G-2d$_2$ Consent for Clinical DNA Sequencing Iowa Institute of Human Genetics **Contact:** Richard JH Smith, MD; Colleen Campbell, PhD, MS, CGC •This completed form must be scanned in Epic•	DATE HOSP.# NAME BIRTH DATE ADDRESS IF NOT IMPRINTED, PLEASE PRINT DATE, HOSP. #, AND NAME

This consent form describes the clinical DNA sequencing test to help you decide if you would like this test. This form provides important information about what you will be asked to do for the test, the risks and benefits of the test, and your rights as a patient.

If you have any questions about or do not understand something in this form, you should ask your healthcare provider for more information. You can discuss this test with anyone you choose such as family or friends. Do not agree to this test unless your healthcare provider has answered your questions and you decide that you want to have this test.

- *If you are the parent/guardian of a child under 18 years old who is considering this test, the word "you" in this document refers to your child. You will be asked to read and sign this document to give permission for your child to have this test.*
- *If you are under 18 years of age, the word "you" in this document refers to you. You will be asked to read and sign this document to indicate your willingness to have this test.*
- *If you are the legally authorized representative of a person who is considering this test, the word "you" in this document refers to the person you represent. You will be asked to read and sign this document to give permission for the person you represent to have this test.*
- *The word "we" in this document refers to the Iowa Institute of Human Genetics.*

CLINICAL DNA SEQUENCING

A. What is the purpose of this test?

To Provide Information to Assist with Your Clinical Care

The purpose of this test is to identify one or more genetic variants that may underlie the medical condition for which you were referred. Genetic variants are changes in your DNA that can cause disease or put you at greater risk to develop disease. A variant that causes disease may be called a "mutation." The identification of such variants may or may not impact your medical care in the following ways:

- Identify a cause for your health condition or symptoms
- Assist you and your healthcare provider in choosing the best treatment for you
- Determine recurrence risks of disease in your family
- Identify predisposition to disease

This test should not be used for prenatal diagnosis.

B. What will happen during this test?

1. Genetic Counseling

A genetic counselor is a healthcare professional trained to explain genetic information to you in a way that is easy to understand. You will meet with a genetic counselor throughout the testing process. Your time with the counselor will include:

- A pre-test genetic counseling appointment. At this appointment, the counselor will discuss how the test is performed, what the test results can and cannot tell you, limitations and risks of the test, and any benefits of the test. The genetic counselor will answer any questions you have about the test. The counselor will also gather information about your personal and family health history.
- You are then free to take time to think and to speak with family members and friends before deciding if you would like to have the test.

- If you decide to have the test, the genetic counselor will complete the rest of this consent form with you and a sample of blood will be drawn as described below. Completion of consent and the blood draw can occur either at the pre-test visit or, if you prefer, at a later appointment that you would schedule.
- When the test results are available, you will meet with the genetic counselor to review the results.
- If at a later date you would like the sequence data from this test to be re-analyzed for a different health condition, you must meet with a genetic counselor first and sign an additional consent form that is different from this form.

2. Cost of the Test

During your genetic counseling appointment the cost of the test will be outlined for you and insurance coverage will be discussed. If you decide you do not want the test done, you will only be charged for the visit with the genetic counselor.

3. Obtaining DNA

We usually obtain DNA from a sample of blood. To do this, we will draw two tablespoons of blood (~1 teaspoon for infants) usually from a vein in your arm using a needle. This will take about 15 minutes of your time. From this blood, we will extract DNA which will be used to perform the genetic test. You may be asked to give an additional sample of blood if the initial sample does not provide enough DNA for the test.

Sometimes we may choose to obtain DNA from tissues other than blood, such as saliva, skin, or a surgery tissue sample. If we require saliva, you will be provided a saliva collection kit. This kit collects one teaspoon of saliva. Obtaining a skin biopsy or surgery tissues will require additional conversations and separate consent forms.

If a child is tested, it may be necessary to study parental DNA samples to interpret the child's results and increase the chance to identify the cause of the disorder. Each parent will need to sign a parental consent form. In such cases a separate parental report will not be issued.

4. Consulting Your Medical Records

To interpret the results of this genetic test we will need to access your medical records, including information about your medical history and any medical tests or procedures you have had.

5. Sequencing Your DNA

This consent is for a genetic test that involves sequencing your DNA. Several types of sequencing tests are available. Your healthcare provider will decide which type of DNA sequencing is best for you, and may order additional DNA testing if necessary. The human genome includes all of the information in our DNA. The portion of the human genome that encodes proteins is called the "exome" and is most frequently studied. This portion of the human genome represents only 1-2% of the human genome.

