fertility Center, LLC, hope to determine the genetic health of your embryos prior to transfer. The purpose is to select and replace only those embryos that appear to be chromosomally normal, so that there will be a reduced probability of losing the pregnancy or carrying a chromosomally abnormal baby to term.

The purpose of this procedure is to select and replace only embryos which do not have certain known chromosomal abnormalities. Chromosomes are the elements within every cell of your body that contain genetic information. Chromosomes are string-like structures found in the center of the cell, the nucleus. Inherited information is housed on the chromosomes. The traits are located in the genes that make up the chromosomes. Aneuploidies (anything other than 2 copies of each chromosome), or errors in development, occur more frequently in eggs and embryos in women over 34 years of age. Normally, there are 22 identical pairs in each cell, plus either XY (male) or XX (female) for a total of 46 chromosomes. Each patient provides 23 chromosomes, but in some children there is an extra chromosome: this is called trisomy. The most well-known trisomy is trisomy 21, also called Down's syndrome. Trisomic embryos usually do not implant, but if they do, this may lead to affected children. These extra chromosomes are usually formed during the final stages of egg ripening. Aneuploidy can happen with any chromosome and it happens during the process of egg and sperm formation over which you have no control. Aneuploidy occurs during the course of natural conception or IVF conception, it can happen to anyone, and we are generally unaware that it has even occurred. The doctors and scientists at Fertility Center, LLC, hope that chromosome testing of your embryos will increase your likelihood of becoming pregnant. They also hope that the test will substantially reduce the chance of conceiving a baby with certain chromosomal abnormalities that occur more frequently in women over 34 years of age. The goal is to reduce risk, not eliminate the risks completely.

The procedure involves techniques to investigate and observe the number of chromosomes in cells removed from the embryos. Cells (blastomeres) from the developing embryos will be analyzed. A tightly cohesive group of cells (usually 10+ cells) will be removed via aspiration with a micropipette (embryo sampling) and using a special laser mounted to the microscope, an opening is made in the protein coating (zona pellucida) surrounding the embryo during its fifth or sixth day of development when the embryo has >80 cells -. The embryo sampling procedure does not significantly alter the ability of embryos to become a viable fetus. In some cases, it may be necessary to remove additional cells according to circumstances. In either of the above cases, the analysis of the biopsied cell(s) uses a technique called array CGH, in which all 46 chromosomes are analyzed to detect gains or losses of chromosomes or segments of chromosomes. A normal embryo has 23 pairs of chromosomes in each cell. The chromosomes present in the cells (blastomeres) extracted from the dividing embryo provide a diagnosis for the genetic status and health of the embryo. The tests are performed exclusively on the removed cells, and the embryo itself remains unaffected. Depending on the number and quality of the embryos produced in a given IVF cycle, the physicians and scientists at Fertility Center, LLC, may recommend canceling the biopsy procedure altogether. About 95% of abnormal embryos can now be detected using these techniques which will be applied to your eggs and embryos. Prenatal testing after the IVF cycle is still strongly advised, since this would confirm the prognosis. Because of the risks described below, your pregnancy will be carefully monitored as should all pregnancies after IVF procedures. Between 10 to 16 weeks, we will recommend chorionic villus sampling, or amniocentesis, where samples of cells are taken from the fluids or placenta beside the developing fetus for similar testing. These tests will provide a comprehensive genetic analysis of the fetus. The fetus will also be monitored with ultrasound to detect its growth and development.

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Risks of PGT

The testing process takes up to 7-10 working days, and results will be brought to the patient and or couple for consultation and discussion of the outcome. Complete testing will, in a majority of cases (more than 95%), eliminate all excess embryos. Most patients will have all embryos that are normal by PGD or PGT, and viable by microscopic appearance, transferred, and excess abnormal or non-viable embryos will be discarded. Occasionally (less than 5% of the time), there may be more embryos that test normal than are safe to transfer. In the case of a day 5 or 6 biopsy, all embryos will be cryopreserved pending the results of the testing.

It should also be understood that this is not an exact science and that research technology may not always produce meaningful results or correct information. You agree that the goal in using this technology is to improve chances of getting pregnant utilizing IVF and to reduce the risk of miscarriage.

