LG-OrT-FR-031	EXOME/GENOME INFORMED CONSENT FORM

PATIENT INFORMATION BARCODE	**NAME SURNAME**		**GENDER**	☐ **FEMALE** ☐ **MALE**
	DATE OF BIRTH		**SAMPLE TYPE AND INFORMATION**	
	ADDRESS		☐ **Peripheral Blood (2-6 ml, EDTA tube)**	
	E-MAIL		☐ **DNA (min 2 µg)**	
	TEL (GSM)		Concentration_____(µg/ml) Volume_____(µl)	
REQUESTING DOCTOR STAMP/SIGNATURE	**NAME SURNAME**		☐ **Other** (specify)_____	
	INSTITUTION			
	TEL		**SAMPLE DATE**	
	E-MAIL		**SAMPLE HOUR**	

TEST SELECTION

TEST	**SAMPLE TYPE**	**CNV ANALYSIS**	**WORK TYPE**
☐ Whole Exome Sequencing (WES)	☐ POSTNATAL	☐ Select for CNV ANALYSIS	☐ SOLO
			☐ DUO (Fill in the fields below for family members.)
☐ Whole Genome Sequencing (WGS)	☐ PRENATAL	CNV ANALYSIS cannot be requested in prenatal cases.	☐ TRIO (Fill in the fields below for family members.)

INFORMATION ABOUT FAMILY INDIVIDUALS

FATHER'S NAME SURNAME		**AGE**		**SELECT IF CLINICALLY AFFECTED ***	☐
MOTHER'S NAME SURNAME					☐
SIBLING/OTHER					☐

*** You can add detailed information for individuals on clinical information section.**

CLINICAL INDICATION/ FINDINGS	**AGE OF ONSET**		
	SELECT IF THE PATIENT IS CLINICALLY UNAFFECTED	☐	
	PARENTAL CONSANGUINITY	☐ **YES**	☐ **NO**
	AFFECTED SIBLING	☐ **YES**	☐ **NO**

CLINICAL INFORMATION

*** You can use the terms "Human Phenotype Ontology" (https://hpo.jax.org/) for clinical findings.**

FAMILY TREE/BACKGROUND INFORMATION

Information About the Test to be Performed

What is Whole Exome/Genome Sequence Analysis?

A genome is the name given to all of a living thing's hereditary material (DNA). Exome is a term used to describe all protein-coding sequences in the genome, i.e. exons. All of the DNA sequences of the genes encoding the proteins needed in order to carry out body functions properly constitute the exome. Genome regions outside the exome play a role in regulating the activity of genes. Changes in the DNA sequence can cause diseases. It is known that the majority of pathogenic DNA changes occur in protein-coding regions, namely exons. However, changes occurring outside of these regions can also cause diseases.

All exome sequencing determines changes in all protein-coding regions. By sequencing the entire genome, changes in the entire genome are determined.

Result Reports

In exome/genome analysis, your results are matched and compared with the reference human genome. Definitive diagnosis cannot always be reached from the data obtained. In our genetic diagnosis centerdata analysis is completed by using clinical and bioinformatics databases. Exome/genome analysis can have one of several outcomes:

Positive: A positive result indicates that variant(s) have been identified that are known to cause the disease symptoms based on the available scientific evidence at the time of testing. This may provide a cause or diagnosis for the patient's health concerns.

Negative: A negative result indicates that no variant has been identified that is known or likely to cause the disease symptoms based on the available scientific evidence at the time of testing. A negative result does not mean that there is not a genetic cause for the patient's health concerns. Future genetic testing may be able to identify additional genetic changes.

Uncertain: A variant of uncertain significance (VUS) indicates that variant(s) have been identified but at this time, there is not enough scientific and medical information to determine if this is a disease-causing variant or not. Testing of additional family members may be recommended to better understand the effect of an uncertain variant. It is the responsibility of the follow-up clinician to request this and new, additional testing (e.g. parents and other family members) or analysis. And it is subject to separate approval. Reanalysis of the data may impose additional financial obligations.

Secondary Findings

WES analyzes many genes all at once, accordingly, it is possible to find some genetic changes that are not related to the patient's current signs and symptoms. These results are called secondary findings. Such findings may have important health implications for patients and their family members. The American College of Medical Genetics and Genomics (ACMG) recommends that laboratories report these findings in all genes that are known to cause specific actionable inherited conditions. These conditions include some cancer syndromes, connective tissue disorders associated with sudden cardiac events, certain types of heart disease, high cholesterol and susceptibility to complications from anesthesia.

Some of these conditions may not present until adulthood and may have a significant impact on the patient's and family members' healthcare and/or reproductive risk. If the patient is found to have a genetic change associated with one of these conditions, the family member samples will be analyzed for the same change. Secondary findings will only be analyzed and reported if the patient, parent, or guardian consents to receive them. Family testing of incidental findings detected in index case is subject to separate consent.

Use of Parental Samples in Whole Exome/Genome Analysis

In all exome/genome analyses, samples belonging to biological parents can also be used to determine the familial transmission of some variants detected in the index case. This requires separate consent and is reported separately. It is possible that this test may reveal unexpected biological relationships (i.e. consanguinity, non-paternity, etc.). In accordance with ethical and legal rules, data other than the purpose of testing are not reported.

