Patient Name:_____

Identification Number:_____

UPMC LIFE CHANGING MEDICINE

WHOLE EXOME & MITOCHONDRIAL GENOME SEQUENCING REQUISTION FORM

☐ **Send Mitochondrial Genome Sequencing to PerkinElmer Genomics (Test Code # UPMC01) refer to page 8**

PATIENT INFORMATION (*Please Print*)			**FAMILY INFORMATION (*Please Print*)**
First Name / MI / Last Name			Name of Family Member #1 / DOB
DOB (mm/dd/yy) / MRN# / Sex M ☐ F ☐			Relationship / Sex M ☐ F ☐
Address / Phone			Name of Family Member #2 / DOB
City / State / Zip Code			Relationship / Sex M ☐ F ☐

Ancestry (check all that apply):

☐ White/Caucasian	☐ Asian	☐ Western/Northern Europe	☐ Native American
☐ Black/African American	☐ Ashkenazi Jewish	☐ Central/South American	☐ Other: (specify)
☐ Hispanic	☐ Eastern/Central Europe	☐ Middle Eastern	

REFERRING PROVIDER INFORMATION (*Please Print*)

Ordering Provider		NPI	Additional Provider		NPI
Address			Address		
City	State	Zip Code	City	State	Zip Code
Phone	Fax	Email	Phone	Fax	Email

PERKINELMER GENOMICS- UPMC Clinical Genomics Lab use only

☐ Extracted DNA provided to PerkinElmer Genomics for Mitochondrial Genome Sequencing (Test Code # UPMC01)

☐ Extracted DNA provided to PerkinElmer Genomics for Mitochondrial Maternal VUS Testing (Test Code # UPMC99)

☐ Bill	Facility/Acct :	Contact:	Phone:	Email:

SAMPLE INFORMATION

DATE OF SAMPLE OBTAINED (mm/dd/yy)	**DOES YOUR PATIENT HAVE A**	**DIAGNOSIS CODING**
☐ Blood in EDTA (3-5 ml in lavender or pink top tube)	☐ History of blood transfusion?	ICD-10 Code(s)
☐ Extracted DNA (Please contact PCGL prior to sending)	☐ History of hematological malignancy?	
☐ Saliva kit	☐ History of allogenic bone marrow transplant?	Clinical Diagnosis
☐ Cultured Fibroblasts	If the answer is yes to any of these questions, please contact the laboratory to discuss before sending a sample.	

STATEMENT OF MEDICAL NECESSITY (*Required*)

I authorize and direct UPMC Clinical Genomics Laboratory (UCGL) to perform the testing indicated. I confirm that the testing requested is reasonable and medically necessary and that the test results may impact medical management and treatment decisions for this patient. I certify that the patient or legal guardian has been informed of the risks, benefits and limitations of genetic testing. The person listed as the ordering provider is authorized by law to order the test(s) requested herein.

_____

Signature of Provider (required) Date

PATIENT CONSENT (*Required*)

By signing this form I acknowledge as the patient/legal guardian that I have read the attached informed consent document and that I authorize the UPMC UCGL to perform whole exome sequencing as described. Genetic variants that are present in a family member but not in the proband will NOT be detected. and therefore not reported.

☐ OPT-IN: Please check this box if you wish to receive reportable secondary findings as identified by the ACMGG. (Family members cannot opt-in unless the patient has opted to receive these findings).

☐ OPT-IN: Please check this box if you wish to be recontacted for research opportunities by your provider.

_____

Print name of Patient/Legal guardian Signature of Patient/Legal guardian Date

PAYMENT OPTIONS (FILL OUT ONE OF THE OPTIONS BELOW)

☐ INSURANCE BILLING (copy front and back of insurance cards)

Primary Insurance	Insurance ID#	Name and DOB of Insured	Patient Relation to Policy Holder Self ☐ Spouse ☐ Child ☐
Secondary Insurance	Insurance ID#	Name and DOB of Insured	Prior Authorization # - Please Attach

☐ PATIENT BILLING

☐ I am electing to self-pay. I agree that neither UPMC Clinical Genomics Laboratory (UCGL) nor I will submit a claim to my insurance for testing. Please discuss with your provider.

☐ INSTITUTIONAL BILLING

Facility	Address	Contact	Phone	Email

Patient Name:_____

Identification Number:_____

UPMC LIFE CHANGING MEDICINE

WHOLE EXOME & MITOCHONDRIAL GENOME SEQUENCING REQUISTION FORM

ITEM CHECKLIST FOR TESTING

Proband Sample:	☐ Included	☐ Signed Consents	☐ Clinical Notes/Family History	☐ Requisition
Maternal Sample:	☐ Included	☐ At a later date	☐ N/A	☐ Requisition w/ clinical notes, if applicable
Paternal Sample:	☐ Included	☐ At a later date	☐ N/A	☐ Requisition w/ clinical notes, if applicable
Other Family Member:	☐ Included	☐ At a later date	☐ N/A	☐ Requisition w/ clinical notes, if applicable

INDICATION FOR TESTING

Please provide the following information regarding the patient to be tested. Phenotypes listed are in HPO terms with the corresponding HPO number (http://human-phenotype-ontology.github.io/). This information is needed to facilitate interpretation of whole exome sequencing results.

☐ Negative/None

PRE/PERINATAL HISTORY
☐ Cystic hygroma [0000476]
☐ Diaphragmatic hernia [0000776]
☐ Encephalocele [0002084]
☐ Increased nuchal translucency [0010880]
☐ Intrauterine growth restrictions [0001511]
☐ Nonimmune hydrops fetalis [0001790]
☐ Oligohydramnios [0001562]
☐ Omphalocele [0001539]
☐ Prematurity GA:___.___[0001622]
☐ Polyhydramnios [0001561]
☐ Prolonged neonatal jaundice [0006579]

GROWTH
☐ Failure to thrive [0001508]
☐ Hemihypertrophy [0001528]
☐ Macrosomia [0001520]
☐ Obesity [0001513]
☐ Short stature [0004322]
☐ Tall stature [0000098]

