

Affix barcode label here	Patient Name		Requested Test	<input type="checkbox"/> Singleton
	Date of Birth			<input type="checkbox"/> Trio (family)

<b>Patient Information</b>			ID / MR#		
First Name	Last Name	MI	Date of Birth	Gender	<input type="checkbox"/> Male <input type="checkbox"/> Female
Address			Ethnicity <input type="checkbox"/> African/African American <input type="checkbox"/> Latino		
Telephone			<input type="checkbox"/> Ashkenazi Jewish <input type="checkbox"/> East Asian <input type="checkbox"/> Other: <input type="checkbox"/> European <input type="checkbox"/> South Asian _____		
Email					

<b>Summary of Clinical Information</b>	
<p>In addition to selecting from the phenotypes on page 2, please include a summary of current symptoms, age of onset, family history, medical history and previous testing.</p>	

<b>Sample Information</b>	
Collection Date	Specimen Type <input type="checkbox"/> Blood <input type="checkbox"/> Saliva <input type="checkbox"/> Amniotic Fluid <input type="checkbox"/> Genomic DNA
Relationship to Proband	Proband's name (if not self)
<input type="checkbox"/> Self <input type="checkbox"/> Father <input type="checkbox"/> Brother <input type="checkbox"/> Other: <input type="checkbox"/> Mother <input type="checkbox"/> Sister _____	

<b>Ordering Healthcare Provider</b>			
First Name	Last Name	Title	NPI #
Facility Name			Telephone / Fax
Facility Address			Email

<b>Additional Report Recipients</b>		
Name	Telephone / Fax	Email
Name	Telephone / Fax	Email

<b>Healthcare Provider's Statement</b>	
<p>By my signature below, I indicate that I am the referring physician or authorized healthcare provider. This test is medically necessary for the diagnosis or detection of a disease, illness, impairment, symptom, syndrome or disorder. The results will determine my patient's medical management and treatment decisions. I have explained the purpose of the test described in this form. The patient has been given the opportunity to ask questions and/or seek genetic counseling. The patient has voluntarily decided to have the test performed by Variantyx for diagnostic purposes.</p>	
Healthcare provider signature _____	Date _____



<b>Billing Information</b>		
<input type="checkbox"/> Insurance Billing	<input type="checkbox"/> Institutional Billing	<input type="checkbox"/> Patient Payment
Insurance Company	Facility Name	Contact Name
Policy #                      Group #	Contact Name	Telephone / Email
Patient Relation to Policy Holder? <input type="checkbox"/> Self <input type="checkbox"/> Spouse <input type="checkbox"/> Child	Facility Address	<input type="checkbox"/> Check (Payable to Variantyx Inc) <input type="checkbox"/> Credit Card (Call 617-209-2090)
Name / D.O.B. of Policy Holder (if not self)	Telephone / Fax / Email	Visa, MasterCard, Amex and Discover are accepted

