Patient Name: _____ Date of Service: _____

EXOME WITH CNV EVALUATION INFORMED CONSENT

This consent provides information about the Whole Exome Sequencing Test With CNV Evaluation. If this consent form is used for a pediatric patient, the word "you" or "your" refers to your child.

WHAT IS WHOLE EXOME SEQUENCING?

Whole Exome Sequencing (WES) is one of the most extensive genetic tests available. Exome testing is different from other types of genetic tests that evaluate only one gene at a time. Each person has thousands of genes which are made of DNA. Genes provide instructions for proteins that are used by the body to develop and function. The DNA is a sequence made up of four letters. Much like a sentence, the sequence of these letters produces a message. Differences in the sequence from one person to the next are what make us different from one another. This is sometimes referred to as normal variation. An example of normal variation is eye color and height.

If a change in the DNA sequence affects the body's ability to complete an important function it may cause a disease or disorder. Most genetic disorders are caused by a variation in a part of the gene called the exon. All the exons together make up what is called the exome. This test will search the sequence of the exome to look for genetic changes known as variants that may be associated with a disorder. This test also includes CNV (copy number variant) analysis. This means it also looks for missing or repeated sections of the sequence.

Exome testing is most commonly requested when your medical history and physical exam findings suggest a genetic condition, but your doctor has not identified the cause of the medical issues or symptom(s), or if no other test is available.

Exome testing frequently identifies hundreds of variants for evaluation. Exome testing is most informative when the patient provides a complete medical and family history, as well as blood samples from both biological parents. This information helps evaluate the variants.

While family samples and clinical history may help with interpretation, they do not guarantee that the test will detect variants related to your medical condition. If disease-associated variants are not detected from this test, it does not mean that your medical condition is not genetic. It is possible that this test is not able to detect the variant, or there is not enough known about the variant at this time. It is important to stay in touch with your doctor. Genetic testing options may change over time and symptoms may evolve that direct your doctor to different tests or to reanalyze the data from this test. Because medical knowledge and information continues to advance, it is important to know that variant interpretation is based on information available to the laboratory at the time of testing and may change in the future.

RISKS AND LIMITATIONS OF THIS TESTING

This test may not provide conclusive results or definitive answers regarding your medical condition. In some instances, this testing may not detect a genetic variant due to limitations in the current medical knowledge or testing technology.

Accurate interpretation of exome results depend on knowing the biological relationships in a family. If those relationships are not reported accurately, this may result in an incorrect interpretation or results. Genetic testing may also reveal that the biological relationships are not as stated. For example, the test may reveal mistaken

paternity, which means the person stated as the father is not the biological father. It may also reveal consanguinity, which means parents (or other relatives) of the person tested are related by blood. These results may be necessary to report to your medical provider.

This test does not have the ability to detect every variant that may be associated with every medical condition you may develop. The purpose of this test is to help determine whether a genetic variant may be associated with the current medical condition for which you are being tested.

GENETIC COUNSELING

Genetic counseling is strongly recommended for anyone undergoing genetic testing. Due to the complicated nature of exome sequencing, it is strongly recommended you and your family receive genetic counseling before and after testing to assist in understanding the result(s) and follow-up recommendations.

To find a genetic counselor in your area please visit the website of the National Society of Genetic Counselors (www.NSGC.org).

TEST RESULT REPORTING AND POSSIBLE RESULTS OF THIS TEST

A written report will be provided directly to the doctor who ordered your test, who will inform you of the results. The report will contain information about genetic variants that may be associated with the medical condition for which the testing was ordered. As discussed in the secondary findings section below, the report may also contain information about genetic variants detected in genes unrelated to your medical condition, but which may have an important impact on your health, if you choose to receive this information. The report will not include variants detected in genes that are not thought to be associated with your health.

You may receive different types of results from this testing:

1. **Positive or Likely Positive**: A positive or likely positive result indicates that the laboratory has detected a genetic variant that may help explain your medical condition. A positive or likely positive result could also have implications for family members who may also possess the variant.

2. **Negative**: A negative result indicates that the laboratory did not detect a genetic variant currently associated with the medical condition for which your doctor ordered testing. This does not mean that the cause of your medical condition is not genetic. It also does not mean that you will be healthy or free of any genetic diseases or medical conditions. This could mean that the exome sequencing technology was unable to detect the variant or that the laboratory has not yet associated the variant(s) detected with your medical condition. Further testing may be necessary.

