Washington University in St. Louis Physicians

Patient Name (LAST, FIRST): _____ DOB: _____

Informed Consent for Clinical Exome Sequencing

About This Form

- The purpose of this form is to guide the consent process and to supplement the pre-test counseling discussion about Clinical Exome Sequencing testing performed by the Department of Pathology & Immunology, Washington University School of Medicine (WUSM).

- Read this consent form and discuss it with your health care provider, or with your child's provider. If you wish to proceed with the test, please sign and date this form. This test is voluntary; it is your choice to have this test or not.

- For the purposes of this consent, "I", "me", and "my" will refer to me or to my child, if my child is the person for whom the healthcare provider has ordered testing.

Test Description

- Clinical Exome Sequencing is a genetic test to identify differences (also called variants) in the human genome that can give rise to genetic disorders. Some genetic tests examine one gene at a time. In Clinical Exome Sequencing, the protein-coding regions (exons) of all of the genes of the human genome are examined. About 20-40% of the time, the test will find a diagnosis or reason for a patient's medical or developmental concerns.

- For the Clinical Exome Sequencing test, the lab will need a specimen from the patient from which to extract DNA for sequencing. It can be helpful to analyze the patient's sequence data alongside sequence data from their biological relatives, especially parents, to determine what variants they have in common. The specimens are referred to as comparator samples. Specimens from comparators should be submitted with the patient's specimen. The patient's doctor will provide to the laboratory clinical information about the patient and any relative who submits a sample to aid in interpretation of the sequence data. Genetic variants identified as potentially related to the patient's medical condition will be included in the patient's report with information about whether they were also observed in the family member. Family members serving as comparators will receive a report documenting the use of their sample and, if requested, any ACMG secondary findings results.

Test Limitations and Potential Risks

- In some cases, testing may not identify a reportable genetic variant even if the patient's disease is genetic. This may be due to limitations in current medical knowledge or testing technology. This test does not sequence every base in the genome and current technology is not able to completely characterize every coding region of the genome. This Clinical Exome Sequencing test detects only single base pair changes or small additions or deletions of DNA. This test does not detect other types of genomic variants, such as repeat expansions, mitochondrial variation, and genomic structural abnormalities.

- Accurate interpretation of test results requires understanding true familial biological relationships. I understand that if I fail to accurately report biological relationships in my family, it could lead to incorrect interpretation of test results, incorrect diagnoses, and/or inconclusive test results. Genetic testing can reveal unexpected biological relationships in a family, including non-paternity (the reported father is not the biological father) or consanguinity (parents are related). I agree to have these findings reported to the healthcare provider who ordered the test, who may share this information with my family. Although non-paternity and consanguinity will not be explicitly stated in the report, in some cases it may be inferred.

- Interpretation of the significance of genetic variants is based on currently available information in the medical literature, research and scientific databases. Because these bodies of scientific knowledge are constantly changing, understanding of the significance of genetic variants may change as new information becomes available. I may wish to periodically check with my provider to see if new information is available.

- Although genetic testing is highly accurate, inaccurate results may occur for reasons including, but not limited to, mislabeled samples, incorrect clinical/medical information, rare technical errors, or unusual circumstances such as bone marrow transplantation, or the presence of variants in some, but not all, of a patient's cells (mosaicism).

- I understand that this test will not predict all of the long-term medical risks that may exist for me. The result of this test does not guarantee my health and additional diagnostic tests may still be required.

- Occasionally, an additional sample may be needed from me, or other family members. This can happen if there are problems with the original specimen or if additional material is required.

Test Result Reporting

- **A written report** for the patient will be provided directly to the healthcare provider who ordered the test, who will inform them 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. Different categories of results that may by generated from this testing include:

    - **Positive**: A positive result occurs when the laboratory detects one or more genetic variants that may help explain the relevant clinical condition. Such a result may also have implications for family members who share that genetic variant.

    - **Negative**: A negative result indicates that the laboratory did not detect genetic variation currently associated with the medical condition for which my doctor ordered testing. This does not mean that the cause of a medical condition is not genetic. It also does not mean that I will be healthy or free of any genetic diseases or medical conditions. This could mean that the genetic sequencing technology was unable to detect the genetic change or that the genetic changes observed have not been associated with my medical condition.

