Alberta Health Services

Department of Medical Genetics
Dr. R. Brian Lowry Genetics Clinic

UNIVERSITY OF CALGARY

PARTICIPANT INFORMATION AND CONSENT FORM
Adult without Capacity Participant

Title of Study: **Silent Genomes: Precision Diagnosis for Indigenous Families with Genetic Conditions**
(Activity 2 of *Silent Genomes: Reducing health care disparities and improving diagnostic success for children with genetic diseases from Indigenous populations*)

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Sponsors: **Genome Canada; Canadian Institutes of Health Research; Provincial Health Services Authority; UBC Faculty of Medicine, BC Children's Hospital Foundation; BC Children's Hospital Research Institute, Michael Smith Foundation for Health Research; Illumina Inc.**

If you are a <u>substitute decision-maker for an adult</u> who may take part in this study, this consent form is also to be signed by you, and the assent (agreement) of the adult for whom you are a substitute decision-maker may also be required.

"We" means the study doctors and other research staff.

1. INVITATION
The person you represent is invited to take part in this research study because:

- They have a medical condition which is not yet understood, and is likely due to a genetic (single gene) cause
  OR
- They are a biological (blood-related) relative of a person who is affected with such a medical condition.

As part of this study the individual you represent is invited to undergo a type of genetic testing called **'Whole Genome Sequencing' (WGS)**, a new technology which can find changes in DNA, sometimes referred to as "genetic changes" or "**variants**." The purpose of this study is to try to find the variants causing the condition in their family and how best to manage their healthcare.

In most cases, the person affected with the condition as well as two additional blood-related relatives will be invited to take part, although sometimes more family members will be invited (depending on the condition). The reason for including relatives without the condition is to compare genetic changes (variants) that may be identified in the affected family member. When both parents of an affected child participate, we can determine whether the child's variants were passed down through the family, or if they are new genetic changes that happened for the first time in the child.

2. THEIR PARTICIPATION IS VOLUNTARY
Their participation is voluntary. You have the right to refuse for them to participate in this study. If you decide to permit them to participate, you may still choose to withdraw them from the study at any time without any negative consequences to their medical care, education, or other services to which they are entitled or are presently receiving.

In order to decide whether or not you wish them to be a part of this research study, you should understand what is involved and the potential risks and benefits. This form gives detailed information about the research study, which will be discussed with you. Once you understand the study, you will be asked to sign this form if you wish them to participate.

Please take time to read the following information carefully and to discuss it with your family, friends, and doctor before you decide.

3. WHO IS CONDUCTING THE STUDY?
This study is being led by the Principal Investigators (study doctors), Drs. Laura Arbour and Anna Lehman, and the other investigators listed on the first page. This study is funded by Genome Canada, Canadian Institutes of Health Research, **Provincial Health Services Authority, UBC Faculty of Medicine, BC Children's Hospital Foundation, BC Children's Hospital Research Institute, and the Michael Smith Foundation for Health Research. Illumina Inc** is providing in-kind donation only.

4. BACKGROUND

Genetic conditions happen in **all populations around the world**. Individually, genetic conditions are rare, but if we group all genetic conditions together, the number is large. 'Rare' genetic conditions affect at least 1 in 50 people, and the number is even higher if we include more common conditions.

What are genes and gene variants?

We each have ~25,000 **genes** in every cell of our body, which we inherited from our parents.
Genes are the 'instructions' for our bodies, which tell our cells, tissues, and organs how to work. Genes are made of **DNA** (deoxyribonucleic acid), a long string of 'genetic letters' that the cells can read. Every person has a slightly different combination of letters, due to changes (**'variants'**) in their DNA. You can think of variants as being similar to 'spelling mistakes' in the DNA. Most of these variants are harmless (**normal variants**), some have an unknown or uncertain effect (**variants of uncertain significance**), while others are known to play a role in disease (**disease-causing variants**).

What is Whole Genome Sequencing (WGS)?

