Informed Consent Form for Participation in a Research Study

**Study Title**: *Evaluation of a Novel Diagnostic Test for Calcium Release Deficiency Syndrome*

**Principal Investigator:** Dr. Habib Khan

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**Sponsor/Funder(s):** Population Health Research Institute

INTRODUCTION

You are being invited to participate in a research study. You are invited to participate in this study because

As a Substitute Decision Maker, you are being asked to provide informed consent on behalf of a person who is unable to provide consent for him/herself. If the participant gains the capacity to consent for him/herself, your consent for them will end. Throughout this form “you” means the person you are representing.

1) You have a diagnosis of Calcium Release Deficiency Syndrome (CRDS) in the presence of a genetic change that causes an underactive RyR2 protein (a protein in the heart). OR

2) You have a diagnosis of Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT). OR

3) You had a cardiac arrest that remains unexplained. OR

4) Your doctor has recommended that you undergo an electrical heart study for a benign electrical heart rhythm called Supraventricular Tachycardia (SVT).

This consent form provides you with information to help you make an informed choice. Please read this document carefully and ask any questions you may have. All your questions should be answered to your satisfaction before you decide whether to participate in this research study.

Please take your time in making your decision. You may find it helpful to discuss it with your friends and family.

Taking part in this study is voluntary. You have the option to not participate at all or you may choose to leave the study at any time. Whatever you choose, it will not affect the usual medical care that you receive outside the study*.*

IS THERE A CONFLICT OF INTEREST?

There are no conflicts of interest to declare related to this study.

If you would like additional information about the funding for this study, or about the role of the doctor in charge of this study, please speak to the study staff or the Patient Relations Office at LHSC at (519) 685-8500 ext. 52036.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to investigate the possibility that pacing the heart and observing the electrical response on ECG can be used to make a diagnosis of CRDS. The rationale for also including CPVT, SVT, and unexplained cardiac arrest patients is to clarify if the electrical response to heart pacing is a specific finding for CRDS patients. We anticipate that CRDS patients will have a temporary, brief prolongation of their QT-interval (a measurement made on the ECG) following the heart pacing, whereas this will not be observed for the CPVT, SVT, and unexplained cardiac arrest patients.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

It is anticipated that about 500 participants will be enrolled in this research study, including 20-50 CRDS patients, 20-50 CPVT patients, 50-400 unexplained cardiac arrest patients, and 100-500 SVT controls. People will take part in this study, from research sites located in several cardiology centres across North America, Europe, Asia, and Australia.

This study should take 5 years to complete and the results of this study may be published as a scientific paper to help other doctors help their patients. The results should be known in about 5 years' time.

WHAT WILL HAPPEN DURING THIS STUDY?

This study is designed to perform 2-4 brief periods of heart pacing (each lasting 5-10 seconds) that are routinely performed as part of a standard EP study or device interrogation and are comparable to those performed on standard clinical ICD testing during routine follow up visits. The first period of heart pacing involves pacing the ventricles (the bottom heart chambers) for 10 beats at 120 beats per minute. The second period of heart pacing involves pacing the ventricles for 10 beats at 150 beats per minute. The third and fourth periods of heart pacing involve repeating the pacing in the atria (the top heart chambers) if an atrial pacing wire is present. We will record the electrical behavior of the heart after the pacing is completed using a 12-lead ECG that runs continuously while the heart pacing is performed.

The study will also collect relevant clinical data for research purposes, including age, sex, race, list of current medications, family history of heart disease, and findings from clinical testing, including ECGs and echocardiograms. The researchers will collect information about you from the hospital’s health records and enter this information into an electronic database. The data will be securely stored, and will be maintained by the security measures at PHRI. The database can only be accessed by people who are involved in research. Please talk to the research team if there is information that you do not feel comfortable sharing.

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HOW LONG WILL PARTICIPANTS BE IN THE STUDY?

Your participation on this study will involve approximately one or two visits.

CAN PARTICIPANTS CHOOSE TO LEAVE THE STUDY?

