Preimplantation Genetic Testing (PGT)
Fresh and Frozen Embryos
Process, Risk, and Consent

PGT analysis is offered to patients that seek to identify a chromosomal abnormality in their embryos prior to initiating a pregnancy.

PGT-A (aneuploidy) analysis for abnormal chromosome number can be utilized to improve pregnancy rates for infertility of an unknown factor or because of an increased risk of chromosomal abnormality due to maternal age and/or previous medical, personal or family history. This genetic testing method cannot predict other birth defects or genetic disorders or all cases of the disorders for which PGT is being performed. PGT-A would also be utilized when gender selection is offered to patients who already have at least one child and wish to gender balance their family. The same risks apply to this purpose as described above.

PGT-M (monogenic/single gene defects) and PGT-SR (structural rearrangements) analysis are offered to couples that seek to identify a single cell defect or genetic translocation in their embryos prior to initiating a pregnancy. PGT-M or SR analysis will be provided because there is an increased risk in one’s family of conceiving a child who can inherit a known genetic disorder. The increased risk is known because of standard genetic screening for the disease or family history. I/We understand this genetic testing method cannot predict other birth defects or genetic disorders or all cases of the disorders described above for which PGT is being performed. The objective of the PGT-M/SR analysis will be to test for specific single gene defect(s) or translocation(s) known to be risk factor(s) for my/our family.

Biopsy and Testing of Embryos During a Fresh IVF Cycle

- Development to blastocyst (80-100 cells or 5-6 days post fertilization) stage of development is required in order for embryo biopsy to be attempted.

IVF (in-vitro fertilization) techniques are necessary in order to undergo PGT testing on embryos even though a couple may not be infertile, therefore I/we agree to participate in the IVF program at Advanced Fertility Care (“AFC”). I/We also understand that our IVF cycle will be conducted in accordance with AFC’s guidelines as summarized in a separate consent, entitled “In Vitro Fertilization – Process, Risk, and Consent”, and coordinated amongst AFC physicians, embryologists, applicable staff and the applicable laboratory that will be performing the biopsy, analysis, and reporting the results of PGT testing.

Embryo biopsy is necessary to obtain and test cells in order to establish the possibility of a defect. An embryo biopsy is the process by which cells are removed from the embryo for genetic analysis. This is accomplished with laser assisted biopsy of the embryos in which a microscopic hole will be created in the embryo membrane with the aid of a computer guided laser beam, allowing for several cells (2-8) to be removed from the outer layer of cells (trophoblast). In performing the biopsy:

- The risk of damage to the embryo is extremely small and this technique has become a regular laboratory practice. If the embryo is damaged during the biopsy process, it may or may not have a negative effect on its ability to survive freezing and subsequent warming in the future, and ultimately influence overall pregnancy outcome.

- The cells will be processed and sent to a genetic laboratory, as noted later in this document, for analysis. Results from the biopsy will usually be available within 2-3 weeks from day of biopsy.

- Once results of the biopsy are available, and assuming there are “normal” embryos for transfer, you will then need to be coordinated for a Frozen Embryo Transfer in a future cycle.
Biopsy and Testing of Frozen Embryos

- Blastocysts must be warmed/thawed, rehydrate and re-expand in order for biopsy to be possible.
- While survival of embryos is very high (>95%), this is not guaranteed. Embryos that do not survive the thaw and achieve normal expansion will not be biopsied, and will be discarded.

In order for the cryopreserved embryos to be tested, the previously frozen embryos will need to undergo the following process:

- Controlled warming of the embryos from their cryopreserved state
- Laser assisted biopsy of the embryos will be performed in which a microscopic hole will be created in the embryo membrane with the aid of a computer guided laser beam, allowing for several cells to be removed from the outer layer of cells (trophoblast).
  a. The risk of damage to the embryo is extremely small and this technique has become a regular laboratory practice.
  b. If the embryo is damaged during the biopsy process, it may or may not have a negative effect on its ability to survive refreezing and subsequent warming in the future, and ultimately influence overall pregnancy outcome.
  c. The cells will be processed and sent to a genetic laboratory, as noted later in this document, for analysis.
- The biopsied embryos will be refrozen in a fashion identical to the initial freeze process using flash freezing or “vitrification” technique.
- Results from the biopsy will usually be available within 2-3 weeks from day of biopsy.

Assisted Hatching

- Assisted hatching involves making a hole in the outer shell (zona pellucida) that surrounds the embryo.
- Assisted Hatching of the zona pellucida is necessary and required in order for the embryologist to biopsy (remove) a number of cells from the trophectoderm of the embryo in order to allow for genetic testing of these cells.
- All embryos that are biopsied MUST be hatched first.

