Clinical Genomics Patient Consent

Genetic Testing Introduction:
Genetic testing can reveal information about your health and potential risks for certain conditions. Your healthcare provider has or will order one or more tests offered by Ambry Genetics. It's important you understand what the testing involves and how your data and sample will be used. Signing this consent confirms that you understand the process, your rights, and that participation to test is voluntary.

Genetic Test Purpose and Specimen:
The submitted blood, body fluid, or tissue specimen is required for isolation and purification of DNA to be used for molecular genetic testing. The purpose of molecular genetic testing is to determine if you or your child have any pathogenic (disease-causing) or likely pathogenic (likely disease-causing) genetic variants associated with a specific condition or risk for developing one. Molecular genetic testing involves the analysis of the genes relevant to the condition for which your healthcare provider ordered testing. See Ambry's website for more information about the specific test(s) ordered by your healthcare provider: www.ambrygen.com

Testing and Analysis:
This testing involves sequencing and analysis of nuclear genes and may include sequencing and analysis of variants in the mitochondrial genome (mtDNA). This process includes genes that have been previously associated with human disease (characterized) and those that have not yet been described to cause a specific genetic condition (uncharacterized/novel). The goal of this testing is to identify the underlying molecular cause of an affected individual's condition.

Several hundred thousand variants will be identified using this type of sequencing, and all variants will be filtered based on the types of variants, minor allele frequencies, and information from various databases. Next, a thorough review is performed by our team to identify clinically relevant variants with overlapping features consistent with the patient's reported clinical features. Analysis begins with characterized gene-disease relationships. If no clinically relevant variants are identified among characterized gene-disease relationships, the case may then move to the second step for analysis of novel genes. Analysis of novel genes is only available when sequencing of the proband plus biologically related parents (traditional trio) is performed. Variants that are considered "relevant findings", meaning they are likely to be related to the patient's clinical features, will undergo further analysis and interpretation by an ABMG-certified laboratory director and will be included in the primary report.

Testing involves sequencing of the patient (proband) with or without up to two additional informative, genetically-related family members (preferably parents). Additional family member samples may be submitted for co-segregation analysis. Analysis of novel genes is only available when sequencing of the proband plus two other informative family members (trio) is performed. If an informative trio is not available, analysis of novel genes will not be performed. Co-segregation analysis is performed for candidate variants when family member specimens are

submitted at the time of testing. Providing family member samples improves the likelihood of a more definitive diagnosis.

Confirmation by orthogonal methods will be performed for all relevant finding variants that fail to meet quality thresholds. Co-segregation results for the family members will be included in the primary report. If no relevant findings are identified in the proband, additional family member samples will not be tested. Testing of family members submitted to Ambry after testing is completed is available at standard pricing.

Family Member Discrepancies:

As with any family-centered genetic testing, there is a possibility that the family's genetic relationships do not align with what is reported by your family. If relationship confirmation results are not as reported to Ambry, your clinicians will be contacted to determine how to proceed with testing. Options include switching from trio to duo testing, sending in another first-degree family member, and modifying family member information in the report.

Results and Interpretation:

The primary report will contain results related to the proband's primary indication for testing. A primary report is considered "positive" if a pathogenic variant is identified in a gene associated with the patient's reported clinical features. If no relevant findings are identified, a negative report is issued. Overall result categories will be dependent on the pathogenicity of the variant along with the clinical overlap of the gene with the proband's reported clinical features. For informative results and the best likelihood of a conclusive diagnosis, it is critical to provide all relevant clinical and family history information to Ambry Genetics. Results will be released to the patient by the ordering clinician, and the final clinical interpretation of results will be made by the ordering clinician, not Ambry Genetics.

When applicable, analysis of novel genes may allow for the discovery of new gene-disease relationships. New scientific information becomes available on a regular basis and could alter the interpretation of previously reported results in the future. In the event of a change in interpretation, an unsolicited reclassification (amended) report may be issued to the ordering clinician. Reanalysis may also be performed by request. Please contact the laboratory for reanalysis options.