MOTOR/COGNITIVE DEVELOPMENT
☐ Absent speech [0001344]
☐ Aggressive behavior [0006919]
☐ Anxiety [0100852]
☐ Autistic Behavior [0000729]
☐ Delayed speech and language development [0000750]
☐ Developmental Regression [0002376]
☐ Global development delay [0001263]
☐ Hyperactivity [0000752]
☐ Intellectual Disability [0001249]
☐ Learning Disability [0001328]
☐ Memory impairment [0002354]
☐ Sleep disturbance [0002360]
☐ Psychiatric [0000708]

CRANIOFACIAL/DYSMORPHISM
☐ Abnormal facial shape [0001999]
☐ Cleft lip and/or palate [0000202]
☐ Coarse facial features [0000280]
☐ Craniosynostosis [0001363]
☐ Dysmorphic features [0001999]
☐ Macrocephaly [0000256]
☐ Microcephaly [0000252]
☐ Short neck [0000470]

STRUCTURAL BRAIN ABNORMALITIES
☐ Abnormal myelination [0012447]
☐ Abnormality of the basal ganglia [0002134]
☐ Abnormality of the brainstem [0002363]
☐ Abnormality of periventricular white matter [0002518]
☐ Abnormality of corpus Collosum [0001273]
☐ Aplasia/hypoplasia of cerebellar vermis [0006817]
☐ Aplasia/hypoplasia of the cerebellum [0007360]
☐ Arnold Chiari malformation [0007099]
☐ Cerebellar atrophy [0007360]
☐ Heterotopia [0002282]
☐ Holoprosencephaly [0001360]
☐ Hydrocephalus [0000238]
☐ Leukodystrophy [0002415]
☐ Lissencephaly [0001339]
☐ Pachygyria [0001302]
☐ Polymicrogyria [0002126]
☐ Ventriculomegaly [0002119]

NEUROLOGICAL FINDINGS
☐ Abnormality of nervous system [0000707]
☐ Ataxia [0001251]
☐ Cerebral palsy [0100021]
☐ Chorea [0002072]
☐ Cortical visual impairment [0100704]
☐ Dementia [0000726]
☐ Dysarthria [0001260]
☐ Dyskinesia [0100660]
☐ Dysphasia [0002357]
☐ Dystonia [0001332]
☐ Encephalopathy [0001298]
☐ Hemiplegia [0002301]
☐ Incoordination [0002311]
☐ Infantile Spasms [0012469]
☐ Migraines [0002076]
☐ Myoclonus [0001336]
☐ Parkinsonism [0001300]
☐ Peripheral neuropathy [0009830]
☐ Seizures [0001250]
☐ Sensory Neuropathy [0000763]
☐ Spasticity [0001257]
☐ Syncope [0001279]
☐ Tremors [0001337]
☐ Vertigo [0002321]

HEARING IMPAIRMENT
☐ Abnormal Newborn Screen: _____
☐ Conductive hearing impairment [0000405]
☐ Mixed hearing impairment [0000410]
☐ Sensorineural hearing impairment [0000407]

CARDIAC FINDINGS
☐ Abnormal heart morphology [0001627]
☐ Amyloidosis [0011034]
☐ Aortic root dilatation [0002616]
☐ Arrhythmia [0011675]
☐ Atrial septal defect [0001631]
☐ Bicuspid aortic valve [0001647]
☐ Bradycardia [0001662]
☐ Coarctation of aorta [0001680]
☐ Dilated cardiomyopathy [0001644]
☐ Heterotaxy [0030853]
☐ Hypertension [0000822]
☐ Hypertrophic cardiomyopathy [0001639]
☐ Mitral valve prolapse [0001634]
☐ Noncompaction cardiomyopathy [0012817]
☐ Patent ductus arteriosus [0001643]
☐ Patent foramen ovale [0001655]
☐ Prolonged QTc interval [0005184]
☐ Sudden death [0001645]
☐ Supraventricular tachycardia [0004755]
☐ Tetralogy of Fallot [0001636]
☐ Ventricular septal defect [0001629]

VASCULAR SYSTEM
☐ Aneurysm [0002617]
☐ Arterial calcification [0003207]
☐ Arterial dissection [0005294]
☐ Arterial tortuosity [0005116]
☐ Arteriovenous malformation [0100026]
☐ Epistaxis [0000421]
☐ Lymphedema [0001004]
☐ Pulmonary arterial hypertension [0002092]
☐ Pulmonary venous hypertension [0030950]
☐ Stroke [0001297]

EYE DEFECTS & VISION
☐ Abnormality of vision [0000504]
☐ Aniridia [0000526]
☐ Anophthalmia [0000528]
☐ Anterior Segment Dysgenesis [0007700]
☐ Cataracts [0000518]
☐ Cataract bilateral congenital [0000519]
☐ Coloboma [0000589]
☐ Corneal dystrophy [0001131]
☐ Ectopia lentis [0001083]
☐ Esotropia [0000565]
☐ Exotropia [0000577]
☐ External ophthalmoplegia [0000544]
☐ Glaucoma congenital [0001087]

Patient Name:_____

Identification Number:_____

UPMC LIFE CHANGING MEDICINE

WHOLE EXOME & MITOCHONDRIAL GENOME SEQUENCING REQUISTION FORM

INDICATION FOR TESTING continued

EYE DEFECTS & VISION
- ☐ Microphthalmia [0000568]
- ☐ Myopia [0000545]
- ☐ Nystagmus [0000639]
- ☐ Optic atrophy [0000648]
- ☐ Optic neuropathy [0001138]
- ☐ Ptosis [0000508]
- ☐ Retinal detachment [0000541]
- ☐ Retinitis pigmentosa [0000510]
- ☐ Strabismus [0000486]

MUSCULOSKELETAL FINDINGS
- ☐ Abnormal connective tissue [0003549]
- ☐ Abnormal form of the vertebral bodies [0003312]
- ☐ Abnormality of the ribs [0000772]
- ☐ Arachnodactyly [0001166]
- ☐ Clinodactyly [0030084]
- ☐ Decreased muscle mass [0003199]
- ☐ Ectrodactyly [0100257]
- ☐ Exercise intolerance [0003546]
- ☐ Hemihypertrophy [0001528]
- ☐ Hypertonia [0001276]
- ☐ Hypotonia [0001252]
- ☐ Joint Hypermobility [0001382]
- ☐ Muscle weakness [0001324]
- ☐ Myalgia [0003326]
- ☐ Myopathic facies [0002058]
- ☐ Osteoarthritis [0002758]
- ☐ Osteopenia [0000938]
- ☐ Pectus carinatum/excavatum [0000766]
- ☐ Polydactyly [0010442]
- ☐ Recurrent Fractures [0002757]
- ☐ Rhabdomyolysis [0003201]
- ☐ Scoliosis [0002650]
- ☐ Skeletal Dysplasia [0002652]
- ☐ Syndactyly [0001159]

