ACIBADEM	
LG-MG-FR-005	**INFORMED CONSENT FORM FOR MONOGENIC DISEASES (PGT-M) AND/OR HLA TYPING (PGT-HLA) PREIMPLANTATION GENETIC TESTING**

Female	**Name-Surname**				**BARCODE**
	Date of Birth				
	Phone				
	E-Mail Address				
	Type of Sample		**Sampling Date-Time**		
Male	**Name-Surname**				**BARCODE**
	Date of Birth				
	Phone				
	E-Mail Address				
	Type of Sample		**Sampling Date-Time**		
Address Details					
Doctor Information	**Name-Surname**				**Stamp/Signature**
	Institution				
	Phone				
	E-Mail Address				
Clinical Information and Family History					
Requested Test Information					

GENERAL INFORMATION ABOUT THE APPLICATION

Preimplantation Genetic Test (PGT) is a method in which genetic tests and IVF applications are applied together in order for a carrier or affected couple to have a healthy baby for a hereditary genetic disease. This process can be successfully used in hereditary single-gene diseases with known causes. Single-gene (monogenic) diseases are hereditary diseases caused by mutations or changes in a specific gene in the DNA of the sick person (such as Spinal Muscular Atrophy (SMA), Beta Thalassemia, Alpha Thalassemia, Cystic Fibrosis, Sickle Cell Anemia).

With the Preimplantation Genetic Test (PGT) method, healthy or affected embryos can be distinguished. There is certainly no such thing as changing genes in the PGT process. For PGT to be performed, it is necessary to determine which gene or genes the expectant mother and father have mutations in before the procedure. PGT procedure consists of the steps of obtaining embryos by combining egg cells taken from the mother and sperm cells taken from the father with the IVF method and transferring embryos that do not carry the disease to the mother by testing the obtained embryos for the disease in question.

The PGT method can be used for different purposes; PGT-M is the process of determining whether the embryos obtained by IVF application of couples known to be carriers for a hereditary single gene disease carry the mutation in the parent. PGT-HLA is the process of determining whether the embryos obtained as a result of IVF are both healthy and HLA compatible in order to perform marrow transplantation to an affected individual with a single gene disease such as Beta Thalassemia and Fanconi Anemia, which can be treated with bone marrow transplantation. Although this application is not hereditary, it can also be applied to individuals with a disease such as leukemia and aplastic anemia, which can be treated with bone marrow transplantation, and in this case, only HLA tissue adaptation in the embryo is examined. Before starting the PGT-M and/or PGT-HLA procedure, a preparation phase called "Pre-Preparation (Setup) Procedure" should be carried out with the DNA obtained from blood or cheek swab samples to be taken from you and your relatives (if any, your children, parents or siblings). In this process, the markers specific to the disease and mutation you carry will be detected and these markers are used to test the embryos during the PGT process. This process is family-specific and takes about 6-8 weeks. For technical reasons, this period can sometimes be extended.

Biopsy samples are sent to the genetics laboratory for examination for genetic testing. Reporting is done after the analysis with the help of the markers obtained as a result of the family-specific setup process. In cases where the test does not give results for any reason or the result obtained is not sufficient for any reason, a second biopsy procedure (rebiopsy) may be required.

LIMITATIONS and GENERAL CONCEPTS

- Potential risks that may arise during embryo development, embryo biopsy, and PGT procedure;

- Failure to perform biopsy due to cessation of embryo development.
- Technical problems for which embryo biopsy is not possible.
- Loss of viability of embryos frozen by biopsy after thawing.
- Failure to obtain informative results after genetic testing or the results remaining below the reliability limit.
- If there is no embryo suitable for transfer, IVF and PGT procedures have to be repeated.

- The PGT-M process in embryos is limited to the DNA mutation in the targeted gene or genes and does not provide information about diseases and disorders that may arise from other variants. Therefore, it does not include any other single gene disease that is not included in this process. It also does not provide information about the numerical and structural chromosomal disorders that may occur in an embryo. For this reason, our institution cannot be held responsible for direct and indirect damages arising from single gene diseases and numerical-structural chromosomal disorders that are not included in this test.

