INFORMED CONSENT FOR PRENATAL EXOME SEQUENCING

Name: _____

DOB: _____

MRN: _____

Name of authorizing provider: _____

This form is to help the consent process. It is also to support the pre-test counseling discussion. It is your choice to have this test or not. Another option is to not have this test. The parents of the baby will sign the last pages of this document if they agree to have the Prenatal Exome Sequencing (ES) test. Please ask any questions about this test.

PURPOSE OF PRENATAL EXOME SEQUENCING (ES)

- To find genetic cause(s) of the baby's health issues.

THE TEST PROCESS

- This genetic test looks at most of the genes in the body at one time. This test is different from most genetic tests that look at one gene at a time.
- This test needs a sample of DNA from the baby. This sample typically comes from amniocentesis. You and your healthcare team should talk about the risks of any procedure to obtain the baby's DNA. The sample will be checked for maternal cell contamination.
- The laboratory will compare the baby's DNA sequence to other family members' (if applicable) DNA sequences. They will also compare it to the reference DNA sequence to see if there are differences compared to the expected spelling of the DNA. Family members' DNA may come from blood or saliva.
- The laboratory will use clinical information (such as ultrasound findings) and family history to decide which of the genetic changes found may be responsible for the baby's signs and symptoms.
- The laboratory will report the genetic changes that may relate to the baby's signs and symptoms to the provider who ordered the test.

LIMITATIONS OF ES TECHNOLOGY

- This test does not sequence every exon.
- The test may not find all changes in each gene.
- ES finds only small genetic misspellings or small extra or missing pieces of DNA. This test does not detect other types of disease-causing variants. This test may not detect mosaic DNA changes, which are changes that are not present in all cells.
- Prenatal ES results can be more difficult to interpret than ES results after the baby is born. This is because clinical information found during the prenatal stage is often only imaging results. It is important to have reliable clinical information and a correct family history to help interpret the prenatal ES results.
- ES testing is more likely to find a genetic cause of a patient's disease when blood or saliva from biological parents are analyzed at the same time.
- Studies of prenatal ES have shown that the chance of getting a diagnosis from this test depends on the baby's specific health problems. Prenatal ES finds a diagnosis less than 50% of the time. Getting a negative or uncertain result does not mean that there is not a genetic reason for the signs and symptoms seen. Sometimes, further testing might need to be done.
- Prenatal ES results do not predict how severe a condition will be. ES results do not predict the age of onset of conditions.

POTENTIAL RISKS OF ES

- No laboratory test, including ES, is 100% accurate.
    - A possible genetic diagnosis may be incorrect.
    - The baby's diagnosis may not be found by this test.
    - The baby may get uncertain results.
    - The results may be reclassified in the future as genetic knowledge evolves. This could change the recommendations for treatment.

- This test may show that the biological relationships in a family, such as fatherhood or blood relation, are not as suspected. The prenatal ES test is not used to establish paternity or biological relationships.
- This test may find genetic changes unrelated to the baby's current signs and symptom. These changes could be connected with other health problems (see sections about incidental and secondary findings for more information). These results may be upsetting.

WHAT IS REPORTED

- Genetic changes that may have caused the baby's signs and symptoms.
- Variants of uncertain significance may be reported if they could provide a diagnosis of the baby's signs and symptoms should the variant classification change to likely pathogenic or pathogenic (e.g. variant in a gene associated with autosomal dominant conditions that fit the baby's features; variant in a gene associated with X-linked disorders that fit the baby's features, and the baby is male; variant that is *in trans* with a pathogenic or likely pathogenic variant in a gene associated with autosomal recessive disorders that fit the baby's features).
- Genetic changes found in genes not related to the patient's condition that may have an important impact on health. You can decide if you want this information.
- Genetic changes found in family members that are related to the patient's signs and symptoms will be included in the patient's report. Family members will not get separate written reports.
- Genetic changes found in genes which may have an impact on health early in life and/or are considered medically actionable in that they may require future medical care, but are unrelated to your baby's current medical conditions, will be reported if you decide to receive them on the report. Please see the information about incidental and secondary findings for further discussion.
- On the written report of the proband, parental origin of each variant will be indicated (unless the variant occurred for the first time in the baby).Parents will not get separate written reports.

WHAT IS NOT REPORTED

- Variants in genes that are not thought to affect one's health.
- Variants found in research studies that may not be connected to disease.
- Variants in genes that are currently known to cause symptoms in adulthood.
- Variants in genes that are not known to be associated with the baby's signs and symptoms and only show carrier status for an autosomal recessive or X-linked disorder.
- Variants of uncertain significance in genes that are associated with the baby's signs and symptoms but only show carrier status for an autosomal recessive or X-linked disorder.
- Variants that predict an increased risk of a disease, but do not cause a disease by themselves.