GASTROINTESTINAL FINDINGS
- ☐ Constipation [0002019]
- ☐ Diarrhea [0002014]
- ☐ Duodenal stenosis/atresia [0100867]
- ☐ Episodic Vomiting [0002572]
- ☐ Failure to thrive [0001508]
- ☐ Feeding difficulties [0011968]
- ☐ Gastroesophageal reflux [0002020]
- ☐ Gastroparesis [0002578]
- ☐ Hepatomegaly [0002240]
- ☐ Hirschsprung Disease [0002251]
- ☐ Inflammatory bowel disease [0002037]
- ☐ Pancreatitis [0001733]
- ☐ Pyloric Stenosis [0002021]
- ☐ Splenomegaly [0001744]
- ☐ Tracheoesophageal Fistula [0002575]
- ☐ Vomiting [0002013]

GENITOURINARY
- ☐ Ambiguous Genitalia [0000062]
- ☐ Cryptorchidism [0000028]
- ☐ Horseshoe Kidney [0000085]
- ☐ Hydronephrosis [0000126]
- ☐ Hypospadias [0000047]
- ☐ Inguinal hernia [0000023]
- ☐ Micropenis [0000054]
- ☐ Nephrolithiasis [0000787]
- ☐ Polycystic Kidney Disease [0000113]
- ☐ Renal Agenesis [0000104]
- ☐ Renal Tubulopathy [0000114]
- ☐ Renal dysplasia [0000110]
- ☐ Umbilical hernia [0001537]

HAIR & SKIN FINDINGS
- ☐ Abnormal Blistering of the Skin [0008066]
- ☐ Abnormal Nails [0001597]
- ☐ Alopecia [0001596]
- ☐ Anhidrosis [0000970]
- ☐ Café-Au-Lait Spots [0000975]
- ☐ Coarse Hair [0002208]
- ☐ Eczema [0000964]
- ☐ Generalized Hypertrichosis [0004554]
- ☐ Hemangiomas [0001028]
- ☐ Hyperextensible skin [0008067]
- ☐ Hyperpigmentation of the skin [0001000]
- ☐ Hypohidrosis [0000966]
- ☐ Hypopigmentation of the skin [0001010]
- ☐ Ichthyosis [0008064]
- ☐ Skin Rash [0000988]
- ☐ Sparse hair [0008070]
- ☐ Telangiectasia [0001009]
- ☐ Velvety skin [0000977]

METABOLIC/RESPIRATORY FINDINGS
- ☐ Abnormal activity of mitochondrial respiratory chain [0011922]
- ☐ Asthma [0002099]
- ☐ Bronchiectasis [0002110]
- ☐ Aminoaciduria [0003355]
- ☐ Elevated hepatic transaminase [0002910]
- ☐ Hyperammonemia [0001987]
- ☐ Hyperglycemia [0003074]
- ☐ Hyperventilation [0002883]
- ☐ Hypoammonemia [0100493]
- ☐ Hypoglycemia [0001943]
- ☐ Hypoventilation [0002791]
- ☐ Increased CPK [0003236]
- ☐ Increased pyruvate [0003542]
- ☐ Lactic acidosis [0003128]
- ☐ Organic Aciduria [0001992]
- ☐ Pneumothorax [0002107]
- ☐ Pulmonary fibrosis [0002206]
- ☐ Respiratory insufficiency [0002093]

HEMATOLOGIC/IMMUNOLOGIC FINDINGS
- ☐ Anemia [0001903]
- ☐ Immunodeficiency [0002721]
- ☐ Neutropenia [0001875]
- ☐ Pancytopenia [0001876]
- ☐ Recurrent infections [0002719]
- ☐ Thrombocytopenia [0001873]

ENDOCRINE
- ☐ Delayed puberty [0000823]
- ☐ Diabetes Insipidus [0000873]
- ☐ Diabetes Mellitus [0000819]
- ☐ Hyperthyroidism [0000836]
- ☐ Hypophosphatemia [0002148]
- ☐ Hypothyroidism [0000821]
- ☐ Hypoparathyroidism [0000829]
- ☐ Maturity-onset diabetes of the young [0004904]
- ☐ Pheochromocytoma [0002666]
- ☐ Paraganglioma [0002668]

CANCER
- ☐ Type of cancer_____
- ☐ Age at Diagnosis_____
- ☐ Family History of Cancer

Additional clinical information (attach copies of other relevant records if desired):

Patient Name:_____

Identification Number:_____

UPMC LIFE CHANGING MEDICINE

WHOLE EXOME & MITOCHONDRIAL GENOME SEQUENCING REQUISTION FORM

INFORMED CONSENT

ABOUT THE UPMC WHOLE EXOME SEQUENCING TEST

Whole exome sequencing is a complex genomic test that looks at thousands of genes at once. It is designed to identify genetic changes in your DNA (genetic material) that may cause the medical condition your provider is concerned about. Most changes that cause disease affect the parts of our DNA called “exons.” Only about 1.5% of all the DNA is located in the exons. However, testing the exons finds many of the genetic changes which are known to cause disease. All of the exons of all the genes together is called the “whole exome.” This test will sequence, or “read” the patient’s whole exome.

The purpose of this test is to determine if there is a possible genetic reason for the patient’s health condition. Finding a genetic cause may improve future medical care and treatment options and inform family planning.

Detailed medical and family history are needed for accurate interpretation of results. Clinical photographs can also be helpful.

Genetic counseling and/or clinical genetics consultation is recommended before and after whole exome sequencing. Clinical reports are released only to the certified healthcare professional(s) listed on the order form. You may choose to request a copy of the clinical report from the healthcare professional who ordered the test.

FAMILY TESTING

Any sample submitted to be used to assist in the analysis of the patient’s exome (such as the parents or a sibling) will have sequencing performed but will not be analyzed separately. They will only be utilized if submitted before the patient’s exome is analyzed, or within 30 days of receipt of proband, whichever is first.