The entire set of genes/DNA in a person is called the human **genome.** The genome contains about 6 billion DNA units ('genetic letters') in total. **Whole Genome Sequencing (WGS)** is a new genetic technology that allows a person's entire genome to be read and studied at once. Since WGS has the ability to study all of your genes at one time, it has the potential to replace many of the current genetic tests that are available which can only look at a single gene or a small number of genes at one time.

Thousands of variants are found in each person undergoing WGS for a genetic condition. Although most of these will be normal variants or variants of uncertain significance, there is about a **30% chance of finding a disease-causing variant** which leads to a new genetic diagnosis and explains the cause of the medical condition your family was being tested for.

Since WGS looks at a person's entire genome, it may unexpectedly reveal harmful variants in *other* genes which are not related to the reason they were tested. These types of variants are called '**incidental findings'**, because they were unexpectedly found while looking for something else. Sometimes incidental findings are '**medically actionable'**, meaning that there is an action that can be taken (for example, treatment or prevention plan) to reduce the chance the variant will affect health. For example, a disease-causing variant in a gene related to cancer risk could be unexpectedly found, and that information could lead to a recommendation for special cancer screening. How we will provide incidental finding results back to you is discussed in detail in section 8 (pages 7-8).

5. WHAT IS THE PURPOSE OF THIS STUDY?

The main purpose of this study is to **find the gene variant(s) causing the suspected genetic condition** in them or their family member. We will do this through WGS testing of family members with and without the condition.

This particular study focuses on Indigenous families in an effort to **reduce the barriers** many Indigenous communities face in accessing genetic testing and diagnosis.

6. WHO CAN PARTICIPATE IN THIS STUDY?

Their family may be able to take part in this study if they self-identify as Indigenous (First Nations, Inuit, or Métis) and/or have Indigenous ancestry and meet the following criteria:

- The affected person in the family has a suspected genetic (single-gene) condition which could

present in childhood (childhood-onset)
- The condition has not been diagnosed through other available medical tests and investigations
- The condition is serious enough to affect the person's health or quality of life
- Learning the diagnosis is predicted to have a positive impact on the family's health and well-being (for example, the diagnosis may help improve health care delivery, help with treatment decisions, reduce uncertainty for family, etc.).

Eligibility to join the study will be decided on a case-by-case basis, after the study team has permission from the family to review the affected family member's medical records. The **Principal Investigator (study doctor)** at each site will make the final decision about eligibility, based on which families have the best chance of finding a disease-causing variant through WGS.

7. WHO SHOULD NOT PARTICIPATE IN THIS STUDY?

The person you represent will **not** be able to take part in this study if:
- The affected person in the family has already received a diagnosis through other medical tests or evaluations
- The affected person's condition is thought to be caused by something non-genetic, such as an infection, injury, or toxic exposure (either during pregnancy or after birth)
- The affected person is suspected to have a genetic condition for which there is a simpler and more cost-effective test available to the family for diagnosis
- The family is not able to provide informed consent or complete the steps required for this study

8. WHAT DOES THE STUDY INVOLVE?

If you agree to have them join this study, you will be asked to do the following steps. Each condition and each family is unique, so not every participant will do all the steps listed below.

Meeting with genetic counsellor (approximately 1 hour)

Once the study team has confirmed their family's eligibility to join the study, the genetic counsellor at your enrollment site will meet with you in person at the medical genetics clinic, by videoconference, or by telephone (depending on what you prefer).
- The genetic counsellor will describe the study to you in detail, provide information about the different types of genetic results the family could receive from WGS testing, and discuss the possible pros and cons of joining this study.
- The genetic counsellor will ask you questions about the condition in their family and about their **family history**. She/he will draw the family tree to understand the biological relationships in the family and who is affected by the condition.
- You will have the opportunity to have your questions answered.
- If you agree to have them join the study, you will be asked to sign this **consent form**

Looking at their medical records

We will ask you to sign an '*Authorization to Release Healthcare Information*' consent form to **review their medical records** so we can better understand the condition in the family, including how it might be affecting them. Looking closely at your medical records will also help us to interpret the WGS results – i.e. whether any gene variants we may find through WGS match the features of the condition in the family. Their records will be requested from the healthcare provider who referred them to the study and/or from other medical facilities they have visited in the past. The types of records reviewed may

include written reports from doctors, results of previous bloodwork (including any genetic testing), and/or imaging results (such as CT-scan or MRI results/images).