SECONDARY FINDINGS

Prenatal ES may find genetic changes that are not related to the baby's current medical concerns. These are called secondary findings. These findings may have important health effects for patients and their family members. For example, the American College of Medical Genetics and Genomics recommends that all labs that perform ES report disease-causing changes in genes that cause certain inherited disorders. These disorders may lead to serious health problems that can be monitored or treated. Some do not cause symptoms until adulthood. These disorders 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. On the other hand, some types of genetic disorders do not have any effective treatment. These may lead to death or lifelong disability. Secondary findings can be included in the baby's report. We will not look for or report these findings if you tell us that you do not want these results. If you choose to get these results, the baby's report will include this information on disease-causing variants. In addition, the report will note if these variants were found in family members who submitted samples.

Please initial one of the following options (adult patient or parent/guardian of minor child must initial):

_____ Option 1: I want results about secondary findings.

_____ Option 2: I do not want results about secondary findings. I understand that I may not be able to get these results later.

INCIDENTAL FINDINGS

Prenatal ES may find changes in other genes that are linked to moderate to severe childhood-onset disorders. These may include neurodevelopmental disorders or metabolic conditions that do not have prenatally detectable features. These are known as **incidental findings**. Receiving this information is voluntary. We will not seek or report these findings if you do not want this type of result. If you choose to receive these results, the report will include incidental findings found in the baby and the parental origin. Parents will not get separate reports about incidental findings.

Please initial one of the following options (adult patient or parent/guardian of minor child must initial):

_____ Option 1: I want results about incidental findings.

_____ Option 2: I do not want results about incidental findings. I understand that I may not be able to get these results later.

CONFIDENTIALITY

- The laboratory will report the test results to the healthcare provider who ordered the test.
- The laboratory will not give test results to anyone else without your written permission.
- The written report will become part of the mother's medical record. The mother's health insurance provider or other parties may have legal access to this information.
- The laboratory can give raw data from the ES testing after the testing is complete to a healthcare provider or researcher. This will only be done with consent from the patient or parents, and upon request from a healthcare provider.

FUTURE OF THE DATA

- The laboratory will store any remaining sample(s) for two years. They may get rid of those samples after two years.
- The laboratory will keep the test report for 20 years.
- The laboratory will keep the genetic information on a secured computer that can only be accessed by certain people.
- The laboratory may contact your healthcare provider if new information is available later about the findings of this test that could affect the patient's medical care.

POST-TEST COUNSELING AND INTERPRETATION

It is recommended that patients get genetic counseling before signing this consent and when final results are available. To find a genetic counselor near you, ask your doctor to refer you to a genetic counselor. Or you can go to www.nsgc.org.

REANALYSIS OF PRENATAL ES RESULTS

An ordering healthcare provider may request one reanalysis of the prenatal ES data after birth of the baby at no additional charge. It is highly recommended that the healthcare provider submit additional postnatal clinical information about the baby with this reanalysis request. If no additional clinical information is available, it is recommended to wait at least 12 months before requesting reanalysis.

Signing this document means that the test and its limitations and risks have been explained to you.

By signing below, I am saying that I have talked about the benefits, risks, and limitations of this genetic test with my provider. ES is an ever-changing field of medicine. The laboratory will use a current clinically appropriate methodology available to the laboratory at this time to find relevant genetic changes that might be causing my or my child's signs and symptoms. Better, more precise technology might be available in the future. I understand and acknowledge the limitations in current laboratory testing that might be surpassed by future testing. Whether or not I am eligible or appropriate for any future testing is an issue to discuss with my healthcare provider when and if that technology becomes available. My questions about the test have been answered. I consent to whole exome sequencing. I will get a copy of this consent form for my records.

Biological **mother** of the baby, if providing a DNA sample, or parent or guardian of a minor individual:		
	Time: Date:	
Signature		Printed Name

Biological **father** of the baby, if providing a DNA sample, or parent or guardian of a minor individual:		
	Time: Date:	
Signature		Printed Name

	Time: Date:	
Witness Signature/Credentials		Printed Name

Note: All individuals providing a DNA sample for analysis must sign above. Only the pregnant patient or their parent/guardian must sign if the baby's DNA sample is submitted without parental samples.

Physician's/Genetic Counselor's statement: I have explained prenatal exome sequencing to this person/family. I take responsibility for determining the appropriateness of this testing for the patient. I have addressed the limitations of the test. I understand that the interpretation of these results within a clinical context is my responsibility.

Physician/Genetic Counselor Signature/Credentials	Printed Name	Date/Time