In Vitro Fertilization with Frozen Embryo Transfer
Process, Risk, and Consent

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.

I/We understand I/we have been unable to become pregnant through conventional treatments for one or more of the following reasons: Non-functioning or absent fallopian tubes, male factor infertility, “hostile cervical mucous”, endometriosis (with or without failed medical and/or surgical treatment), polycystic ovaries, autoimmune factors, or unexplained infertility. Alternatively, we have opted to undergo In Vitro Fertilization (IVF) as part of our infertility treatment without undergoing other more conservative approaches that we were offered.

Once biological specimens such as eggs and/or embryos are cryopreserved using the In Vitro Fertilization (IVF) process, additional processes and procedures must be undertaken both in the laboratory as well as in the recipient in order to prepare these specimens for successful transfer into the uterus of a woman. These processes will also be outlined below.

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.

This consent also reviews the process necessary for preparation of cryopreserved embryos for transfer into a uterus, including potential 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 encountered during the thawing, laboratory manipulation, and transfer process that are not yet clarified or even suspected at the time of this writing.

I/We wish to attempt to become pregnant using In Vitro Fertilization and Embryo Transfer (IVF & ET). I/We understand the following are basic steps and events to be taken for IVF and ET:

- Completion of preliminary screening (eg. infectious diseases, autoimmune tests when indicated, endocrine evaluation, semen testing, assessment of uterine cavity with sonohysterogram and/or hysteroscopy, Pap's smear, mammogram, cervical cultures, and possible genetic testing and/or psychological consultation).
- IVF Education and Consent Consultation with the clinical staff, and an injection training session. All injectable prescriptions need to be filled prior to this training session and brought to the session. Any one administering injections also needs to attend this session, unless previously attended. Additional medications not initially prescribed may be ordered later in the cycle.
- Prophylactic treatment with oral antibiotics (both male and female).
- Treatment with hormonal agents (oral contraceptives, Lupron, Microdose Lupron, Ganirelax and/or Cetrotide) to initially take control of female reproductive hormones.
- Treatment with injectable fertility drugs (Repronex, Menopur, Bravelle, Low-dose hCG, Folistim, Gonal-F, and/or Growth Hormone) to induce the development of multiple eggs.
- Serial evaluation of hormonal blood levels (estradiol, luteinizing hormone, progesterone) and transvaginal ultrasounds to assess the efficacy of the fertility medications. (Visits will be scheduled before 10 AM)
- A timed injection of hCG (eg. Profasi, Pregnyl, Novarel, or other equivalent).
- Ultrasound guided transvaginal egg retrieval (under anesthesia).
- Production of a fresh semen specimen on the day of egg retrieval (if applicable). If using frozen donor sperm, this MUST have been shipped and in AFC/AARL possession at least 2 weeks prior to retrieval. If fresh specimen is being used, partner/spouse MUST remain available on the day of retrieval if a second sample is needed.
• Discharge from Advanced Fertility Care within 1 hour after oocyte retrieval procedure. A responsible adult must be available to drive the patient home and to take care of the patient for at least 18 hours post retrieval.

• Frozen Embryo Transfer will be performed several weeks after egg retrieval is completed and the ovaries return to normal size and will require coordinated ovarian suppression and preparation of the uterus for implantation. In some cases, fresh embryo transfer may occur 2 to 5 days after egg retrieval depending on physician recommendation.

• Progesterone and Estradiol blood tests approximately three days after day of embryo transfer.

• Serial blood pregnancy tests ~ 8 days to 3 weeks following embryo transfer.

• Two to three OB ultrasounds will be performed assuming successful pregnancy.

My initials at the bottom of the page signify that I/we understand that the following are some of the risks and discomforts associated with the preparation for egg retrieval:

• Blood draws and injections: Mild discomfort and a slight risk of developing a bruise.

• Vaginal ultrasounds: Mild vaginal / pelvic discomfort.

• Psychological stress.

• Unanticipated sources of physical and non-physical discomfort.

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 (2013), newer reports may not yet be incorporated into this document.