If **other family members' medical records** are important in understanding the condition in the family, we will ask you whether it would be OK for you to approach the relative(s) to provide an information letter about the research study and a form to sign if they give us permission to review their records too. This part is optional. We understand some family members may not agree to us reviewing their medical records, but the individual you represent will still be eligible for the study.

Photography

We may ask to take photographs as a way of documenting the features of the condition in the family. Photos may include their face. Photos can help the study team remember and discuss the condition, especially if the photos show something that cannot be described as well in words. However, photos are optional. You can say 'no' to having photos taken and still take part in this study. **At the end of this consent form, you will be given the choice of whether or not you consent to photos of the individual you represent.**

Any photos taken will be part of their research data and will be kept under the same secure conditions as the rest of their data, but separate from their other research data. They will only be available to the research team members. If it is important to include their photos in a future scientific presentation or publication to help other scientists and doctors understand this condition better, we will re-contact you to ask for **separate consent**, and you will have the right to say 'yes' or 'no'.

Digital photos will be kept as required for 5 years after the study is completed, and then they will be destroyed.

DNA sample collection

WGS testing will be done on a DNA sample collected from them. DNA can be collected in different ways, including through a blood, saliva, or cheek-swab sample. Occasionally, we can obtain DNA from a stored tissue sample if other options are not available or some individuals may have DNA banked from a previous blood sample. A blood sample is the preferred way to collect DNA for WGS, as DNA taken from blood is more likely to give the best results. If required, we will provide you with the paperwork to have a blood sample drawn through **LifeLabs**, a clinical laboratory with many different locations and partner labs, or through the Alberta Children's Hospital outpatient lab. A LifeLabs (or partner lab) or Alberta Precision Laboratories (APL) staff member will draw their blood sample in a location that is most convenient to you. The blood sample will be taken from a vein, most often the arm, in the usual way. Depending on age and size, somewhere between 4mL – 10 mL (~1-2 teaspoons) of blood will be drawn. For children, no more than 1 mL (1/5 teaspoon) of blood per 1 pound of body weight will be taken.

In cases where blood collection is not possible, LifeLabs may be able to arrange saliva or cheek-swab collection instead.

DNA handling and storage

After their blood (or saliva, stored issue/DNA or cheek-swab) sample has been collected by **APL** or **LifeLabs**, it will be sent to their lab in Ontario. Once their DNA is extracted as required, LifeLabs will remove all the information that identifies them (i.e. name, date of birth, personal health number, address) from their sample, and instead label their sample with a **unique study code or barcode** which will not allow direct identification of them. Their **coded (de-identified) DNA sample** will then be sent to our research lab (the **Genome Sciences Centre, GSC)** in Vancouver, BC, where WGS testing will be done and their sample will be stored.

Only the study doctor and genetic counsellor at your enrollment site, and the central site study team members located at Children's and Women's Health Centre of BC in Vancouver will have access to the key that links their unique study code and research data back to their name and other identifying information. We need to be able to link back to their name since we will need to re-contact you to provide WGS results and to do further confirmation tests if possible disease-causing variants are found.

If a possible disease-causing gene variant is found through WGS, the GSC will send a **coded** sample of their DNA back to LifeLabs, who will do a **test to confirm the gene variant** and issue a clinical report in their name. We will send their name and other information that identifies them to LifeLabs along with their original sample but they will not have access to any of their other research information.

They are the owner of their DNA, and it is considered to be "on loan" to us for the purpose of this research. Their DNA will only be used for the purposes of this particular study. We will *not* sell their DNA, we will *not* use it to make money, and we will *not* share it with others without your knowledge and permission. If we wish to use their DNA for any other research beyond the purpose of this study, we will come back to you and ask permission. If you want their DNA destroyed or sent back to you at any time, we will do that.

