Consent form - *Next Era testing*

Genomic testing is being offered to you/your child/your ward to determine the cause of your/their health problem. The information on this form briefly summarizes the information about genomic testing that was discussed with you by your healthcare provider. If you have any questions or concerns about this testing, please contact your healthcare provider or the Alamya Health team to discuss further. As well, if you decide to proceed with genomic testing, we recommend that you review all of the findings in this report with your healthcare professional.

Purpose

Whole genome sequencing looks for changes or variations throughout one's DNA. Such DNA variations can cause a gene or a group of genes to function improperly.

Alamya Health offers the most cutting edge, comprehensive genomic testing available: Next Era test. The Next Era test includes: clinical grade short-read genome sequencing with mitochondrial sequencing, research grade, long-read genome sequencing, long read methylation analysis (aka methylome) and when indicated, RNA sequencing (aka transcriptome). Long-read genome sequencing can identify certain genetic changes not usually detectable by standard clinical grade short-read genome sequencing: 1) variants in regions of the genome refractory to short read sequencing, 2) some structural changes, and 3) modifications of the DNA or RNA, e.g., DNA methylation alterations. Next Era genomic analyses can provide comprehensive genomic information about the cause of the health concerns and possible management options.

How it is performed

Genomic testing is performed on DNA that is obtained from a small blood sample. Analysis and reporting of the testing data are guided by detailed clinical information and family history information along with up to date published medical and scientific information. In some cases, samples from other family members are needed to interpret the results of the individual with health concerns (e.g., samples from parents along with a child's sample). Alamya Health will provide a test report to the healthcare provider who ordered the test. This healthcare provider will be responsible for discussing the result with the individual/family and determining whether it would be appropriate to confirm any findings in a clinical diagnostic laboratory (see below). If relevant, the test report will indicate if a genetic change was inherited from one or both of the parents. Reports are, however, typically not issued for family members whose samples were used to guide interpretation for the individual with the health concerns unless testing for secondary findings has been requested (see below section on "Secondary Findings").

Types of results

Positive genetic result: A genetic change was found that is the likely cause of the health concerns. These genetic changes are termed pathogenic variants or likely pathogenic variants.

Positive epigenetic results: Two types of DNA methylation changes can be found in support of the pathogenicity (cause of the health concern) of certain genetic variants. One type is a methylation alteration that is localized to a specific genomic region. The second type is a specific genome-wide pattern of DNA methylation alterations which constitutes a signature characteristic of a specific disorder. It is possible that a DNA methylation change indicative of a genetic disorder is detected without an associated genomic variant; in such instances, further testing might be indicated.

Positive transcriptome result: Sequencing of RNA provides support for the pathogenicity of the genetic or epigenetic variant.

Positive pharmacogenomic result: Specific changes can indicate the potential for an altered response to certain medications. As with any positive test finding, this should be discussed with your healthcare provider(s) especially as your response to a medication can be influenced by multiple factors.

Negative: No genetic, epigenetic, or transcriptomic changes were found to explain the health concerns. This might be due to current limitations in scientific and medical knowledge and/or testing technology. Such results do not, however, completely rule out the possibility of an underlying genetic disease. Reanalysis or retesting in future might be indicated, and you should discuss this with your healthcare provider (see below section on “Variant(s) of uncertain significance” and “Sample retention, data storage, and database participation”).

Variant(s) of uncertain significance (VUS): Change(s) was/were found, but it is unclear whether this change is the cause of the health concerns. If relevant, changes in the epigenome and transcriptome might also be reported. The interpretation could remain uncertain until additional information becomes available. Such information could include published scientific articles indicating that the finding is pathogenic or that the finding does not cause health concerns (benign).

OPTIONAL TEST RESULTS: please initial your choice of whether or not to include these options

Secondary findings: The test might reveal findings, termed secondary findings. Such findings are not related to the current reasons for testing but could have important

implications for current and/or future health. The American College of Medical Genetics (ACMG) has recommended the reporting of genetic variants in 81 select genes associated with various genetic disorders that are considered to be medically actionable in childhood or in adulthood (https://www.acmg.net/PDFLibrary/Secondary-Findings-v3.1.pdf). You can choose to have the ACMG list of secondary findings analyzed in yourself/your child/ward, and any pathogenic or likely pathogenic variants in these genes will be reported. Alternatively, you can decline to have the ACMG list of secondary findings analyzed in yourself/your child/ward. The decisions you make regarding the reporting of secondary findings in yourself/your child/ward will not impact the analysis and reporting of findings related to the presenting health concerns. The decision to report/not report secondary findings should be discussed with your healthcare provider.