You can choose to end your participation in this research (called withdrawal) at any time without having to provide a reason. If you choose to withdraw from the study, you are encouraged to contact the research team.

You may withdraw your permission to use information that was collected about you for this study at any time by letting the research team know. However, this would also mean that you withdraw from the study.

If you choose to enter the study and then decide to withdraw at a later time, you have the right to request the withdrawal of your information collected during the study. This request will be respected to the extent possible. Please note however that there may be exceptions where the data will not be able to be withdrawn. For example, where the data has been shared with another research institution or where the data has been merged with other data. If you would like to request the withdrawal of your data please let your study doctor know. Information that was recorded before you withdrew will be used by the researchers for the purposes of the study, but no information will be collected after you withdraw your permission.

CAN PARTICIPATION IN THIS STUDY END EARLY?

Your participation in the study may be stopped early, and without your consent, for reasons such as:

* New information shows that the research is no longer in your best interest
* The research team decides to stop the study
* The research ethics board withdraws permission for this study to continue

If you are removed from this study, the research team will discuss the reasons with you.

WHAT ARE THE RISKS OR HARMS OF PARTICIPATING IN THIS STUDY?

For the CRDS, CPVT, and unexplained cardiac arrest patients: The pacing maneuvers included in the study protocol are modifications of pacing that are routinely performed as part of your standard clinical care when your ICD is checked. The potential and very unlikely risk from heart pacing is the possibility to trigger a fast heart rhythm that could trigger a dangerous fast heart rate leading to fainting or a shock from your ICD. As the heart pacing is for very brief periods and the heart rates are not very fast, it is anticipated that the likelihood of this occurring is extremely low (the clinical experts leading this study believe the likelihood is less than 1 in 1,000). In the unlikely event that a dangerous fast heart rate developed, the ICD would deliver a shock in order to restore sinus rhythm.

For SVT controls: The heart pacing included in the study protocol are slight modifications of heart pacing performed as part of the EP studies you are scheduled to undergo. As such, they are not anticipated to introduce any additional risk to you should you choose to participate. Given how brief they are (4 maneuvers lasting 5-10 seconds each), they are also not anticipated to increase the duration of your invasive EP study.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY

For CRDS patients: The anticipated benefit of this study for you and your family members is the potential development of a test that will correctly diagnose this condition. This may benefit both you and your family members because a correct diagnosis will enable optimal medical care and effective screening of your family members.

For CPVT patients: The anticipated benefit of this study for you and your family members is the development of a diagnostic test that may help distinguish CRDS from CPVT. As both conditions develop due to genetic changes in RyR2, a test that helps clarify if a patient has CRDS rather than CPVT will help ensure that both groups of patients receive appropriate treatment.

For Unexplained Cardiac Arrest patients: The anticipated benefit of this study is to potentially clarify if you have a diagnosis of CRDS. In the event that you have CRDS, this may lead to changes in the medical treatment you receive and lead to screening and identification of potentially vulnerable family members.

For SVT patients: Participation in this study may be of no direct benefit to you.

HOW WILL PARTICIPANT INFORMATION BE KEPT CONFIDENTIAL?

If you decide to participate in this study, the research team will only collect the information they need for this study.

Records identifying you at this centre will be kept confidential and, to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document.

Authorized representatives of the following organizations may look at your original (identifiable) medical records at the site where these records are held, to check that the information collected for the study is correct and follows proper laws and guidelines.

* Population Health Research Institute, the Sponsor of this study
* The research ethics board who oversees the ethical conduct of this study in Ontario
* This institution and affiliated sites, to oversee the conduct of research at this location

The Quality Assurance and Education Officers from Lawson Health Research Institute (Lawson) may audit this research study for quality assurance purposes.