Once this study is complete and the results of the study have been published, any remaining DNA at the GSC will be destroyed unless you specifically request that their sample be returned to you or moved to a different study or biobank that you have provided separate consent for.

Whole Genome Sequencing (WGS) genetic testing
WGS will be done at our research lab (the GSC in Vancouver, BC), using their **coded (de-identified) DNA sample**. All electronic (computer) data resulting from WGS will be stored on a highly secure server at the GSC, and sent to the central study site at **BC Children's Hospital Research Institute (BCCHRI)** through a secure File Transfer Protocol (FTP). All data from their WGS testing will be securely backed up on the BCCHRI servers.

❖ *Types of WGS results*
Our research team will study their data from WGS and create a list of possible disease-causing gene variants. Decisions about which variants might be disease-causing will be made by our research team, made up of doctors, genetic counsellors, data specialists, and lab staff.
There are four different types of possible results from WGS testing:

1) **A disease-causing gene variant is found that explains the condition that their family was originally being tested for ('positive' result):** This would provide an explanation for the condition in their family.
2) **No gene variant is found to explain the condition in their family ('negative' result)**: This

does not mean that there is no genetic cause – it may be that we just can't find it with our current technology.

3) **Variant(s) of Uncertain Significance (VUS) are found**: Everyone has many gene variants in their DNA. Some variants cause disease, others do not. Sometimes there is not enough information available to decide if a variant might cause a health condition. When the meaning of a variant is unclear, we refer to it as a VUS.
4) **Incidental Findings (IFs) are found**: Sometimes, by chance, WGS finds a gene variant that may cause a completely *different* health condition –something we were not looking for. Please read the next section to learn more about IFs and the choices you will need to make about them.

It is important to understand the limitations of the WGS performed for this study. This study focuses on finding disease-causing gene variants *related to the specific condition* in the affected person in their family, and not on finding gene variants that may cause other *unrelated* diseases. Therefore, **the WGS performed for this study is not a full analysis of all their genes, and a 'negative' result does not mean that they do not have any genetic risk factors.**

❖ *Incidental (unexpected) findings*

Gene variants that cause health conditions *unrelated to the original reason for testing* are called **Incidental findings (IFs)**. Although we will not purposely look for gene variants related to *different* diseases and will try to lower the chance of finding them, they may be found unexpectedly. IFs can be found in anyone who has WGS testing- even in healthy people.

Some IFs have a relatively high risk of causing health conditions where screening, prevention, or treatments are available to help improve health. These are called '**medically actionable' IFs**. It is not always clear which IFs fit this category, so our team as a whole will review each possible one and come to an agreement about it.

In this study, there are two types of medically actionable IFs that participants might have to face:

1) **Childhood-onset IFs**: These IFs predispose to health conditions where disease features can occur in childhood. Examples of conditions in this category are neurofibromatosis (a genetic condition of the skin and nervous system) and Long QT syndrome (a genetic condition affecting heart rhythm).
2) **Adult-onset IFs**: These IFs predispose to health conditions where features do not usually occur until adulthood. Examples include gene variants that increase the risk for certain types of cancer or heart disease.

❖ *How will WGS results be given back to you?*

We will provide their WGS results to the healthcare provider who referred them to the study, and it will be his/her responsibility to share the results with you. Your healthcare provider will have the option of including the study genetic counsellor and/or study doctor in the results appointment, and follow-up genetic counselling will be available to you as part of this study.

We will inform your healthcare provider of your results from this study, even if nothing of significance is found. The types of results you may get back include:

- **Negative result,** which means that no gene variants believed to be related to the condition in

the family were found. This result does not guarantee there is no genetic cause- it may be that we just cannot find it with our current technology.

- **Disease-causing gene variant(s)** that explain the *original condition being tested for* or that explain *some of the features/symptoms* you have.

- **Certain Variants of Uncertain Significance (VUS) that are decided by the study team to be possibly disease-causing** for the *original condition being tested for* or for *some of the features/symptoms* you have.