Family members are ONLY used for better interpretation of the patient’s whole exome sequencing findings. Genetic variants that may be in a family member, but are NOT present in the proband, will not be detected and therefore are not reported.

Genetic testing may reveal that the true biological relationships in a family are not as they were reported. This includes non-paternity (the stated father of an individual is not the biological father) and consanguinity (the parents of an individual are related by blood). Incorrect information about the biological relationships in your family may result in incorrect interpretation of results, incorrect diagnoses, and/or inconclusive test results. If you have any concerns about any such issues, please discuss them confidentially with your genetic counselor or ordering provider.

WHOLE EXOME SEQUENCING RESULT REPORTING

In general, the laboratory will only report results that may explain the patient’s clinical features.

You can also choose to receive secondary findings. The American College of Medical Genetics and Genomics (ACMGG) identified 59 genes and disorders for which treatment is available that may reduce morbidity and/or mortality. These findings may be unrelated to the reason for referral but may impact medical decision-making if identified. Only DNA changes known to cause disease will be reported. For more information about the ACMGG recommendations, refer to www.nature.com/articles/gim2016190

Due to limited knowledge on their genetic causes, variants related to complex multifactorial diseases such as asthma, lupus and type 2 diabetes, will not be reported.

Genetic variants not known to be clinically relevant will not be reported.

One report is generated for the patient. If samples from parents or siblings were utilized as part of the interpretation of the patient’s exome test, the results will indicate if the variant(s) were de novo (new event), or inherited from the mother, the father or present in a sibling.

Patient Name:_____

Identification Number:_____

UPMC LIFE CHANGING MEDICINE

WHOLE EXOME & MITOCHONDRIAL GENOME SEQUENCING REQUISTION FORM

INFORMED CONSENT continued

POSSIBLE TEST RESULTS

The genetic variants found by whole exome sequencing will be classified according to the guidelines from the American College of Medical Genetics and Genomics (ACMGG). Three possible test results include:

- Positive: pathogenic or likely pathogenic variant) a variant was found that likely caused the patient's condition or carries an increased risk for developing the disorder in the future. This result may be important for other family members.
- Negative: no disease-causing variants were found. This result does not eliminate the possibility of a genetic condition not discovered by this test.
- Variant of uncertain clinical significance (VUS): A genetic variant was found, but it is currently unknown whether that change could have caused the patient's condition. A VUS may be benign or disease-causing, but more research is needed.

Because the literature, medical and scientific knowledge are constantly changing, new information that becomes available in the future may replace or add to the information UPMC Clinical Genomics laboratory used to interpret the results.

RISKS & LIMITATIONS

As with all laboratory testing, there is a small risk of getting an erroneous result.

Because many different genes and conditions are being analyzed, there is a risk that genetic information will be revealed that is not directly related to the reason WES was ordered. This information might relate to diseases or symptoms that may develop in conditions that have no current treatment. The severity and clinical course of the genetic condition may not be known.

Additional variants may exist and may contribute to or cause disease but not be identified by this analysis. Whole exome sequencing has technical limitations and generally is not able to detect larger deletions/duplications or structural rearrangements, low level mosaicism, deep intronic variants, methylation abnormalities or repetitive sequence changes.

Interpretation of findings is limited by what is currently known about the genes and diseases being tested.

DATA & UPDATED INFORMATION

Information about genetic disease is continually changing. Additionally, a patient's clinical presentation or family history may also change over time. It is the responsibility of the patient and ordering provider to be aware of any changes in the patient's symptoms and to communicate them to the laboratory. The laboratory will also re-contact the referring physician if the lab learns that new information about the gene(s) tested has been identified.

The physician can initiate a request for variant interpretation review, reanalysis of sequencing data and release of raw data. There may be a charge associated with this request.

Sharing health history and genetic information can ultimately help health care providers deliver better care for their patients and provide researchers opportunities to make discoveries. UPMC submits de-identified information to public databases to contribute to the advancement of medical knowledge.

PRIVACY/PATIENT CONFIDENTIALITY

The United States Federal Government has enacted the Genetic Information and Non-discrimination Act (GINA) that prohibit discrimination, based on genetic test results, by health insurance companies and employers. These laws also prohibit unauthorized disclosure of this information. For more information you can visit https://www.eeoc.gov/laws/statutes/gina.cfm However, this law does not consider the possible impact these results may have on obtaining disability or life insurance.

Data and personal information will be stored and protected in strict confidence complying with regulatory requirements (e.g., HIPAA and equivalent protections), and I acknowledge that I have read and understand UPMC's privacy policy.

Patient Name:_____

Identification Number:_____

UPMC LIFE CHANGING MEDICINE

WHOLE EXOME & MITOCHONDRIAL GENOME SEQUENCING REQUISTION FORM

INFORMED CONSENT continued

CANCELLATION OF TESTING

Request to cancel testing will be required within one business day of sample receipt. If the laboratory has already started the testing process, I will be responsible for the cost of the test. Written documentation of the request to stop testing will be required. My provider can contact the laboratory for the cancellation form.

INTERPRETER'S STATEMENT

Execute if an interpreter is provided to assist the individual in understanding this informed consent form:

I have translated the information and advice presented orally to the individual to be treated by the person obtaining this consent.

In addition, I have sight translated the consent form (read it aloud in his/her language). To the best of my knowledge and belief he/she understood this explanation.

_____

Cyracom ID (if applicable)

_____

Print Name

_____

Signature (Not required if a Cyracom Interpreter Was Used)

PerkinElmer For the Better | PerkinElmer GENOMICS

Patient Name: _____

Identification Number: _____

U.S. CLINICAL INFORMED CONSENT FORM

PerkinElmer Genetics, Inc., ("PerkinElmer") requires a completed Patient's Informed Consent Form (ICF) for testing to be performed. The ICF must be completed by the patient, or a legally authorized representative of the patient (or by the healthcare provider where permitted under applicable law or regulation). For any patient below the age of majority, the ICF must be completed by the patient's legally authorized representative.