3. **Variant of Uncertain Significance (VUS)**: An inconclusive result indicates that there was a genetic variant detected, but the laboratory is currently uncertain if this variant is associated with your medical condition. This is not considered to be a positive or negative result. Additional information or testing, including testing of additional family members, may be recommended to help clarify the inconclusive result.

If applicable, information regarding genetic variants identified in family members and related to your medical condition will be included in your report. Family members will not receive separate written reports. You may want to ask for a copy of the report from your doctor to keep for your records or to share relevant information with family members who may also be at risk for inheriting the genetic variants that are detected.

COST OF TEST

This is a clinical laboratory test. The results may help in your diagnosis, treatment and care. You or your health insurer will be billed for this test.

GENETIC INFORMATION NONDISCRIMINATION ACT

Since some genetic variations can help to predict future health problems for you and your relatives, this information might be of interest to health care providers, life insurance companies, and others. Federal and State laws provide some protections against discrimination based on genetic information. For example, the Genetic Information Nondiscrimination Act (GINA) makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information. However, it does not prevent companies that sell life insurance, disability insurance, or long-term care insurance from using genetic information as a reason to deny coverage or set premiums. For more information, please visit www.genome.gov/10002328.

SECONDARY FINDINGS

Exome sequencing may identify variants associated with disease that are not related to the medical condition or symptoms for which you are being tested, but may nonetheless have important health implications for you and potentially your family members. For example, if WES is ordered in connection with an epileptic condition the test may also identify a variation in a gene that is associated with cancer or another serious health condition. These other variants, which are not related to the current medical condition being evaluated by your doctor, are called secondary findings.

The American College of Medical Genetics and Genomics (ACMG) recommends that certain disease-associated secondary findings be reported, whether or not they are related to the patient's medical condition, as monitoring or treatment may be available. Please refer to the ACMG Recommendations for Reporting of Secondary Findings in Clinical Exome and Genome Sequencing, update 2021 ACMG SFv3.0, for a list of the genes and associated medical conditions for which ACMG recommends reporting. Some patients want to know about these secondary findings, and other patients do not. Secondary findings will not be included in the report provided to your doctor unless your doctor confirms that s/he has obtained your consent to include secondary findings in the report and affirmatively indicates to the laboratory that secondary findings should be included in the report.

Family members who undergo testing to help inform your results may discover that they have the same variant(s). Family members will not, however, receive a separate report or secondary findings. If you are found to have a variant or a secondary finding, your family members may be at risk to also have the genetic variation(s). It is recommended that family members speak with their doctor and/or genetic counselor in order to make an informed decision about genetic testing as related to their own health.

If no ACMG secondary findings are identified, it does not guarantee the absence of disease-associated variants. If a genetic syndrome is suspected in you or a family member, genetic testing specific to that genetic syndrome may be recommended.

I understand that the ACMG recommends that certain disease-associated secondary findings be reported, whether or not they relate to the medical condition for which I am being tested, as monitoring and treatment may be available. I understand that if I choose to receive secondary findings, the report may include results that, although unrelated to the condition for which I am currently being tested, may affect my health now or in the future. I understand that if I choose to not receive secondary findings, the report will not include results that, although unrelated to the condition for which I am currently being tested, may affect my health now or in the future.

_____Yes. Please order ACMG-recommended secondary findings.

_____No. Please DO NOT order ACMG-recommended secondary findings.

PATIENT ATTESTATION OF INFORMED CONSENT:

My doctor or his/her designee (such as a genetic counselor) has given me information about the Quest Diagnostics Exome Sequencing with CNV Evaluation. I understand the purpose of the test and the possible benefits and risks of the test. I have been given a full opportunity to ask questions that I may have about the test. I voluntarily agree to undergo this testing. I understand that I will receive a copy of this consent form.

Patient Name (Print): _____

Patient Signature: _____

If signing on behalf of a minor child, please complete below:

Authorized Guardian Name (Print): _____

Authorized Guardian Signature: _____

Relationship to the Minor (eg, mother, father, court-appointed guardian): _____

Date: _____