SUPPLEMENTARY INFORMED CONSENT REQUIREMENTS: Whole Genome and Whole Exome Sequencing

Overview:

Sequencing, and the use of sequences, have associated risks to research participants that are not currently known in their entirety, and which may increase over time. Privacy, confidentiality, and return of results have been identified as areas of ethical concern when it comes to sequencing that require attention in the informed consent process.

A primary privacy concern in genomics research is the risk of re-identification of an individual's entire genome/exome sequence. Since an individual's genomic sequence is unique to them it should be considered identifying information. The risk of re-identification can extend beyond the individual to their family members or their community. Researchers have demonstrated that participants can be re-identified by combining de-identified genomic information with other publicly available information for specific groups of individuals (such as genealogy databases), which is ever expanding. Additionally, researchers have been able to distinguish individuals within summary-level genomic data. Therefore, access to full sequences may result in re-identification.

How the data is stored is a key consideration of the privacy risks to the participant. Data repositories may protect against the possibility of re-identification by controlling access to and use of the data. However, it is not possible to completely eliminate the risk of re-identification, or the use of sequences required or allowed by current or future laws. Unrestricted and/or public access and further data sharing pose risks to individuals who contribute their whole genome sequence (WGS) or whole exome sequence (WES) to research. Consequently, the continued existence of a whole genome/exome sequence may become risker to the individual over time, as other data becomes available and the possibility of re-identification increases.

Return of results is another risk associated with WGS and WES. Research ethics guidelines in Canada require that there be a plan to deal with any material incidental findings associated with research. In the WGS context, that has been interpreted as any medically actionable genetic findings. Returning results carry the risk of causing emotional harm to participants and have consequences for third party family members as well. During the informed consent process, participants should be given the opportunity to make their preferences known in terms of return of results.

When engaging in this kind of research, research participants must be provided with information that will help them make voluntary, informed decisions about whether to begin or continue participating in a research study. Furthermore, where sequences on humans are banked for future use ('unspecified research'), additional information must be shared during the consent process. The TCPS and the Information & Privacy Commissioner of Ontario expect that banking of samples or data, including genomic sequences, only be done with express consent, and that individuals have the option to not consent to the banking activities without affecting their participation in the main research study.

Purpose:

This Guideline describes the minimum privacy requirements for consenting participants to whole genome sequencing and whole exome sequencing of a human/person (i.e., not a virus or part of a human genome, such as a tumor DNA). It considers all relevant sections and information required for the participant to make a voluntary and informed decision about the project's whole genome or exome sequencing activities and associated privacy risks. The Guideline is applicable to all projects that collect, use, and disclose any whole sequences.

Scope:

This Guideline considers consent requirements for research participants aged 18 and older. Consent and/or assent requirements for research participants under the age of 18 are under review – please contact the Unity Health Privacy Office to request additional guidance.

Instructions:

Part 1

- *Consent forms or discussions must include all sections (rows) below and address all probing questions listed in the Required Content column, though content can be conveyed in any order or alongside other content (i.e., related to research activities not involving sequencing).*
- *All content should be written or stated in plain language.*

Part 2 (development of requirements currently underway)

- *Where sequences or samples will be banked for future use, the optional banking content must also be included. Broad consent for future use, for yet unknown research questions, requires the same degree of rigor and detail in the consent process as consent for specific uses.*

PART 1: REQUIRED CONTENT FOR ALL WGS/WES CONSENT FORMS		
Required Sections:	**Required Content:** *The answer to each question or instruction must be addressed at some point in the informed consent form or discussion, unless not applicable (as indicated below).*	**Recommended Text:** *Where indicated, please include language that is similar to the samples below. Where there are is no sample language, please include answers to the probing questions.*
Explanation of Sequencing	1. What are genes and gene variants? 2. What is WGS/WES?	Sample language: *Every person has their own unique set of genes, or "genome". Genes carry the information that helps to determine your characteristics. Genes are made up of DNA; between people, the DNA sequence of a gene can vary slightly. These differences in DNA sequence are called variants. These variants may or may not be harmful.* *This study uses a type of genetic test called "genomic sequencing". Genomic sequencing looks at every letter of a person's DNA and shows us a large number of variants to better understand whether they may be linked to increased risks of diseases.*
Purpose	1. What experiment is being performed (e.g. WGS, WES or more targeted sequencing)? 2. Why is WGS/WES being completed?	To be provided by study team as it is determined on a case-by-case basis. Please make sure language is consistent throughout the document (e.g., if you discuss WGS then keep referring to the experiment as WGS).
Procedures	1. What is the process for the collection of samples? 2. Which samples are being used for WGS/ WES (e.g. blood, tissue, saliva)? 3. How is the sample analyzed? 4. Will the sample be stored? (Yes/No) 5. Will samples and sequences be de-identified and coded with a study ID? 6. Will sequences be compared to family members or population controls? (include answer, if yes) 7. What are the limitations of the method, e.g. it cannot detect every mutation, it will not predict severity of disease or onset of disease?	Sample language for question #2 & #3: *We will extract DNA from your [blood/saliva/other] sample. We will then send some of the DNA for testing. This is usually done in [country] or, rarely, it may be sent to international facilities.* *Sample language for Question #4 (if "Yes"):* *We will store your DNA and any other samples in a secure 'bank' called a biorepository in [location]. We will label your samples and sequences with a unique code instead of your personal information. This means that researchers accessing*