- **Medically actionable IF** results will be handled in different ways, depending on whether the participant is a child, dependent adult (who has a legal substitute decision-maker), or competent adult who is capable of making his/her own decisions. Our approach, explained below, is based on current Canadian guidelines for reporting IFs:

  - **Dependent adult participant (requiring legal substitute decision-maker):** Given that a dependent adult is not able to make his/her own healthcare decisions, we **will** give back results for any medically actionable IFs that are found. This is in the best interest of the participant, to be sure that he/she has the opportunity to receive appropriate healthcare and take preventative actions to reduce harms related to the IF.

Please note that if any information related to paternity (who a child's father is) or other unexpected family relationship is discovered during this research study, it will not be disclosed to participants.

❖ *Confirming disease-causing gene variants and medically actionable IFs*

If a **disease-causing variant**, a **VUS suspected to be disease-causing**, or a **medically actionable IF*** is found through WGS, their result will be confirmed by a repeat genetic test at LifeLabs before being given back to you and their referring healthcare provider. Since these types of results may affect their healthcare, it is important to make sure the result is correct by double-checking it in a **clinical** (non-research) lab before letting you know about it. Once confirmed, LifeLabs will give these results back to their healthcare provider as a **clinical report**, which will include their name and other identifying information.

If a **clinical report** of their genetic test result is issued, i*t will no longer be only research data, but will become part of their medical record*, like all of their other health records. These reports are also stored long-term in the LifeLabs clinical genetics database. Unlike your research data, clinical reports may be read by any healthcare providers involved in their care, either now or in the future.

❖ *Re-testing and follow-up*

Throughout the length of this study (approximately 4 years), we will likely re-test their DNA sample and/or re-analyze their data as our knowledge and WGS capabilities grow. Therefore, it is possible that you may receive new gene variant results at a later date, or that the interpretation of their results may change over the course of the study. New or changed results will be given back as explained in the *'How will WGS results be given back to you?'* section above.

Possible additional tests - optional

Throughout this study, we may suggest extra procedures to help understand the full nature of the condition in their family. This may involve the study of additional tissues such as another blood sample, hair sample, urine sample, skin biopsy, or tissue biopsy from a previous surgery. If this is the case, a **separate consent form** will be presented to you and you can decide whether you want to consent to the individual you represent having the additional studies done.

If a gene variant is found that we suspect may be disease-causing but additional studies are required to be sure, we may wish to send their sample to a researcher who specializes in that particular gene for further analysis. In such cases, **a separate consent form** will be presented to you. If you consent to sending their sample for further analysis, only their de-identified (coded) sample will be shared with the other researchers and their identity will be protected.

Re-contact for future research studies - optional
At the end of this consent form, you will be given the choice of whether you would like to be re-contacted about other research opportunities in the future.

9. WHAT ARE MY RESPONSIBILITIES?
Please keep in contact with us to let us know of any change their address or contact details. If there are significant health changes in the study participant related to the suspected genetic condition being tested for, it would be helpful for you to let us know.

10. WHAT ARE THE POSSIBLE HARMS AND DISCOMFORTS?
Discomfort of blood draw
The risks of drawing blood may include some minor local discomfort, light-headedness (dizziness or fainting), and/or minor infection or bruising around the area where the needle was inserted. If they are planning to have blood drawn as part of your routine clinical care, we will make every effort to coordinate their study blood draw so it can be done at the same time.

Risks related to WGS and Incidental Findings (IFs)
❖ *Potential psychological impact*:
When you donate their blood or tissue for genetic testing or research, they are sharing genetic information, not only about themselves, but also about biological (blood) relatives who share their DNA. If you learn that they have a genetic condition, there may be other family members, including those alive now or those who may be born in the future, who may also be at risk of having the same condition. This knowledge may provide you or their family with important information that could be used either to prevent the disease (if possible) or to inform other health care decisions. However, there is also a risk that simply having this knowledge may cause worry or stress. For some people, genetic results may influence their decision to have a child or affect other lifestyle decisions. This is one of the reasons that families have access to a genetic counsellor as part of the study. Genetic counselling helps each family to assess the pros and cons of the testing and understand what their results might mean for their wider family.