IVF and Frozen Embryo Transfer Procedures

Medications for IVF Treatment and Frozen Embryo Transfer with Hormonal Support of Uterine Lining

• 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.

• Successful attachment of embryo(s) to the uterine lining depends on adequate hormonal support.

• Progesterone, given by the intramuscular, oral, and/or vaginal route, is routinely prescribed for this purpose.

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. Low-dose hCG (human chorionic gonadotropin) can be used in lieu of LH. 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 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.

Concerns have been raised that the risk of ovarian cancer may increase with the use of fertility drugs, but recent studies have not confirmed this. A major risk factor for ovarian cancer is infertility per se, and early reports may have falsely attributed the risk resulting from infertility to the use of medications to overcome it (see 2.b.2 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 has not been associated with any fetal malformations, however you should discontinue use of the GnRH-a immediately if pregnancy is confirmed.

- **GnRH-antagonists (ganirelix acetate or cetrorelix acetate) (Ganirelix®, 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 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 oil based injections or 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, very rarely, 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 vaginal 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.

### Transvaginal Oocyte (Egg) Retrieval

- Eggs are removed from the ovary with a needle under ultrasound guidance.
- Anesthesia is provided to make this comfortable.
- Complications 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 laparoscopy or trans-abdominal 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 0.1%. 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 may require surgical repair and possibly loss of the ovary. The need for blood transfusion is rare. (Although very rare, review of the world experience with IVF indicates that unrecognized bleeding may 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 very low.

**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.

**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. Modern anesthesia is relatively safe and uneventful so that virtually everyone can be afforded its benefits. There are several types of anesthesia available. Your surgeon has chosen intravenous for your surgical procedure. This anesthesia technique is designed to reduce your anxiety and pain. It provides the patient with partial or, in most cases, total amnesia. Medications (Versed, Fentanyl, and/or Diprovan (i.e. Propofol) are injected into the bloodstream inducing a semi-conscious state. Most patients will sleep through the procedure, waking up shortly after the procedure is finished.

You will need to fast (not eat or drink anything) for at least 8 hours before the scheduled procedure.

Due to the nature of anesthesia, fatigue or sleepiness can be expected for up to 24 to 36 hours after the procedure, so the patient undergoing anesthesia MUST be accompanied by a responsible adult who can drive her home and care for her for at least 18 hours following the procedure in the event of an emergency. In addition, the patient may not drive during the immediate 18 hours after the procedure.

Risks and hazards of intravenous sedation, although rare, can occur regardless of the experience, care and skill of your anesthesia provider. The risks and hazards of intravenous sedation include, but are not limited to: injury to a blood vessel (phlebitis), vertigo (dizziness), post-operative nausea and vomiting, an unconscious state which can lead to depressed breathing, allergic reaction to one of the drugs used (which in extreme cases can lead to anaphylaxis and even death). Your anesthesia provider will do his/her very best to protect you from harm but no guarantee as to the outcome of your anesthesia can be made.

Advanced Fertility Care will provide for a licensed physician anesthesiologist to provide intravenous anesthesia for the surgical procedure. The anesthesiologist administering the intravenous sedation will have full charge of the administration and maintenance of the anesthesia, and that it is an independent function from surgery.

My initials at the bottom of the page and signature(s) at the end of this document indicate my informed consent to receive anesthesia for Egg Retrieval.
In Vitro Fertilization and Embryo Culture

- Sperm and eggs are placed together in specialized conditions (culture media, controlled temperature, humidity and light) to achieve fertilization.
- Culture medium is designed to permit normal fertilization and early embryo development, but the content of the medium is not standardized.
- Embryo development in the lab helps distinguish embryos with more potential from those with less or none. On average, only 30-50% of embryos will normally develop to the blastocyst stage.

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

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

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

It is important to note that since some eggs and embryos may be 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 many factors including 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.
- An egg 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.

