

**THE FERTILITY CENTER, LLC  
CONSENT FOR  
PRE-IMPLANTATION GENETIC DIAGNOSIS (PGD)**

**PURPOSE**

Pre-implantation Genetic Diagnosis (PGD) is used in conjunction with in vitro fertilization to detect numerical or structural anomalies in the chromosomes of embryos, as well as conditions caused by single gene defects. When embryos are affected by certain chromosomal conditions, these can prevent implantation to the uterine lining, lead to pregnancy loss, or result in the birth of a child with physical problems and/or mental retardation.

PGD can help prevent adverse outcomes by identifying affected embryos in the laboratory and thus preventing them from being transferred to the uterus.

**PGD for ANEUPLOIDY**

Normal human cells contain 46 chromosomes in 23 pairs. We receive 23 chromosomes from the sperm and 23 from the egg. The first 22 pairs of chromosomes are the same for male and female. The 23rd pair determines sex. A female has two "X" chromosomes, and a male has an "X" and a "Y." Woman can only pass an X to her child. The man passes either the X or the Y, therefore determining the sex of the child. If an error occurs, and the egg or sperm has an extra or missing chromosome, the embryo created by that egg or sperm will have an extra or a missing chromosome resulting in a condition called aneuploidy. Having an extra chromosome is known as trisomy and having a chromosome missing is known as monosomy. When aneuploidy involves the larger chromosomes, the embryo may not attach to the wall of the uterus or may stop developing soon after attaching, leading to a miscarriage. When aneuploidy involves chromosomes such as the 13, 18, 21, X or Y, the pregnancy may result in birth, even though there is a chromosomal disorder. The most common of these is an extra number 21, known as Down syndrome or trisomy 21 (three 21 chromosomes). Other common aneuploidies are Klinefelter syndrome (XXY), trisomy 13, and trisomy 18. The features of the chromosome condition depend upon which chromosome is extra or missing, but can include physical differences and mental retardation.

PGD for aneuploidy is often used in patients undergoing in-vitro fertilization (IVF) who are 35 years or older. Patients in this age group are at increased risk of miscarriage or birth defects due to aneuploidy. PGD may help reduce these risks. PGD for aneuploidy may also be used in patients of any ages who have failed several IVF cycles. Other patients who may consider PGD are those with a history of miscarriages or who have had an aneuploidy pregnancy in the past. In summary, the purpose of PGD for aneuploidy is to select chromosomally normal embryos for transfer in order increase the chance of pregnancy, reduce the chance of miscarriage, and reduce the children born with conditions caused by aneuploidy.

## **BIOPSY OF BLASTOMERES**



A blastomere is a cell within the embryo. To perform PGD on an embryo a blastomere is removed from the embryo. An opening is made in the covering of the embryo when the embryo has 5 to 10 cells. A blastomere is removed via aspiration with a pipette. The embryo is then returned to the incubator and the removed cell is analyzed.

## **ANALYSIS**

The biopsied cells are analyzed using a technique called *fluorescence in-situ hybridization* or FISH. This technique uses probes, small pieces of DNA that are a match for the chromosomes analyzed, to count the chromosomes present. These probes are different colors. The probes are applied to the biopsied cell and attach to the chromosomes. Under a microscope, we then count the number of chromosomes of each type (color) that are in that cell. The geneticist can tell normal cells from cells with aneuploidy. Testing of the cells destroys them because they must be glued to a glass slide and repeatedly heated and cooled. Therefore, the cells cannot be used for another purpose or returned to the embryo. The slides are kept for future reference. This analysis is accomplished in one day.

## **LIMITATIONS**

We are unable to study all of the chromosomes via PGD, and we are also unable to study the structure of the chromosomes. Because of these limits, prenatal testing after the IVF cycle with PGD is strongly advised in order to confirm the diagnosis and review the number and structure of all the chromosomes. This prenatal testing may be done in the first trimester via chorionic villus sampling (CVS) or during the second trimester via amniocentesis. CVS is a procedure done in the late first trimester that takes cells from the placenta and analyzes them for chromosomal abnormalities. Amniocentesis is a procedure usually done between 12 and 20 weeks of pregnancy that takes fluid from around the baby and analyzes the baby's cells in the fluid for chromosomal abnormalities.