- The PGT-M process does not detect chromosomal anomalies. PGT-A (Preimplantation Genetic Test for Screening for Aneuploidy) or PGT-SR (Preimplantation Genetic Test for Translocation) tests can be applied to detect chromosomal anomalies. Since PGT-A and PGT-SR tests are different from PGT-M procedures, separate written consent must be given for PGT-A and PGT-SR procedures.
- The following possibilities may arise in line with the test results in which molecular genetic diagnosis is made in single gene diseases. These possibilities are based on the classification of variants in single gene diseases genetic analysis reports according to their disease-causing effects. This classification is made following the criteria proposed by the "American College of Medical Genetics (ACMG)"1. According to the variant classification made according to these criteria*,

-Pathogenic (P); In cases where pathogenic variants that explain the patient's clinic and whose disease-causing effect has been reported in the literature are reported,

-Likely Pathogenic (LP); PGT-M can be applied in cases where possible pathogenic variants that explain the patient's clinic but whose disease-causing effect has not been reported in the literature are reported.

-Variant of Uncertain Significance (VUS)

-Likely Benign

-Benign

A DNA variant included in one of the above-mentioned classes may be included in another class with varying scientific data. Therefore, the targeted DNA variant in the PGT-M process may not be the main gene and DNA variant causing the disease in the family in which the process was conducted. In particular, it should be considered that variants of uncertain significance (VUS) can be classified as benign or pathogenic with new processes.

All responsibility for the targeted gene/genes and variant in PGT-M procedures performed according to the genetic test results processed in the external center belongs to the center and family working on the diagnostic test or carrier screening test.

In the consent form, details about the clinical diagnosis, gene/genes and target variant should be written in the process area.

- Our institution cannot be held responsible for direct and indirect damages arising from sick childbirth associated with genes/genes and variants that are not covered by the patient’s decision.
- The reliability of PGT-M tests depends on the safety of the genetic data of the family members with the index case examined and the correct classification of the variants in the report subject to the procedure. The classification of variants may vary with the increase of information in databases over time, and a previously classified variant may be defined in another class in the light of new information.
- PGT applications for HLA haplotyping alone do not detect inherited single gene diseases or chromosomal disorders.
- The probability of misdiagnosis with PGT-M and PGT-HLA is around 1-2% per application2. The reliability of the test is 98%. Testing the biopsy sample may not show any evidence of the embryo as a whole. Trophectoderm cells and embryonal cells may be different. Feto-placental differences may occur. These tests do not provide information about multifactorial diseases or microdeletion syndromes, ploidy disorders (triploidy, tetraploidy, etc.), and balanced chromosomal changes (translocation, inversion). Therefore, the results of the test must be confirmed by invasive prenatal diagnostic techniques (CVS, amniocentesis and cordocentesis).
- The marker regions determined as informative from the DNA of men and women can show certain proportions of concordance. The results may be affected by biological factors such as the loss of genetic material due to crossing-overs or allele drop-out (ADO) of gene and STR regions, situations caused by application and analysis, damages during embryo biopsy, performance of simultaneous devices, errors caused by human and test systems, and possible de novo (new formation). Depending on these, the tests may be repeated, the time to get results may be prolonged, the result may not be reached or it may be evaluated incorrectly.
- Couples need to abstain or be protected to avoid the risk of an unplanned pregnancy during PGT-supported IVF application. Our institution cannot be held responsible for direct and indirect damages that may occur if the patient has a child due to the pregnancy that may occur before or after the fresh or frozen embryo transfer with PGT-M or HLA test.
- Embryo biopsy samples delivered to our laboratory and not processed will be stored for a maximum of 3 years after they reach our laboratory and will be destroyed at the end of the period.