The types of sequencing tests covered by this consent include:

Disease-Specific Targeted Capture Sequencing
A subset of genes which are known to cause disease can be tested, such as all genes known to cause hearing loss. The advantage of this type of testing is that it is simpler to do and easier to interpret. The disadvantage is that it is limited and so if your disease is caused by a gene not yet known to cause your disease, the disease-causing variant you carry will not be identified.

Exome sequencing (WES)
Exome sequencing is targeted capture sequencing of all exons. Exome sequencing screens the coding portion of almost every known gene, including the mitochondrial genome. The advantage of exome sequencing is that this test is more comprehensive and should detect most DNA variants in the protein-coding portions of the human genome. The disadvantages are: 1) the test is still limited because it does not cover the entire exome; 2) data analysis is more complicated because there are more genes to study; 3) the thoroughness with which the genes can be analyzed is often less with WES as compared to Disease-Specific Targeted Capture Sequencing.

Whole genome sequencing (WGS)
Whole genome sequencing screens the entire human genome for genetic variants. The advantage of whole genome sequencing is that the entire genome is studied. The disadvantages are: 1) data analysis is extremely complicated because the large amount of data; and 2) the thoroughness with which the entire genome can be analyzed is often less than the thoroughness with which WES or Disease-Specific Targeted Capture Sequencing data can be studied. 3) WGS will identify many variants, and we may not yet be able to determine which are medically important.

6. Analyzing and Reporting on Your Sequencing Data

Once we have your sequence data, to analyze your sequence data we use computers. Computers compare your sequence data with sequence data from thousands of other persons including persons with medical conditions similar to yours. We do this type of comparison to assess whether variants are potentially medically important.

7. Validation of Your Sequencing Data

If we are able to identify a genetic sequence variant(s) that may be causing your health condition, this variant may be validated by a second DNA test such as Sanger sequencing. To do this, we will use your original DNA sample to verify the DNA variant(s).

C. What information will I receive from this test?

1. Findings Related to Your Primary Condition

All individuals who are tested will receive a report describing genetic findings related to their primary condition. A genetic counselor and your physician will explain these results to you. The report will include the following findings:

- Variants reported to cause your primary condition.
- New variants highly likely to cause your primary condition if these variants are in genes known to cause your primary condition.

2. Incidental and Secondary Findings

Incidental findings are variants in genes associated with your primary condition that are predicted/expected to cause symptoms that **differ** from the symptoms you are experiencing and for which you are being tested. (For example, if you are being tested for genetic causes of hearing loss and a variant is identified in a gene that causes hearing loss but the variant is predicted/expected to cause infertility **not** hearing loss, that variant is called an "incidental finding".) It will not be possible to predict the symptoms associated with all incidental findings.

If you **want** to receive information on incidental findings, initial here. _____

Secondary findings are findings unrelated to your primary condition. These genes are **not included** in the analysis and therefore **no** secondary findings are reported.

D. What information will not be provided by this test?

- This test will not report on issues of paternity/non-paternity.
- Because we do not yet fully understand the human genome, we will not be able to interpret your genetic data with complete accuracy.
- The laboratory will not return the remaining DNA sample, but it may be possible to perform additional tests on the remaining DNA sample at your request. The DNA sample can be destroyed at your request. Otherwise, the DNA sample will remain in the laboratory for future use as you indicate in Section J of this consent form.

E. What are the limitations of this test?

- The variant causing your primary finding may not be detected because: some types of variants are very difficult to identify; and it may not be included in the sequenced/studied region.
- If the variant is identified, it may **not** be recognized as disease-causing because our understanding of the genome is **not** complete and we are unable to predict with 100% accuracy the effect of new variants that are identified.
- Interpretation of results is based on the current understanding of the human genome and human health and disease. The test may detect variants of uncertain clinical significance. Efforts will be made to limit these types of results.
- The results may be unclear and testing of other family members may be necessary to interpret your test results, however this testing would require your approval and the consent of your family members.
- The ability to identify the variant responsible for your condition is highly dependent on the clinical information provided to the laboratory.
- If the cause of your condition is identified, it may not be possible to predict the severity of the disorder.

F. What are the risks of this test?

You may experience physical discomfort or bruising from the needle prick if blood is drawn from your arm. Potential risks from a skin biopsy include infection, bleeding, pain or scarring at the biopsy site.