❖ *Potential risk of disclosure of your genetic information:*
There is a small risk of loss of privacy for them and their family. Despite our best efforts to protect their privacy, we cannot guarantee that their data will remain completely anonymous in all situations. If we decide to publish results from this study in a scientific medical journal, we will not include any

information about their identity (such as their name, community, birth date, etc.). However, it is possible that somebody somewhere - perhaps, for example, someone who looked after them in hospital - may realize the unnamed person in the study could be them. Studies published in medical journals are distributed worldwide and are mainly read by doctors and scientists, but could be read by non-doctors too.

There is always a risk of computer systems or research offices being broken into and data stolen, although the chance is estimated to be very small. Every effort will be made to protect their privacy and the confidentiality of your genetic results.

If you decide to reveal their genetic test results to others, there is a chance it could lead to discrimination towards them and/or their blood relatives. A federal government law enacted in May 2017, called the *Genetic Non-Discrimination Act* bans discrimination based on genetic characteristics and makes it illegal for insurance companies (such as life insurance companies) and employers to require people to reveal their genetic test results. Insurance companies and employers are not allowed to use their *genetic test results* against them (for example, they cannot use this information to decide whether to offer them life insurance or whether to hire them for a job). See *GNA* fact sheet available at: https://www.cagc-accg.ca/doc/S201%20fact%20sheet%20-%20final%20copy%20-%20May%2017%202017.pdf. Although this law is helpful, it does not prevent insurance companies from using information about their current symptoms or family history of a health condition, or the results of *other types of medical tests* to decide if they will insure them (even if that health condition has a genetic basis). Also, laws sometimes change over time, so no one can guarantee that the *GNA* will always be in place to protect them.

As discussed in the '*Confirming disease-causing gene variants and medically actionable IFs'* section on page 9, if you receive a **clinical report** of their genetic test results from LifeLabs, it will become part of their medical record and may be read by any healthcare providers involved in their care, either now or in the future. These reports are also stored long-term in the LifeLabs clinical genetics database. Having genetic test results enter their medical record would remove your choice to keep your results private from your healthcare providers.

11. WHAT ARE THE POSSIBLE BENEFITS OF PARTICIPATING?

No one knows whether or not they will directly benefit from taking part in this study. It is possible that you will receive a genetic explanation for the condition in their family, which in some cases is helpful in guiding the medical care and support of affected family members. Some people find it helpful to learn the reason for the medical condition in their family.

We hope that the information learned from this study can be used in the future to benefit other people with suspected genetic conditions.

12. WHAT ARE THE ALTERNATIVES?

It is important for you to know that you can choose for them not to take part in the study. Choosing not to participate will in no way affect their health care. The availability of genomic testing varies across Canada – If you choose for them not to join this study, WGS testing may or may not be available through the medical system in their region.

13. WHAT IF NEW INFORMATION BECOMES AVAILABLE THAT MAY AFFECT MY DECISION TO PARTICIPATE?

You will be told of any new information that becomes available that may affect your willingness to have them remain in the study. You may be asked to provide renewed consent if new information is learned that may affect your decision to have them take part in the study.

14. WHAT HAPPENS IF I DECIDE TO WITHDRAW MY CONSENT FOR THEM TO PARTICIPATE?

You may withdraw them from this study at any time without giving reasons. If you choose to have them enter the study and then decide to withdraw them at a later time, you have the right to request the withdrawal of their information (and/or samples) collected during the study. This request will be respected to the extent possible. Please note however that there may be exceptions where the data (and/or samples) will not be able to be withdrawn, for example where the data (and/or sample) is no longer identifiable (meaning it cannot be linked in any way back to their identity) or where their data have been combined with other data. If you would like to request the withdrawal of their data (and/or samples), please tell the study doctor at their site. If their participation in this study includes any optional studies or long-term follow-up, you will be asked whether you wish to withdraw them from these as well.