    - **Variant of Uncertain Significance (VUS)**: The finding of a variant of uncertain significance means that there is a genetic variant in the DNA but the laboratory is currently uncertain if this variant is associated with my 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.

- **Secondary findings.** Clinical Exome Sequencing may detect genetic variants that are not related to the patient's reason for undergoing testing but may have important health implications for them and their family members. These are known as secondary findings. The American College of Medical Genetics and Genomics (ACMG) recommends that patients undergoing Clinical Exome Sequencing be offered reporting of clinically-significant variation in a select list of genes associated with conditions for which prevention or treatment is available. Examples of such conditions include those causing elevated risk for cancer, heart conditions, high cholesterol, and susceptibility to complications from anesthesia. Secondary findings are available for relatives being sequenced as comparators as well as the patient.

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

___ **Yes, include ACMG-recommended secondary findings in my report**. I choose to receive results regarding any actionable, disease-associated variation I may have in genes included in the current ACMG secondary findings list. I understand that 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.

___ **No, DO NOT include ACMG-recommended secondary findings in my report**. I choose not to receive results regarding any actionable, disease-associated variation I may have in genes included in the ACMG secondary findings list.

- To maintain confidentiality, the test results will only be available to the referring health care provider, to the ordering laboratory, to me, to other health care providers involved in my diagnosis and treatment, or to others with my consent or as permitted or required by law. Federal laws prohibit unauthorized disclosure of this information. More information can be found at: *www.genome.gov/10002077*

- It is recommended that I receive genetic counseling before and after having this genetic test. I can find a genetic counselor in my area at: *www.nsgc.org*. Further testing or additional consultations with a healthcare provider may be necessary.

Future of the Data

- **Specimen Retention**. After testing is complete, de-identified DNA from my sample may be used for test development and improvement, internal validation, quality assurance, and training purposes. DNA samples are not returned to individuals or to referring health care providers unless specific prior arrangements have been made.

- **Database Participation**. De-identified health history and genetic information can help health care providers and scientists understand how genes affect human health. It is not uncommon for laboratories to share such de-identified health history and genetic information with genetic databases. Although it is unlikely that I could be identified based on the genetic and health information that is shared, this risk is greater if I have already shared my genetic or health information with public resources, such as genealogy websites.

Patient Name (LAST, FIRST): _____ DOB: _____

- **Re-contact for Research Participation**. The laboratory may collaborate with scientists, researchers and drug developers to advance knowledge of genetic diseases and to develop new treatments. If there are opportunities to participate in research relevant to the disorder in my family, and if I have consented for re-contact, I may be re-contacted for research purposes, such as the development of new testing, drug development, or other treatment modalities. ***Please initial one of the following options (Adult patient or parent/ guardian of minor child must initial):***

___ **Yes, I agree to be re-contacted for research studies.**
___ **No. I do not want to be re-contacted for research studies.**

Signatures

Physician's/Genetic Counselor's statement: *I have explained this test to this individual. I have addressed the limitations of the test and have answered all stated questions.*

Signature: _____ **Date: _____**

Provider Name (print): _____ Provider Phone #_____

Adult patient, comparator, or parent/ guardian of minor child's statement: *I have read, or have had read to me, all of the above statements and understand the information regarding Clinical Exome Sequencing testing at WUSM. I acknowledge that I have discussed the benefits, risks, and limitations of this genetic test with my physician or genetic counselor. I have had the opportunity to ask questions about this test. By signing this form, I authorize the Department of Pathology and Immunology at Washington University School of Medicine to perform this testing. I will receive a copy of this consent form for my records.*

Patient Name (Print): _____ Date: _____

Signature (*Adult patient, comparator, or parent/ guardian of minor child*):

_____

Print Name: _____ Relationship to Patient: _____

Individual's role in testing *(must select one):*

☐ **Patient/Proband** (Individual with medical condition seeking a molecular diagnosis)

☐ **Comparator** (Family member of patient)
Each comparator must complete a copy of this form.

If individual completing the form is patient/proband, please indicate if additional family members are undergoing sequencing: ☐ Yes ☐ No

If yes, please use the space below to record their information and relationship to you.

Patient Name (LAST, FIRST): _____DOB: _____

Name (Print):

DOB: _____

_____

Relationship to patient:

_____

Name (Print):

DOB: _____

_____

Relationship to patient:

_____