Given the nature of this test we may find thousands of genetic variants. We will not report such variants as part of the clinical diagnostic test.

As with any genetic test, the information you learn about the genetic cause or predisposition to your condition may have clinical or reproductive implications for yourself or your family members. In addition, you may learn about symptoms you do not yet have.

G. Are there other testing options?

Other testing options available to you depend on your medical condition and the specific clinical question. Before you decide whether or not to have this test, your doctor and/or genetic counselor will discuss the other options, their risks and benefits, and help you make an informed choice.

H. Medical advice

Our report will not provide medical advice. The results will include information your healthcare provider can use in combination with professional knowledge and clinical information to determine what might be causing your symptoms, and the best medical course of action. You should not ignore any symptoms you experience or discontinue treatment based on the content of your report.

I. Analysis of your sequencing data

By having this test you are allowing the clinical information related to your medical condition and genetic information from your sequencing test to be placed in a database that we maintain. To interpret your data, we have to compare it to data from thousands of other persons, some of whom have your medical condition. Only a select group of individuals will have access to your name and medical records. Family members will not be permitted access to genetic information generated by this test.

J. Future use of your DNA sample and genetic data (collectively known as "Genetic Information")

To improve this test and our ability to help patients, we would like to continue to compare your Genetic Information to the genetic information of thousands of other persons, some of whom have your medical condition. Therefore, we are asking for your permission to store your DNA sample and genetic data so we can study them in the future.
If you do **not** wish to have your Genetic Information used in this manner, please initial here. _____

Your Genetic Information, stripped of all identifying information, may be placed in a national repository.
If you do **not** wish to have your data used in this manner, please initial here. _____

It is possible that your Genetic Information might be used to develop products or tests that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.
If you do **not** wish to have your Genetic Information used in this manner, please initial here. _____

It is possible we may publish the results of aggregated data in which the results of multiple genetic tests (targeted, WES, or WGS) are combined and individual identification is not possible in the medical literature. These publications will not include any information that will identify you personally.
If you do **not** wish to have your Genetic Information used in this manner, please initial here. _____

It is possible to make a cell line and DNA from cells removed from the blood samples. Cell lines are produced by growing blood cells in a laboratory and allow us to have a source of the DNA without having to redraw your blood. These blood cells can be stored for decades or more. The cell lines and DNA and data may be made available to researchers trying to learn more about the cause of diseases. Your blood sample may be used to make a cell line.

If you do **not** wish to have your blood sample used in this manner, please initial here. _____

It is possible to use your Genetic Information in the future. This may include but is not limited to test development and/or validation, or research. Refusal to consent for use of your DNA sample in this manner will not affect your medical care. If you consent now to future use of your DNA sample, but decide in the future that you would like to have it removed from future research, you should contact the Iowa Institute of Human Genetics.

If you **do** wish to have your Genetic Information used in this manner, please initial here. _____

K. Reporting of results

This is a diagnostic test. The purpose is to identify genetic changes which may be responsible for your **primary** disease or condition. Results will be returned to the healthcare provider who ordered the test and your genetic counselor. We are unable to provide results back directly to you. We will only report back results for your **primary** condition and genes associated with that condition (primary genes). A healthcare team will review your clinical and family history and the candidate variant list prior to reporting it back to your healthcare provider. The report will tell your healthcare provider what region of the gene(s) or genome we were unable to analyze sufficiently. This report will be included in your medical record.

L. Will my health information be used during this test?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires University of Iowa Health Care to obtain your permission for the diagnostic team to access or create "protected health information" about you for purposes of this diagnostic test. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this test and for your healthcare. Once your healthcare provider has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under "Confidentiality."

You cannot have this test unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any alternative tests available to you. Your signature on this Consent Document authorizes your healthcare provider to give us permission to use or create health information about you.

M. Signatures

This Informed Consent Document is not a contract. It is a written explanation of what this testing involves if you decide to have it. You are not waiving any legal rights by signing this Informed Consent document. Your signature indicates that this test has been explained to you, that your questions have been answered. You will receive a copy of this form.

Patient Signature: _____ Date: _____ Time: _____

Signature _____ Date: _____ Time: _____
(Parent/Guardian or Legally Authorized Representative

Printed Name (if not patient): _____ Relationship to Patient: _____

Statement of Person Who Obtained Consent

I have discussed the above points with the patient or, where appropriate, with the patient's legally authorized representative. It is my opinion that the patient understands the risks, benefits, and procedures involved with this testing.

Signature: _____ Title: _____ Date: _____ Time: _____