

Biobank Protocol

Name of the Bank: International Pediatric Brugada Registry – Optional Substudy on Biological Samples (Saliva, blood and/or oral mucosa)

Person in Charge of the Bank: CECILIA GONZALEZ-CORCIA, MD, Investigator, Metabolic and Cardiovascular Health, Sainte-Justine University Hospital Center (SJUHC), is the Director of the Bank.

Version Date : July 01st,2026

1. Applicable Principles and Standards

This Governance Framework acknowledges the importance and primacy of the participants' rights.

This Bank is managed in agreement with generally recognized and applicable principles, including autonomy, dignity, benevolence, privacy and justice, while promoting scientific progress in Pediatric Brugada.

The Bank is governed in accordance with this Governance Framework, CHU Sainte-Justine's policies and procedures, the Research Information and Consent Form signed by the participants and/or their legal representative, and applicable laws and standards in Québec and Canada.

2. Context and Objectives

2.1. Objectives

The purpose of this bioabank is to expand the Pediatric Brugada Registry (PBR) protocol to include optional biospecimen sub-studies in severely affected pediatric patients. The collection of saliva, blood and/or oral mucosa samples will allow genomic, molecular, and biomarker investigations to complement the clinical and ECG dataset both in the child and the parent. These sub-studies will support ongoing national and international collaborations and help refine genotype–phenotype correlations and precision medicine approaches in Brugada syndrome.

The Bank cannot be used for purposes other than scientific research.

2.2. Source of Funding

The Bank is funded by local Researcher Funds, SJUHC and Startup fund of the Université de Montréal.

2.3. Economic Aspect

The Bank is a non-profit entity. The Bank, including its content, cannot be sold.

3. Governance Structure

3.1. Director

The Director is Cecilia Gonzalez-Corcia, MD, Investigator, and has research privileges at CHU Sainte-Justine, Metabolic and Cardiovascular Health.

Director has acquired an expertise in the field of Brugada syndrome and built inter-institutional network. She supervises and manages the Bank. Director does not own the biological samples stored in the Bank. Director acts as a trustee. Director notably ensures the efficient progress of the Bank's activities and confidentiality of the biological samples stored.

Director may recruit personnel as needed, and purchase the equipment necessary to safely carry out the Bank's activities. Director is liable for the actions of the team members.

Director also ensures compliance with applicable administrative, legal and ethical standards.

3.2. Access Committee

Access Committee is comprised of:

- Cecilia Gonzalez-Corcia, MD
- Gregor Andelfinger, MD
- Fabiola Breault, B.Sc.inf. Clinical research coordinator
- Frédérique Provencher, B.Sc.inf. Clinical research coordinator
- Rocio Gutierrez Rojas, M.Sc, Research project manager

Access Committee assesses all requests to access for research purposes, including that each request aligns with the Bank's objectives, and determines if access can be granted.

3.3. Infrastructures

CHU Sainte-Justine's infrastructures are used to manage and conduct the Bank's activities.

4. Participants

The Bank aims to store, with participants' and/or their legal representative's consent, data and biological samples collected from participants taking part in the research project International Pediatric Brugada Syndrome Registry 2023-5047.

Table 1 : Inclusion Criteria for Participating in the Bank

Inclusion Criteria
• Must be enrolled in the registry (International Pediatric Brugada Syndrome Registry 2023-5047) • And meeting the definition of <i>severely affected</i> (life-threatening arrhythmia, aborted sudden cardiac death, or early severe electrical disease) • Or being the parent of a severely affected child

4.1. Number of Participants Expected

Between 30 and 40 families.

Recruitment

Recruitment is conducted through a self-enrolment framework. Participants already enrolled in the International Pediatric Brugada Syndrome Registry (2023-5047) who meet the eligibility criteria are identified by the CHUSJ coordinating team. They are contacted by email to receive detailed study information and are invited to complete online consent via a secure platform prior to any participation. A mandatory virtual meeting with the research team is scheduled before consent validation to verify identity, assess capacity to consent (for adults), confirm understanding of the study, and answer any questions. Consent will only be validated if adequate understanding can be confirmed in French, English, or Spanish.

4.2. Consent

Participants', and/or their legal representatives', electronic consent will be obtained before any participation, and before collecting and storing their biological samples in the Bank. Recruitment is managed by the CHUSJ coordinating team using the existing self-enrolment framework. Eligible participants will be contacted to receive detailed study information and online consent.