Physicians and scientists of Fertility Center, LLC, are uncertain of the risks involved in microsurgery on the embryos, but believe them to be acceptably low. Numerous animal studies and some human studies show that the microsurgery of the embryo needed to remove the cells, does not affect the normal development of the baby. This procedure, however, has been performed in a limited number of studies on human embryos, so the precise negative effects, if any, are unknown. In animal studies there have been no apparent problems and preliminary evidence with human eggs and embryos suggests that this is also true. Although a rare occurrence (0.1%), it is possible that some or all egg(s) or embryo(s) may be accidentally damaged during biopsy. Furthermore, a relatively large number of the eggs or embryos may be abnormal providing a very limited number of embryos for replacement. It is possible that in some cases, none of the embryos may be normal, and embryo replacement should then not be performed. It is also possible that no reading is available on one or more embryos. While this is a disappointing outcome, it is likely that the cycle would have failed without PGS or an abnormal conception would have occurred. Finally, the tests may fail in any individual case because of unforeseen technical malfunctions. It is therefore not possible to guarantee pregnancy after PGS or even to promise that there will be benefits for any individual case.

When any pregnancy is achieved after an IVF procedure, physicians and scientists of Fertility Center, LLC, strongly recommend a comprehensive genetic analysis of the fetus between 10-18 weeks. This can be chorionic villus sampling or amniocentesis, which provide samples of cells taken from the fluids of the placenta. The risks and benefits of this testing should be discussed with your obstetrician. The fetus should also be checked with ultrasound to monitor growth and development.

Benefits of PGT

The utilization of preimplantation genetic screening may result in the following benefits…

It is possible that the chance of pregnancy is increased after performing these procedures because embryos which are genetically affected only rarely develop into fetuses. Chromosomally normal embryos have higher chances to develop to term. By replacing only chromosomally normal embryos, your chances of becoming pregnant may increase. The chance of pregnancy and delivery of a healthy child, however, is reduced in patients over 34 years (normally less than 50%) due to problems inherent to the IVF procedure. As mentioned above, this study will be able to identify most chromosomal abnormalities at risk of arriving to term. These abnormalities are more common in women older than 34, and occur in 1 in 25 babies from women 40 or older. It is possible that some information about your embryos could be beneficial to you in case of future IVF attempts. The study doctors and scientists of Fertility Center, LLC, hope to learn more about the connection between chromosomes and failed development and implantation of your embryos. You may benefit from this study, and future patients may also benefit from the information obtained.

It is not possible to guarantee pregnancy after this study or to promise that you will receive any benefits from this study, because not all genetic disorders can be identified.

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Voluntary Participation

Your decision whether or not to have aneuploidy testing will not prejudice your future relations with Fertility Center, LLC, and the treatment you are now undergoing at this site. If you decide to participate, you are free to discontinue participation at any time. By signing this consent you have not waived any other legal rights, which you would otherwise have as a patient, or a subject in a research study or released any party from liability for negligence. Your participation is voluntary and your refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled.

_____ / _____ I/we want to have PGT performed on available embryos.
(If choosing to do PGT testing additional forms will need to be completed.)

_____ / _____ I/we choose ***do not*** want to have PGT performed on available embryos.

Disposition of Genetically Tested Embryos

By initialing my/our selection, I/we understand that genetic abnormalities commonly exist in embryos and that live born infants do not usually result from genetically abnormal embryos except in rare cases of Down's Syndrome and/or Turner's Syndrome. As a result, the physicians of Fertility Center, LLC do not recommend transferring genetically abnormal embryos in an effort to become pregnant and the embryos are typically discarded.

If pre-implantation genetic testing (embryo sampling and subsequent PGT) results show abnormal embryos, our wish for their disposition is

_____ / _____ To have Fertility Center, LLC keep the abnormal embryos in cryo-storage until further notice, in which cryo-storage fees will be incurred on a yearly basis.

_____ / _____ To allow Fertility Center, LLC to use the genetically abnormal embryos for training or research, at which time the embryos would be subsequently discarded and would never again be available to attempt to establish a pregnancy.

_____ / _____ To have Fertility Center, LLC discard genetically abnormal embryos upon receipt of genetic testing results and would never again be available to attempt to establish a pregnancy.