Quality control in the lab is extremely important. On occasion, immature or unfertilized eggs, sperm or abnormal embryos that would normally be discarded may be used for quality control and training purposes prior to being discarded, in accordance with normal laboratory procedures and applicable laws. This material would not be capable of establishing a pregnancy or a cell line.
Starting with Cryopreserved Embryos

In most cases, the embryos will have been frozen at the blastocyst stage of development (5-6 days after fertilization or approximately 80-100 cells). In more rare circumstances, embryos may have been frozen after initial fertilization of the egg “2PN stage” or after 3 days after fertilization (6-10 cells).

In cases where freezing occurred earlier than at the blastocyst stage of development, the embryos must be thawed in the laboratory and cultured in special media for 2-5 days to ensure adequate survival and cell growth and division.

Published reports indicate approximately 90-95% of all cryopreserved blastocysts survive the thawing process if they were initially frozen using the most current flash freezing techniques known as “vitrification”. However, it is difficult or impossible to predict how many of the thawed embryos will survive and/or continue to develop and be suitable for transfer.

Embryo transfer will ONLY occur if the thawed embryo(s) are determined to be medically suitable for transfer to the uterus. Embryo(s) will NOT be transferred into the patient’s uterus if the embryo(s) do not survive the thawing process and/or do not develop. **Embryos that do not divide and/or survive the freeze/thaw process will be discarded.**

Embryo transfer

- **When starting with cryopreserved embryos, embryos are considered to be viable and suitable for transfer if at least 50% of the cells survive the thawing process.**
- **The number chosen for transfer influences the pregnancy rate and the multiple pregnancy rate.**
- **The age of the egg used to create the embryo, the visual appearance of the developing embryo, and the internal genetic composition of the embryo have the greatest influences on pregnancy outcome.**
- **Using ultrasound guidance, embryos are placed in the uterine cavity with a thin tube.**
- **In some situations, your physician may recommend a fresh embryo transfer. After a few days of development, the best appearing embryos are selected for transfer.**
- **The number chosen influences the pregnancy rate and the multiple pregnancy rate.**
- **A woman’s age, genetic makeup, and the appearance of the developing embryo have the greatest influences on pregnancy outcome.**
- **Embryos are placed in the uterine cavity with a thin tube.**
- **Excess embryos of sufficient quality that are not transferred during a fresh cycle can be frozen.**

One to two embryos are selected for transfer to the uterine cavity. In the case of embryo thaw, the number of embryos thawed and intended for transfer will be predetermined by the recipient(s) in consultation with the physician and as noted on the “Embryo Thaw and Transfer Plan” which you will discuss with your physician and sign prior to starting injections to prepare the uterus for implantation. If a fresh embryo transfer is indicated by your physician, after a few days of development following fertilization, one or more embryos are selected for transfer to the uterine cavity. In either case, 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 2017 recommend limits on the number of embryos to transfer (see Tables below). These limits should not necessarily 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.

At AFC, in women under age 35 who have at least 3 blastocysts of good quality that develop and are available for transfer on day 5, elective SINGLE BLASTOCYST is strongly encouraged; AFC and AARL internal data support minimal if any compromise in subsequent pregnancy rate when compared to transfer of two or more embryos in the same population, however, with drastically reduced rates of multiple pregnancies.

### Recommended MAXIMUM LIMITS on the number of embryos to transfer (ASRM 4/2017)

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In some cases where fresh transfer is indicated, there may also 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.

**Hormonal support of the uterine lining**

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

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

- ICSI is used to increase the chance of fertilization when fertilization rates are anticipated to be lower than normal.
- Overall success rates with ICSI are similar to those achieved with conventional insemination.
- An increased risk of genetic defects in offspring is reported.
- ICSI will not correct oocyte defects.

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 similar 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 surgically collected from the epididymis or the testis by a urologist.

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

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

Some men with extremely low or absent sperm counts have small deletions on their Y chromosome. When viable sperm can be obtained to fertilize eggs with ICSI, sperm containing a Y chromosomal microdeletion may result in male offspring who also carry the microdeletion and may be infertile. A Y chromosome microdeletion can often, but not always, be detected by a blood test.