4.3. Risks and Benefits

4.3.1. Risks

If the participant chooses the option of providing a blood sample, one of the known risks associated with a blood draw is that it may be uncomfortable and can cause bruising, dizziness, fainting, or, more rarely, an infection. There are no other risks nor inconveniences in participating in this Bank other than a potential breach of confidentiality. Measures are taken to limit this risk.

4.3.2. Benefits

Participants will not directly benefit from taking part in the Bank. Results will contribute to the advancement of scientific knowledge and may help improve patient care in the future.

4.4. Recontact at Adulthood

Where a participant is a minor at time of consent, reasonable efforts will be made to contact the participant once he or she reaches adulthood, provided that up-to-date contact information is available, to inform him or her of his or her participation in the Bank and right to withdraw. No intrusive tracing will be undertaken if contact information is no longer available.

4.5. Right to Withdraw

Participants can withdraw from the Bank at any time and without prejudice. To do so, they can contact Director. A participant's decision to withdraw from the Bank will have no impact on the quality of care and services to which the participant is otherwise entitled or on the participant's relationship with the teams.

Where a participant (and/or through legal representative) withdraws from the Bank, participant's biological samples will no longer be available for research purposes. Participant's biological samples will be removed from the Bank and destroyed according to CHU Sainte-Justine's applicable standards, except for those already shared, accessed, used and/or analysed, which cannot be destroyed.

4.6. Access and Rectification

Participants (and/or legal representative) have the right to consult and verify their data gathered, and to have it rectified if needed.

5. Biological Samples

Director ensures that all biological samples collected and stored is relevant and required to meet the Bank's scientific objectives.

5.1. Biological Samples

Biological samples collected and stored are the following:

- a) Saliva (DNA and biological marker)
- b) Blood (DNA extraction, biological marker and plasma preparation)
- c) Oral mucosa (transcript)

The samples will be collected as part of the research study. The amount of blood drawn will depend on the patient's weight to ensure that the allowable volume is respected, which ranges between 5 and 10 mL. Blood samples may be collected at the participant's usual clinical center, solely for sample collection purposes, and not as part of research site activities.

Regarding saliva, a sample of approximately 2 mL is required. Saliva samples may be collected at home or at the centre where the participant receives follow-up care.

Data collected from participants as part of the International Pediatric Brugada Syndrome Registry (2023-5047), to which participants have already consented, may be linked to biological samples stored in the Bank for the purposes of research analyses (e.g. genotype–phenotype correlations, biomarker studies).

6. Access

6.1. Administrative Level Access

Director has access to the Bank for administrative purposes (e.g. data management, providing access and overseeing security measures).

Research team members who have access to the Bank for administrative purposes can have different roles such as researcher, research auxiliary, student and research intern (supervised by Director).

Research team members, including Director and members of the Access Committee, must agree, in writing, maintain the confidentiality of the biological samples. They must complete relevant training as required by CHU Sainte-Justine.

Research team members, including Director and members of the Access Committee, are also subject to the terms and conditions set forth in this Governance Framework in order to access, for research purposes, to the biological samples (see in particular, sub-section 6.2. [Research Access]).

6.2. Research Access

Researchers, including Director and members of the Access Committee, may request access to use, for research purposes, the biological samples.

6.2.1. Request to Access Process

Any researcher wishing to access and use the biological samples must first submit a request to the Access Committee.

The Access Committee decides according to the following criteria:

- i) Research project is related to Brugada, and is adequately governed by a research protocol.
- ii) Intended use of the biological samples complies with the Bank's objectives, this Governance Framework and the participants' (and/or legal representatives') consent.
- iii) Research project is approved by a competent Research Ethics Board of Québec, and an approval letter is available.
- iv) Research project is scientifically relevant.

The researcher is informed, in writing, of Access Committee's decision. Director records the Access Committee's decision and keeps a copy of the ethics approval letter for the research project for which access is requested.