EVALUATION OF THE RESULTS

Normal: These embryos can be transferred.

Affected: Embryos detected as homozygous mutant in autosomal recessively inherited diseases after PGT-M or heterozygous in cases with autosomal dominant inheritance. These embryos can not be transferred.

Carrier: Embryos detected as heterozygous in autosomal recessive cases do not show a clinical finding. However, in the future, in the case of a spousal marriage with the same gene variant, they may have affected children.

In diseases transferred due to the X chromosome, the carrier female embryos themselves may also show some signs of the disease and there is a risk of having a affected male child in the future. Our institution cannot be held responsible for direct and indirect damages incurred if this group embryo transfer is requested.

ADO: The amplification of only one of the maternal or paternal gene copies (allele) is called allele drop-out (ADO). In this case, if the detected allele is normal, the embryo can be transferred for recessive diseases with the information that the embryo is carrier or normal. Transfer of embryos with autosomal dominant, ADO detected is not recommended.

Insufficient Data: It refers to situations where low reliability and insufficiently informative results are encountered or no results can be obtained. In this case, it is recommended to take a biopsy again and repeat the tests.

INCORRECT DIAGNOSIS CASES

PGT-M and PGT-HLA have a 1-22% risk of misdiagnosis. “False positivity” is among the most important causes of errors. “False positivity” means abnormal detection of normal embryos. Conversely, there is a possibility that abnormal embryos are detected as “normal”, that is, there is a possibility of “false negatives”.

A second important cause is contamination. Contamination means that maternal, paternal or foreign DNA molecules mix with the DNA of the sample to be analyzed before or during the procedure and affect the results. To prevent contamination; culture conditions, embryo biopsy process and all laboratory procedures should be carried out under highly sterile conditions to prevent possible foreign genetic material that may come from outside.

Since PGT-M application is performed with a very small number of cells, the target gene region on the DNA from the mother or father cannot be reproduced by PCR in some embryos. This may lead to a lack of results. In addition, the ADO condition, which occurs as a result of the reproduction of only one copy of the relevant gene region of the mother and father, may also cause misdiagnosis.

Our institution cannot be held responsible for direct and indirect damages caused by faulty diagnoses, including false positivity or false negativity, due to the technical and biological limitations of the tests in terms of diagnosis.

COST AND CONFIDENTIALITY

In accordance with the provisions of the “Tıbbi Laboratuvar Hizmetleri ve İleri Teknoloji Tıbbi Laboratuvar Uygulamaları Hakkında Yönetmelik” in force, the service breakdown and unit prices for the services provided for the examinations are arranged in detail and a copy is given to the parent upon request.

In accordance with the provisions of the relevant legislation, test takers have the right to request that their personal information, health conditions, diagnosis and treatment information, as well as their visits during diagnosis and treatment, be kept confidential. Such information may only be shared with legal authorities if necessary.

Persons in charge of providing health services may only access the health data of the person concerned, provided that it is limited to the requirement of the health service to be provided.

Our institution cannot be held responsible for direct and indirect damages caused by patients who share limited/incomplete health data due to incomplete data sharing.

CERTIFICATION

In accordance with the provisions of the “Biyoloji ve Tıbbın Uygulaması Bakımından İnsan Hakları ve Haysiyetinin Korunması Sözleşmesi 3” and the “Tıbbi Laboratuvar Hizmetleri ve İleri Teknoloji Tıbbi Laboratuvar Uygulamaları Hakkında Yönetmelik“ in force, genetic examination is not performed for the purpose of gender determination only without medical indication at each step of PGT procedures from the beginning to the end. In cases other than gender-related diseases, gender is not specified in preimplantation genetic test reports.

