MASSACHUSETTS GENERAL HOSPITAL
VINCENT REPRODUCTIVE MEDICINE AND IVF

INFORMED CONSENT FOR EMBRYO BIOPSY

FOR USE IN PREIMPLANTATION GENETIC DIAGNOSIS

This consent form describes pre-implantation genetic diagnosis (PGD), which is used to diagnose a genetic abnormality in eggs fertilized through in vitro fertilization. PGD involves taking one or two cells from each fertilized egg (embryo) after they have grown to at least 6 cells in the culture dish. We will then test these cells to look for a chromosome or gene problem before the fertilized eggs are selected to be transferred (replaced) into the uterus. PGD has been offered to you because you or your partner are at increased risk of having a child with a chromosomal abnormality or a specific gene mutation and have decided to undergo in-vitro fertilization. If you choose to undergo PGD, your embryo analysis will be directed to the genetic risk of concern. Our methods cannot predict all genetic disorders.

For couples with a balanced chromosomal translocation, the purpose of PGD is to evaluate your embryos for the chromosomes involved in the translocation. Embryos containing unbalanced rearrangements of these chromosomes will not be transferred as they would lead to an abnormal baby or a miscarriage. You will not know whether the embryos transferred into your uterus are normal embryos or balanced embryos (carrying the balanced translocation).

For couples at risk for a specific genetic disease, embryos will be tested for that gene. Embryos affected with the disease will not be transferred back into the uterus. If an embryo is not affected with the disease, but carries one copy of the recessive disorder gene for the disease ("carrier embryos"), then we will discuss this situation with you, including potential risks and options.

For women who are carriers of an X chromosome-linked disorder and test for whole chromosome number (FISH), only female embryos will be transferred, as half of the male embryos would be affected.

For couples at risk for aneuploidy, the purpose of PGD is to evaluate the embryos for chromosomal abnormalities frequently seen in spontaneous abortions. Embryos thought to have abnormalities in the number of chromosomes (3 chromosomes instead of two, one chromosome instead of two), will not be transferred as they could lead to either an abnormal baby or a miscarriage. One important thing to remember is that your embryos will be tested only for those chromosomal abnormalities frequently seen in spontaneous pregnancy losses. The test normally evaluates 5-12 pairs of chromosomes. Each embryonic cell normally contains 23 pairs of chromosomes. Therefore, your embryo could test normal for those 12 pairs of chromosomes and still have an abnormality in another chromosome pair that we do not have the ability to test for.

In cases where there are concerns about the quality of the probes binding the chromosomes or quality of the first cell biopsied, an additional cell may be biopsied.

As part of the PGD screening process, you will visit with a genetic counselor to discuss your particular risks of having a chromosomally or genetically abnormal pregnancy. He/she will take a detailed family history including specific questions about possible single gene disorders in your

family. If you decide to undergo PGD, blood testing will generally first be performed on both of you to be sure that our methods can find your specific chromosome abnormality.

You will have approximately 10 visits that are required for a typical In Vitro Fertilization (IVF) treatment cycle. Embryo genetic testing may help us to transfer back into your uterus only those embryos found not to be abnormal. However, we also recommend an amniocentesis (taking a sample of fluid from around the baby) or chorionic villus sampling (biopsy of the placenta), through your obstetrician specialist when you are pregnant.

You understand that your IVF cycle may be discontinued if, upon controlled ovarian hyperstimulation, there are not enough mature follicles produced in the ovaries or if the eggs are released from the ovaries before the eggs can be retrieved surgically. In addition, if the female partner is thought to be at risk for the illness Ovarian Hyperstimulation Syndrome, the IVF cycle may have to be canceled.

The PGD procedure involves microscopic removal of one or two cells from the embryos after fertilization. First, a small hole is created in the zona pellucida (outer coating) of the embryo, a procedure that also "assists" with the hatching of the embryo later in the development. A cell of each normally dividing embryo is then removed. Genetic analysis of this cell will be performed directed by the condition for which you are at increased risk. After the cells are removed for testing, the embryos will be grown in culture for a short period, prior to transferring them back into the uterus.

The cells that are removed will be prepared for genetic diagnosis by placing them in special tubes and sent by courier to the laboratory performing the genetic test.

1) For couples at risk for a specific genetic disease, embryos will be tested for that gene at the GenesisGenetics Institute in Detroit, Michigan. You will have already contracted GenesisGenetics Institute to perform the genetic testing on the cells that we send. When Genesis Genetics laboratory has completed the testing on the cells, they will notify you and our office. At that time, we will all discuss which embryos should be transferred to your uterus for the initiation of a pregnancy.