Men who are infertile because of congenital bilateral absence of the vas deferens (CBAVD) are affected with a mild form of cystic fibrosis (CF). When sperm aspiration and ICSI results in conception, the CF gene will be passed on to the offspring. Men with CBAVD and their partners should be tested for CF gene mutations prior to treatment. However, some CF mutations may not be detected by current testing, so that some parents who test negative for CF mutations could still have affected children.

Assisted Hatching

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

The cells that make up the early embryo are enclosed within a flexible membrane (shell) called the zona pellucida. During normal development, a portion of this membrane dissolves, allowing the embryonic cells to escape or "hatch" out of the shell. Only upon hatching can the embryonic cells implant within the wall of the uterus to form a pregnancy.
Assisted hatching is the laboratory technique in which an embryologist makes an artificial opening in the shell of the embryo. The hatching is usually performed on the day of transfer, prior to loading the embryo into the transfer catheter. The opening can be made by mechanical means (slicing with a needle or burning the shell with a laser) or chemical means by dissolving a small hole in the shell with a dilute acid solution.

In the case of frozen embryos, assisted hatching is routinely performed due to the hardening of the embryo membrane associated with the freezing process; this technique has been shown to improve implantation rates, and ultimately, live birth rates. In the case of fresh embryo transfers, some programs have also incorporated artificial or "assisted hatching" into their treatment protocols in certain situations because they believe it improves implantation rates, and ultimately, live birth rates although definitive evidence of this is lacking.

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

Cryopreservation

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

Freezing (or "cryopreservation") of eggs or embryos is a common procedure. Since multiple eggs (oocytes) are often produced during ovarian stimulation, on occasion there are more embryos available than are considered appropriate for transfer to the uterus. Such embryos can be frozen for future use. Alternatively, some eggs can be frozen before being exposed to sperm. Both strategies save the expense and inconvenience of stimulation to obtain additional eggs in the future. Furthermore, the availability of cryopreservation permits patients to transfer fewer embryos during a fresh cycle, reducing the risk of high-order multiple gestations (triplets or greater). 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). 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 cryopreservation: There are several techniques for embryo cryopreservation, and research is ongoing. Older methods include “slow,” graduated freezing in a computerized setting, and current modern methods incorporate “rapid” freezing methods, called “vitrification.” Current techniques deliver a high percentage of viable eggs and embryos thawed after cryopreservation, but there can be no certainty that eggs and embryos will thaw normally, nor be viable enough to divide and eventually implant in the uterus. Cryopreservation techniques could theoretically be injurious to the embryo. Extensive animal data (through several generations), and limited human data, do not indicate any likelihood that children born of embryos that have been cryopreserved and thawed will experience greater risk of abnormalities than those born of fresh
embryos. However, until very large numbers of children have been born following freezing and thawing of embryos, it is not possible to be certain that the rate of abnormalities is no different from the normal rate.

**If you choose to freeze eggs or embryos, you MUST complete and/or notarize the separate document entitled “Specimen Storage Agreement” before freezing. This document outlines the choices you have with regard to the disposition of biological specimens including eggs, semen, and embryos in a variety of situations that may arise. You are free to submit a statement at a later time indicating different choices, provided you both agree in writing. It is also incumbent upon you to remain in touch with the clinic regarding your residence, and to pay for storage charges as they come due.**

**Risks to the Woman**

**Ovarian Hyperstimulation Syndrome**

The intent of giving gonadotropins is to mature multiple follicles, but some women have an excessive response to the medications and are at risk for ovarian hyperstimulation syndrome (OHSS). This is the most serious side effect of ovarian stimulation. Its symptoms can include increased ovarian size, nausea and vomiting, accumulation of fluid in the abdomen, breathing difficulties, an increased concentration of red blood cells, kidney and liver problems, and in the most severe cases, blood clots, kidney failure, or death. The severe cases affect only a very small percentage of women who undergo in vitro fertilization—0.2 percent or less of all treatment cycles—and the very severe are an even smaller percentage. Only about 1.4 in 100,000 cycles has 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. A final answer may require decades of follow-up to resolve. Note that an increased chance for “borderline” ovarian tumors has been observed with IVF, even when compared to the subfertile population (see reference section for citation). More research is required to examine what the long-term impact fertility drugs may have 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. This was demonstrated in an Australian study that reviewed adverse obstetric and perinatal outcomes in sub-fertile women conceiving without ART (see Table below). 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-conceived Pregnancies

