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Genome-wide Sequencing Ontario

CHEO Genetics Diagnostic Laboratory
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Tel: (613) 738-3230
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gsontario.ca | gso@cheo.on.ca

Patient name:

Date of Birth (DD-MM-YYYY):

Gender: ☐ *Male* ☐ *Female* *MRN:*

Address:

Telephone #:

Ontario health card #: *Version:*

GENOME-WIDE SEQUENCING: PROBAND

Ordering physician:

Name: _____

Institution: _____

Address: _____

Phone: _____

Fax: _____

Email address: _____

Copy report to:

Name: _____

Institution: _____

Address: _____

Phone _____

Fax _____

Sample information:

Date obtained (DD-MM-YYYY): _____-_____-_____

Your referring laboratory reference #: _____

☐ Blood in EDTA (purple top tube): min. 2 x 4 mL (0.5-3 mL for newborns)

☐ DNA: min.5 ug in low TE buffer (Source: _____)

☐ Tissue* (Source:_____)

*Please contact the laboratory directly to discuss prior to sample submission

Bone marrow transplant / Transfusion

Has the patient undergone bone marrow transplant? ☐ Yes ☐ No

Date of bone marrow transplant (DD-MM-YYYY): _____-_____-_____

Testing for patients who have received an allogenic bone marrow transplant must be completed on a pre-transplant sample or a non-hematologic sample.

Has the patient received a blood transfusion? ☐ Yes ☐ No

Date of last transfusion (DD-MM-YYYY): _____-_____-_____

Blood obtained for genetic testing should ideally be collected at least 2-4 weeks after the date of the last transfusion

For laboratory use only:

Date (DD-MM-YYYY) | **Time Received**:

_____-_____-_____ | _____h

Order #: _____

Specimen type, amt & # of tubes: _____

Comments:

_____

Requested Genome-Wide Sequencing (GWS)

☐ **Singleton**
☐ **Duo**
☐ **Trio**
☐ **Quad**

Biological parent/family member information

A separate family member requisition **must** be completed for each individual.

Mother ☐ Not available

First name		Last name	
MRN	**DOB (DD-MM-YYYY)**	**Ethnicity**	**Clinical status:** ☐ Asymptomatic ☐ Symptomatic
Comments			

Father ☐ Not available

First name		Last name	
MRN	**DOB (DD-MM-YYYY)**	**Ethnicity**	**Clinical status:** ☐ Asymptomatic ☐ Symptomatic
Comments			

Other

First name		Last name	
MRN	**DOB (DD-MM-YYYY)**	**Ethnicity**	**Clinical status:** ☐ Asymptomatic ☐ Symptomatic
Relationship to the proband			
Comments			

GWS submission requirements:

Consent:
The test has been discussed with the patient, the consent form has been completed, and decisions have been documented on page 5.

Clinical information:
The following information has been provided for the proband and family:

- Previous testing history
- Phenotypic information
  (☐ Clinical data sheet or ☐ PhenoTips if available)
- Family history (pedigree)
- Relevant clinic note(s) and/or letter(s)

Eligibility:
The eligibility criteria for GWS have been met and have been documented on page 4

Proband name: _____ MRN: _____ DOB: _____

CLINICAL DATA SHEET

Previous genetic testing:

☐ Single gene/Gene panel (1): _____
Result: _____

☐ Single gene/Gene panel (2): _____
Result: _____

☐ Microarray: _____

☐ Other: _____
Result: _____

Pre/Perinatal History

☐ Cystic hygroma
☐ Increased nuchal translucency
☐ Intrauterine growth retardation
☐ Nonimmune hydrops fetalis
☐ Oligohydramnios
☐ Polyhydramnios
☐ Prematurity GA: _____
☐ Other: _____

Growth:

☐ Growth delay
☐ Overgrowth
☐ Failure to thrive
☐ Hemihypertrophy
☐ Short stature
☐ Tall stature

Structural Brain Abnormalities

☐ Abnormal myelination
☐ Abnormality of basal ganglia
☐ Abnormality of brainstem
☐ Abnormality of periventricular white matter
☐ Abnormality of the corpus callosum
☐ Aplasia/hypoplasia of cerebellar vermis
☐ Aplasia/hypoplasia of cerebellum
☐ Cerebellar atrophy
☐ Chiari malformation
☐ Cortical dysplasia
☐ Encephalocele
☐ Heterotopia
☐ Hemimegalencephaly
☐ Holoprosencephaly
☐ Hydrocephalus
☐ Leukodystrophy
☐ Lissencephaly
☐ Pachygyria
☐ Polymicrogyria
☐ Ventriculomegaly
☐ Other: _____

