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 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: An implementation Pilot for Rare Disease Diagnostics" (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).
    - 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.