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

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

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

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

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

**Risks to Offspring**

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

**Overall Risks**

Since the first birth of an IVF baby in 1978, more than 5 million children have been born worldwide following IVF treatments. Numerous studies have been conducted to assess the overall health of IVF children and the majority of studies on the safety of IVF have been reassuring. A major problem in interpreting the data arises from the fact that comparing a group of infertile couples to a group of normally fertile couples is not the proper comparison to make if one wants to assess the risk that IVF technology engenders. Infertile couples, by definition, do not have normal reproductive function and might be expected to have babies with more abnormalities than a group of normally fertile couples. This said, even if the studies suggesting an increased risk to babies born after IVF prove to be true, the absolute risk of any abnormal outcome appears to be small. In addition, 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%, and is slightly higher among infertile patients. Most of this risk is due to delayed conception and the underlying infertility issues. In a recent large study performed in Australia (see reference), the risk of birth defects was not increased among women who had routine IVF treatment, but was higher among those who employed ICSI as part of the treatment. No higher risk was seen in frozen embryo transfer and donor egg cycles.

**Imprinting Disorders.** These are rare disorders having to do with whether a maternal or paternal gene is inappropriately expressed. In two studies of children with the imprinting disorder called Beckwith-Weidemann Syndrome, more were born after IVF 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. Further studies have not supported this finding.

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

### Potential Risks in Singleton IVF Pregnancies

<table>
<thead>
<tr>
<th>Risk</th>
<th>Absolute Risk (%) in IVF Pregnancies</th>
<th>Relative Risk (vs. non-IVF pregnancies)</th>
<th>Relative Risk for infertile women without ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm birth</td>
<td>11.5%</td>
<td>2.0 (1.7–2.2)</td>
<td>1.32 (1.05-1.67)</td>
</tr>
<tr>
<td>Low birth weight (&lt; 2500 g)</td>
<td>9.5%</td>
<td>1.8 (1.4–2.2)</td>
<td>1.44 (1.11-1.85)</td>
</tr>
<tr>
<td>Very low birth weight (&lt; 1500 g)</td>
<td>2.5%</td>
<td>2.7 (2.3–3.1)</td>
<td></td>
</tr>
<tr>
<td>Small for gestational age</td>
<td>14.6%</td>
<td>1.6 (1.3–2.0)</td>
<td></td>
</tr>
<tr>
<td>NICU (intensive care) admission</td>
<td>17.8%</td>
<td>1.6 (1.3–2.0)</td>
<td></td>
</tr>
<tr>
<td>Birth</td>
<td>1.2%</td>
<td>2.6 (1.8–3.6)</td>
<td></td>
</tr>
<tr>
<td>Neonatal mortality</td>
<td>0.6%</td>
<td>2.0 (1.2–3.4)</td>
<td>2.19 (1.10-4.36)</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>0.4%</td>
<td>2.8 (1.3–5.8)</td>
<td></td>
</tr>
<tr>
<td>Genetic risks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-imprinting disorder</td>
<td>0.03%</td>
<td>17.8 (1.8–432.9)</td>
<td></td>
</tr>
<tr>
<td>-major birth defect</td>
<td>4.3%</td>
<td>1.5 (1.3–1.8)</td>
<td></td>
</tr>
<tr>
<td>-chromosomal abnormalities after ICSI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-of a sex chromosome</td>
<td>0.6%</td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>-of another chromosome</td>
<td>0.4%</td>
<td>5.7</td>
<td></td>
</tr>
</tbody>
</table>

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 a Multiple Pregnancy

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

Prematurity accounts for most of the excess perinatal morbidity and mortality associated with multiple gestations. IVF twins deliver on average three weeks earlier and weigh 1,000 gm less than IVF singletons. Triplet (and greater) pregnancies deliver before 32 weeks (7 months) in almost half of cases. 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 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.