Alternative Treatment Options

Similar techniques can be used to test any embryos which might be affected by a genetic disease known to be present in your family. Such procedures are applied in order to select embryos which are not affected by the disease. You can choose to have no genetic diagnosis performed on the embryos, and to have the embryos transferred. In that case, the only way of determining possible genetic deformities during early pregnancy would be by testing through chorionic villus sampling or amniocentesis from 10 weeks gestation onwards. You do not have to participate in this study in order to have IVF.

Costs

You (or your insurance) will be responsible for the costs of the study procedure as described above. Fees for PGT are in addition to the cost of the IVF cycle, over and above those related to your normal IVF procedure. Those fees will be presented on another document.

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

EMBRYO SERVICES
Keeping Dreams Alive

Ongoing Storage of Embryos

Ongoing storage of embryos, eggs, or sperm, will be administered by our sister company, Embryo Services LLC. Six months from the initial date of freezing, if you have either remaining embryo(s) egg(s) or sperm, you will receive your first invoice from Embryo Services LLC. If you qualify for a Univfy Package, billing for your storage will begin upon completion of your package, or upon the successful delivery of a child. If you elect a yearly billing cycle you will receive an invoice of $420.00 on or near the anniversary date of the initial freeze. If you elect for a monthly billing cycle you have the option to be set up on an automatic draft of your preferred bank account for $35.00 per month to maintain storage and that amount will be withdrawn on the anniversary day of the initial freeze. Billing notifications and invoicing will take place via email, unless otherwise requested.

Preferred Billing Method

☐ Annual eInvoice $420.00 YR

☐ Monthly eInvoice $35.00 MO

☐ Monthly Bank Draft $35.00 MO

Billing Email _____

☐ Standard Cycle ☐ Univfy Cycle

Your monthly, or yearly, payment will serve as notice to continue storage. If you choose to discontinue payment, or fail to notify Fertility Center or Embryo Services, at (423) 899-0500, of any changes to your address or billing information, then Embryo Services will assume that you no longer want to continue storage. It is your responsibility to request any changes of status in writing. If at any point you wish to transfer, retrieve, discard, donate to another couple or specified individual, or donate for training or research purposes, you must request from us the appropriate consent form to complete, have notarized, and return to us. Only at that point can those wishes be honored, unless otherwise allowed by circumstances of death, divorce, abandonment, or by reaching the age of 55.

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Disposition of Embryos

Because of the possibility of you and/or your partner's separation, divorce, death or incapacitation after embryos have been produced, it is important to decide on the disposition of any embryos (fresh or cryopreserved) that remain in the laboratory in these situations. 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. It is understood and agreed that all parties will abide by any applicable federal or state requirements and regulations. I/We understand and agree that any embryos created are regulated by the Food and Drug Administration and the Tennessee State Department of Health, and any changes in federal or state rules and regulations may affect the future use of embryos created during this cycle.

Currently, the alternatives are:

- Discarding the cryopreserved embryo(s)
- Donating the cryopreserved embryo(s) for approved training and/or research purposes.
- Donating the cryopreserved embryos to another couple in order to attempt pregnancy. (In this case, you may be required to undergo additional infectious disease testing and screening due to Federal or State requirements.)
- Use by one partner with the contemporaneous permission of the other for that use.

This agreement provides several choices for disposition of embryos in these circumstances: death of the patient or the patient's spouse or partner, separation or divorce of the patient and her spouse/partner, successful completion of IVF treatment, decision to discontinue IVF treatment, failure to pay fees for frozen storage, or failure to determine disposition of embryos by the age of 55.

I/We agree that in the absence of a more recent written and witnessed consent form, the Clinic is authorized to act on our choices indicated below, so far as it is practical.

DEFAULT DISPOSITION: **I/We understand and agree that in the event that if our chosen dispositional choices are not available or we fail to preserve any choices made herein, whether through nonpayment of storage fees or otherwise, the clinic is authorized, without further notice to us, to discard and destroy our embryos. Note…**

- Embryos cannot be used to produce pregnancy against the wishes of the partner. For example, in the event of a separation or divorce, embryos cannot be used to create a pregnancy without the express, written consent of both parties, even if donor gametes were used to create the embryos.