The purpose of this ICF is to provide you with a description of the Test ordered, known risks and benefits of the Test, anonymization of personal health information ("PHI"), sample and data retention, research opportunities, and the reporting of secondary findings, if applicable. Given the complexity of the type of the Test, it is recommended that you and/or your child receive genetic counseling by a trained genetics professional before and after the testing is performed.

TEST INFORMATION

Your healthcare provider ("HCP") has recommended that you, or your child, receive enzymatic, biochemical or molecular genetics clinical testing ("Test") indicated on the submitted Test Requisition Form ("Requisition"). For more information on the reasons your HCP has ordered the Test, and the disorders your HCP is having you tested for, please consult with your HCP. You are free to decide if you want this Test performed or not. Providing a Sample and undergoing the Test is voluntary and you may withdraw your consent without penalty at any time.

Enzyme/Biomarker Test: This type of test measures the presence or absence of enzymes/biomarkers and/or their level of activity in an individual. Only the enzymes/biomarkers identified on the requisition will be tested. Results from this type of Test may indicate the presence of a specific condition or conditions, and follow-up confirmatory testing may be recommended.

Genetic/Genomic Test: This type of Test analyzes one or more segments of your DNA depending on the assay requested. This Test is used to identify what, if any, DNA variant(s) you or your child is carrying which is causing the specific disease or condition you are being tested for. Identifying the mutation may be useful for diagnostic and treatment purposes, and allows at-risk family members to be tested. Only the genes identified on the Requisition will be analyzed. In some cases, we may not be able to determine with certainty which gene is actually causing the disease.

TEST METHOD

If you consent to the Test, your HCP will take a sample of your and/or your child's blood, saliva, body fluid, tissue or other sample type. Your Sample will be sent to PerkinElmer's laboratories in the United States for the Test; the majority of testing will be performed at our laboratory headquarters in Pittsburgh, PA.

Under some circumstances, including inadequate or poor quality sample, an additional Sample may be required for Tests to be performed.

TEST RESULTS

Your treating HCP has sole responsibility for all decisions concerning the possible management of your diagnosis and disease; PerkinElmer will not provide a diagnosis. PerkinElmer will report Test results only to your HCP via secure email, a secure internet portal, or fax. Your HCP is responsible for communicating with you regarding the results of the Test and may refer you or your child to a specialist for further clinical evaluation and confirmation of diagnosis, if applicable. Possible results for Genetic/Genomic Tests include:

1. *Positive:* A positive genetic test result may indicate that you are a carrier of, predisposed to, or have the specific disease or condition being tested for. A positive genetic test may limit your access to health insurance or life assurance coverage; for example, a life insurance company might ask you to provide genetic information indicating a disorder if this information is available to you.
2. *Negative:* A negative result indicates that no disease-causing variant was identified in the Test performed. No Test can rule out all genetic diseases or conditions. A negative result does not guarantee that you are free from genetic disorders or other medical conditions.
3. *Inconclusive/Variant of Uncertain Significance:* A variant of uncertain significance (VOUS) result indicates that a DNA change was detected, but it is currently unknown if the variant is associated with a genetic disorder. A VOUS is not the same as a positive result and does not clarify whether there is an increased risk to develop a genetic disorder. The variant could be a benign change or it could be indicative of disease/disease-causing.
4. *Unexpected Results:* In rare instances, this Test may reveal an important genetic change that is not directly related to the reason for ordering this test. This information would be disclosed to your HCP if it potentially impacts medical care, and you have consented to receive this type of result

TEST REPORT

Reported disease-causing variants are described as pathogenic variant(s), likely pathogenic variants(s), or variant(s) of uncertain significance in genes interpreted to be responsible for, or potentially contributing to, a disease or condition. In addition, variants in genes not known to be associated with disease but for which there is evidence to suggest an association with disease may also be reported. For testing performed on prenatal samples or for screening of apparently healthy individuals, only variants classified as pathogenic or likely pathogenic will be reported.

When Whole Exome Sequencing (WES) or Whole Genome Sequencing (WGS) tests are ordered by your HCP, you have the option to receive some findings not directly related to the reason for ordering the Test called "Secondary Findings". When Secondary Findings are requested, only Pathogenic or Likely Pathogenic findings will be reported, where applicable. Please read the Secondary Findings sections on page 3 and/or 4 of this consent form for more information, and available reporting options. For prenatal samples, secondary findings for the proband are not available.

INFORMATION ABOUT PARENTAL AND FAMILIAL SAMPLES

In some circumstances, it may be helpful for additional family members to undergo testing in order to provide information that can aid in the interpretation of the WES/WGS test results. These Tests could be part of a TRIO Test or as stand-alone targeted testing. PerkinElmer, in consultation with the HCP, will decide if other family members need to be tested. If the HCP recommends testing for additional family members, only the Test performed will be reported. If undergoing a TRIO WES or WGS test, family members will have the option to receive information about secondary findings either as a part of the proband report or as a standalone parental report. A full analysis of the parental samples for secondary findings will only be completed if standalone reports are selected (for an additional charge). If family members elect to receive information about secondary findings either as part of the proband report or as a standalone report, the family member must sign all applicable sections on page 3 and/or 4 of this form.

TEST LIMITATIONS

Due to current limitations in technology and incomplete knowledge of diseases and genes, some variants may not be detected by the Test ordered. There is a possibility that the Test result that is uninterpretable or of unknown significance may require further testing when more information is gained. In rare circumstances, Test results may be suggestive of a condition different from that which was originally considered for the purpose of consenting to this Test. The Test may also find variants or genes that lead to conditions for which you currently do not have symptoms or may not be related to your current condition.

TEST RISKS

Patients and family members may experience anxiety before, during, and/or after testing. Testing multiple family members may reveal that familial relationships are not biologically what they were assumed to be. For example, the Test may indicate non-paternity (the stated father of an individual is not the biological father) or consanguinity (the parents of an individual are closely related by blood). These biological relationships may need to be reported to the HCP who ordered the test.

Taking a blood or tissue sample from you and/or your child may lead to mild pain, bruising, swelling, redness, and a slight risk of infection. Light-headedness, fainting or nausea may occur if your HCP collects blood or tissue samples. These side-effects are typically brief and transient, but you should contact your HCP if you and/or your child require treatment. Under some circumstances an additional sample may be required for Tests to be performed.