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. When genetic testing of the embryo is requested, hatching is initially performed on the third day of embryo development to enable the cells to protrude from the embryo and allow for biopsy of these cells. This hatching process is once again repeated prior to the transfer of frozen embryos. 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.

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.
Summary – Preimplantation Genetic Testing of Fresh or Frozen Embryos

I/We understand that the biopsy (removal of cells) from the embryos for the purpose of PGT analysis will be performed at Arizona Advanced Reproductive Laboratory (“AARL”). We also acknowledge that the genetic testing of the cells removed from the embryo is to be performed by a laboratory outside of AARL and therefore, neither AARL nor any of its employees or affiliated organizations are responsible for the outcome of such testing.

I/We have been appropriately counseled on alternative options available to us to avoid having a child with chromosomal abnormalities, which may include the use of donor egg or donor sperm, adoption, and/or prenatal screening after pregnancy begins by means of chorionic villus sampling or amniocentesis with the option to terminate if the fetus is affected with a genetic disorder.

I/We understand that the purpose of this procedure is to have a child that does not have a genetic or chromosomal disorder for which we are at an increased risk, improve pregnancy rate, or to select the gender of our child. Preimplantation genetic testing of embryos will usually result in at least some embryos being found to have an abnormal chromosome complement or number (“aneuploidy”). If transferred into the uterus, these embryos are likely to result in no pregnancy, abnormal pregnancy resulting in miscarriage, or birth of an affected child with significant health issues. In cases of genetic testing for specific gene mutations, pregnancy resulting from genetically abnormal embryos would lead to an abnormal pregnancy or fetus affected with a particular disease. Therefore, abnormal embryos are considered nonviable and the recommendation of AFC and AARL physicians is that they be discarded upon obtaining the results of the testing. AFC’s physicians and embryologists exercise the right to use reasonable medical judgment to determine if the embryo(s) are non-viable or not medically suitable for use for embryo transfer. Under no circumstances will the AFC physicians transfer a known genetically tested abnormal embryo into a woman’s uterus. AFC is not obligated to transfer these embryos at any point in the future if any medical evidence and/or any other experience indicate that the risk of transfer outweighs the benefits of transfer.

I/We understand that the following are potential risks of PGT analysis:

- Due to the limitation of the genetic testing process, the results of genetic testing embryonic cells may not be 100% accurate and as a result may be subject to both false positive and false negative outcomes
- The risk of Ovarian Hyperstimulation Syndrome (OHSS) may be greater in a normally fertile female than in a female with infertility
- The embryos may not survive the freezing or thawing process if cryopreserved; and
- The inherent risks of an IVF procedure, as outlined in the In Vitro Fertilization Consent.

I/We understand the financial responsibility for PGT is ours and that the costs incurred are in addition to any standard charges for the Frozen Embryo Transfer at AFC. As the cost of PGT testing is usually not covered by most insurance companies, pre-payment of all charges associated with PGT are expected to be paid to AFC prior to testing of the embryos.
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.

Laboratory Performing Genetic Testing

- [ ] Natera/Spectrum Genetics Lab
- [ ] Invitae Genetics
- [ ] Other: __________________________

Indications for Preimplantation Genetic Testing

Choose ALL that apply:
- [ ] PGT-A (Aneuploidy Screening and/or Family Balancing if within AFC guidelines)
- [ ] PGT-SR (Structural Rearrangement)
- [ ] Reciprocal Translocation
- [ ] Robertsonian Translocation/Inversion
- [ ] PGT-M (Monogenic/Single Gene Defect): __________________________

Initials: _____ / _____

FRESH EMBRYOS

- [ ] N/A: I/We wish to test previously frozen embryos ONLY

Desire and Consent to Biopsy and Freeze Fresh Embryos

I/We hereby authorize and consent to the biopsy of my/our embryos that reach the blastocyst stage of development. In addition, we understand that we have the following options when it comes to the biopsy of our embryos and our initials below indicate the choices we have made for our upcoming IVF cycle.

YOU MUST SELECT one of the two options listed below:

- Option 1 (Freeze All Plan): I/We choose to have all embryos that achieve sufficient quality and development be biopsied for the purpose of genetic testing and then immediately frozen, regardless of number of embryos that can be biopsied (i.e. no minimum). We understand that embryo development varies and there is a possibility that none of the embryos will be able to be biopsied, in which case, there will be no embryos for transfer. We understand that by selecting this option, there will be NO option for a fresh transfer. Should there be embryos to biopsy and freeze, a future frozen embryo transfer cycle will be required in order to attempt pregnancy, assuming results of the genetic analysis of the cells are favorable.