Information that is collected about you for the study (called study data) may also be sent to the organizations listed above. Representatives of Clinical Trials Ontario, a not-for-profit organization, may see study data that is sent to the research ethics board for this study. Your name, address, email, or other information that may directly identify you will not be used. The records received by these organizations may contain your *participant code, sex, and age*. This research study is also collecting information on ethnicity because this characteristic may influence your test results. Providing information on your ethnic origin is voluntary.

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during this study will be published as a scientific paper to help other doctors help their patients. However, your privacy will be protected and you will never be identified by name or by a description of you.

Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated.

A copy of the consent form that you sign to enter the study may be included in your health record/hospital chart.

Other future research

Participants with CRDS may also be asked to participate in another study called the CRDS Registry, which aims to collect further data on this very rare disease. Those who consent to participate in the CRDS Registry, will have data from this study (Diagnose CRDS) shared in the registry's study database. If you do not consent to participate in the registry, your data will not be shared.

WHAT IS THE COST TO PARTICIPANTS?

Participating in this study will not involve any additional costs to you or your private health care insurance.

ARE STUDY PARTICIPANTS PAID TO BE IN THIS STUDY?

You will not be paid for taking part in this study.

WHAT ARE THE RIGHTS OF PARTICIPANTS IN A RESEARCH STUDY?

You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study.

You have the right to be informed of the results of this study once the entire study is complete.

If you wish to be contacted about the study results please keep your contact information up to date so that the study staff can contact you when the study results are written.

In the event that a discovery may be found relating to your heart health and that of your family,

the investigators are dedicated to informing you and your health caregiver so that appropriate

information and care can be delivered to you.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form, you do not give up any of your legal rights against the researcher/study doctor, sponsor or involved institutions for compensation, nor does this form relieve the researcher/study doctor, sponsor or their agents of their legal and professional responsibilities.

You will be given a copy of this signed and dated consent form prior to participating in this study.

WHOM DO PARTICIPANTS CONTACT FOR QUESTIONS?

If you have questions about taking part in this study, or if you suffer a research-related injury, you can talk to the research team, or the person who is in charge of the study at this institution. That person is:

Dr. Habib Khan, Investigator:  Tel.: 519-663-3746

For more information about your rights as a study participant contact, you may contact Patient Relations Office at LHSC at (519) 685-8500 ext. 52036.

This study has been reviewed by the Hamilton Integrated Research Ethics Board (HiREB). The HiREB is responsible for ensuring that participants are informed of the risks associated with the research, and that participants are free to decide if participation is right for them. If you have any questions about your rights as a research participant, please call the Office of the Chair, Hamilton Integrated Research Ethics Board at 905.521.2100 x 24013.

**Evaluation of a Novel Diagnostic Test for Calcium Release Deficiency Syndrome**

**Informed Consent Signature Page**

SIGNATURES

* All of my questions have been answered,
* I understand the information within this informed consent form,
* I allow access to medical records and related personal health information as explained in this consent form,
* I do not give up any of my legal rights by signing this consent form,
* I understand that my family doctor/health care provider may be informed of study participation
* I agree, or agree to allow the person I am responsible for, to take part in this study.

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Signature of Participant/ PRINTED NAME Date

Substitute Decision-Maker

If consent is provided \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

by Substitute Decision Maker: PRINTED NAME of Participant

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Signature of Person Conducting PRINTED NAME & ROLE Date

the Consent Discussion

The following attestation must be provided if the participant is unable to read or requires an oral translation:

**Evaluation of a Novel Diagnostic Test for Calcium Release Deficiency Syndrome**

**Informed Consent Signature Page Continued**

**If the participant is assisted during the consent process, please check the relevant box and complete the signature space below:**

[ ]  The person signing below acted as an interpreter, and attests that the study as set out in the consent form was accurately sight translated and/or interpreted, and that interpretation was provided on questions, responses and additional discussion arising from this process.

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PRINT NAME of Interpreter Signature Date

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Language

[ ]  The consent form was read to the participant. The person signing below attests that the study as set out in this form was accurately explained to the participant, and any questions have been answered.

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PRINT NAME Signature Date

of witness

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Relationship to Participant