A positive test result may limit your access to health insurance or life assurance coverage; for example, a life insurance company might ask you to provide genetic information indicating a disorder if this information is available to you. Please refer to information on the Genetic Information Nondiscrimination Act (GINA) and applicable local laws for more information.

250 Industry Drive, Pittsburgh, PA 15275 • T 866-354-2910 • F 412-220-0785

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Patient Name: _____

Identification Number: _____

U.S. CLINICAL INFORMED CONSENT FORM

CONFIDENTIALITY

You have the right to confidential treatment of the Sample and your PHI. Your HCP will provide PerkinElmer with Personal Health Information ("PHI") such as your name, date of birth, gender and clinical symptoms to help track your sample and report results. To maintain confidentiality, the test results will only be released to the referring health care provider, to the ordering laboratory, to the patient/guardian, to other health care providers involved in your diagnosis and treatment, or as otherwise required by law or regulation. Unless required by law, PerkinElmer will not disclose your PHI to any person or entity except with your written consent.

You and your HCP can control how your Sample and PHI are processed. You have the right to request access to your PHI, request corrections of any errors in recorded PHI, or where PHI may be missing or incomplete ask that it be completed. You also have the right to ask that your PHI be erased, subject to law or regulation. You can contact your HCP for such requests and your HCP will contact PerkinElmer, or you can contact PerkinElmer directly by visiting www.perkinelmergenomics.com. If requests for access, correction, completion, or erasure cannot be fulfilled, you will be informed and provided with the reasons why your requests cannot be fulfilled.

SAMPLE AND DATA RETENTION

Pursuant to laboratory best practices, your DNA sample will be retained by PerkinElmer for a minimum of two years and then destroyed. Additionally, your PHI, the data from the Tests (including those performed before any withdrawal of consent) and the related reports will be retained by PerkinElmer indefinitely, unless otherwise noted. In some instances, it may be beneficial to you for PerkinElmer to retain your sample for a longer period of time in order to conduct additional testing, and PerkinElmer will do so with appropriate documentation from you or your HCP.

PerkinElmer is requesting consent to keep you and/or your child's anonymized sample and data indefinitely for ongoing test development, scientific research, and/or other activities. This consent is optional, and the Test will be performed whether or not you provide consent to the following:

- PerkinElmer will anonymize and retain your Sample indefinitely for internal quality control, test validation, assay development and improvement. By allowing PerkinElmer to retain your Sample, you understand and agree that you give up any property rights you may have in the Sample and are donating it to PerkinElmer Genetics, Inc. If you withdraw your consent, no additional tests or anonymization will be carried out on your Sample; no results will be reported and your sample, reports and data that have not been anonymized will be destroyed.
  - ❑ Check here if you would like to opt out of anonymized sample retention (NY State residents, please see section below). Note, if not checked, this is interpreted as "consent given"
- PerkinElmer will anonymize your data and retain the anonymized data and related anonymized reports from your Tests indefinitely for internal statistical, quality analysis, research, scientific and technical development, and market research.
  - ❑ Check here if you would like to opt out of anonymized data retention. Note, if not checked, this is interpreted as "consent given"

REQUIRED FOR SAMPLES COLLECTED IN NEW YORK STATE ONLY

No tests other than those authorized shall be performed on the biological sample submitted for testing, and any material derived from the sample (i.e., DNA); this includes testing for internal research and/or quality control purposes. The sample shall be destroyed no more than 60 days after the sample was taken or at the end of the testing process, whichever occurs later, unless indicated below.

❑ By checking here and signing at right, I consent to PerkinElmer keeping my sample for longer than 60 days, and to using my de-identified sample for internal research and/or quality control purposes. Note, if not checked and signed, this is interpreted as "consent not given."

_____
Patient/Guardian Signature

RESEARCH OPTIONS

PerkinElmer may collaborate with scientists, researchers and drug developers to advance knowledge of genetic diseases. If there are opportunities to participate in future research relevant to the disease in you and/or your child, PerkinElmer may contact you or your HCP about the development of new testing, drug development, or other treatments. PerkinElmer may also work with scientists or researchers from academic or commercial institutions who have received the necessary approvals to conduct a research study. In some instances, these scientists or researchers may like to contact you directly about your interest in participating in a specific research study.

❑ By checking here I would like to opt out of PerkinElmer being able to provide my contact information to outside researchers to contact me directly about applicable research studies.

WITHDRAWAL OF CONSENT

I understand this consent is voluntary and is valid until I withdraw my consent. I understand I may withdraw my consent to sample and data retention, and to the Test at any time, that PerkinElmer will not perform the Test unless I provide consent to the Test. If I withdraw any consent, it will not affect actions taken before I withdrew my consent, including any anonymization of data or of my Sample. I understand that if I wish to withdraw my consent I should contact PerkinElmer via email at: Genomics@perkinelmer.com or toll-free by telephone +1-866-354-2910 to request withdrawal.

PATIENT CONSENT TO TESTING

❑ By checking this box I attest:

I have read and understood the Informed Consent Form in its entirety, including the explanation of why my sample is being tested, how genetic testing is performed and the risks associated with genetic testing. I have had the opportunity to ask my HCP questions about the information contained herein, and understand that I am entitled to a copy of this ICF. My signature below acknowledges my free consent to the Test, and to any additional consents indicated above, and such testing in no way guarantees my health, the health of an unborn child, or the health of other family members.

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

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

FAMILY MEMBER CONSENT TO TESTING (if applicable)

❑ By checking this box I attest: I have read and understood the Informed Consent Form in its entirety, including the explanation of why my sample is being tested, how genetic testing is performed and the risks associated with genetic testing. I have had the opportunity to ask my HCP questions about the information contained herein, and understand that I am entitled to a copy of this ICF. My signature below acknowledges my free consent to the Test, and to any additional consents indicated above, and such testing in no way guarantees my health, the health of an unborn child, or the health of other family members.

_____ _____ _____ _____
Family Member Signature Date Family Member Name Relationship to Patient

FAMILY MEMBER CONSENT TO TESTING (if applicable)

❑ By checking this box I attest: I have read and understood the Informed Consent Form in its entirety, including the explanation of why my sample is being tested, how genetic testing is performed and the risks associated with genetic testing. I have had the opportunity to ask my HCP questions about the information contained herein, and understand that I am entitled to a copy of this ICF. My signature below acknowledges my free consent to the Test, and to any additional consents indicated above, and such testing in no way guarantees my health, the health of an unborn child, or the health of other family members.