- Embryo donation to achieve a pregnancy is regulated by the FDA (U.S. Food and Drug Administration) as well as state laws, as donated tissue; certain screening and testing of the persons providing the sperm and eggs are required before donation can occur.

- You are free to revise the choices you indicate here at any time by completing another form and having it notarized.

- Your wills should also include your wishes on disposition of the embryos and be consistent with this consent form. Any discrepancies will need to be resolved by court decree.

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Death of Patient

In the event the patient dies prior to use of all the embryos, we agree that the embryos should be disposed of in the following manner (check only one box):

☐ Award to patient's spouse or partner, which gives complete control for any purpose, including implantation, donation for research, or destruction. This may entail maintaining the embryos in storage, and the fees and other payments due the clinic for these cryopreservation services.

☐ Donate to another couple or individual for reproductive purposes. This may entail maintaining the embryos in storage, and the fees and other payments due the clinic for these cryopreservation services. If you wish, you may designate a couple or individual to receive the embryos. In the event the designated couple or individual is unable or unwilling to accept the embryos, the clinic will control the donation.

Please donate to:
Name _____
Address _____
_____
Telephone _____
Email _____

Special note for embryos created with gamete donors: If your embryos were formed using gametes (eggs or sperm) from a known third party donor, your instruction to donate these embryos to another couple or individual must be consistent with and in accordance with any and all prior agreements made with the gamete donor(s). If anonymous donor gametes were used, written authorization from the gamete donor must be obtained to use these gametes for anything other than reproduction or destruction of the embryos.

☐ Donate for training and/or research purposes which may result in the destruction of the embryos but will not result in the birth of a child.

☐ Destroy the embryo(s).

☐ Other disposition (please specify): _____

Death of Partner

In the event the patient's spouse or partner dies prior to use of all the embryos, we agree that the embryos should be disposed of in the following manner (check one box only):

☐ Award to patient, which gives complete control for any purpose, including implantation, donation for research, or destruction. This may entail maintaining the embryos in storage, and the fees and other payments due the clinic for these cryopreservation services.

☐ Donate to another couple or individual for reproductive purposes. This may entail maintaining the embryos in storage, and the fees and other payments due the clinic for these cryopreservation services. If you wish, you may designate a couple or individual to receive the embryos. In the event the designated couple or individual is unable or unwilling to accept the embryos, the clinic will control the donation.

Please donate to:
Name _____
Address _____
_____
Telephone _____
Email _____

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Special note for embryos created with gamete donors: If your embryos were formed using gametes (eggs or sperm) from a known third party donor, your instruction to donate these embryos to another couple or individual must be consistent with and in accordance with any and all prior agreements made with the gamete donor(s). If anonymous donor gametes were used, written authorization from the gamete donor must be obtained to use these gametes for anything other than reproduction or destruction of the embryos.

☐ Donate for training and/or research purposes which may result in the destruction of the embryos but will not result in the birth of a child.

☐ Destroy the embryo(s).

☐ Other disposition (please specify): _____

Simultaneous Death of Patient and Partner

In the event the patient and her spouse or partner die at the same time, prior to use of all the embryos, we agree that the embryos should be disposed of in the following manner (check one box only):

☐ Donate to another couple or individual for reproductive purposes. This may entail maintaining the embryos in storage, and the fees and other payments due the clinic for these cryopreservation services. If you wish, you may designate a couple or individual to receive the embryos. In the event the designated couple or individual is unable or unwilling to accept the embryos, the clinic will control the donation.

Please donate to:
Name _____
Address _____
_____
Telephone _____
Email _____

Special note for embryos created with gamete donors: If your embryos were formed using gametes (eggs or sperm) from a known third party donor, your instruction to donate these embryos to another couple or individual must be consistent with and in accordance with any and all prior agreements made with the gamete donor(s). If anonymous donor gametes were used, written authorization from the gamete donor must be obtained to use these gametes for anything other than reproduction or destruction of the embryos.

☐ Donate for training and/or research purposes which may result in the destruction of the embryos but will not result in the birth of a child.

☐ Destroy the embryo(s).

☐ Other disposition (please specify): _____

Divorce or Dissolution of Relationship

In the event the patient and her spouse are divorced or the patient and her partner dissolve their relationship, we agree that the embryos should be disposed of in the following manner (check one box only):

☐ A court decree and/or settlement agreement will be presented to the Clinic directing use to achieve a pregnancy in one of us or donation to another couple for that purpose.