- Option 2 (Possible Fresh Transfer): In the case when three (3) or more embryos achieve sufficient quality and development to be biopsied for the purpose of genetic testing, I/we choose to have all embryos biopsied (as per the PGT Freeze All Plan as described above in Option 1) and then immediately frozen. We understand that embryo development varies and there is a possibility that none of the embryos will be able to be biopsied, in which case, there will be no embryos for transfer. If by Day 5 of embryo development, LESS THAN three (3) embryos are deemed adequate for biopsy by the embryology staff, we wish to forego biopsy and proceed with a fresh embryo transfer of the best two (2) embryos. Any embryos that may progress to freezable quality by Day 6 will then be frozen without biopsy and genetic testing. I/We understand that by selecting this option, we will need to be trained and instructed to start progesterone therapy due to the possibility of a fresh transfer pending outcome of embryo development. Should there be embryos to biopsy and freeze, I/we will require a future frozen embryo transfer cycle in order to attempt pregnancy, assuming results of the genetic analysis of the cells are favorable.

Initials: _____ / _____

Continued on next page

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Initials: Partner #1_________/Spouse or Partner #2__________
FROZEN EMBRYOS:  ☐ N/A: I/We do not have frozen embryos to be tested

I/We hereby authorize and consent to the thawing of my/our embryos that are currently frozen for the purposes of biopsy and subsequent genetic testing. I/We understand that the embryos that survive thawing and biopsy will then need to be refrozen using rapid freezing “vitrification” techniques. Assuming that genetic testing of embryos yields genetically normal embryos, those embryos will once again need to be thawed for the purposes of embryo transfer.

I/We have ______ embryos frozen and available for thawing and possible biopsy for genetic testing purposes. I/We understand that only embryos that successfully survive the thawing process will be biopsied, and not all embryos that are thawed will be able to be biopsied.

My/Our desire is to have ☐ ALL EXISTING - or- ☐ ______ (specify #) blastocysts thawed, biopsied and subsequently refrozen, assuming survival of those embryos.

Initials: ______ / ______

Assisted Hatching of Embryos

I/We acknowledge that my physician has counseled me/us on the fact that Assisted Hatching is a mandatory and required step for biopsy of the embryos for the purposes of Preimplantation Genetic Testing. I/We understand, agree and consent that: Laser Assisted Hatching of Embryos WILL BE PERFORMED to enable biopsy of any embryo(s) that will undergo Preimplantation Genetic Testing.

Initials: ______ / ______

Disposition of Abnormal Embryos

UNLESS Check Box Below is selected, your initials indicate your consent for AFC/AARL to:

DISCARD ALL GENETICALLY ABNORMAL EMBRYOS: I/We UNDERSTAND, AGREE, and CONSENT that ALL embryos found to be chromosomally abnormal will be AUTOMATICALLY discarded by AFC/AARL and not be available for future transfer.

Please note it is our policy in certain cases to send abnormal embryos to the reference genetics laboratory. This will allow the genetics laboratory to perform quality control testing on existing and new genetic testing methods with abnormal non-viable embryos. All abnormal embryos not sent to the genetics laboratory will be discarded or used for internal quality control/training purposes. “Discarded” embryos are never cultured to viability, donated, or cryopreserved for future attempts at producing a pregnancy. Please keep in mind that these are embryos that cannot be used to help you achieve a pregnancy.

☐ CONTINUE CRYOPRESERVATION of any embryos with ABNORMAL genetic test results. I/We UNDERSTAND and AGREE, that any embryos deemed genetically abnormal will NOT BE available for future transfer at Advanced Fertility Care. Annual storage fees will apply as long as they are maintained in cryostorage. AFC’s physicians and embryologists exercise the right to use reasonable medical judgment to determine if the embryo(s) are non-viable or not medically suitable for use for embryo transfer. Under no circumstances will the AFC physicians transfer a known genetically tested abnormal embryo into a woman’s uterus. AFC is not obligated to transfer these embryos at any point in the future if any medical evidence and/or any other experience indicate that the risk of transfer outweighs the benefits of transfer.

Initials: ______ / ______
Our signatures below acknowledge that all of our questions regarding PGT of my/our embryos have been answered completely. We understand that the analysis is performed at my/our request and I/we voluntarily request that AFC proceed with the analysis as discussed herein. I/We understand that we may revoke this consent at any time prior to the testing being initiated.

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 Preimplantation Genetic Testing process and its benefits, limitations, and risks, and agree to go forward with this procedure as our signatures below testify.

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