Participant Information and Consent Form

Genetic differences in pharmacodynamic safety endpoints with propofol anesthesia in children

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Emergency 24-Hour Contact: 604-875-2161; *Ask to page the anesthesiologist on call*

Non-Emergency Contact: 604-875-2711

If you are a parent or legal guardian of a child who may take part in this study, permission from you and the assent (agreement) of your child may be required. When we say "you" or "your" in this consent form, we mean you and/or your child; "we" means the doctors and other staff.

1. Invitation

You are being invited to take part in this research study because you are undergoing surgery or other procedures under general anesthesia at BC Children's Hospital (BCCH).

2. Your participation is voluntary

Your participation is voluntary. You have the right to refuse to participate in this study. If you decide to participate, you may still choose to withdraw from the study at any time without any negative consequences to the medical care, education, or other services to which you are entitled or are presently receiving.

You should be aware that there is a difference for both you and your doctor between being a patient and being a research participant. As a patient, all medical procedures and treatments are carried out for your benefit only according to standard accepted practice. As a research participant, you and your doctor also must take into account the requirements for the research study. These may include procedures and treatments that are not part of standard practice or are not yet proven. This consent form describes the diagnostic and treatment procedures that are being carried out for research purposes. Please review the consent document carefully when deciding whether or not you wish to be part of the research and sign this consent only if you accept being a research participant.

If you wish to participate in this study, you will be asked to sign this form.

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 this study?

This study is being conducted by the Pediatric Anesthesia Research Team (PART), a division of the Department of Anesthesia at BC Children's Hospital.

No investigator is receiving any financial compensation from any outside funding agency for conducting or being involved with any part of this study, and there is no possibility of benefit to the investigators from commercialization of any research findings.

4. Background

Sedation and anesthesia are important parts of care for children undergoing surgery or other procedures or investigations that are painful, uncomfortable, or that require them to lie still for a long time.

Propofol is a drug that is widely used, in this hospital and elsewhere, for sedation and general anesthesia. Propofol has to be given in carefully measured doses as there is only a small difference in the amount required to make somebody unconscious and the amount

that will make them stop breathing. There is also a lot of difference between patients in the amount of this drug that is needed to get to these '*pharmacodynamic endpoints'*.

In the past, anesthesiologists have always been the ones to sedate and anesthetize children. But increasing demand means that sedation is now sometimes given by non-anesthesia doctors. Given that different patients need different amounts of propofol to lose consciousness and to stop breathing, its use by a non-anesthesia doctor could cause problems if even a little too much propofol is given to a particular patient.

There are many different reasons why people need different amounts of propofol, but researchers have found that adults with different genetic ancestry can require very different amounts of propofol to lose consciousness or stop breathing. This idea has not been properly studied in children.

5. What is the purpose of the study?

The purpose of this study is to investigate the doses of propofol needed to make children (a) become unconscious and (b) stop breathing. Both of these points are normal and desired occurrences when an anesthesiologist is preparing a patient for a procedure.

We also aim to identify genetic differences that will help us to understand why some children need more propofol and some need less. Self reported ancestry will be compared to genomic ancestry to see if this will be a useful measure for physicians planning their care.

6. Who can participate in this study?

You may be able to participate in this study if:

- You are between the ages of 3 and 18 years
- Your anesthesiologist plans to use propofol at the start of your anesthesia

7. Who should not participate in this study?

You will not be eligible to participate in this study if:

- You need a sedative premedication before you go into the operating room
- You have a brain disorder that means you will need less propofol
- You or a family member are unable to tell us the countries your family originally comes from
- You weigh less than the 3rd centile for your age, or more than the 97th centile

8. What does the study involve?

In the anesthetic care unit, about 360 families will be asked to provide the countries of family origin for the participating child, parents and grandparents.

In the operating room, your anesthesiologist will insert an intravenous cannula (a thin tube inserted into a vein, called an IV) as they normally would, and propofol will be given through the IV at a steady rate. We expect you to become sleepy within 60 seconds and unconscious 1-2 minutes later. We will gently stroke your eyelash regularly, which is a routine way to find out exactly when you do become unconscious. If you are a parent accompanying your child to the OR, you will leave the OR at this point (as is also the case if you choose not to participate).

As a normal part of your standard care, your anesthesiologist will want you to stop breathing for your procedure so the anesthesia machine can breathe for you. In this study, to measure exactly when this happens, once you are asleep we will put nasal prongs in your nostrils and the anesthesia monitoring machine will tell us when you have not taken a breath for 20 seconds. This will then be the end of the study and from this point onward you will receive routine care.