☐ Donate for training and/or research purposes which may result in the destruction of the embryos but will not result in the birth of a child.

☐ Destroy the embryo(s).

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Abandonment

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 an annual 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 5 years or fees associated with embryo storage have not been paid for a period of 5 years and the clinic is unable to contact the patient after reasonable efforts have been made (via registered mail at last known address), the embryo(s) may be destroyed by the clinic in accordance with normal laboratory procedures and applicable law.

If I/we fail to pay the overdue storage fees within 30 days from the date of said mailing, such failure to pay constitutes my/our express authorization to the clinic to follow the disposition instructions we have elected below without further communications to or from us (check one box only):

☐ Donate for training and/or research purposes which may result in the destruction of the embryos but will not result in the birth of a child.

☐ Destroy the embryo(s).

Determination by age 55

If I/we elect not to utilize the cryopreserved embryos for a future pregnancy it is agreed that before the 55th birthday of the patient (_____ /_____ /_____), a decision will be made and the cryopreserved embryo(s) must be thawed and implanted, donated, transported elsewhere or otherwise discarded. If no disposition has occurred by the above date, I/we hereby waive any and all interest in said cryopreserved embryo(s) and the cryopreserved embryo(s) shall become the sole and exclusive property of Fertility Center, LLC/Embryo Services, LLC. In this event, I/we prefer to:

☐ Donate for training and/or research purposes which may result in the destruction of the embryos but will not result in the birth of a child.

☐ Destroy the embryo(s).

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Risks to the Woman

Ovarian Hyperstimulation Syndrome

To increase the number of eggs that develop, a series of hormone shots are given to support the simultaneous growth of numerous follicles instead of just one. The hormones used in this regimen are known to have, or 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, 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 lead 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 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 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 Obstetrics & Gynecology, vol. 109, no. 4, pages 967-77, 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. There may be additional risks related to the IVF procedure per se, but it is difficult to assign the relative contributions.

Potential Risks in Singleton IVF Pregnancies

	Absolute Risk (%) in IVF-conceived Pregnancies	Relative Risk (vs. non IVF-conceived Pregnancies)
Pre-eclampsia	10.3%	1.6 (1.2--2.0)
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)
Cesarean delivery *	26.7%	2.1 (1.7--2.6)

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 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. 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.

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

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. 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.

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 treatments with methotrexate (a weak chemotherapy drug) or surgery to treat the abnormal pregnancy. Side effects of methotrexate include nausea or vomiting, diarrhea, cramping, mouth ulcers, headache, skin rash, sensitivity to the sun and temporary abnormalities in liver function tests. Risks of surgery include the risks of anesthesia, scar tissue formation inside the uterus, infection, bleeding and injury to any internal organs.

Risks to Offspring

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 and 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.

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.

Imprinting Disorders. These are rare disorders having to do with whether a maternal or paternal gene is inappropriately expressed. In two studies approximately 4% of children with the imprinting disorder called Beckwith-Weidemann Syndrome were born after IVF, which is more than expected. A large Danish study however found no increased risk of imprinting disorders in children conceived with the assistance of IVF. Since the incidence of this syndrome in the general population is 1/15,000, even if there is a 2 to 5-fold increase to 2-5/15,000, this absolute risk is very low.

Childhood cancers. Most studies have not reported an increased risk with the exception of retinoblastoma: In one study in the Netherlands, five cases were reported after IVF treatment which is 5 to 7 times more than expected.

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

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

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.

Potential Risks in Singleton IVF Pregnancies

	Absolute Risk (%) in IVF Pregnancies	Relative Risk (vs. non-IVF Pregnancies)
Preterm birth	11.5%	2.0 (1.7--2.2)
Low birth weight (< 2500 g)	9.5%	1.8 (1.4--2.2)
Very low birth weight (< 1500 g)	2.5%	2.7 (2.3--3.1)
Small for gestational age	14.6%	1.6 (1.3--2.0)
NICU (intensive care) admission	17.8%	1.6 (1.3--2.0)
Stillbirth	1.2%	2.6 (1.8--3.6)
Neonatal mortality	0.6%	2.0 (1.2--3.4)
Cerebral palsy	0.4%	2.8 (1.3--5.8)
Genetic risks		
-imprinting disorder	0.03%	17.8 (1.8--432.9)
-major birth defect	4.3%	1.5 (1.3--1.8)
Chromosomal abnormalities (after ICSI):		
-of a sex chromosome	0.6%	3.0
-of another chromosome	0.4%	5.7

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 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. The numbers in parentheses (called the "Confidence Interval") indicate the range in which the actual Relative Risk lies.