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Phenotype(s) / History (check all that apply)		
<b>Cognitive/Physical Development</b>	<b>Muscular</b>	<b>Skin/Integument</b>
<input type="checkbox"/> Developmental regression <input type="checkbox"/> Global developmental delay <input type="checkbox"/> Intellectual disability <input type="checkbox"/> Fine motor delay <input type="checkbox"/> Gross motor delay <input type="checkbox"/> Speech articulation difficulties <input type="checkbox"/> Speech delay	<input type="checkbox"/> Dysphagia <input type="checkbox"/> Exercise intolerance/easy fatigue <input type="checkbox"/> Hypertonia <input type="checkbox"/> Hypotonia <input type="checkbox"/> Mobility limitations <input type="checkbox"/> Muscle fasciculations <input type="checkbox"/> Muscle wasting <input type="checkbox"/> Muscle weakness <input type="checkbox"/> Muscular dystrophy <input type="checkbox"/> Myotonia <input type="checkbox"/> Abnormal muscle biopsy	<input type="checkbox"/> Abnormal hair or nails: _____ <input type="checkbox"/> Abnormal connective tissue <input type="checkbox"/> Abnormal pigmentation <input type="checkbox"/> Abnormal sweating <input type="checkbox"/> Abnormal temperature regulation <input type="checkbox"/> Icthyosis
<b>Behavioral</b>		<b>Skeletal</b>
<input type="checkbox"/> Autism spectrum disorder <input type="checkbox"/> Self-injurious behavior <input type="checkbox"/> Stereotypic behavior		<input type="checkbox"/> Club foot <input type="checkbox"/> Craniosynostosis <input type="checkbox"/> Multiple joint contractures <input type="checkbox"/> Scoliosis <input type="checkbox"/> Vertebral anomalies
<b>Brain Anomalies</b>	<b>Endocrine</b>	<b>Cardiac</b>
<input type="checkbox"/> Abnormalities of basal ganglia <input type="checkbox"/> Agenesis of the corpus callosum <input type="checkbox"/> Brain atrophy <input type="checkbox"/> Cerebellar hypoplasia <input type="checkbox"/> Cortical dysplasia <input type="checkbox"/> Dandy-Walker malformation <input type="checkbox"/> Encephalocele <input type="checkbox"/> Heterotopia <input type="checkbox"/> Holoprosencephaly <input type="checkbox"/> Hydrocephalus <input type="checkbox"/> Lissencephaly <input type="checkbox"/> Molar tooth sign <input type="checkbox"/> Periventricular leukomalacia <input type="checkbox"/> Polymicrogyria	<input type="checkbox"/> Adrenal hyperplasia <input type="checkbox"/> Adrenal insufficiency <input type="checkbox"/> Cushing syndrome <input type="checkbox"/> Hypothyroidism <input type="checkbox"/> Hypoparathyroidism <input type="checkbox"/> Hypogonadism <input type="checkbox"/> Pheochromocytoma/paraganglioma <input type="checkbox"/> Type 1 Diabetes Mellitus <input type="checkbox"/> Type 2 Diabetes Mellitus	<input type="checkbox"/> Arrhythmia <input type="checkbox"/> Cardiomyopathy <input type="checkbox"/> Pulmonary venous return <input type="checkbox"/> Septal defect: _____ <input type="checkbox"/> Syncope <input type="checkbox"/> Structural heart malformation <input type="checkbox"/> Tetralogy of Fallot
	<b>Metabolic</b>	<b>Gastrointestinal</b>