A sample of your saliva will be taken using a swab while you're asleep. This sample will be taken to a lab in the hospital's research institute for genetic analysis.

Genetic research

Cells in your body contain a type of molecule called deoxyribonucleic acid, or DNA for short. DNA is what your genes are made of. Your cells also contain another type of molecule called Ribonucleic acid (RNA for short) that works closely with your genes. Changes in genes or RNA may affect a person's chance of developing certain diseases or how they respond to medications. These changes may be inherited (i.e. passed on in families from parents to children) or they may be somatic (arising in a single body cell at some point during life and generally cannot be passed on to children). "Genetic research" is a type of research that studies these changes, and will hopefully provide a better understanding of the links between the genetic changes and specific diseases, and eventually develop new ways to prevent, detect and treat these diseases.

Incidental (unexpected) findings and genetic research

It is possible that genetic testing may discover a finding that the researchers were not looking for, such as a genetic change being present that indicates that you (or a family member who may carry the same genetic change) are at greater risk for developing a condition for which screening or prevention strategies are available or which presents an important risk to your health. This is called a "clinically relevant incidental finding". If an incidental finding of this type is discovered and something can be done about it, you have the right to know. Should this occur, your primary care provider at BC Children's Hospital will be given information about the finding and they will contact you with details on how to proceed, including information about receiving genetic counselling.

9. What are my responsibilities?

There are no additional responsibilities or requirements necessary for you to participate in this study.

10. What are the possible harms and discomforts?

You may not be willing or able to tell us where your family originates from. We understand if you choose that you do not want to share this personal information.

Our study procedures in the operating room will be very similar to the care you would receive otherwise. We will be giving the propofol more slowly and steadily than usual and this means going to sleep will take a little longer: it would usually be less than a minute, but in this study, we expect it to take between 1 and 2 minutes.

Risks related to genetic testing and incidental findings

When you donate your saliva sample for genetic testing or research, you are sharing genetic information, not only about yourself, but also about biological (blood) relatives who share your genes or DNA. While the risk of your information being accidentally released is estimated to be extremely small, disclosure of genetic research data could result in discrimination by employers or insurance providers toward you or your biological (blood) relatives. This is because there is currently no law in Canada that specifically protects against genetic discrimination. For example, no law prevents an insurance company in British Columbia from requesting information about the result of a person's genetic test as part of the process of assessing risk to determine whether to grant coverage and to set premiums. When you apply to an insurance company for new insurance coverage, it is possible that the personal results of any genetic testing performed in connection with this study could be requested by that insurance company, particularly if the results are shared with you or your physician. If you wish to participate in this study and do not already have insurance coverage in place, you may wish to seek some advice about whether participation could affect your insurability. You might consider applying for and obtaining insurance before participating in research that could return genetic information to you. Even if you already have insurance in place, results from genetic testing could have implications for your ability to renew your coverage if, for example, you try to change the terms of your insurance coverage or if your policy reviews eligibility after set periods of time.

If you become aware that you have a disease-related genetic change, this knowledge may provide you or your family with important information that could be used to either prevent the disease (if possible) or to inform other health care decisions related to the finding. However, there is also a risk that simply having this knowledge may cause anxiety or distress and alter your decision to have a child or other lifestyle decisions for you or a family member who may have the same genetic change. Every effort will be made to protect your privacy and the confidentiality of these results. Because technology changes so quickly, the potential future use of genetic information is unknown and therefore the potential future risks also are unknown. You should be aware that genetic information cannot be protected from disclosure by court order. Incidental findings that are found during participation in a research

study will be confirmed in a laboratory that is not associated with the research study before they are used for your health care and other important decisions. In this situation, it is your responsibility for covering the cost of the confirmation tests and the costs of genetic counselling that you may have as part of the process of finding out the results. Please know that these services may not be covered by your provincial health care plan and are only be available if you pay for them. In such instances, the confirmation testing would only be done with your permission and the total cost to you for the testing and genetic counselling may be more than $1000.

11. What are the potential benefits of participating?

There are no known direct or immediate benefits to research participants. Testing of your saliva is experimental, individual results will not be communicated to you. However, we hope that the information learned from this study can be used in the future to benefit other children needing propofol for sedation or anesthesia.