Developmental/Behavioral

☐ Aggressive behavior
☐ ADHD
☐ Anxiety
☐ Autistic Behavior
☐ Autism spectrum disorder
☐ Cognitive impairment
☐ Delayed speech & language development
☐ Developmental regression
☐ Fine motor delay
☐ Gross motor delay
☐ Speech delay
☐ Gait disturbance
☐ Global developmental delay
☐ Hyperactivity
☐ Incoordination
☐ Intellectual disability
  ☐ Mild ☐ Profound
  ☐ Moderate ☐ Severe
☐ Learning disability
☐ Memory impairment
☐ Obsessive-compulsive disorder
☐ Sleep disturbance
☐ Stereotypy

Neurological

☐ Ataxia
☐ Chorea
☐ Cortical Visual Impairment
☐ Dementia
☐ Dysarthria
☐ Dyskinesia
☐ Dysphasia
☐ Dystonia
☐ Encephalopathy
☐ Headaches
☐ Hemiplegia
☐ Infantile Spasms
☐ Migraines
☐ Myoclonus
☐ Myopathic facies
☐ Myopathy
☐ Muscle weakness
☐ Muscle dystrophy
☐ Neuropathy
  ☐ Motor ☐ Sensory ☐ Sensorimotor
☐ Parkinsonism
☐ Seizures
☐ Spasticity
☐ Tremors

Craniofacial dysmorphic features

☐ Craniosynostosis
Specify: _____
☐ Macrocephaly
☐ Microcephaly
☐ Head shape Specify: _____
☐ Facies Specify: _____
☐ Forehead Specify: _____
☐ Ears Specify: _____
☐ Eyes Specify: _____
☐ Nose Specify: _____
☐ Cleft lip and/or palate
☐ Coarse facial features
☐ Short neck
☐ Synophrys
☐ Other: _____

Ophthalmological

☐ Anophthalmia
☐ Cataracts
☐ Coloboma
☐ Corneal opacity
☐ Ectopia lentis
☐ External ophthalmoplegia
☐ Microphthalmia
☐ Myopia
☐ Nystagmus
☐ Optic atrophy
☐ Ptosis
☐ Retinal detachment
☐ Retinitis pigmentosa
☐ Strabismus
☐ Other: _____

Hearing Impairment

☐ Abnormal Newborn Screen: _____
☐ Conductive hearing impairment
☐ Sensorineural hearing impairment

Haematological or Immunologic

☐ Anemia
☐ Coagulation disorder
☐ Immunodeficiency
☐ Neutropenia
☐ Pancytopenia
☐ Recurrent infections
☐ Thrombocytopenia
☐ Other: _____

Integumental

Skin

☐ Abnormal blistering of the skin
☐ Anhidrosis
☐ Café-Au-Lait macules
☐ Cutis laxa
☐ Hemangiomas
☐ Hyperpigmentation of the skin
☐ Hypopigmentation of the skin
☐ Ichthyosis
☐ Skin rash
☐ Telangiectasia
☐ Vascular skin abnormality
☐ Other: _____

Hair

☐ Abnormal texture, distribution, colour, whorls
Specify: _____
☐ Alopecia
☐ Coarse hair
☐ Sparse hair
☐ Other: _____

Dental

☐ Specify: _____

Nails

☐ Specify: _____

Proband name: _____ MRN: _____ DOB: _____

CLINICAL DATA SHEET

Cardiac
- ☐ Aortic root dilation
- ☐ Arrhythmia / Conduction defect
  - ☐ Bradycardia
  - ☐ Prolonged QTc interval
  - ☐ Ventricular tachycardia
- ☐ Cardiomyopathy
  - ☐ Dilated
  - ☐ Hypertrophic
  - ☐ Noncompaction
- ☐ Congenital heart defect
  - ☐ Atrial septal defect
  - ☐ Bicuspid aortic valve
  - ☐ Coarctation of aorta
  - ☐ Hypoplastic left heart
  - ☐ Patent ductus arteriosis
  - ☐ Patent foramen ovale
  - ☐ Tetralogy of Fallot
  - ☐ Ventricular septal defect
- ☐ Heterotaxy
- ☐ Mitral valve prolapse
- ☐ Sudden death
- ☐ Syncope
- ☐ Other: _____