	<input type="checkbox"/> CPK abnormalities <input type="checkbox"/> Elevated alanine <input type="checkbox"/> Elevated pyruvate <input type="checkbox"/> Ketosis <input type="checkbox"/> Lactic acidosis <input type="checkbox"/> Low plasma carnitine <input type="checkbox"/> Organic aciduria <input type="checkbox"/> Abnormal metabolic testing: _____	<input type="checkbox"/> Abdominal wall defect <input type="checkbox"/> Chronic intestinal pseudo-obstruction <input type="checkbox"/> Constipation <input type="checkbox"/> Diarrhea <input type="checkbox"/> Elevated hepatic transaminases <input type="checkbox"/> Gastroesophageal reflux <input type="checkbox"/> Gastroschisis/Omphalocele <input type="checkbox"/> Hirschsprung disease <input type="checkbox"/> Pyloric stenosis <input type="checkbox"/> Recurrent vomiting <input type="checkbox"/> Tracheoesophageal fistula
<b>Neurological</b>	<b>Constitutional</b>	<b>Genitourinary</b>
<input type="checkbox"/> Ataxia/Spasticity <input type="checkbox"/> Chorea <input type="checkbox"/> Dysmyelination <input type="checkbox"/> Dystonia <input type="checkbox"/> Foot drop <input type="checkbox"/> Neurodegeneration <input type="checkbox"/> Neurodevelopmental NOS <input type="checkbox"/> Neuromuscular NOS <input type="checkbox"/> Neuropathy <ul style="list-style-type: none"> <li><input type="checkbox"/> Distal motor neuropathy</li> <li><input type="checkbox"/> Proximal motor neuropathy</li> </ul> <input type="checkbox"/> Pes cavus <input type="checkbox"/> Pressure palsy <input type="checkbox"/> Psychiatric <input type="checkbox"/> Recurrent headache/migraine <input type="checkbox"/> Reduced/absent deep tendon reflexes <input type="checkbox"/> Seizures <input type="checkbox"/> Sleep apnea <input type="checkbox"/> Stroke-like episodes <input type="checkbox"/> Tremor <input type="checkbox"/> Vocal cord paresis <input type="checkbox"/> Other movement disorder <input type="checkbox"/> Abnormal CT <input type="checkbox"/> Abnormal EEG <input type="checkbox"/> Abnormal EMG <input type="checkbox"/> Abnormal MRI <input type="checkbox"/> Abnormal nerve biopsy <input type="checkbox"/> Abnormal nerve conduction velocity	<input type="checkbox"/> Dysmorphic features <ul style="list-style-type: none"> <li><input type="checkbox"/> Cleft lip/palate</li> <li><input type="checkbox"/> Syndactyly</li> <li><input type="checkbox"/> Polydactyly</li> </ul> <input type="checkbox"/> Failure to thrive <input type="checkbox"/> Macrocephaly <input type="checkbox"/> Microcephaly <input type="checkbox"/> Obesity <input type="checkbox"/> Overgrowth <input type="checkbox"/> Short stature <input type="checkbox"/> Tall stature	<input type="checkbox"/> Ambiguous genitalia <input type="checkbox"/> Hydronephrosis <input type="checkbox"/> Hypospadias <input type="checkbox"/> Kidney malformation <input type="checkbox"/> Renal agenesis <input type="checkbox"/> Renal tubulopathy <input type="checkbox"/> Undescended testis <input type="checkbox"/> Other abnormality: _____
	<b>Ophthalmology/Auditory</b>	<b>Prenatal Anomalies</b>
	<input type="checkbox"/> Blindness <input type="checkbox"/> Cataracts <input type="checkbox"/> CPEO (ophthalmoplegia) <input type="checkbox"/> Coloboma <input type="checkbox"/> Optic atrophy <input type="checkbox"/> Ptosis <input type="checkbox"/> Retinitis pigmentosa <input type="checkbox"/> Visual impairment <input type="checkbox"/> External ear malformation <input type="checkbox"/> Hearing loss/deafness <input type="checkbox"/> Ototoxicity (aminoglycoside-induced)	<input type="checkbox"/> Intrauterine growth retardation <input type="checkbox"/> Oligohydramnios <input type="checkbox"/> Polyhydramnios <input type="checkbox"/> Premature birth <input type="checkbox"/> Cystic hygroma
		<b>Other</b>