CONSENT TO STORAGE AND USE

Consent For Storage	**Consent to Use**
DNA samples may need to be used for additional genetic testing in the future. The obtained DNA samples (belonging to family members and embryo biopsies) are kept for 5 years.	Test results are an important resource for researchers to investigate genetic diseases and improve their diagnosis and treatment. In this case, personal data is anonymized and/or encrypted. After anonymization, the rights regarding the data and material will belong to Acıbadem Maslak Genetic Diseases Diagnosis Center. Accordingly, I consent to the storage and use of my test results in the database for scientific purposes, to improve and facilitate the identification of diseases and to provide statistical information.
□ I accept. **□I do not accept, my samples should be destroyed when legal obligations are eliminated.**	**□ I accept.** **□ I do not accept, it should be kept only for the purpose of being used for additional processes approved by me.**

CONSENT

By signing this request form, I consent to the PGT-M /PGT-HLA test being performed voluntarily. I have received comprehensive information on the indication, procedure, chance of success, limitations and results of the proposed test, as well as the duration and cost of this test. The applications to be performed, their duration, possible consequences and complications, risks, and consequences were explained in detail. In the event that this information is not sufficiently understood by me, I know that the experts are ready to explain all aspects of the relevant issues.

All genetic data are processed, recorded and stored by you within the scope of personal consent for the purposes specified in this document. I have been informed about my rights as the relevant person within the scope of Article 11 of the 6698 sayılı Kişisel Verilerin Korunması Kanunu5 that my data obtained and processed by Acıbadem in line with the purposes specified in the relevant legislation and this document can be shared with the companies included in the Acıbadem Group, all kinds of judicial authorities, their authorized representatives, domestic and foreign institutions from which you receive consultancy, regulatory and supervisory institutions, business partners and other third parties with whom they cooperate in order to realize or improve the services offered, including official authorities; in the physical archives and/or information systems of Acıbadem, both in the digital environment and in the physical environment.

According to the need of the process, we were informed that there is a possibility to include our children in the process by taking blood from our first or second degree relatives, if any, and that the blood collection will be included in the process by obtaining a separate consent with the **Genetic Tests Consent Form.**

I have read a copy of the informed consent, understand and accept that no result has been committed to me by the application of the said tests, that these tests have limitations and that I cannot impose any defects and liability on those who perform the test due to direct and indirect damages incurred in these cases. We authorize this practice to be carried out without any pressure and direction, completely of my own free will, and we request this practice to be carried out. We consent this practice to be carried out voluntarily.

I know that I can withdraw this permission partially or completely at any time without giving any reason, provided that I convey it in writing and signed, and that I have the right not to receive information about the test results.

We have read, understood and fully accepted all the above-mentioned stages.

Please, write "I have read, I understand and I accept" in your handwriting in this field.

Gene(s) to be Processed	
Class of Variant*	

Wife Name-Surname/Signature/Date)	**Husband (Name-Surname/Signature/Date)**	**Witness (Name-Surname/Signature/Date)**	**Physician (Name-Surname/Signature/Date)**

Report Delivery Preference: All genetic data is personal and cannot be shared with third parties. In our center, only your physician who made the test request is informed by e-mail. If you give your consent, your final report may be sent to the physician or physicians who make the request and follow you clinically, to you or to another person you authorize. For this, you need to indicate your authorization request in your handwriting.

Authorization to Receive Information on the Result:

REFERENCES

1-Richards S. et al; ACMG Laboratory Quality Assurance Committee. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015 May; 17(5):405-24.

2-Greco E. et al; Preimplantation Genetic Testing: Where We Are Today. Int J Mol Sci. 2020 Jun 19;21(12):4381.

3-In accordance with Law No. 5013 "Biyoloji ve Tıbbın Uygulaması Bakımından İnsan Hakları ve Haysiyetinin Korunması Sözleşmesi"

4-Dated Ocotober 24, 2025 and numbered 33057 "Tıbbi Laboratuvar Hizmetleri ve İleri Teknoloji Tıbbi Laboratuvar Uygulamaları Hakkında Yönetmelik"

5-Dated June 21, 2019 and numbered 30808 "Kişisel Sağlık Verileri Hakkında Yönetmelik"

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