Endocrine
- ☐ Early puberty
- ☐ Delayed puberty
- ☐ Diabetes Insipidus
- ☐ Diabetes mellitus
- ☐ Hyperparathyroidism
- ☐ Hypoparathyroidism
- ☐ Hyperthyroidism
- ☐ Hypothyroidism
- ☐ Hypogonadism
- ☐ Hypophosphatemia
- ☐ Rickets
- ☐ Other: _____

Gastrointestinal
- ☐ Chronic intestinal pseudo-obstruction
- ☐ Duodenal stenosis/atresia
- ☐ Diaphragmatic hernia
- ☐ Elevated transaminases
- ☐ Exocrine pancreatic insufficiency
- ☐ Feeding difficulties
- ☐ Gastroesophageal reflux
- ☐ Hepatomegaly
- ☐ Hepatic failure
- ☐ Hirschsprung disease
- ☐ Inflammatory bowel disease
- ☐ Intrahepatic biliary atresia
- ☐ Laryngomalacia
- ☐ Omphalocele
- ☐ Pyloric stenosis
- ☐ Splenomegaly
- ☐ Tracheoesohageal fistula
- ☐ Other: _____

Genitourinary
- ☐ Ambiguous genitalia
- ☐ Cryptorchidism (undescended testes)
- ☐ Cystic renal dysplasia
- ☐ Horseshoe kidney
- ☐ Hydronephrosis
- ☐ Hypospadias
- ☐ Inguinal hernia
- ☐ Infertility
- ☐ Micropenis
- ☐ Nephrolithiasis
- ☐ Polycystic kidney disease
- ☐ Renal agenesis or dysgenesis
- ☐ Renal tubulopathy
- ☐ Other: _____

Musculoskeletal
- ☐ Abnormal connective tissue
- ☐ Abnormal form of the vertebral bodies
- ☐ Abnormality of the digits
  - ☐ Arachnodactyly
  - ☐ Clinodactyly
  - ☐ Ectrodactyly
  - ☐ Polydactyly
  - ☐ Syndactyly
- ☐ Abnormality of the limb(s)
  Specify: _____
- ☐ Abnormality of the ribs
- ☐ Arthralgia
- ☐ Arthrogryposis
- ☐ Contractures
- ☐ Decreased muscle mass
- ☐ Exercise intolerance
- ☐ Hypertonia
- ☐ Hypotonia
- ☐ Joint hypermobility
- ☐ Myalgia
- ☐ Osteoarthritis
- ☐ Osteopenia
- ☐ Pectus carinatum
- ☐ Pectus excavatum
- ☐ Recurrent fractures
- ☐ Scoliosis
- ☐ Skeletal dysplasia
- ☐ Other: _____

Respiratory
- ☐ Bronchiectasis
- ☐ Pneumothorax
- ☐ Pulmonary fibrosis
- ☐ Respiratory insufficiency
- ☐ Other: _____

Tumour / Malignancy
Type: _____
Location: _____
Age of onset: _____

Vascular System
- ☐ Angioedema
- ☐ Aneurysm
- ☐ Arterial calcification
- ☐ Arterial dissection
- ☐ Arterial tortuosity
- ☐ Arteriovenous malformation
- ☐ Bruising susceptibility
- ☐ Epistaxis
- ☐ Lymphedema
- ☐ Pulmonary hypertension
- ☐ Stroke

Metabolic
- ☐ Abnormal activity of mitochondrial respiratory chain
- ☐ Abnormal Newborn Screen: _____
- ☐ Elevated CPK
- ☐ Elevated hepatic transaminase
- ☐ Hypoammonemia
- ☐ Hyperammonemia
- ☐ Hypoglycemia
- ☐ Hyperglycemia
- ☐ Increased serum pyruvate
- ☐ Ketosis
- ☐ Lactic acidosis
- ☐ Rhabdomyolysis
- ☐ Plasma AA: _____
- ☐ Urine OA: _____
- ☐ Other: _____