6.2.2. Access Granting Process

Once a researcher has received approval from Access Committee ("**Researcher-User**"), Researcher-User must, in particular:

- i) Comply with CHU Sainte-Justine's Confidentiality Agreement and/or a signed Data Transfer Agreement, as applicable;
- ii) Commit to:
 - a. Maintain confidentiality;
 - b. Conduct research responsibly and in accordance with recognized applicable ethical standards;
 - c. Use biological samples for the sole purpose of the research for which access is granted and/or in accordance with signed agreement(s);
 - d. Not attempt to identify the participants;
 - e. Disseminate, publish or communicate any research result in a form that prevents participant identification (e.g. at conferences or publications).

7. Return of Results

7.1. General Results

General results may be disseminated, published or communicated only in a form that prevents participant identification.

General results will be dealt with in articles, presentations, posters or general discussions.

7.2. Individual results

Individual findings may be communicated to participants (or their representatives). The sharing of results pertains exclusively to genes associated with inherited arrhythmias. No systematic screening for unrelated

incidental findings will be performed. Only clinically significant and actionable results directly related to arrhythmic risk may be communicated, within an appropriate clinical framework.

8. Commercialisation

New commercial products can be developed from biological samples and generate profits. However, participants will not be entitled to any financial gain thereof.

9. Confidentiality and Security Measures

Biological samples will be stored securely. To this end, security measures described below will be taken.

9.1. Storage Place and Process

The Bank is located at CHU Sainte-Justine, in the department of Cardiology.

- Biological samples: they will be stored in the Sainte-Justine biobank for saliva, blood and oral mucoasa collections. The Sainte-Justine Biobank (CRA-CHUSJ) is located at 5750 Hudson Road, Room 3967 in Montreal. The samples will be sent to Génome Québec for more advanced sequencing analyses. Génome Québec is located within the Sainte-Justine facility.

9.2. Period

No foreseen end date for the Bank's activities. Biological samples will be stored for as long as Director can ensure its proper management, notably that administrative, ethical and scientific standards are followed. Change of Director to pursue the Bank's activities can only occur with prior approval from CHU Sainte-Justine's Research Ethics Board. The Bank will be subject to periodic review by the CHUSJ Research Ethics Board.

9.3. Coding

Biological samples are coded. Each participant is assigned a unique code before storing his or her biological samples. The key to the code is safely stored in a separate secure file in the trust of Director. When biological samples are transmitted to a Researcher-User, no directly identifiable information is shared. A new code is then assigned (double-coding).

9.4. Logbooks

Director maintains and updates a logbook of research team members who are given administrative access to the Bank, specifying their names, titles and type of access.

Director also maintains and updates a logbook of access requests for research purposes, specifying notably the name of the researcher requesting access, project title, Access Committee's decision and decision date, name of Research Ethics Board that gave ethics approval and approval date.

9.5. Destruction

Where applicable, biological samples stored in the Bank is destroyed in accordance with CHU Sainte-Justine's applicable standards.

9.6. Incident or Accident

In the event of a breach of confidentiality, including unauthorized access or loss of biological samples, Director will promptly notify CHU Sainte-Justine's Research Ethics Board in order to agree on measures to be taken in accordance with CHU Sainte-Justine's applicable standards

10. Ethics Approval and Oversight

This Governance Framework is approved by CHU Sainte-Justine's Research Ethics Board.

CHU Sainte-Justine's Research Ethics Board ensures the ongoing ethics oversight of the Bank's activities. Director must, annually, submit a report describing the Bank's progress, including a copy of the logbook of access requests for research purposes, to CHU Sainte-Justine's Research Ethics Board.

11. Closure

If the Bank's activities are discontinued, biological samples stored in the Bank will be destroyed, except those already shared, accessed, used and/or analysed, which cannot be destroyed. All logbooks, records, decisions and other documents related to the Bank's activities will be safeguarded in accordance with CHU Sainte-Justine's applicable standards.

12. Contact

Table 2 provides contact information for any question, information or request to access.

Table 2 : Contact

Director :	CECILIA GONZALEZ-CORCIA, MD, Investigator, Metabolic and Cardiovascular Health, Sainte-Justine University Hospital Center (SJUHC), is the Director of the Bank.
Contact for participants :	514-345-4931 ext. 5410, cecilia.gonzalez-corcia.med@ssss.gouv.qc.ca Research team: 514-345-4931 ext. 5407

APPENDIX

Pediatric Brugada Registry

An International Initiative for Risk Assessment and Management

New section: Optional Substudy on Biological Samples (Saliva, blood)

1.1 Purpose

The purpose of this amendment is to expand the Pediatric Brugada Registry (PBR) protocol to include optional biospecimen sub-studies in severely affected pediatric patients and his parents. The collection of saliva, blood and/or oral mucosa samples will allow genomic, molecular, and biomarker investigations to complement the clinical and ECG dataset. These sub-studies will support ongoing national and international collaborations and help refine genotype–phenotype correlations and precision medicine approaches in Brugada syndrome.