Risks of Multiple Pregnancy

The most important maternal complications associated with multiple gestation are preterm labor and delivery, pre-eclampsia, and gestational diabetes (see prior section on Risks to Woman). 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 also can occur. Triplets and above increase the risk to the mother of more significant complications including post-partum hemorrhage 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 (where one or more fetuses are selectively terminated) reduces, 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.

Multiple fetuses (including twins) that share the same placenta have additional risks. Twin-twin transfusion syndrome in which there is an imbalance of circulation between the fetuses may occur in up to 20% of twins sharing a placenta. Excess or insufficient amniotic fluid may result from twin-to-twin transfusion syndrome. Twins sharing the same placenta have a higher frequency of birth defects compared to pregnancies having two placentas. Twins sharing the same placenta appear to occur more frequently after blastocyst transfer.

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Placenta previa (placenta extends over the cervical opening) and vasa previa (where one or more of the blood vessels extends over the cervical opening) are more common complications in multiple gestations. Abruptio placenta (premature separation of the placenta) also is more common and postpartum hemorrhage may complicate 12% of multifetal deliveries.

Consequences of multiple gestations include the major sequelae of prematurity (cerebral palsy, retinopathy of prematurity, and chronic lung disease) as well as those of fetal growth restriction (polycythemia, hypoglycemia, necrotizing enterocolitis). It is unclear to what extent multiple gestations themselves affect neuro-behavioral development in the absence of these complications. Rearing of twins and high-order multiples may generate physical, emotional, and financial stresses, and the incidence of maternal depression and anxiety is increased in women raising multiples. 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 Selective 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 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 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%.

In general, the risk of loss after MFPR increases if the number of fetuses at the beginning of the procedure is more than three. While there is little difference between the loss rates observed when the final number of viable fetuses is two or one, the loss rate is higher in pregnancies reduced to triplets. Pregnancies that are reduced to twins appear to do as well as spontaneously conceived twin gestations, although an increased risk of having a small for gestational age fetus is increased when the starting number is over four. The benefit of MFPR can be documented in triplet and higher-order gestations because reduction prolongs the length of gestation of the surviving fetuses. (This has been demonstrated for triplets; triplets have a 30-35% risk of birth under 32 weeks compared to twins which is 7 to 10%)

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

3rd Party Considerations

If applicable, the following is a list of considerations that one must take into account when using any 3rd party eggs, sperm, or embryos