Limitations of Tests

This test may not sufficiently cover all targeted regions to accurately determine if a pathogenic variant is present. Due to current technical limitations, exome/genome sequencing does not analyze all genes and all types of genetic changes. It is possible that this test may not identify the genetic change responsible for the patient's medical concerns. This test may identify a change in a gene, but does not have the ability to predict long-term prognosis. Interpretation of results is based on our current understanding of genetics. It is possible that results may change in the future upon reanalysis. It is important to have reliable clinical information and an accurate family history in order to interpret results from exome/genome sequencing correctly. Misinterpretation of results may occur, if the provided information is inaccurate and/or incomplete. Results from WES may indicate that additional tests should be considered. The genetic test to be performed is only for the disease /clinical findings described by the referring physician in this form. Test results may indicate that additional tests should be considered. It should be noted that the test performed requires a series of laboratory procedures. This may lead to the possibility of false positive/negative results due to simple errors such as labeling error, secretariat error. It is the physician's responsibility to request re-analysis and or repeat testing in the presence of clinical incompatibility with the report, accompanied by clinical evaluation.

Exome/Genome Sequencing Consents Section

Our Genetic Diagnosis Center needs your approval in order to legally conduct genetic analysis. For the whole exome/genome sequencing analysis, it is mandatory to obtain written consent from the patient or parent/a legally authorized relative and sign the form. **This form becomes valid as signed by the patient. And it means that the signing patient approved the content of this 4-page file. It is also signed by the physician.** Your physician has

advised you (or for someone who is in your custody or accompanying you) to perform a whole exome/genome sequence analysis to clarify the diagnosis/symptoms stated on this form.

Test: Whole Exome/Genome Sequencing

Test Material: Genetic Testing aims to investigate the hereditary substance (DNA). The sample used for this purpose is mostly a peripheral blood sample. For this purpose, it will be sufficient to take 5-10 ml of blood from the veins in the arm by means of a needle. There is no known health risk, except rarely mild bruising, mild pain, and very rare infection, possible nerve-vascular damage due to the traumatizing effect of the needle. If the DNA sample is insufficient or to confirm the diagnosis, a resampling may be required. In cases where sufficient DNA secondary products cannot be obtained and/or the desired quality cannot be achieved, a new sample may be requested.

Turnaround Time: Turnaround times specified on our website or by our physician or staff to conclude the tests are the average times under normal conditions. However, due to patient-specific differences or the need for further examination, or the need to collaborate with other domestic/foreign laboratories, turnaround times may be exceeded.

Consent of Storage	Consent to Use
Your remaining blood sample will be retained and destroyed during the legal process. Obtained DNA sample and data are stored for 5 years. The DNA sample may need to be used for additional genetic testing in the future. The data obtained will be important for clinical follow-up. For example, analysis can be repeated and expanded on the data without the need for new samples or a new test.	Test results are an important resource for physicians, scientists and researchers to investigate genetic diseases and improve the diagnosis and treatment of patients. In this case, personal data are anonymized and/or encrypted. You can request the removal of non-anonymous test data at any time. After anonymization, rights regarding data and material will belong to Acibadem Labgen Genetic Diagnosis Center. I consent to my test results being stored and used in a database for scientific purposes, to improve and facilitate the identification of diseases and to provide statistical information.
□ **I accept.**	□ **I accept.**
□ **I do not accept, My samples will be removed when legal obligations are removed.**	□ **I do not accept it, it should be kept only to be used for additional studies consented by me.**

Secondary Findings: I consent to the reporting of secondary findings to me or to my physician (Please see "Secondary findings" section.) **(Secondary findings are not analyzed in prenatal samples.)**

□ **I accept** □ **I do not accept**

Report Delivery Preference: All genetic data are personal and cannot be shared with third parties. In our center, preliminary information is provided by e-mail only to the physician who requests the test. The report with wet signature has to be delivered by hand. If you give your consent, your final report can be delivered to your physician or physicians who have made the request and followed you clinically, or to you or another person authorized by you. For this, you need to specify your authorization request in your handwriting.

Authority to Receive Information on the Result:

Consent of the Patient or Custodian

I learned about the whole exome/genome sequencing test, received a written explanation, read and understood it. I was fully informed about the technical features and limitations of the analysis. I understood that there are possibilities of false positive/negative results, the need to rerun and/or analyze the test, to re-sample and to request additional samples. The medical terms in the article were explained and sufficient time was allowed to ask questions and make decisions. I know that I have the right to request additional information at any time. I declare that I am aware of my responsibilities regarding genetic diagnosis and that I accept genetic diagnosis without any threat or financial or moral pressure. And I declare that I permit "whole exome/genome sequencing" to be performed.

I know that I can withdraw this consent in whole or in part at any time without any justification and I have the right not to receive information about the test results.

PATIENT/CUSTODIAN (Name, Surname/Signature/Date)	WITNESS (Name, Surname/Signature/Date)	REFERRING PHYSICIAN (Name, Surname/Signature/Date)