1.2 Design

Optional sub-studies are added:

a. Saliva DNA and/or Oral mucosa transcript Sub-study (primary option for self-enrolled and international participants)

- The CHU Sainte-Justine (CHUSJ) Biobank will prepare and mail saliva self-collection kits containing preservative tubes or coverslip prepaid return mailers.
- Participants and their parents will self-collect saliva or oral mucosa sampling themselves by following the provided instructions and will return the kits by post.
- DNA and/or transcript will be extracted and stored for future research on Brugada syndrome and related arrhythmias.

b. Blood Sub-study (priority for sites with capacity)

- Peripheral blood samples will be drawn by qualified personnel at the local clinical site or at CHUSJ for the child and the parent.
- Samples will be shipped to CHUSJ Biobank for DNA extraction and plasma preparation.
- Plasma aliquots will be stored at –80 °C for biomarker and autoantibody analyses.

Saliva, blood or oral mucosa collections are optional and do not affect a participant’s eligibility or participation in the main registry.

Role of International Collaborating Centers: International collaborators are not research sites for this substudy.

International collaborators have been informed that this optional biospecimen substudy is conducted as a strictly monocentric initiative under CHUSJ REB oversight. Because of the regulatory complexity associated with multi-jurisdictional biological sample governance, this substudy does not involve international centers as research sites. Participation of their patients occurs exclusively through voluntary self-enrollment and direct contact with the CHUSJ research team. Collaborating centers

remain free to decide whether or not to share information about this optional substudy with their patients. Their decision has no impact on their participation in the main Pediatric Brugada Registry. This approach preserves the integrity of international collaborations while ensuring compliance with local ethical and regulatory requirements.

The role of collaborating centers is limited to:

- Informing potentially eligible families about the existence of the optional substudy.
- Directing interested families to contact the CHUSJ research team directly.

They do not:

- Obtain consent
- Collect samples for research purposes
- Transfer identifiable data
- Store or analyze biological samples
- Act as co-investigators in this substudy

1.3 Eligibility and Recruitment

Participants already enrolled in the registry and meeting the definition of *severely affected* (life-threatening arrhythmia, aborted sudden cardiac death, or early severe electrical disease) are eligible. Parents are also asked to provide a saliva, blood or oral mucosa sample. Recruitment is managed by the CHUSJ coordinating team using the existing self-enrolment framework. Eligible participants will be contacted to receive detailed study information and online consent.

This optional biospecimen substudy is strictly monocentric and conducted exclusively under the authority and REB approval of CHU Sainte-Justine (CHUSJ). No international center is considered a research site for this substudy. No research procedures are conducted outside CHUSJ. No new clinical data will be extracted from external medical records for the purpose of this substudy.

International centers may inform eligible families about the existence of the substudy, but all enrollment, consent, and study-related procedures are conducted directly between participants and the CHUSJ research team.

For participants followed in Quebec, recruitment may occur either during routine clinical follow-up at CHUSJ or through voluntary self-enrollment.

1.4 Consent Procedure

Consent and assent are obtained electronically via the online registry portal.

Participants (or parents/guardians) are presented with additional checkboxes to indicate agreement for:

- Saliva DNA and biological marker collection
- Blood DNA extraction, biological marker and plasma collection

- Oral mucosa (transcript)
- Future re-contact for related studies

Assent is obtained from children old enough to understand as appropriate. Consent and assent language specifies optional participation and the right to withdraw at any time.

Before electronic consent is finalized, a mandatory virtual meeting (via Microsoft Teams or equivalent secure platform) will be conducted between a CHUSJ research team member and the participant or legal guardian.

During this meeting, the research team member will:

- Verify participant identity
- Assess capacity to consent (for adult participants)
- Confirm understanding of study objectives, procedures, risks, and voluntary nature
- Provide opportunity for questions

Consent will only proceed if adequate comprehension can be confirmed in English, French, or Spanish.