Multiple fetuses that share the same placenta, as in most identical twins, have additional risks. Twin-twin transfusion syndrome, in which excess or insufficient amniotic fluid results from an imbalance of circulation between the fetuses, may occur in up to 20% of twins sharing a placenta. Twins sharing the same placenta have a higher frequency of birth defects compared to twins with two placentas. After the first trimester, death of one fetus in a twin pregnancy is more common with a shared placenta and may cause harm to the remaining fetus.

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

**The Option of Multifetal Pregnancy Reduction:** The greater the number of fetuses within the uterus, the greater is the risk for adverse perinatal and maternal outcomes. Patients with more than twins are faced with the options of continuing the pregnancy with all risks previously described, terminating the entire pregnancy, or undergoing a procedure called multifetal pregnancy reduction. By reducing the number of fetuses, multifetal pregnancy reduction (MFPR) decreases risks associated with preterm delivery, but often creates important 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%, although this risk increases when the number of fetuses prior to the procedure is greater than three.

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

**Psychosocial Effects of Infertility Treatment**
A diagnosis of infertility can be a devastating and life-altering event that impacts 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 anxiety, 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.

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.

Patients may consider working with mental health professionals who are specially trained in the area of infertility care, as well as with their health care team, to minimize the emotional impact of infertility treatments. National support groups are also available, 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).
Alternatives to IVF
Using donor sperm, donor eggs, adoption, or not pursuing treatment are all 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 or ethical issues relating to disposition of any cryopreserved embryos. Sperm and egg freezing are now considered well established and successful procedures.

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 for 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, data aggregation and/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.

Summary – IVF & Frozen Embryo Transfer (ET) Consent
Success rates with IVF are dependent on individual factors and may range from less than 10% to more than 70%.

My/our initials at the bottom of the page signify that I/we understand that all procedures related to IVF will be performed in conjunction with the physician(s)/staff of Advanced Fertility Care, PLLC (“AFC”), and the embryology and andrology team of Arizona Advanced Reproductive Laboratory, LLC (“AARL”). Egg retrieval and embryo transfer procedures will occur at Arizona Advanced Surgery Center, LLC (“AASC”).

In addition, I/we have read and understand the outlined preliminary testing and sequence of events noted in this document pertaining to IVF and Embryo Transfer which will be performed in conjunction with Advanced Fertility Care, Arizona Advanced Reproductive Laboratory, and Arizona Advanced Surgery Center.

I/We understand that no warranty or guarantee has been made to us that eggs will: be retrieved, fertilize, cleave, be placed in the uterus, implant, produce a pregnancy, lead to a delivery, or produce a live born child. I/We have been assured that all information about us obtained during this procedure will be handled confidentially and that neither our identity nor our specific medical details will be revealed without our prior written consent. We acknowledge that specific anonymous medical details may be revealed in professional publications and to the SART licensing board as long as our identity is concealed. In addition, it is mandatory that data from our ART procedure be provided to the Centers for Disease Control and Prevention (CDC) as required by law and protected under the provisions of the Public Health Service Act, Section 308(d) excluding disclosure of identifying information without your consent.

It is understood that should we suffer any physical injury as the result of participation in the IVF procedure, AFC and staff will make available any treatment and necessary facilities, emergency treatment, and professional services. However, these additional treatments will incur additional expenses not covered by our payment of fees for the IVF & ET procedure. It is also understood that in the event of injury resulting from this procedure, Advanced Fertility Care is not able to offer financial compensation or to absorb the costs of medical treatment.