Other investigations
(Please provide copy or report if possible)

Echo: _____
EEG: _____
EMG: _____
MRI: _____
Muscle biopsy: _____
Ultrasound: _____
X-ray: _____

Additional clinical findings:
_____
_____
_____
_____
_____
_____

FAMILY HISTORY

Please draw or attach pedigree
- ☐ Consanguinity

Requisition and samples must be accompanied by additional clinical notes

Proband name: _____ MRN: _____ DOB: _____

PATIENT SUMMARY (all sections must be completed)

Phenotypic category
- ☐ Syndromic developmental delay (DD) or intellectual disability (ID)
- ☐ Moderate-severe isolated DD or ID
- ☐ Single system disorder without DD or ID
- ☐ Multisystem disorder without DD or ID
- ☐ Multiple congenital anomalies without DD or ID

Age of onset
- ☐ Prenatal
- ☐ At birth (<12mo)
- ☐ Childhood (1-10yrs)
- ☐ Adolescence (11-17yrs)
- ☐ Adulthood (>18)

Ethnicity (all applicable)
- ☐ Black, African-American, African
- ☐ East Asian ☐ South Asian
- ☐ White ☐ Indigenous
- ☐ French-Canadian
- ☐ Middle Eastern, North African
- ☐ Latino, Hispanic, Spanish
- ☐ Unknown ☐ Other: _____

Previous test history (all applicable)
- ☐ No previous genetic testing
- ☐ Chromosome microarray
- ☐ Single gene test
- ☐ Gene panel (<100 genes)
- ☐ Gene panel (≥100 genes)
- ☐ Targeted testing (e.g. Prader-Willi)
- ☐ Unknown

CLINICAL GWS TESTING CRITERIA (as defined by the Ontario Ministry of Health)

Clinical Presentation (must meet ≥ 2 items):

YES	NO	
☐	☐	Moderate to severe developmental or functional impairment
☐	☐	Multisystem involvement
☐	☐	Progressive clinical course
☐	☐	Differential diagnosis includes ≥ 2 well defined conditions requiring evaluation by multiple targeted gene panels
☐	☐	Suspected severe genetic syndrome NYD for which multiple family members are also affected, or where parents are consanguineous

Management Impact (must meet ≥ 1 item):

YES	NO	
☐	☐	Will limit further invasive diagnostic investigations
☐	☐	Results allow for specific and informed reproductive decision making (for patient or parents)
☐	☐	Will enable identification of at-risk family members and facilitate early intervention

Attestation (must meet <u>all</u> items):

YES ☐ NO ☐ **I <u>confirm</u> that all the following conditions have been met:**
- Detailed phenotypic characterization (physical examination, investigations) has been documented
- Pretest genetic counseling and consent has been completed
- Chromosomal microarray has been completed and does NOT explain the patient's phenotype (applicable to patients with developmental delay, intellectual disability, multiple congenital anomalies, and dysmorphic features)
- Other causative circumstances (e.g. environmental exposures, injury, and infection) do NOT explain the patient's clinical presentation, based on the most complete clinical history
- Previous targeted testing was unrevealing where appropriate (e.g. specific monogenetic disorder suspected)
- Previous comprehensive panel testing has NOT been completed in the last 3 years (the panel contained virtually all known genes for the clinical indication)
- Previous whole exome sequencing has NOT been performed

YES ☐ NO ☐ **I <u>confirm</u> that the patient does NOT have:**
- Isolated mild intellectual disability or learning disabilities
- Isolated non-syndromic autism
- Isolated neurobehavioural disabilities (e.g. attention deficit disorder)
- A phenotype highly specific to a known genetic condition for which an optimized genetic panel exists, or for which all known gene-disease associations could be assessed. If so, then the targeted gene panel should be given priority assuming it is more sensitive (e.g. Noonan spectrum disorders)

YES ☐ NO ☐ **I <u>confirm</u> that I:**
- Practice in the area of genetics (as a geneticist/genetics consultant or in a clinic where a genetic counsellor has been integral to the care of the patient)
- Have expertise in performing a clinical genetics evaluation including family history, genetic-focused medical history and physical examination, and have a critical understanding of the prior genetic evaluations undertaken in the patient
- Have expertise in determining whether clinical GWS is the test of choice for the specific clinical indication, prioritizing other available tests as appropriate
- Have expertise in providing adequate pre-test counseling, including informed consent for primary and incidental findings
- Have the ability to interpret the results of the clinical GWS and provide adequate post-test counseling

PROVIDER ATTESTATION

By signing here I attest that the above the information is an accurate and comprehensive summary of this patient's clinical history.