_____ _____ _____ _____
Family Member Signature Date Family Member Name Relationship to Patient

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Patient Name: _____

Identification Number: _____

U.S. CLINICAL INFORMED CONSENT FORM

ACMG RECOMMENDED SECONDARY FINDINGS: REQUIRED ONLY FOR WES/WGS

Since many different genes and conditions are being analyzed during the genetic Test, some findings not directly related to the reason for ordering the Test may be revealed. These findings are called "secondary" and can provide information that was not anticipated when the Test was ordered. Secondary findings are variants found in genes that are unrelated to the individual's reported clinical features. One such group of secondary findings available to individuals undergoing WES or WGS are diagnostic findings in genes defined as highly penetrant and medically actionable by the American College of Medical Genetics and Genomics. Please see below for additional information.

The American College of Medical Genetics and Genomics (ACMG), has recommended that secondary findings should be offered for a specific subset of highly penetrant and medically actionable genes associated with various inherited disorders for all individuals undergoing WGS or WES. Please refer to the latest version of the ACMG Recommendations for Reporting of Secondary Findings in Clinical Exome and Genome Sequencing for complete details of genes and conditions at www.acmg.net. Medically-actionable conditions are those for which there is currently recommended treatment or preventative actions that can be taken to reduce the risk of developing the disease. An example would be hereditary cancer syndromes such as Lynch syndrome.

We are unable to guarantee that the Test will find all medically-actionable conditions for which you have a pathogenic or likely pathogenic variant. You may have a pathogenic or likely pathogenic variant for a condition in which there was little or no coverage in the Test and therefore will not be detected. Additional testing for health purposes should be discussed with your doctor or genetic counselor.

Secondary findings will only be reported if consent is given by the Patient or Parent/Guardian. Each individual receiving secondary findings will need to fill out the appropriate section(s) below to indicate which secondary findings that they will receive. If a box is not checked or this form is not returned, it is assumed that the applicable individual does not want to receive the corresponding secondary finding(s).

PATIENT SECONDARY FINDINGS CONSENT

Not available for prenatal samples.

❑ Check this box if you wish to receive a report on pathogenic or likely pathogenic findings in genes defined as highly penetrant and medically actionable by the American College of Medical Genetics and Genomics.

If ACMG recommended Secondary Findings are elected above, please choose if you would like only pediatric findings, only adult findings, or both as defined by Table 1 in PMID:27854360. The lack of selection will result in return of ALL results ("both"). Please note, it is recommended that the patient be 18 years or older for the return of adult findings.

❑ Pediatric Findings Only ❑ Adult Findings Only ❑ Both Pediatric and Adult Findings

❑ Check this box if you do NOT want to receive ACMG-recommended secondary findings.

_____ _____

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

_____ _____

Patient Name Name and Relationship (Parent/Guardian if patient is minor)

FAMILY MEMBER(S) SECONDARY FINDINGS CONSENT

*Please note that this section is **required** if family members included as part of TRIO would like to receive secondary findings either as part of a proband report or as a standalone report.*

- *Return of Secondary Findings results as part of the proband report will include only the parental inheritance of those findings reported in the proband. No other findings will be commented on. This option is not available for prenatal reports.*
- *Return of findings as a standalone report will include a full analysis of all selected Secondary Finding sections for each family member. A standalone family member report will only be issued if an appropriate test selection is made on the test requisition form AND this section is filled out entirely.*

❑ Check this box if you wish to receive a report on pathogenic or likely pathogenic findings in genes defined as highly penetrant and medically actionable by the American College of Medical Genetics and Genomics.

If ACMG recommended Secondary Findings are elected above, please choose if you would like only pediatric findings, only adult findings, or both as defined by Table 1 in PMID:27854360. The lack of selection will result in return of ALL results ("both"). Please note, it is recommended that the patient be 18 years or older for the return of adult findings.

❑ Pediatric Findings Only ❑ Adult Findings Only ❑ Both Pediatric and Adult Findings

❑ Check this box if you do NOT want to receive ACMG-recommended secondary findings.

_____ _____

Family Member Signature Date

_____ _____

Family Member Name Relationship to Patient

FAMILY MEMBER(S) SECONDARY FINDINGS CONSENT

*Please note that this section is **required** if family members included as part of TRIO would like to receive secondary findings either as part of a proband report or as a standalone report.*

- *Return of Secondary Findings results as part of the proband report will include only the parental inheritance of those findings reported in the proband. No other findings will be commented on. This option is not available for prenatal reports.*
- *Return of findings as a standalone report will include a full analysis of all selected Secondary Finding sections for each family member. A standalone family member report will only be issued if an appropriate test selection is made on the test requisition form AND this section is filled out entirely.*

❑ Check this box if you wish to receive a report on pathogenic or likely pathogenic findings in genes defined as highly penetrant and medically actionable by the American College of Medical Genetics and Genomics.

If ACMG recommended Secondary Findings are elected above, please choose if you would like only pediatric findings, only adult findings, or both as defined by Table 1 in PMID:27854360. The lack of selection will result in return of ALL results ("both"). Please note, it is recommended that the patient be 18 years or older for the return of adult findings.

❑ Pediatric Findings Only ❑ Adult Findings Only ❑ Both Pediatric and Adult Findings

❑ Check this box if you do NOT want to receive ACMG-recommended secondary findings.