- Although great care is taken with all specimens, a laboratory accident may result in loss of or damage to the eggs, sperm or embryos.
- A pregnancy may result in the birth of a baby or babies with congenital anomalies, although the odds for such an outcome are no greater with assisted reproduction. A genetic amniocentesis or chorionic villus sampling may be done when appropriate.
- No one can guarantee the physical or mental characteristics of any children resulting from these procedures. The recipient couple as well as their successors, offspring and assigns release and agree to hold harmless from liability the physicians, associates and staff of THE CENTER for complications resulting from pregnancy or childbirth following assisted reproduction procedures; from liability for any mental, emotional and physical problems; and from liability for physical or mental disabilities of any children produced following these procedures.
- Although egg donors are carefully screened for infectious diseases as governed by the FDA, no test is 100 percent accurate.
- The recipient couple indicates by signing this consent form their agreement to release the anonymous donor from any legal or financial responsibilities from an established pregnancy or medical costs related to that pregnancy and delivery. The couple and their heirs will release the anonymous donor from any financial and legal responsibility for the children from conception forward and also release the physicians, their associates, and the staff at THE CENTER from any financial responsibilities for the children from conception forward.
- The recipient couple is free to discontinue participation in the ART program at any time, either verbally or in writing. Their decision to discontinue participation will in no way prejudice other treatment that may be received from THE CENTER. If there is a decision to discontinue participation in the program, the recipient couple will be personally responsible for all the expenses incurred prior to such discontinuation and related to anonymous egg donor screening and/or treatment in the program.
- The results of treatment or any aspect of treatment may be published in medical literature. If publication of data occurs, all reasonable precautions will be taken to protect the anonymity of all parties. Participants in the ART program grant permission for related statistics to be published, provided names are not used.
- Anonymity is required for the egg donor as well as the recipients. The donor has signed a consent agreeing not to try under any circumstances to contact the recipients and is aware that absolutely no information will be given to her from this program concerning either the recipient or partner. The donor has agreed to relinquish any rights to responsibility or claims to any children or embryos resulting from her donation of eggs.
- The recipient couple releases the physicians, their associates and the staff at THE CENTER from any responsibilities or legal liabilities related to the recruiting of the anonymous donors from the surrounding communities.
- In most cases your chosen donor sperm bank has screened the donor(s) for HIV/AIDS and other medical conditions. I/We also understand that the Fertility Center, LLC has not screened the donor(s) or sperm. I/We understand that despite such screening it is possible to acquire an infectious disease, including HIV, from the insemination with donor sperm procedure.
- So far, there is no evidence that insemination with donor sperm causes an increased chance of abnormalities in the fetus(es). The risk of birth defects may or may not be higher than the usual risk of birth defects (two to five percent) when conception occurs through intercourse.
- Legal Status. I/We understand that there may be future changes in the law related to insemination with donor sperm, including anonymity. I/We have had an opportunity to seek independent legal counsel
- The pregnancy rate with a frozen egg is 56%. This means that the transferred embryos may not implant or the pregnancy may not be carried to term. The rate of pregnancy complications is the same as in naturally-occurring pregnancies.
- If pregnancy occurs, the possibility of a twin pregnancy is 25%. The possibility of triplets or more is 5%. The probability of a tubal or ectopic pregnancy is about 5%.
- Because egg freezing is a new and emerging technology, there is very little information available about potential birth defects. Our experience with frozen embryos, however, has not shown any greater incidence of major or minor birth defects compared to children conceived naturally.
- Each couple must decide if this technology is appropriate for them. Psychological counseling is available for all who are uncertain whether or not to use this technology.

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

Ethical and Religious Considerations

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

A diagnosis of infertility can be a devastating and life-altering event that impacts on 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

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 outcome 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) (if my/our clinic is a member of this organization). The CDC may request additional information from the treatment center or contact me/us directly for additional follow-up. Additionally, my/our information may be used and disclosed in accordance with HIPAA guidelines in order to perform research or quality control. All information used for research 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.

Initials: _____ / _____

FERTILITY CENTER, LLC
7407 Ziegler Road – Chattanooga, TN 37421
10408 Jackson Oaks Way – Knoxville, TN 37922

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 ART Program is located. We acknowledge that the ART Program 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.

In accordance with Federal regulations, we are obliged to inform you about Fertility Center's policy in the event physical injury occurs. If, as a result of your participation, you experience physical injury from known or unknown risks of the research procedures as described, immediate medical care and treatment, including hospitalization if necessary, will be available. No monetary compensation, however, is available and you will be responsible for the costs of such medical treatment, either directly, or through your medical insurance and/or other forms of medical coverage.

My/Our signature(s) below certifies that I/We have been advised of the risks of these procedures and that I/We fully understand these risks. I/We hereby certify that I/We have been given ample opportunity to discuss questions or concerns with my physician and I/We release the physician, the Center, and associates of the Center from liability if I/We fail to discuss my/our concerns before signing.

_____ _____ /_____ /_____
Patient Name (Print) Date of Birth

_____ _____ /_____ /_____
Patient Signature Date

_____ _____ /_____ /_____
Partner Name (Print) Date of Birth

_____ _____ /_____ /_____
Partner Signature Date

Notary Public

Sworn and subscribed before me on this _____ day of _____, _____.

_____ _____
Notary Signature My Commission Expires

Alt. Witness 1* _____ Date _____ /_____ /_____

Alt. Witness 2* _____ Date _____ /_____ /_____

*Fertility Center office staff only. Document must be notarized if signed outside of the office.

Initials: _____ / _____