Ordering physician signature: _____ Date: _____

Proband name: _____ MRN: _____ DOB: _____

Genome-wide Sequencing Ontario: Acknowledgement and Consent Form

ACKNOWLEDGEMENT

- I understand that I will be undergoing genome-wide sequencing to possibly identify the cause(s) and genetic variant(s) responsible for myself/my family member's condition. I am aware of the benefits, limitations, and risks of genome-wide sequencing (GWS).
- I understand how my de-identified genomic and health data will be managed and shared now and in the future as outlined on the GSO Information Sheet.

CONSENT FOR CLINICAL DATA SHARING

- It is critically important that laboratories share data to improve test performance and ensure that we are providing the best possible test for your family and for other patients. With your consent, we will share your/your child's GWS coded (information that can identify you will be replaced by a code) data and clinical features (details available on GSO Information Sheet) as a part of Ontario's Clinical Genomic Knowledge Base, and similar institutionally-approved Knowledge Bases in Canada, as described on the GSO Information Sheet. You will be asked to indicate your choice below.

CONSENT TO CONTACT FOR RESEARCH

- GSO can also support direct contact with you regarding approved research studies to better understand rare diseases and test new treatments. If there are opportunities to participate in research or share your data, do you wish to be contacted?

☐ I **consent** to be contacted by the CHEO Department of Genetics for future research opportunities

E-mail address: _____ Phone number: _____

How often may we contact you about research opportunities (check one): ☐ Once per year ☐ Up to twice per year ☐ No preference

☐ I do not **consent** to be contacted by the CHEO Department of Genetics for future research opportunities

DECISIONS AND SIGNATURES

Proband

By signing below I consent to undergo GWS and I have indicated my decisions as follows:

☐ I **consent** to share my coded data in Clinical Genomics Knowledge Network(s) approved by CHEO
☐ I **do not consent** to share my coded data in Clinical Genomics Knowledge Network(s) approved by CHEO

I have reviewed the information on secondary findings on the GWS information sheet and have outlined my choices below:

☐ Patients under 18: I **decline** the reporting of adult-onset *medically actionable* secondary findings
☐ Patients 18 and over: I **decline** the reporting of all *medically actionable* secondary findings

Signature: _____

Name of signee: _____

Relationship of signee: _____

Date (DD-MM-YYYY): _____

Family Member 1

By signing below I consent to undergo GWS and I have indicated my decisions as follows:

☐ I **consent** to share my coded data in Clinical Genomics Knowledge Network(s) approved by CHEO
☐ I **do not consent** to share my coded data in Clinical Genomics Knowledge Network(s) approved by CHEO

I have reviewed the information on secondary findings (SF) on the GWS information sheet and understand that SF that I share with the proband will be reported unless specified below:

☐ I **decline** for the laboratory to report on the presence or absence of the proband's SF in me
☐ **Not applicable** as the proband declined the reporting of SF (note: only applicable for probands >18 years)

Name: _____

Relationship to proband: _____

Signature of individual/guardian: _____

Date (DD-MM-YYYY): _____

Family Member 2

By signing below I consent to undergo GWS and I have indicated my decisions as follows:

☐ I **consent** to share my coded data in Clinical Genomics Knowledge Network(s) approved by CHEO
☐ I **do not consent** to share my coded data in Clinical Genomics Knowledge Network(s) approved by CHEO

I have reviewed the information on secondary findings (SF) on the GWS information sheet and understand that SF that I share with the proband will be reported unless specified below:

☐ I **decline** for the laboratory to report the presence or absence of the proband's SF in me
☐ **Not applicable** as the proband declined the reporting of SF (note: only applicable for probands >18 years)

Name: _____

Relationship to proband: _____

Signature of individual/guardian: _____

Date (DD-MM-YYYY): _____

Family Member 3

By signing below I consent to undergo GWS and I have indicated my decisions as follows:

☐ I **consent** to share my coded data in Clinical Genomics Knowledge Network(s) approved by CHEO
☐ I **do not consent** to share my coded data in Clinical Genomics Knowledge Network(s) approved by CHEO

I have reviewed the information on secondary findings (SF) on the GWS information sheet and understand that SF that I share with the proband will be reported unless specified below:

☐ I **decline** for the laboratory to report the presence or absence of the proband's SF in me
☐ **Not applicable** as the proband declined the reporting of SF (note: only applicable for probands >18 years)

Name: _____

Relationship to proband: _____

Signature of individual/guardian: _____

Date (DD-MM-YYYY): _____

GENOME-WIDE SEQUENCING ONTARIO: INFORMATION SHEET

Your physician has offered you/your child a diagnostic test, known as genome-wide sequencing (GWS), to try to identify the cause(s) and genetic variant(s) responsible for your/your child's condition. This test is performed by the CHEO Genetics Diagnostic Lab and SickKids Genome Diagnostics Lab as a part of an Ontario-wide clinical collaboration, also known as "Genome-Wide Sequencing Ontario" (GSO). The purpose of this information sheet is to supplement the pre-test counselling discussion. This test is voluntary; it is your choice to have this test or not. Please discuss any questions about this test and options for alternative testing with your doctor or genetic counsellor. You/your child will be referred to as "the patient" in each section below.

PURPOSE OF GENOME-WIDE SEQUENCING (GWS)

- This genetic test allows us to look broadly at the patient's DNA, to identify potential genetic cause(s) of their medical condition.

HOW IS GWS PERFORMED

- GWS is performed on DNA that, typically, has been extracted from blood. The sequence of DNA between people is very similar (>99%), but there are still millions of differences in a person's DNA that can be detected with GWS. Some of these differences, also known as genetic variants, can cause medical conditions.
- In order to guide the analysis of these differences, it is beneficial to compare the patient's genetic variants to variants identified in family members who are either healthy or who have the same or similar medical condition.
- The laboratory will use the patient's clinical information, family information and the current medical knowledge to evaluate which of the identified genetic variants might be responsible for their medical condition.
- The laboratory will report the genetic variants likely to be associated with the patient's medical condition to the doctor who ordered this test. The patient will be informed of all test results, and these results will be put in the patient's medical record.

WHAT IS REPORTED

- Genetic variants which are identified in the individuals submitted for testing and are related to the patient's symptoms will be included in the report. Family members who do not have the medical condition will not receive a separate written report related to the primary findings in the patient.
- **Primary findings:** The laboratory will report variants in genes that may explain the patient's medical condition.
    - Different categories of changes in these genes will be reported: variants that are known to cause the medical condition (pathogenic), variants that are highly likely to cause the medical condition (*likely pathogenic*), and variants for which the impact cannot be determined at this time (called *variants of uncertain significance*).
    - It is possible that the classification of a genetic variant or gene will change over time, as we learn more about the causes of different medical conditions. The interpretation of the patient's GWS results may also change over time due to new scientific knowledge.
    - Please keep in touch with your doctor to learn of any changes in the classification or interpretation of your results.
- Variants associated with unrelated adult-onset conditions for which there is no prevention, early detection, or treatment, as well as carrier status for recessive genetic disorders unrelated to the disorder for which testing has been offered, will not be reported.
- **Secondary Findings**: As GWS can look at all of a person's genes; this test can identify disease-causing variants in genes that are not related to the primary medical conditions for which the test has been offered, but which may cause other medical conditions during childhood and/or later in life. These variants are known as *medically actionable secondary findings* because there are clear medical recommendations that can be made to reduce the risk that they will impact a person's health in the future. The laboratory will search for variants in specific disease genes, as defined by the American College of Medical Genetics and Genomics (ACMG) guidelines (detailed list available at gsontario.ca). Findings expected or known to be disease-causing that are identified in a gene that is not included in the ACMG gene list may also be reported if considered to be medically actionable (i.e. Incidental findings).
    - **In children,** secondary findings that reveal a risk for a condition that is *medically actionable during childhood* will be reported to the parents/caregivers. Parents/caregivers can choose to receive, or not, the analysis of variants in genes that are associated with adult-onset medically actionable conditions for their children. Mature minors, may choose for themselves to receive, or not, the analysis of variants in genes that are associated with adult-onset medically actionable conditions.
    - **In incompetent adults**, secondary findings will be reported to the legal representative, unless the patient expressed wishes to the contrary while still competent.
    - **In competent adults**, reporting of secondary findings is optional.
    - The patient's choice regarding secondary findings will not impact the results of their test.
    - Family members participating in GWS may choose whether they wish to have the inheritance of secondary findings identified in the patient reported for themselves.