Secondary Findings:

This testing may result in the identification of other variants unrelated to the indication for testing (aka "secondary findings"). When requested, pathogenic and likely pathogenic variants are reported in alignment with American College of Medical Genetics and Genomics recommendations (Green, 2013; Kalia, 2016; Miller 2021; Miller, 2022; Lee, 2025). For ongoing pregnancies undergoing exome sequencing, the Childhood Onset Diseases Secondary Findings are also available at no additional charge. Analysis for secondary findings is optional. Secondary findings results are available for the proband and each family member sequenced as part of the

duo or trio. The family members chosen as the duo or trio are at the discretion of the laboratory. Thus, not all consented members may receive secondary findings reports. Each duo or trio family member who opt-in will receive their own secondary findings analysis and report. Pathogenic or likely pathogenic variants identified within secondary findings genes are reported in duo or trio members even if the pathogenic or likely pathogenic variant was not identified in the proband.

Technical Testing Limitations:
While this test is designed to identify most detectable pathogenic and likely pathogenic variants in the genes analyzed, it is still possible that there are pathogenic and likely pathogenic variants that the testing technology is unable to detect. In addition, there may be other genes associated with the specific genetic condition you were tested for that are not included in this testing or that are not known at this time.

Standard Laboratory Limitations:
Inaccurate results may occur because of (but not limited to) the following reasons: sample mixup, inaccurate or misleading information about you, your clinical condition or that of your family members, or technical problems. Due to limitations in technology and incomplete knowledge of genes, some changes in DNA or protein products that cause disease may not be detected by the test. There is a possibility that the findings will be uninterpretable or of uncertain significance.

Genetic Discrimination:
Federal laws, such as the Genetic Information Nondiscrimination Act (GINA), protects against genetic discrimination by health insurers and employers, but does not cover life, long-term care, or disability insurance. State laws may offer additional protections.

Data and Sample Uses:
The test(s) will generate health data about you and Ambry Genetics or the reference lab may receive health data from your medical record in connection with the test(s). Your identifiable data is subject to legal requirements regarding its use and protection. Ambry Genetics may use and disclose the test results and your other health data as described in its notice of privacy practices (NPP) at www.ambrygen.com/legal/notice-of-privacy-practices.

Ambry Genetics reserves the right to:
- Contact you to share additional genetic testing or clinical trial opportunities that may help understand your clinical genotyping.
- Retain your deidentified sample and may utilize the remaining deidentified sample for laboratory quality control or for laboratory test validation optimization purposes.
- Use deidentified data from your records (including from your genetic testing) for research and other purposes permitted by law.

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Clinical Genomics Patient Consent - Page 4 of 4

Patient Acknowledgement:

- You understand that genetic testing is voluntary, and you may choose not to have your sample tested.
- You have read and understand the information provided in this consent, and all your questions have been answered.
- You acknowledge that the information you provided to your healthcare provider is true and correct.
- You have had the opportunity to ask questions about the purpose of testing, about the test procedure, the test results, the risks, the limitations to testing, and your rights prior to signing this informed consent.
- If the law requires you to consent to these terms but you have been unable to sign, provision of your sample to Ambry Genetics indicates your consent.

For NY Residents*: I am aware that genetic counseling is available to me prior to signing this form and after testing is complete.

☐ By checking this box, I agree that Ambry Genetics will retain my sample for 6 months after the testing above has been completed. By not checking this box, I understand that under New York State law, Ambry Genetics must discard my sample after the longer of (a) testing completion and (b) 60 days after the Date of Collection above.

***Please ensure the patient's consent to retain the sample is also documented on the paper test requisition form or within AmbryPort.**

Please consult your healthcare provider if you have any questions.

Patient Signature (or Parent/Guardian if patient is a minor) _____ Date _____

Name and Relationship (Parent/Guardian if patient is a minor) _____ Date _____

Provider Signature _____ Date _____

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