



# Consent for Preimplantation Genetic Diagnosis (PGD) for a Balanced Translocation

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Print Patient's Name

Date

## Purpose & background

The purpose of the procedure is to select and transfer to the uterus those embryos that can be diagnosed as chromosomally normal.

Chromosomes are string-like structures found in the center of the cell, the nucleus. Chromosomes carry our inherited information in genes that are made of DNA. During the process of cell division, occasionally chromosomes may become attached to each other, or pieces of different chromosomes may interchange – this is known as a chromosomal translocation. The change may take place so that there is no extra or missing chromosomal material, or the break in the chromosome may not affect gene function, and there is no effect on the individual. If there is no additional or missing chromosome material, the translocation is considered to be “balanced”; if there is extra or missing chromosomal material, the translocation is “unbalanced”.

Individuals with balanced translocations typically have no medical problems, although some do have reduced fertility. Although an individual with a balanced translocation may be healthy, a problem can arise if the egg or sperm of that individual has an unbalanced chromosome make-up that leads to an unbalanced translocation in the resultant embryo or pregnancy.

The presence of an unbalanced translocation can lead to failed implantation of an embryo, a miscarriage during pregnancy, or a child being born with mental and physical problems. Therefore, individuals with a translocation may experience multiple pregnancy losses or have a child affected with physical and mental problems that may be lethal. A child that appears to have the same balanced translocation as the parent may have a new tiny change in chromosomal material that leads to physical or mental problems. The new change may not be detected by standard chromosome analyses.

There are two types of translocations: Reciprocal and Robertsonian. Reciprocal translocations involve any 2 chromosomes. Breaks occur in the chromosomes allowing pieces to be exchanged between them. Approximately 1 in 625 individuals has a reciprocal translocation. Approximately 1 in 900 individuals has a Robertsonian translocation. These translocations involve chromosomes 13, 14, 15, 21 and 22. Robertsonian translocations result from breaks in the middle of the chromosomes and subsequent fusion of 2 bottoms of the chromosomes.

## Procedure

The procedure consists of five different steps, usually performed by a team of experts in two laboratories. (i) The first part is in vitro fertilization (IVF) in which eggs are harvested from the female patient and fertilized with the male partner's sperm in order to produce embryos. (ii) The second part is embryo biopsy where one cell is removed from the embryo for analysis. (iii) The processing of the cell, in this case called cell fixation (iv) The analysis of the cell is performed by a reference laboratory (v) The final step, the transfer of the embryos to the patient, is done by your physician.

This consent form is for the fourth part, the analysis of the biopsied blastomeres by the reference laboratory. You will also be presented with other consent forms, including one for embryo biopsy and cell processing (fixation) and another for IVF and embryo transfer.

### **Abstention from intercourse**

It is critical that Patients refrain from sexual intercourse for a period of time beginning fifteen (15) days prior to the date that the Patient's eggs are retrieved, and ending not before the date the Patient receives conclusive results of a pregnancy test performed by the Patient's physician. Abstention from intercourse is required because sperm can survive up to fifteen (15) days in vivo. As such, it is possible that sperm from intercourse may result in fertilization and implantation of an embryo, in addition to, or instead of, fertilization and implantation that results from IVF. This would negate the results of PGD testing.

### **Biopsy and blastomere fixation**

A blastomere is a cell from an embryo. To test the blastomere, an embryologist from the IVF laboratory makes an opening in the covering of the embryo on the third day of development, when the embryo has 5 to 10 cells, and removes a blastomere via aspiration with a pipette. The embryo is returned to an incubator and the cell that was removed from the embryo is fixed to a glass slide and sent to an outside reference laboratory for analysis. Please read and sign the consent form for embryo biopsy and fixation given to you by Dr. Miller, which will explain the risks of this procedure.



## **Cell transport**

After the cells have been biopsied and fixed, the embryologist sends the slides to an outside reference laboratory for analysis by same-day or next-morning delivery couriers.

## **Analysis**

The fixed cells are analyzed by an outside reference laboratory 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 to be analyzed, to count the chromosomes present. The probes attach to the chromosomes when they are applied to the biopsied cell, and each appears in a different color.

Under a microscope, the numbers of chromosomes, identified by color, are counted and the geneticist can distinguish normal cells from cells with aneuploidy. The cells must be glued to a glass slide and repeatedly heated and cooled before testing, and are destroyed in the process. Therefore, the cells cannot be used for another purpose or returned to the embryo. The analysis is usually accomplished in one day, and the slides are kept for future reference.

## **Limitations**

The reference laboratory is unable to study all of the chromosomes, or study their structure via PGD. Because of these limitations, 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.

Prenatal testing may be carried out in the first trimester of pregnancy via chorionic villous 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 usually done between 15 and 20 weeks of pregnancy; this procedure takes amniotic fluid from around the baby and analyzes cells from the baby found in the fluid for chromosomal abnormalities.

## **Risks**

### **The risk of embryo biopsy**

PGD does not guarantee the birth of a normal baby. It is not known whether biopsied embryos are less likely to implant than embryos that have not been biopsied. Embryo biopsy itself, without the assay results, may lower implantation rates slightly, but selection of chromosomally normal embryos via PGD will more than compensate for any negative effect of embryo biopsy, and increase the probability that the embryos transferred will implant.



If an embryo is damaged by the procedure, it will stop growing and will not be suitable for transfer into the uterus. The risk of damaging an embryo during removal of the cell(s) is less than 1%. The future fetus will be complete even if one or two cells are removed from the embryo. The procedure may delay cell division by a few hours, after which the embryo continues its development.