GENOME-WIDE SEQUENCING ONTARIO: INFORMATION SHEET

POTENTIAL RISKS OF GWS

- Because GWS is performed as a family analysis, the same genetic variants that are identified in the patient may also be found in the other family members that have given a sample for testing.
- GWS results may reveal that biological relationships in a family are not as they were reported to the healthcare provider. This includes non-paternity and non-maternity (the stated father/mother of an individual is not the biological parent) and consanguinity (the parents of an individual are related by blood). As incorrect information about biological relationships and health status may prevent the accurate interpretation of GWS results, it may be necessary to report these findings to the health care provider who ordered your test.

LIMITATIONS OF GWS TECHNOLOGY

- GWS does not always lead to a definitive explanation for a person's medical condition. This is due to current limitations in medical knowledge and/or testing technologies.
- GWS does not detect all types of genetic variants. When GWS does not identify a causative variant, it does not rule out the possibility that a genetic variant may be causing your medical condition.
- As with all laboratory tests, there is a small possibility of error or sample failure.

CONFIDENTIALITY

- Results of GWS will only be reported to the health care provider(s) who ordered the test. The laboratory will not give test results to other individuals without the patient's written permission, or unless required by law. The written report will become part of the patient's **permanent** medical record.
- Analysis of the patient's GWS data will be completed using a secure external IT platform. The external IT platform provider will have access to a limited set of anonymized data for the purpose of quality assurance and improvement of the platform as a whole. The external IT platform has been reviewed and approved for use by CHEO and SickKids Legal and Privacy.
- To help healthcare providers and laboratories deliver better care to patients, laboratories share their interpretation of genetic results. De-identified (i.e., information that can identify the patient has been permanently removed) genetic results and diagnoses may be shared with healthcare providers, genetic testing laboratories, and/or submitted to public databases, including those outside of Canada, for these purposes.
- With consent, coded (i.e., information that can identify the patient will be replaced by a code) GWS data and clinical features will be shared through Ontario's Clinical Knowledge Base to ensure that GSO is providing the best possible test for all patients. This data may also be shared with institutionally approved Clinical Knowledge Bases within Canada. Coded data shared in Clinical Knowledge Base(s) can include: demographic information (sex, age, and ethnicity), details of the patient's clinical presentation, diagnoses, and genetic variants. This data will only be accessible to professionals working in diagnostic laboratories in Canada.
- Only the laboratory where the patient's test is performed will have access to an individual patient's full dataset.
- The patient's coded or anonymous results and data may also be used for education, publication and metric reporting with appropriate approval.
- Please speak with your genetic counsellor, clinician, or reach out gso@cheo.on.ca if you have questions about how your genomic data will be shared.

SAMPLE STORAGE / FUTURE USES

- After GWS has been completed, the sample(s) from the GWS analysis will be stored at the CHEO and/or SickKids laboratories for a limited time (2 years, unless an ethics committee determines otherwise).
- The remaining sample may be used for additional clinical genetic testing that the patient consents to, as offered by your healthcare provider(s). It may also be used for test development/validation and quality assurance procedures in the laboratory, after it has been de-identified.
- The patient may request that their complete GWS data be shared with their health care provider or a research program with Research Ethics Board approval.

CONSENT TO CONTACT FOR RESEARCH

- GWS is a test that was developed to try to diagnose patients with very rare genetic conditions. Enabling research helps improve our understanding and treatment of such rare conditions.
- GSO can support direct contact with you regarding approved research studies to better understand rare diseases and test new treatments. Examples of such research include sharing of GWS data with researchers to identify the cause of a rare disease, understanding current management of a rare disease, gaining insight into the natural history of a rare disease, and participating in clinical trials.
- You will be given the option to provide your contact information on the requisition if you are interested in being contacted by the Department of Genetics at CHEO to hear about future research opportunities.

GENETIC COUNSELLING

- All patients and family members should receive genetic counselling before proceeding with testing, and once final results are available.