My/our initials and signatures on this document acknowledges my/our voluntary participation in this procedure, but does not release the medical staff from their professional and ethical responsibility to me.
I/We have had the opportunity to ask any questions we might have about our participation. I/We understand that our alternatives include, donor egg IVF, adoption, foster parenting and foregoing parenting. If other medical or surgical therapies were possible these avenues have already been attempted and/or are not practical or suitable to us. I/We are aware that participating in an Assisted Reproduction Program may have serious psychological consequences with respect to, but not limited to the parent/child and patient/partner relationships.

Insurance may not cover any or part of the procedures. By consenting to this procedure, I/we, the patient & partner, agree that we will be responsible for all expenses resulting from this treatment. These expenses may consist of the facility charges, laboratory charges, anesthesia charge, and the physician’s professional fees. If physical injury results from voluntary participation in this program, Advanced Fertility Care will provide acute care but will not provide free medical care, or compensation for injuries.

Notice of Arbitration

It is understood that any and all disputes relating to this Agreement or its breach, or to medical malpractice, that is, as to whether any medical services rendered under this contract were unnecessary or unauthorized or were improperly, negligently or incompetently rendered, shall be settled by arbitration in Scottsdale, Arizona (Maricopa County), in accordance with Arizona’s Revised Uniform Arbitration Act (A.R.S. §12-3001, et seq.), and utilizing the then-current procedural rules of the American Arbitration Association. I/We, by entering into this contract, are giving up my/our constitutional right to have any such dispute decided in a court of law before a jury, and instead are accepting the use of arbitration. Judgment upon the arbitration award may be entered in any court having jurisdiction hereof. The arbitrator or, if necessary, a court of competent jurisdiction, shall award the costs of arbitration, including reasonable attorneys’ fees, to AFC/AARL/AASC provided that any of them are the substantially prevailing party in the arbitration and/or in any subsequent litigation to enforce an arbitration award. Any arbitration shall be conducted in the English language and the award rendered in the United States dollars. Should I/we, or either of us, dismiss or abandon a claim or counterclaim before the arbitration hearing, AFC/AARL/AASC shall be deemed the “substantially prevailing party” for purposes of this section. Service of any petition to confirm the arbitration award shall be complete on personal delivery or the deposit of the petition and notice in the United States mail.
**IVF Treatment Plan**

My/Our selections below, along with our initials and signatures on this document indicate our desired plan for treatment as previously discussed with my/our physician.

**IVF Protocol**

My/our physician has recommended and I/we have agreed to the following plan:

- **IVF/Frozen Embryo Transfer (FET):** Egg Retrieval, Fertilization, Embryo Culture with:
  - STANDARD: Freezing of all appropriate blastocysts. **No Fresh Transfer will be performed.**
  - Anticipated Low Number of Embryos: Potential fresh transfer based on number and quality of embryos.

- **IVF with Fresh Embryo Transfer (Due to insurance requirement)**

**Provider of Sperm**

I/We plan to use sperm from:

- Spouse / partner Type:  
  - Fresh  
  - Frozen  
- Donor (specify name or number):  

**Intended Carrier of embryos**

I/We plan to transfer the embryos into:

- Myself (Partner #1)  
- My spouse/partner (Partner #2) (Name:________________________)  
- A Gestational Carrier — if known, her name: __________________________

**Method of Insemination**

I/We acknowledge that I/we have discussed the possibility of the need for ICSI with our (my) physician and understand, agree and consent that:

- Intracytoplasmic Sperm Injection (ICSI) will be used for fertilization

- Conventional Insemination will be used, unless the sperm at time of egg retrieval is sub-optimal, less than 5 eggs are retrieved, or the initial fertilization is poor. I/we will be notified if ICSI is recommended and will need to provide verbal consent at that time, acknowledging this will incur additional fees.

- We DO NOT consent to ICSI under any circumstances. This choice may have a significant negative impact on the success of the cycle.
### Number of Eggs to be Inseminated

- **STANDARD:** Attempt to Fertilize ALL Mature Eggs

- **Limited:** Attempt to Fertilize ONLY SOME of the Mature Eggs  
  *(Not Recommended)*  
  Number or fraction of mature eggs to be exposed to sperm: ____% of eggs (or) ____ # of eggs

  **If Limited option selected, plan for eggs that are not exposed to sperm:**
  - ☐ Freeze for my later use (requires Specimen Storage Agreement), and additional fees will apply
  - ☐ Donate to:  
    - ☐ Research
    - ☐ Another person designated in the Specimen Storage Agreement
  - ☐ Discard: This disposal will follow ASRM Ethical Guidelines.