15. CAN THEY BE ASKED TO LEAVE THE STUDY?

If they are not able to complete the steps of the study, we may ask you to withdraw them from the study. If they are asked to leave the study, the reasons for this will be explained to you and you will have the chance to ask questions about this decision. They could also be removed from the study if we are no longer able to contact you (e.g. moved, no forwarding address).

16. HOW WILL THEM TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

Their confidentiality will be respected. However, research records and health or other source records identifying them may be inspected in the presence of the Investigator or his/her designate by representatives of Health Canada, the study sponsors, or the Research Ethics Board at the University of Calgary and the University of British Columbia for the purpose of monitoring the research. No information or records that disclose their identity will be published without your consent, nor will any information or records that disclose their identity be removed or released without your consent unless required by law.

Their rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that their privacy is respected. You also have the legal right of access to the information about them that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request.

They will be assigned a unique study code as a participant in this study. This code will <u>not</u> include personal information that could identify them (e.g. it will not include their name, health card number, SIN, date of birth, address etc.). This code will be used on their data and samples collected during the course of this study, so that their identity will be kept confidential. Only the study doctors, their designated study team members, and LifeLabs will be able to match their name to the unique study code that is used on their research-related information. The key matching their name to their study code will not be released to anyone else without your consent, unless required by law.

Most of their study data (such as their WGS data, medical details about their condition, photographs,

etc) will be labelled only with their unique study code and will be stored in password-protected files on the computer servers at the study doctors' institutions, which are protected by strict security measures. Any photographs taken of them will be stored in a separate file from their other study data. The list matching their name to unique study code will be stored on the same secure servers, but in separate password-protected files.

Hard-copies of paperwork which could contain their personal information (i.e. medical records received for this study, signed consent form, family tree drawn by the genetic counsellor during the research visit, and records of the study team's communications with you) will be kept in a file in a lockable cabinet behind a locked door at their study doctor's institution and will only be accessed by the study doctor and genetic counsellor at their local site.

If we present or publish any study results for other scientists or health care providers, we will not include any personal information about them. If we wish to include their photographs in a future scientific presentation or publication, we will re-contact you to ask for separate consent, and you will have the right to say 'yes' or 'no'. Any scientific papers we write from this study will be reviewed by our Indigenous oversight committee before being published.

As discussed in previous sections, if you receive a **clinical report** of their genetic test results from LifeLabs, it will contain their name and other identifying information on it and will become part of their medical record. It will also be stored long-term in the LifeLabs clinical genetics database. As part of your medical record, it may be read by any healthcare providers involved in their care, either now or in the future. Safeguards are in place, as the privacy of medical records is protected by law.

Authorized representatives from the University of Calgary and the Conjoint Health Research Ethics Board may look at their identifiable medical/clinical study records held at the Alberta Children's Hospital for quality assurance purposes.

17. WHAT HAPPENS IF SOMETHING GOES WRONG?

By signing this form, you do not give up any of their legal rights and you do not release the study doctor, participating institutions, or anyone else from their legal and professional duties. If they become ill or physically injured as a result of participation in this study, medical treatment will be provided at no additional cost to you. The costs of their medical treatment will be paid by their provincial medical plan and/or by the study sponsors.

18. WHAT WILL THE STUDY COST ME?

All research-related medical care and any tests that they have during your participation in this study will be provided at no cost to you.

19. WHO DO I CONTACT IF I HAVE ANY QUESTIONS ABOUT THE STUDY DURING THEIR PARTICIPATION?

If you have any questions or would like further information about the study at any time, or if you feel you have suffered any adverse effects from the study, **please contact:**

Calgary site – Brenda McInnes (study coordinator/genetic counsellor) at 403-955-7028; Brenda.McInnes@ahs.ca

20. WHO DO I CONTACT IF I HAVE ANY QUESTIONS OR CONCERNS ABOUT THEIR RIGHTS AS A PARTICPANT?

If I have any questions concerning the rights of a possible participant in this research, or research in general, I can contact the Chair of the Conjoint Health Research Ethics Board, University of Calgary at (403) 220-7990.