If adequate understanding cannot be ensured, participation in the biospecimen substudy will not proceed.

Participants experiencing logistical difficulties (e.g., sample collection or return shipping) may contact the CHUSJ research team for additional guidance via virtual meeting or secure email communication.

Collection of Postal Address: The participant's postal address will be collected during the mandatory virtual consent meeting solely for the purpose of shipping the collection kit. The address will be recorded in a secure project log accessible only to authorized CHUSJ research personnel. Postal information will be stored separately from coded research data. When feasible, postal address information will be deleted after confirmation of sample receipt.

1.5 Sample Handling and Storage

All biospecimen activities are conducted in collaboration with the CHUSJ Biobank under protocol #2023-5047. The samples will be sent to Génome Québec for more advanced sequencing analyses. Génome Québec is located within the Sainte-Justine facility.

- Samples are labeled using coded identifiers corresponding to registry IDs.
- Chain of custody and temperature logs are maintained by the Biobank.
- DNA and plasma are stored at -80 °C in access-controlled freezers.
- The link between identifiers and participant identities is held securely by the principal investigator.

1.6 Shipping and International Participants

The CHUSJ Biobank will prepare international kits compliant with postal and biosafety regulations. Saliva collection and oral mucosa is the preferred method for international participants. Blood collection is restricted to sites with logistical capacity.

All biospecimen shipment procedures are developed in accordance with applicable national and international regulations governing the transport of biological substances.

The CHUSJ Biobank and institutional biosafety team have been consulted to ensure compliance with relevant biosafety, packaging, and shipping standards.

All shipments will comply with IATA and Transport Canada regulations for Biological Substance Category B (UN3373).

Participants are not responsible for verifying export regulations. The CHUSJ research team will provide standardized shipping materials and instructions compliant with international regulations. Participants are only required to return the pre-packaged kit using the provided instructions.

All samples will be classified and shipped as Biological Substance Category B (UN3373), in compliance with IATA Packing Instruction 650.

No declaration regarding infectious status beyond regulatory classification will be made.

1.7 Risks and Benefits

Risks are minimal: mild discomfort or bruising for blood draws; none for saliva collection. The main study risk remains confidentiality breach, mitigated by existing REDCap and biobank safeguards (encryption, restricted access, coded samples, and audit logs).

To assure patients' confidentiality, all electronic data are stored within secure CHUSJ institutional servers protected by encryption, role-based access control, and audit trails.

There is no direct personal benefit to participants. The collected data will contribute to improving understanding and management of severe pediatric Brugada syndrome.

1.8 Withdrawal and Destruction

Participants may withdraw at any time without affecting ongoing participation in the registry. Upon withdrawal, any remaining samples will be destroyed upon request. Data or results already derived from the samples may be retained unless the participant explicitly requests their deletion.

1.9 Data Linkage and Governance

Each biospecimen is assigned a code linked

The key linking code to identity is stored separately and securely under the principal investigator's

custody.

Future use of biospecimens will require REB approval and authorization by both the Pediatric Brugada Databank Access Committee and the CHUSJ Biobank Access Committee.

2.0 International Data Transfer and Legal Considerations.

International participants provide explicit consent for the transfer of their biological samples and associated coded data to CHU Sainte-Justine in Canada. No directly identifiable information is transferred outside CHUSJ. All data are stored and processed within secure CHUSJ infrastructure in compliance with Quebec and Canadian privacy legislation. Participants are informed that privacy protections applicable in Canada may differ from those in their country of residence (including the European Union General Data Protection Regulation, GDPR). Data processing is based on explicit informed consent.

Confidentiality and Coding Procedures: Each biospecimen is assigned a coded identifier. The coded identifiers is stored exclusively at CHU Sainte-Justine under the custody of the Principal Investigator.

Samples are shipped using coded identifiers only, without direct personal identifiers. Access to the code key is restricted to authorized CHUSJ personnel and protected within secure institutional infrastructure.

2.1 Management of Genetic Findings

Only clinically actionable findings directly relevant to inherited arrhythmia risk may be considered for return to participants. Return of results, when applicable, will occur within an appropriate clinical framework, including referral to specialized cardiogenetic or genetic counseling services. Participants are informed that genetic interpretation standards and return-of-results policies are governed by Canadian regulations and institutional policies.