It is estimated that more than 2000 babies have been born from IVF with PGD with no reported increase of congenital abnormalities above the general population rate. The rate of malformations in the general population is 3-5%. This procedure, however, has not yet been performed sufficiently to rule out any detrimental effect on embryo development. Therefore, we still strongly recommend chorionic villus sampling or an amniocentesis in order to confirm the preimplantation diagnosis.

## **The risk of fixation**

After embryo biopsy, the biopsied cell is glued (fixed) to a glass slide and an acid solution removes all but the center of the cell, the nucleus, which contains the chromosomes to be studied. After this process, the cells are no longer viable in any way and can only be used for analysis. A fraction of cells may not have a test result. Some cells may not have a nucleus and will not yield a result, some cells may be lost during the fixation process, and others may have suboptimal fixation rendering the cell inadequate for analysis. Embryos without analysis may still be transferred, but the advantages of PGD do not apply.

## **The risk of transport**

Once the cells are fixed a third party transports the cells to the reference laboratory for analysis using same day or next morning delivery services. Weather and air travel conditions may delay the receipt of samples. Rarely samples do not arrive in the reference laboratory or are damaged during transport.

## **The risk of the PGD analysis**

When the reference laboratory personnel analyze the cells, the risk of a clinical misdiagnosis resulting in a fetus or baby with chromosome abnormalities after a PGD is less than 1%.

Due to the chance of misdiagnosis, as well as the presence of types of chromosome problems for which we cannot or do not test; your pregnancy should be carefully monitored. Again, we strongly recommend prenatal testing by CVS or amniocentesis. CVS and amniocentesis offer higher accuracy and lower misdiagnosis rates than PGD, and may yield more information.



**NO EMBRYOS FOR FREEZING** - If most of your embryos that are tested are found to be abnormal, you may only have a few embryos for transfer, and none left for freezing. This is common.

**NO NORMAL EMBRYOS** - It is possible that none of your embryos are found to be normal or balanced, and embryo transfer will not take place. This occurs in approximately 20% of cases.

**NO DIAGNOSIS AND PARTIAL DIAGNOSIS** - Due to the fact that some cells may lack a nucleus, or due to the fixation process, some embryos will not have a diagnosis. Embryos without a test result can still be transferred, but all the possible advantages of PGD will not apply. In addition, occasionally the test result may not be clear for one of the chromosomes; this embryo could be transferred, but the advantages of PGD do not apply.

Because of the possibility of misdiagnosis, your pregnancy should be carefully monitored. Between 10 to 18 weeks, we strongly recommend that you have chorionic villous sampling (CVS) or amniocentesis performed. The fetus should also be monitored with ultrasound examination to check its growth and development. There is no guarantee that a child will be normal after IVF with PGD.

### Possible Benefits

In the majority of cases, embryos with unbalanced translocations are indistinguishable morphologically and developmentally from those that are chromosomally normal. Thus, without genetic testing, an embryologist cannot differentiate the normal or balanced embryos from unbalanced embryos and could transfer the unbalanced embryos to you.

Most chromosomally abnormal embryos either do not implant or spontaneously abort after implantation. Whereas PGD for translocation considerably reduces the chance of miscarriage for patients that have been tested thus far, this may not apply in your individual case and a miscarriage may still occur. PGD will not cause you any physical discomfort other than that experienced during a regular IVF cycle.

### Alternatives

Alternatives to PGD during pregnancy include standard prenatal testing for abnormalities (chorionic villous sampling, amniocentesis, ultrasound examination). You are not obliged to undergo PGD even if your physician recommends it. You should undergo recommended prenatal testing that is based on your age and medical history.

The risks, benefits and alternatives of this testing should be discussed thoroughly with your genetic counselor, obstetrician or the person performing/ordering the tests. If you wish to be referred to a genetic 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.



## Confidentiality

Confidentiality of your records will be maintained in accordance with applicable state and federal laws at all times.

## Genetic consultation before PGD

It is recommended that you have a consultation with a genetic counselor that specializes in PGD before undergoing PGD. This can be arranged through Women's Fertility Center [Subject to state law requirements].

## Specimen retention

The cells to be tested will be destroyed during the process of the analysis. This will usually occur within 5 days of the biopsy. After testing has occurred, the reference laboratory will retain blood, chromosomes and/or the DNA until three months after the birth of the baby; the specimen is retained for follow up and preparation of future cycles.

## Follow up

Testing of a pregnancy can be done via chorionic villous sampling (CVS) or amniocentesis. Your obstetrician, or someone he or she refers you to, 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.

If a pregnancy loss occurs, we request that chromosome studies be performed on the products of conception. All results from genetic testing of the pregnancy or the child up to the age of one year will be forwarded to the PGD Program Coordinator at the reference laboratory. This information will remain confidential and will be used to monitor outcomes of the PGD program.

## Costs

Fees for PGD are in addition to the cost of the IVF cycle. If the PGD procedure is paid for but not performed, your payment will be refunded less the cancellation fee. You are also responsible for any additional medical costs incurred as a result of complications or other medical care required as a result of receiving preimplantation genetic diagnosis.

Insurance cover for all or any part of this total procedure may not be available, and you are personally responsible for payment of such costs including hospital and laboratory charges, and physician's professional fees.



## Declaration

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 wish to proceed with PGD for translocations.

We also understand that undergoing PGD for translocations does not eliminate the need for standard prenatal testing such as chorionic villous sampling or amniocentesis. The need for these tests remains the same whether or not PGD for translocations 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 genetic 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, genetic counselor or nurse.

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Patient's Signature	Print name	Date
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Partner's Signature	(if not applicable, write NA)	Date
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Witness Signature	Print name	Date
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You may request a copy of this form for your records.

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Signature of Nora Miller, MD	Date
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