If I have any concerns or complaints about the person I represent as a research participant and/or my experiences while participating in this study, I can also contact the Research Participant Complaint Line in the University of British Columbia Office of Research Ethics by e-mail at RSIL@ors.ubc.ca or by phone at 604-822-8598 (Toll Free: 1-877-822-8598). By giving the study reference number (H18-00726) when I call the Complaint Line, the staff will be better able to help me.

I can also contact the Vancouver Island Health Authority (VIHA) Research Ethics Board at 250-519-6726; researchethics@viha.ca

21. AFTER THE STUDY IS FINISHED:

This study is expected to last at least 4 years, although there is a possibility the study will be renewed for a longer period. Once all the testing and data analysis are complete and the findings are published, any remaining DNA samples will be destroyed, unless you specifically request that they be returned to you or transferred to another study or biobank that you have provided separate consent for. If you prefer that we return any remaining sample to you instead of destroying it at the end of the study, you may request this by contacting the study team (see section 19, above).

As required, the data from this study will be stored for at least 5 years after the study is finished.

PRECISION DIAGNOSIS FOR INDIGENOUS FAMILIES WITH GENETIC CONDITIONS

PARTICIPANT CONSENT

My signature on this consent form means:

- I have read and understood the information on this consent form.
- I have had enough time to think about the information provided.
- I have been able to ask questions and have had satisfactory responses to my questions
- I understand that their participation in this study is voluntary.
- I understand that I am completely free at any time to refuse for them to participate or to withdraw from this study at any time, and that this will not change the quality of care that they receive.
- I authorize access to their health records as described in this consent form.
- I understand that we **will** receive results for any medically actionable IFs that are found.
- I understand that if a disease-causing or likely disease-causing variant is found in them, then their genetic test result will be confirmed in a clinical lab and will become part of their medical record, which all of their healthcare providers can look at.
- I understand that there is no guarantee that this study will provide any benefits to them.
- I understand that I am not waiving any of their legal rights as a result of signing this consent form.

I will receive a signed copy of this consent form for my own records. I consent for the individual I represent to take part in this study.

LEGAL SUBSTITUTE DECISION-MAKER consent for dependent adult participant who is incapable of consent:

The parent/guardian or substitute decision-maker (legally authorized representative) and the investigator are satisfied that the information contained in this consent form was explained to the child/participant to the extent that he/she is able to understand it, that all questions have been answered, and that the child/participant assents to participating in the research.

Printed name of adult participant (ward): _____

_____	_____	_____
Printed name of parent/guardian **OR** substitute decision-maker	Signature	Date

_____	_____	_____
Printed name & role of person obtaining consent	Signature	Date

PRECISION DIAGNOSIS FOR INDIGENOUS FAMILIES WITH GENETIC CONDITIONS

OPTIONAL CONSENT CHECKBOXES– DEPENDENT ADULT participant

Printed name of dependent adult (ward): _____

OPTION 1 – Photographs: Photographs, including photos of his/her face, may help the study doctors better understand the condition in the family and help with the interpretation of Whole Genome Sequencing results. I understand that I have the option of deciding whether or not to have photos of the person I represent taken. Any photos taken will only be viewed by the study team members, and will have the same protections as the rest of their research data but will be stored separately from the other research data. If the study doctors feel it is important to include photos in a future scientific presentation or publication, I will be re-contacted and asked for **separate consent**, and I will have the right to say 'yes' or 'no' to this.

Please check one box below.

☐ **YES, I agree** to have photographs of the person I represent taken for the purposes of this research study.

☐ **NO, I do NOT agree** to have photographs taken.

OPTION 2 – Re-Contact for Future Research Studies

I understand that new research studies may be of interest to the family. I can choose whether I wish to be re-contacted about future research opportunities for the person I represent. If I agree to be re-contacted, it does not mean the person I represent has to participate in any future research projects. I will have the right to say 'yes' or 'no' to participating in any future studies that are presented to me.

Please check one box below.

☐ **YES, I agree** to be contacted in the future to learn about a new research study.

☐ **NO, I do NOT agree** to be contacted in the future to learn about a new research study.