12. What are the alternatives to the study treatment?

If you choose not to participate in this study or to withdraw at a later date, your child will receive the standard anesthetic medications that are used at BCCH, which will quite likely include propofol. In this case, your anesthesiologist may or may not choose to give the propofol in the same way as we will in the study.

You can discuss these options with your doctor before deciding whether or not to participate in this research project.

13. What if new information becomes available that may affect my decision to participate?

If you choose to enter this study and at a later date a more effective treatment becomes available, it will be discussed with you. You will also be advised of any new information that becomes available that may affect your willingness to remain in this study.

14. What happens if I decide to withdraw my consent to participate?

You may withdraw from this study at any time without giving reasons. If you choose to enter the study and then decide to withdraw at a later time, all information about you collected up to the point of your withdrawal will be retained for analysis in order to protect the integrity of the research, which may benefit future research participants and patients. However, no further information will be collected.

15. Can I be asked to leave the study?

If you are not able to follow the requirements of the study or for any other reason, the study doctor may withdraw you from the study and will arrange for your care to continue. On

receiving new information about the treatment, your research doctor might consider it to be in your best interests to withdraw you from the study without your consent if they judge that it would be better for your health. If you are asked to leave the study, the reasons for this will be explained to you and you will have the opportunity to ask questions about this decision.

16. How will my taking part in this study be kept confidential?

Your confidentiality will be respected. However, research records and health or other source records identifying you may be inspected in the presence of the Investigator, or his or her designate, by representatives of the UBC C&W Research Ethics Board for the purpose of monitoring the research. No information or records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law.

You will be assigned a unique study number as a participant in this study. This number will not include any personal information that could identify you (e.g., it will not include your Personal Health Number, SIN, or your initials, etc.). Only this number will be used on any research-related information collected about you during the course of this study, so that your identity will be kept confidential. Information that contains your identity will remain only with the Principal Investigator and/or designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected. You also have the legal right of access to the information about you and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to your study doctor.

Data transferred out of Canada

Sometimes de-identified research data is made publically available so that other researchers can investigate whether the study results are valid. Any study related data sent outside of Canadian borders may increase 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. However, all study related data that might be transferred outside of Canada will be coded (this means it will not contain your name or personal identifying information) before leaving the study site. By signing this consent form, you are consenting to the transfer of your information to organizations located outside of Canada.

17. What happens if something goes wrong?

By signing this form, you do not give up any of your legal rights and you do not release the study doctor, participating institutions, or anyone else from their legal and professional duties. If you 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 your medical treatment will be paid by your provincial medical plan.

18. What will the study cost me?

All research-related medical care and treatment and any related tests that you will receive during your participation in this study will be provided at no cost to you. There will be no additional cost for you to participate and you will not receive any payment for participation.

19. Who do I contact if I have questions about the study during my participation?

If you have any questions or desire further information about this study before or during participation, you can contact Dr Simon Whyte at (604) 875-2711.

20. Who do I contact if I have any questions or concerns about my rights as a participant?

If you have any concerns or complaints about your rights as a research participant and/or your experiences while participating in this study, 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). Please reference the study number H19-00188 when contacting the Complaint Line so the staff can better assist you.

21. After the study is finished

Study results and publication(s) may be available at the conclusion of the study; however you will not be given individual results regarding the analyses undertaken in this research project. If you are interested, you will be able to obtain general information on the progress of this research project by visiting our official website at http://part.bcchr.ca.

Participant Consent

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My signature on this consent form means:

- I have read and understood the information in this consent form.
- I have had enough time to think about the information provided.
- I have been able to ask for advice if needed.
- I have been able to ask questions and have had satisfactory responses to my questions.
- I understand that all personally identifying information collected will be kept confidential.
- I understand that de-identified data may be shared or made publicly available and that the results will only be used for scientific purposes.
- I understand that I will not receive individual genetic results except for actionable incidental findings.
- I understand that my participation in this study is voluntary.
- I understand that I am completely free at any time to refuse to participate or to withdraw from this study at any time, and that this will not change the quality of care that I receive.
- I authorize access to my health records as described in this consent form.
- I understand that I am not waiving any of my legal rights as a result of signing this consent form.
- I understand that there is no guarantee that this study will provide any benefits to me.

The parent(s)/guardian(s)/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.

I will receive a signed copy of this consent form for my own records.

I consent to participate in this study.

Participant's Name			
Participant/Parent/Guardian Signature	Printed Name		Date
Signature of person obtaining consent	Name of person obtaining consent	Study Role	Date