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### Informed Consent and Authorization

The benefits and risks of the Genomic Unity™ test are explained below. It is recommended that you receive genetic counseling from a licensed healthcare provider who can answer your questions about genetic testing and provide information about alternatives. Information about genetic counselors in your area is available at <https://www.nsgc.org/>.

#### Background

DNA is organized into coding regions that make up the approximately 20,000 genes which provide instructions for making proteins. These proteins are responsible for growth and development as well as traits such as eye color. Non-coding regions help control how and when genes are used. Genetic disorders may be caused by changes (variants) in the DNA. The purpose of genetic testing is to identify changes in the DNA sequence that are the cause of an affected individual's condition.

This test sequences the entire genome using a PCR-free protocol that produces comprehensive and consistent coverage of all exons. The resulting data is subjected to in-silico analyses optimized for small sequence changes, structural variants (including CNVs), short tandem repeats and mitochondrial variants. Additional information about Genomic Unity™ test is available from your healthcare provider and on the Variantyx website at <https://www.variantyx.com/>.

#### Technical Limitations

Genetic testing is accurate, but may not always identify a genetic variant even though one exists. This test attempts to evaluate the entire DNA sequence, but may not be able to detect all DNA changes due to limitations in current technology. Certain regions of the DNA may not be well covered. Certain variant types may not be detectable such as methylation abnormalities, variants in genes with highly homologous pseudogenes and variants in regions that are difficult to assay based on current technology. Unusual circumstances including bone marrow transplantation, blood transfusion, and variants that exist in only a small fraction of cells (mosaicism) may interfere with variant identification. Additionally, interpretation of the results is limited by the current medical understanding of disease and available scientific information.

This test requires high-quality DNA. In some cases, an additional sample may be needed if the volume, quality and/or condition of the initial specimen is not adequate. This test does not consider somatic mutations.

#### Possible Test Results

Test results will be issued as a single clinical report for the patient, even if additional family member samples are included in the analysis. If the patient chooses to receive incidental findings, those findings will be included in a separate section of the clinical report. For each family member who chooses to receive incidental findings, a separate incidental finding report will be issued. Possible results of this test include:

**Positive result** - A positive result indicates that one or more genetic variants were identified that either explain the cause of the disorder or indicate an increased risk of developing the disorder in the future.

**Negative result** - A negative result indicates that no genetic variant explaining the disorder was identified by this test. This reduces the likelihood of, but does not exclude the possibility of, the disorder being genetic in nature.

**Uncertain result / Variant of uncertain significance (VUS)** - A variant of uncertain significance was identified by this test. This means that a genetic variant was identified, but based on available information in the medical literature and research and scientific databases it is not certain whether the variant may cause the disorder. The variant could be a normal genetic difference that does not cause medical problems, or it could be a variant causing an abnormality. Without further information, the effects of the variant cannot be known and an inconclusive result may be reported. The uncertainty may be resolved over time if additional information becomes available. Periodic reanalysis of the sequence data or further analysis, including testing of additional family members, may be recommended.

All variants in the clinical report will be categorized as pathogenic, likely pathogenic or a variant of uncertain significance (VUS) utilizing the American College of Medical Genetics and Genomics (ACMG)/Association for Molecular Pathology (AMP) guidelines as published by Richards et al 2015 (for more information see: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4544753/>). Variants included in the clinical report will be labeled as primary or secondary. A primary label indicates that the variant has strong phenotypic correlation with the reported patient phenotype(s) and is considered a strong causal candidate for the disorder. A secondary label indicates that the variant has some phenotypic overlap with the reason for testing but does not appear to be the sole genetic cause for the phenotype(s) in the patient.

Even if this test finds DNA changes that are responsible for the reported symptoms, the testing may not completely predict the severity of the disorder, possible future problems, or response to treatment.

#### Incidental Findings

This test may identify genetic variants, called incidental findings, that are not directly related to the disorder or symptoms that prompted the test. The American College of Medical Genetics and Genomics (ACMG) has recommended that incidental findings identified in a subset of 59 medically-actionable genes associated with a variety of inherited disorders be reported for patients undergoing WES or WGS. Only known pathogenic or likely pathogenic variants in these genes will be reported. The disorders strongly linked to variants in these genes include cancer predisposition risk, later-onset cardiac syndromes and connective tissue syndromes. The identification of incidental findings may result in the identification of a condition for which the individual has not yet experienced symptoms.

You may choose whether or not to have incidental findings reported. If you do not specifically opt-in to receive incidental findings, none will be reported. If you choose to receive incidental findings there may be implications for other family members. For example, identification of a genetic variant that

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indicates an increased risk for an individual of developing cancer may infer that other family members may also be at increased risk of developing cancer. Family members may need to pursue clinical genetic testing through their healthcare provider if concerned about their own risk.

If you choose to receive incidental findings, only findings in the ACMG gene list will be reported, and only if there is enough evidence. The absence of incidental findings does not mean that there are no disease-causing genetic variants in the ACMG genes or in other genes.