	8. Will participants have access to their sequence. If no, provide explanation as to why it will not be accessible.	*your whole genome sequence and any other data about you will not see your identifiable information such as your full name, address, or OHIP number.* *If "No" to Question #4, please indicate that it will not be stored and that it will be destroyed once sequenced.*
Safeguards	1. Are WGS/WES staying inside Canada or being sent outside Canada? Explain what laws are applicable to your study. 2. What physical and technical protections will be instituted for the sequences? 3. What administrative safeguards are implemented? 4. Who will have access to my information? 5. What legal safeguards are in place to protect against genetic discrimination?	Sample language for question # 1, if sequences are being sent outside of Canada: *Any information sent outside of Canadian borders may alter the risk of disclosure of information because the laws in those countries dealing with protection of information may not be as strict as in Canada. All study data that are transferred outside of Canada will be coded (this means it will not contain any personal identifying information such as your name, address, medical health number or contact information), but this does not eliminate the risk that you may be re-identified.* Sample language for question # 1, if sequences are staying in Canada: *All sequences are created, stored and transferred in accordance with federal and provincial privacy laws.* Sample language for questions #2 and 3: *Your sample will be securely stored at the [name] biorepository in [name of hospital/research centre, country] for quality purposes.* *All study data [note all relevant data: sequence, health records, questionnaire data etc.] will be stored in secure, controlled-access databases that meet international security standards and [country] laboratory accreditation requirements. Only the [study doctors, study researchers and personnel] working directly with this study will have access to the database.* *Sample language for question # 4:*

		Besides authorized persons from the study team, your [personal information, health records and any information collected and stored by the study doctors during the research project] might be accessed during audit and inspections by other bodies, such as regulatory authorities. This is to ensure that the study team is complying with the approved study design and procedures. This review may be done by the ethics committee that approved this research project, regulatory authorities, or as required by law. In these circumstances, these parties will review only, not collect or record, your personal information. *Sample language for question #5:* *Despite strict security measures, the potential unintentional release of your genetic and clinical research data could lead to loss of privacy and to possible future discrimination against you or your biological relatives. In Canada, there are laws to protect against discrimination based on your genetic information (the Genetic Non-Discrimination Act). The Genetic Non-Discrimination Act bans discrimination based on genetic test results and makes it illegal for insurance companies and employers to require people to reveal their genetic test results. Insurance companies and employers are not allowed to use your genetic test results against you. Your healthcare provider will not provide your results to an insurance provider without your permission.*
Voluntary Participation	1. Is WGS and WES voluntary?	Sample language: *Your decision to participate is voluntary and you are free to withdraw from the study at any stage.*
Risks of Sequencing	1. What are the current known and foreseeable risks to the individual, the individual's family, and the individual's community? 2. Potential loss of confidentiality (i.e., privacy breach) 3. Physical risks related to collecting the sample(s) 4. Is there a potential to reveal non-paternity (including studies testing multiple family members)?	Sample language for #1 and #2 (REB to provide additional review and language for inclusion): *Your samples, sequences and health information will be kept confidential and will not be released to other parties, unless required by law.*