_____ _____

Family Member Signature Date

_____ _____

Family Member Name Relationship to Patient

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Patient Name: _____

Identification Number: _____

U.S. CLINICAL INFORMED CONSENT FORM

SUPPLEMENTAL SECONDARY FINDINGS OPTIONS: REQUIRED ONLY FOR WES/WGS

Since many different genes and conditions are being analyzed during the genetic Test, some findings not directly related to the reason for ordering the Test may be revealed. These findings are called "secondary" and can provide information that was not anticipated when the Test was ordered. Secondary findings are variants found in genes that are unrelated to the individual's reported clinical features. In addition diagnostic findings in genes defined as highly penetrant and medically actionable by the American College of Medical Genetics and Genomics, PerkinElmer also offers individuals the ability to receive Secondary Findings from three additional categories as defined below:

1. **Pharmacogenetic variants:** This category of Secondary Findings will include changes in the DNA that do not cause a disease but may be related to how your body processes certain medications, such as chemotherapy drugs, antipyretics, antidepressants, anticoagulants, and others. These variants may not be important to you if you are not taking the medications involved, but may tell you how well the medications will work or if you will have side effects if you do take the medications now or in the future.
2. **Carrier status (ex. cystic fibrosis):** This category of Secondary Findings will include carrier findings for autosomal recessive conditions. A recessive condition is one in which two disease-causing variants in the same gene are required in order to show symptoms of the disease (one variant is inherited from each parent). Someone who has only one disease-causing variant does not show symptoms and is called a carrier. However, if we find a disease-causing variant in a recessive gene that is related to your disease, we will report it as a diagnostic finding. Please note that only Pathogenic or Likely Pathogenic variants will be reported if this category of Secondary Findings is selected. Further testing may be necessary to look for a second disease-causing variant in that gene not identified by WES/WGS. The Test is not designed to be a comprehensive carrier test. We are unable to guarantee that all conditions for which you are a carrier will be determined by the Test. You may be a carrier for a condition in which there was little or no coverage in the Testing and therefore will not be detected. Additional carrier testing for reproductive purposes should be discussed with your doctor or genetic counselor.
3. **Diagnostic findings in all other disease-causing genes not related to your clinical features:** This category of Secondary Findings will include conditions that are medically-actionable but not included in the ACMG-recommended list, as well as conditions that are not medically-actionable (do not have recommended treatment or preventative measures), which may be childhood or adult onset. An example would be Alzheimer's disease. Please note that only Pathogenic or Likely Pathogenic variants will be reported if this category of Secondary Findings is selected. Furthermore, we are unable to guarantee that the Test will find all disease-causing variants in all disease-causing genes. You may have a disease-causing variant for a condition in which there was little or no coverage in the Test and therefore will not be detected. Additional testing for health purposes should be discussed with your doctor or genetic counselor.

Secondary findings will only be reported if consent is given by the Patient or Parent/Guardian. Each individual receiving secondary findings will need to fill out the appropriate section(s) below to indicate which secondary findings that they will receive. If a box is not checked or this form is not returned, it is assumed that the applicable individual does not want to receive the corresponding secondary finding(s).

PATIENT SECONDARY FINDINGS CONSENT

Not available for prenatal samples.

❑ Check this box if you wish to receive a report on pharmacogenetic variants (see category #1 above for details).
❑ Check this box if you wish to receive a report on carrier status – (see category #2 above for details).
❑ Check this box if you wish to receive a report including pathogenic or likely pathogenic findings in all other disease-causing genes (see category #3 above for details).

If you selected to receive Secondary Findings from category #3 above, please choose if you would like only pediatric findings, only adult findings, or both. The lack of selection will result in return of ALL results ("both"). Please note, it is recommended that the patient be 18 years or older for the return of adult findings.

❑ Pediatric Findings Only ❑ Adult Findings Only ❑ Both Pediatric and Adult Findings

❑ Check this box if you do NOT want to receive any of the secondary finding categories discussed on this page.

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

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

FAMILY MEMBER(S) SECONDARY FINDINGS CONSENT

*Please note that this section is **required** if family members included as part of TRIO would like to receive secondary findings either as part of a proband report or as a standalone report.*

- *Return of Secondary Findings results as part of the proband report will include only the parental inheritance of those findings reported in the proband. No other findings will be commented on. This option is not available for prenatal reports.*
- *Return of findings as a standalone report will include a full analysis of all selected Secondary Finding sections for each family member. A standalone family member report will only be issued if an appropriate test selection is made on the test requisition form AND this section is filled out entirely.*

❑ Check this box if you wish to receive a report on pharmacogenetic variants (see category #1 above for details).

This category of secondary findings for family members is only available when a standalone report is ordered for the family member. Parental inheritance of pharmacogenomic variants will not be included on a proband report.

❑ Check this box if you wish to receive a report on carrier status – (see category #2 above for details).
❑ Check this box if you wish to receive a report including pathogenic or likely pathogenic findings in all other disease-causing genes (see category #3 above for details).

If you selected to receive Secondary Findings from category #3 above, please choose if you would like only pediatric findings, only adult findings, or both. The lack of selection will result in return of ALL results ("both"). Please note, it is recommended that the patient be 18 years or older for the return of adult findings.

❑ Pediatric Findings Only ❑ Adult Findings Only ❑ Both Pediatric and Adult Findings

❑ Check this box if you do NOT want to receive any of the secondary finding categories discussed on this page.

_____ _____
Family Member Signature Date

_____ _____
Family Member Name Relationship to Patient

FAMILY MEMBER(S) SECONDARY FINDINGS CONSENT

*Please note that this section is **required** if family members included as part of TRIO would like to receive secondary findings either as part of a proband report or as a standalone report.*

- *Return of Secondary Findings results as part of the proband report will include only the parental inheritance of those findings reported in the proband. No other findings will be commented on. This option is not available for prenatal reports.*
- *Return of findings as a standalone report will include a full analysis of all selected Secondary Finding sections for each family member. A standalone family member report will only be issued if an appropriate test selection is made on the test requisition form AND this section is filled out entirely.*

❑ Check this box if you wish to receive a report on pharmacogenetic variants (see category #1 above for details).

This category of secondary findings for family members is only available when a standalone report is ordered for the family member. Parental inheritance of pharmacogenomic variants will not be included on a proband report.

❑ Check this box if you wish to receive a report on carrier status – (see category #2 above for details).
❑ Check this box if you wish to receive a report including pathogenic or likely pathogenic findings in all other disease-causing genes (see category #3 above for details).

If you selected to receive Secondary Findings from category #3 above, please choose if you would like only pediatric findings, only adult findings, or both. The lack of selection will result in return of ALL results ("both"). Please note, it is recommended that the patient be 18 years or older for the return of adult findings.

❑ Pediatric Findings Only ❑ Adult Findings Only ❑ Both Pediatric and Adult Findings

❑ Check this box if you do NOT want to receive any of the secondary finding categories discussed on this page.

_____ _____
Family Member Signature Date

_____ _____
Family Member Name Relationship to Patient