## **THE RISK OF EMBRYO BIOPSY**

There is risk of damage to an embryo during the biopsy. This risk is relatively low and is influenced by the experience of the embryologist and the quality of the embryos. If an embryo is damaged by the procedure it will stop growing and will not be suitable for transfer into the uterus. The future fetus will be complete even if one or two cells are removed from the embryo. The procedure merely delays cell division for a few hours, after which the embryo continues its development.

## **MISDIAGNOSIS**

The accuracy of PGD of aneuploidy is approximately 90%. This means that the chance of the diagnosis being wrong is about 10%. One type of misdiagnosis is a false negative result, where a problem is not detected. Another is a false positive result, where you are told there is a problem when there is not. There is also the possibility that the testing will not work and not give a result. A mosaicism can also occur. A mosaicism means the same embryo has cells with different chromosomal make-up. Typically, all cells of the embryo have the same chromosomal make-up as they originate from the same fertilized egg. However, it is possible for cells of the same embryo to have differing numbers of chromosomes. A mosaicism can result in a specific type of false negative or false positive result. For example, if we analyze a cell that has normal chromosomal content, but another cell in the same embryo has an extra chromosome, we would erroneously diagnose that embryo as being chromosomally normal. Due to the chance of misdiagnosis, as well as the presence of types of aneuploidy for which we do not test, we recommend prenatal testing by CVS or amniocentesis. CVS and amniocentesis offer higher accuracy and lower misdiagnosis rates than PGD, in addition to more information.

If most of your embryos that we test are found to be abnormal, you may only have a few embryos for transfer. It is possible that none of your embryos will be found to be normal. In this case the embryo transfer will not be performed.

## **POSSIBLE BENEFITS**

PGD may reduce the miscarriage rate and the chance of having a child with aneuploidy by allowing the identification of chromosomally normal embryos for transfer; PGD may also increase the implantation rate. This benefit increases when more embryos are analyzed. If there are fewer than 6 embryos, there may not be any increase in implantation rate. When a patient produces fewer than 6 embryos, it may be appropriate to cancel the PGD. This decision should be discussed with your physician prior to the cycle start.

Genetic diagnosis of your embryos may increase the likelihood that you become pregnant with a healthy fetus. PGD will not cause you any physical discomfort other than what is experienced during a regular IVF cycle.

## **ALTERNATIVES**

Alternatives to PGD include standard prenatal testing for abnormalities once pregnant (chorionic villus sampling, amniocentesis, blood tests for Down syndrome, ultrasound). You are not obligated to undergo PGD even if your physician recommends it. You should undergo recommended prenatal testing that is based on your age and medical history even if you do PGD. The risks, benefits and alternatives of this testing should be discussed thoroughly with your obstetrician or the person performing/ordering the tests. You may also discuss your options with a genetics counselor. If you desire referral to a genetics counselor in your area please inform us. *Although these tests may serve as alternatives to PGD, PGD is not a substitute for routine prenatal testing.*

## **FOLLOW-UP**

Testing of a resulting pregnancy can be done via chorionic villous sampling (CVS) or amniocentesis. Your obstetrician, or someone to whom he or she refers you, can perform these tests locally. If prenatal diagnostic testing is not performed, chromosome analyses should be performed on cord blood at the time of delivery. We request that all results from genetic testing of the pregnancy or the child be forwarded to our IVF Coordinator at The Fertility Center, LLC address of 130 Leader Heights Road, York, PA 17403. This information will remain confidential and will be used to monitor outcomes of the PGD program.

**LEGAL STATEMENT**

**We have read the entire consent form, or it has been read to us. We understand that PGD has benefits and risks, some of which may be unknown at this time. We want to proceed with PGD.**

**We also understand that undergoing PGD *does not eliminate* the need for standard prenatal testing such as chorionic villus sampling or amniocentesis. The need for these tests *remains the same* whether or not PGD for aneuploidy is performed. We understand that if we have questions about CVS or amniocentesis we may ask our obstetrician or we may request a referral to a genetics counselor.**

**We have been given an opportunity to ask questions about the PGD procedure and the contents of this consent form. If we think of additional questions, we may contact our physician.**

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Female Partner's Signature

Date

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Male Partner's Signature

Date

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Witness' Signature

Date

You may request a copy of this form for your records.

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