**Testing of Family Samples**

In the case of trio and/or larger cohort analysis, and for parental confirmation of singleton analysis, sequencing and analysis of family samples, may be used to improve the interpretation of genetic variants identified in the patient’s DNA. Accurate interpretation of test results requires accurate assignment of family relationships. Analysis of the sequenced DNA is performed with the assumption that correct family relationships have been provided. It is possible that this test may identify misattributed paternity, for example identifying that the stated father of the patient is not the true biological father, and that it may be necessary to report these findings. Family samples are analyzed only with regard to the patient's condition. Incidental findings will be reported for family members only if specifically requested, as separate reports.

**Patient Confidentiality**

To maintain confidentiality, test results will only be released to the ordering healthcare provider or ordering laboratory, and upon your request, to additional healthcare provider(s) indicated on this test requisition form. Personnel at Variantyx will not release test results directly to patients and will not discuss the test results with anyone except the medical professional who ordered the test or has been authorized to receive the results. Test results will only be disclosed to others by your written consent and/or if demanded by a court of competent jurisdiction. It is your responsibility to consider the possible impact of test results on insurance rates, the ability to obtain disability, life or long-term care insurance and employment. The Genetic Information Non-discrimination Act (GINA), enacted by the US Federal Government, provides some protection against discrimination by health insurance companies and employers based on genetic test results, but does not cover life, disability or long-term care insurance. Information about GINA is available at <https://www.genome.gov/10002328>.

Anonymized information obtained from the test may be included in variant and allele frequency databases used to help healthcare providers and scientists understand human disease, as well as in scientific publications. Names and personal identifying information will not be revealed. Separate from the above, if there are opportunities to participate in research relevant to your condition, and you have consented for recontact, Variantyx may contact you or your healthcare provider for research purposes.

**Specimen Retention**

DNA extracted from submitted specimens will be stored for at least 3 months following completion of testing and will be discarded thereafter. DNA samples are not returned unless requested prior to testing (additional fees apply). After completion of testing, anonymized DNA may be used for test development and improvement, internal validation, quality assurance and training purposes before being discarded.

**Statement of Consent**

I have read the Informed Consent and Authorization section of this document. I have discussed Genomic Unity™ test with my healthcare provider including the purpose and procedure, risks, benefits and alternatives. I have been given an opportunity to ask questions about the test, and any questions I had were answered to my satisfaction. I acknowledge that I have sufficient information and understanding to give this informed consent.

1. I give permission to Variantyx and their affiliates to sequence my DNA and perform genetic testing as described.
2. In the case of direct insurance billing: I acknowledge that the information provided by me is true and correct. I authorize my healthcare provider and/or insurer to share medical information with Variantyx related to my/my child’s condition, diagnosis and treatment as relevant to my/my child’s genetic testing, as well as information about my healthcare plan benefits. I authorize Variantyx to release my/my child’s medical information concerning my/my child’s testing to my insurer. I authorize Variantyx to be my designated representative for purposes of appealing any denial of benefits as needed and to request additional medical records for this purpose. I understand that Variantyx will notify me if my out of pocket costs are determined to exceed \$100. I authorize my insurance benefits to be paid directly to Variantyx.
3. I give permission for my anonymized DNA to be used by Variantyx and their affiliates for test development or improvement, internal validation, orthogonal variant confirmation at an outside referral laboratory and/or quality assurance and training purposes.
4. I give permission for my anonymized sample and clinical information to be included in variant and allele frequency databases and publications. My name or other personal identifying information will not be used in or linked to any databases or publications.
5. I  give /  do not give permission for Variantyx to contact me or my healthcare provider about participation in research studies. 
6. I choose  to receive /  not to receive incidental findings. 

Patient (or legal guardian) first name \_\_\_\_\_ Last name \_\_\_\_\_

Patient (or legal guardian) signature \_\_\_\_\_ Date \_\_\_\_\_ 