Please check ONE of the following:

___ YES, I DO want secondary findings to be reported in myself/my child/ward

___ NO, I DO NOT want secondary findings to be reported in myself/my child/ward

The following test options are offered to individuals providing consent for their own testing:

Carrier testing: Determining carrier status for approximately 1,300 genetic disorders that could pose risks for offspring if both parents are carriers. For example, you might be found to carry a variant in one copy of a specific gene pair. Specific testing could then be considered for your partner to assess the potential risk for your offspring and to guide prenatal testing options.

Typically, being a carrier is not associated with health concerns beyond reproductive planning, although variants detected in a small subset of genes in this category might have health implications for individuals who are identified to be carriers. This report will include potential health risks and management resources if these are detected in your test.

Please check ONE of the following:

___ YES, I DO want carrier findings to be reported in myself

___ NO, I DO NOT want carrier findings to be reported in myself

Repeat expansion disorders: a number of genes contain repeated sequences of DNA. The number of repeats can vary between individuals and across generations but they do not typically vary within an individual; that is, repeat sequence sizes remain

relatively stable across one's lifespan. If one of these repeat sequences has expanded more than it should, it can lead to a specific disorder in that individual. These disorders often involve neurological impairment, and this impairment can be progressive. For a number of these disorders, for example Huntington disease, there might not be an effective treatment. The decision of whether or not to include repeat expansion test results in your report is entirely up to you.

Please check ONE of the following:

___ YES, I DO want the results of repeat expansion testing to be reported in myself

___ NO, I DO NOT want the results of repeat expansion testing to be reported in myself

Risks and limitations

- There may be standard risks associated with blood draw (e.g., bruising, bleeding).
- Inaccurate results can occur due to:
  i) mislabeled samples regardless of strict clinical and laboratory protocols in place to minimize this risk
  ii) inaccurate or incomplete reporting of medical and family history information
  iii) rare technical errors
  iv) other reasons
- This test might reveal biological relationships that were previously unrecognized, such as non-paternity or non-maternity.
- Genomic data might provide ancestry information (e.g. ethnicity) which could be used for the sole purpose of aiding the analysis of this test.
- Due to limitations in current medical knowledge or testing technology, a genetic variant might not be identified even though one exists and may contribute to or cause health problems.
- Genetic testing might identify the diagnosis for the health problems in you/your child/ward; however, the test cannot predict the severity and precise clinical course of the genetic disorder. Your healthcare provider can discuss these issues with you.
- Genetic test results can trigger difficult emotions and, in some cases, cause tension within a family since identifying a genetic diagnosis can have implications for other family members.

- Test results might impact insurance coverage and rates, as well as employment. There may be local laws that help protect individuals undergoing genetic testing against discrimination. Please consider discussing this with your healthcare provider.

- This testing currently comprises both clinically validated testing and research testing and is undertaken in an accredited laboratory. In some situations, follow up confirmatory testing may be recommended.

Sample retention, data storage and database participation

After testing, Alamya Health will store the biological sample(s), if available, and genomic data for the option of reanalysis and reinterpretation in the future. Upon request by a health provider, Alamya Health will determine whether reanalysis or retesting would be preferred.

Alamya Health and its partners adhere to rigorous standards for personal health data storage as guided by laboratory regulatory bodies.

Alamya Health will share de-identified genomic and phenotypic (i.e. clinical) information with select genomic data repositories in order to improve the medical and scientific community's understanding of genetic information. Although sharing such information could support my/my child's/my ward's diagnosis and health management, this could also result in no personal benefit. See notices of privacy practice for more details relative to the sharing of genetic information.

After testing is complete, an individual's sample and/or data may be de-identified and used for testing and analytics validation, quality improvement, and product development.

Billing

This test is only available via private pay. Some insurance plans may cover a portion of the test (i.e. short-read genome sequencing) and you may wish to review your policy for coverage specifics.

I have reviewed this consent form with my healthcare provider and have been given the opportunity to ask questions. By signing below, I consent to testing by Alamya Health as described in this consent form.	
Name (print)	**Date of birth** (MM-DD-YYYY)

Signature (if applicable)	**Date** (MM-DD-YYYY)
Name and relationship of legal decision maker to patient (print)	**Signature of legal decision maker**