		Due to the rapid pace of technical advances, there is always a small risk that sequencing your genome may lead to you being re-identified. Despite strict security measures, the potential unintentional release of your genetic and clinical research data could lead to loss of privacy and to possible future discrimination against you or your biological relatives. *Although your genomic information is unique to you, you share some genomic similarities with your family, and other blood relatives. Therefore, learning your research results could mean learning something about your family members and might cause distress. Before joining the study, it may be beneficial to talk with your family members about whether and how they want you to share your results with them.* *If you are a First Nations or Indigenous person who has contact with spiritual Elders, you may want to talk to them before you decide to participate in this research study. Elders may have concerns about some research procedures including genetic testing*.
Potential Benefits	Please consult the REB for this section	Potential language to be determined with the REB
Legal Rights if Harmed	Provide assurance that participants have not waived any rights to legal recourse in the event that they experience harm associated with the storage and/or use of their data or samples.	Sample language: *You do not give up any of your legal rights, nor release the study investigator, study sponsor, or involved institutions from their legal and professional responsibilities.*
Financial Reimbursement	Please consult the REB for this section	Potential language to be determined with the REB
Commercialization	1. Will there may be any future commercial use of samples or sequences (e.g. distribution of cell lines derived from samples, commercial development of genetic tests or algorithms)? 2. Will there be any production and distribution of derivatives, like cell lines? (include answer, if yes) 3. Is it likely that participants will receive any future profits if the research results in products that are eventually developed and sold for commercial purposes?	Sample language for #1 and #2: *XX organization will use your sample and data only for research. We will not sell them; however, where a sample and/or data is provided to external researchers or organizations, a fee may be charged to recover part, or all of the costs incurred in storing and managing the sample and/or data. The results of this research might someday lead to the development of products (such as a commercial cell line, a medical or genetic test, a drug, or other medical product) that may have commercial*

		value and could be sold by a company. You will not receive money from the sale of any such product.
Withdrawing	1. How will a participant's request for withdrawal to the sequencing of their sample be handled? If they do, will that impact their participation in the study at large? 2. (If yes to #1) How does the participant withdraw their consent to sequence? 3. (If yes to #1) What will happen to their sample and data generated from the sample / sequences? Please include a note that sample destruction will be completed upon request (mandatory requirement under the TCPS-2).	Potential language to be determined by the REB. Sample language for consideration: *You are free to withdraw from the study at any stage by contacting the study team. Your withdrawal will not impact your medical care or access to laboratory tests.* *You can change your mind at any time during the study. We will stop using your samples and/or de-identified data and we will destroy your samples and/or data upon request. We cannot retrieve samples and information that has already been analyzed or already used in presentations or conferences.*
Open access & Open publishing* (*Where a sponsor or publication body requires that the raw data used in a publication or report of final results be make available to other researchers to confirm results or for similar, but new, research questions.)	Specific informed consent must be obtained prior to publishing portions of sequences to any public location. Include the answers to these questions if de-identified raw data (not including whole sequences) will be made available to other researchers at the end of the study. **NOTE:** Researchers may not publish, post, or contribute whole sequences to any repository, without following the BANKING requirements below. 1. What data will be published? (e.g. specific genes, snippets) 2. What is the purpose of publishing publicly? 3. Where will data be published? (include answer, if known) 4. What are the anticipated uses and users of the data, and any requirements for users to access the data (e.g. researchers only, researchers with REB approvals, any member of the public)?	Sample Language: *Some of the data about you that we collect or create may be put into a repository [insert name if available] outside of Unity Health, along with information from many other people like you. Only [snippets of your sequence], not your whole sequence, will be available for [public use/by people who are researchers].* *Some of the data about you that we collect or create may be stored online, in controlled-access databases. Only authorized researchers will have access to it. An independent committee will determine whether to grant researchers access to your information. These researchers can come from anywhere in the world and they may work for universities as well as commercial companies, such as pharmaceutical companies.*

Clinical results and incidental findings	Please consult the REB for this section 1. What types of sequencing / testing results are possible (e.g., material incidental finding)? 2. What plan is in place for addressing material incidental findings? This should already have been considered within REB/ICF requirements. 3. Will the results be given back to the participant? If yes, how will they be provided? 4. Will the results be clinically validated? If so, who will validate the results or how could the participant submit them for validation?	Potential language to be determined with the REB.
Consent for future contact	Please consult the REB for this section	Potential language to be determined with the REB.
Contact healthcare provider	1. Will you contact the participant's healthcare provider during the study? If so, for what purposes?	Sample language: *With your consent, we will contact your family doctor for the purposes of [collecting more health information such as XX]. [OR]* *No, we will not contact your healthcare provider.*