2) The cells removed from embryos of couples at risk for chromosomal abnormalities will be evaluated at the ReproGenetics laboratory in New Jersey. You will have already contracted ReproGenetics laboratory to perform the genetic testing on the cells that we send. When ReproGenetics laboratory has completed the testing on the cells, they will notify you and our office. At that time, we will all discuss which embryos should be transferred to your uterus for the initiation of a pregnancy.

Following embryo transfer, you will be monitored with routine blood tests for human chorionic gonadotropin (hCG) pregnancy. Once you are pregnant, your pregnancy will be followed in a routine fashion. We request permission to contact your obstetrician for the results of your chrorionic villus sampling (biopsy of a piece of placenta for chromosomal or gene analysis), or amniocentesis (testing of cells in the fluid around the baby for chromosomal or gene analysis), prenatal care and delivery, and to contact your child's pediatrician for growth and development information.

Do you agree to allow us to contact your obstetrician for information regarding the amniocentesis, CVS, prenatal care and delivery and your pediatrician for information about your child's growth and development?
Yes ____ No ____

RISKS AND DISCOMFORTS

- Embryos may be damaged during the biopsy procedure reducing their ability to initiate a normal pregnancy.
- Risks of the genetic testing of cells of the embryo are that the cells could test normal when, in fact, other cells in the embryo are abnormal, leading to transfer of an abnormal embryo. The scientific literature reports that this occurs in about 0.3% to 5.6% of the cells that are diagnosed.
- Alternatively, the cell biopsy may test abnormal when the remainder of the embryo is in fact normal, but not transferred due to this error.
- Additionally, at this time we are unable to test for all chromosomal abnormalities; therefore, even if embryos test normal for the chromosomes tested, other abnormalities could be missed, leading to an abnormal pregnancy.
- Birth defects and other types of problems may occur in pregnancies that are completely normal chromosomally and would not be found by our testing.
- There is a possibility that none of your embryos will test normal and that none will be recommended for transfer.

BENEFITS

- We believe that the benefit of PGD is to decrease the chance of a miscarriage or having a baby that has the specific chromosome problem or specific genetic disease you face as a couple.

ALTERNATIVES

- Conceive a pregnancy on your own and have an abnormal pregnancy terminated once the diagnosis is made by amniocentesis or chorionic villus sampling,
- Conceive a pregnancy on your own and carry an abnormal pregnancy to term,
- Insemination of the female patient with sperm from a donor that has proven to not carry the gene for the disease,
- Use of eggs obtained from an egg donor who has been proven to not carry the gene for the disease, or
- Adoption

COSTS

PGD costs are separate from IVF. There will be charges for the embryo biopsy procedure. In addition, there will be the charges for the genetic diagnosis that is performed on the cells removed from the embryos. An outside diagnostic laboratory that you have contracted with to do this work is performing these tests. You understand that you will be responsible for all of the costs for this procedure, including the cost of standard IVF. You understand that you are responsible for paying these costs prior to the cycle if not covered by your insurance. Such costs

do not include the IVF medications, which you will receive from the pharmacy of your choice and pay for yourself if not covered by insurance.

DISPOSITION OF EMBRYOS BIOPSIED FOR PGD

As explained above (p.2), following the receipt of PGD test results, we will discuss with you which embryos should be transferred to your uterus for the initiation of a pregnancy. Other remaining embryos that have undergone PGD, where biopsied cells tested abnormal or with uncertain results as to normalcy, will be disposed of in accordance with your wishes below. Such remaining embryos may be photographed and/or preserved for diagnostic and teaching purposes.

Please choose one option below for the disposition of your embryos that have undergone PGD and are not suitable for transfer:

- ❑ **Donate to research or activities related to improving assisted reproductive therapies (ART)**:
  - The research and activities related to improving ART may include, for example, studies of ways to improve techniques or fertility success rates or studies that may improve our understanding of infertility and reproductive medicine.
  - The research also may include embryonic stem cell research. In this case, MGH would contact us to provide more information about a particular study and to ask whether or not we consent to donate embryos to the study. MGH would retain a link between my/our embryos and limited information about me/us in order to contact us about such research.
- ❑ **Discard** according to standard hospital and program procedures.

Initials of Patient and Partner: ____ ____

CONSENT

This consent will function as an addendum to the consent form entitled Informed Consent for In Vitro Fertilization, which we executed previously, except that the Disposition section immediately above will govern the disposition of embryos that have undergone PGD and are not suitable for transfer.

We, the undersigned, have read this document, understand the purposes, risks, and benefits of this procedure and have been given the opportunity to ask questions about it, which have been answered to our satisfaction. We consent to having our embryos biopsied for use in preimplantation genetic diagnosis and disposed of in accordance with our wishes herein.

Female patient	Partner
Print Name	Print Name
Date of Birth	Date of Birth
Date	Date