### Assisted Hatching of Embryos

Laser Assisted Hatching of my/our embryos will be performed for the purposes of embryo biopsy (if selected) and/or prior to all Frozen Embryo Transfers, as well as in some cases of fresh embryo transfer (i.e. age of egg provider ≥ 38 years old, prior failed implantation).

### Freezing Plan *(Freezing embryos also requires separate signed Specimen Storage Agreement)*

- **STANDARD:** ALL AVAILABLE EMBRYOS WILL BE FROZEN if deemed appropriate by AARL staff  
  **All embryos that do not develop appropriately will be discarded.**

- **Limited:** Freeze ONLY SOME or NONE of remaining blastocysts for my/our future use

  Number to be frozen:  
  - ☐ None  
  - ☐ Up to ____ embryos

  **If Limited option selected, plan for embryos not frozen for my/our future use:**
  - ☐ Donate to:  
    - ☐ Research
    - ☐ Another person designated in the Specimen Storage Agreement
  - ☐ Discard. This disposal will follow ASRM Ethical Guidelines. Extra embryos will no longer be available for attempting a pregnancy.

### Plan for Preimplantation Genetic Testing / Screening

- **PGT GENETIC TESTING** of embryos

  - ☐ Desire for Family Balancing  
    - ☐ YES  
    - ☐ NO  
    - ☐ INELIGIBLE

  **Eligibility Criteria:**
  - You and/or your partner must currently have at least one living child
  - You prefer family balancing for a specific gender rather than transfer of the best quality embryo

  **PRIOR REQUIRED testing and arrangements have ALREADY been completed and our wishes have been documented on the separate PGT Consent Form.**

- **NO PGT GENETIC TESTING** of embryos

  - Initials: _____ / _____
I/WE ACKNOWLEDGE THAT WE HAVE READ AND FULLY UNDERSTAND THIS INFORMED CONSENT/AGREEMENT IN ITS ENTIRETY. I/WE HAVE BEEN ENCOURAGED TO AND HAD THE OPPORTUNITY TO ASK QUESTIONS AND OUR QUESTIONS REGARDING THESE PROCEDURES HAVE BEEN ANSWERED TO MY/OUR COMPLETE SATISFACTION. I HAVE ALSO RECEIVED INFORMATION ABOUT ALTERNATIVE PROCEDURES TO ALLOW ME TO BECOME PREGNANT IF THEY EXIST. I/WE UNDERSTAND THAT I/WE MAY WITHDRAW CONSENT AT ANY TIME TO PARTICIPATE IN THIS PROGRAM, WITHOUT PREJUDICE.

I/We acknowledge that I/we have read and understood the information provided above regarding the IVF and Frozen Embryo Transfer process and its risks, and agree to go forward with this treatment as my/our signatures below testify.

If any clause, sentence, provision, or other portion of this Agreement is, or becomes illegal, null, void or unenforceable for any reason, or is held by any court of competent jurisdiction to be so, the remaining portions shall remain in full force and effect.

NOTICE: BY SIGNING THIS CONTRACT, YOU ARE AGREEING TO HAVE ANY ISSUE OF MEDICAL MALPRACTICE OR LEGAL ISSUE RELATED TO THIS AGREEMENT DECIDED BY NEUTRAL ARBITRATION, AND YOU ARE GIVING UP YOUR RIGHT TO A JURY OR COURT TRIAL. SEE PAGE #14 OF THIS CONTRACT.

<table>
<thead>
<tr>
<th>Partner #1 (Print):</th>
<th>Sign:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spouse/Partner #2 (Print):</td>
<td>Sign:</td>
<td>Date:</td>
</tr>
</tbody>
</table>