Congenital Heart Surgeons' Society (CHSS) Biobank Genomic Registry

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I. Project Team:

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II. Background:

The genomics of congenital heart disease is an emerging science with enormous potential. Yet individual centers of excellence in congenital heart disease do not have either the critical mass of tissue for study, or the extensive resources to undertake these expensive research efforts. Therefore the CHSS conceived a mechanism to foster multi-center genomic studies by creating a central registry database, maintained by the CHSS Data Center, to inform potential researchers of what tissue specimens are available within our various members' Biobanks for study.

The primary purpose of the CHSS Biobank Genomic Registry is to provide a searchable merged list of all specimens from congenital heart disease patients that are contained within each participating institution's Biobank. The Registry database will identify how many samples for a specified diagnosis have been collected and may be available for collaborative use. Its major goal is to encourage collaboration among researchers and reduce duplication of effort. The CHSS Biobank Genomic Registry is therefore a Registry of Registries. It is not a Patient Registry as defined by the Agency for Healthcare Research and Quality. [1]

The CHSS Biobank Genomic Registry will contain the institutional names and very limited, coded personal health information (PHI) (i.e., specific diagnosis). The coded PHI is held in the registry in a well-protected format. No PHI is available to the registry users. The registry data are accessible to the registry users only in aggregate, non-identifying format. Specimens within each participating member's Biobank will remain within that Biobank (i.e., no samples will be transferred to or managed by the CHSS Data Center). By searching the CHSS Registry for the total number of specimens available, a researcher could easily determine whether a critical mass of tissue or fluid is available. The member could then determine the interest of a proposed study and if sufficient, recruit a working group to develop a research proposal. Such a research proposal would require an Institutional Review Board (IRB)/Research Ethics Board (REB) review and approval before initiating the study. Therefore the CHSS registry of registries is a mechanism to help initiate genomic research among participating institutions.

III. Objective:

The CHSS Biobank Genomic Registry is a service to CHSS member institutions. Its objective is to provide an inventory list of diagnosis-specific specimens that are stored within the Biobanks of participating CHSS institutions. To date, there are 8 CHSS institutional Biobanks that have expressed interest in participating. Among these Biobanks there are > 10,000 congenital heart patients who have provided informed consent to store their tissue or fluids in the various Biobanks. Each institutional biobank has its own IRB/REB approval according to its own local requirements. All patient consents will continue to be confined to the individual Biobanks.

The CHSS Registry is not a research study per se. Rather, it is a merged data set consisting exclusively of five data fields (institutional name, primary diagnosis, secondary diagnosis, diagnostic category and CHSS #). The data are accessible to registry users only in aggregate, non-identifying format. The CHSS #s, although held within the registry database, are not accessible to the registry users.

Any research studies arising from the CHSS Biobank Registry will require IRB/REB review and approval within those institutions involved, as appropriate. These studies are beyond the mandate and scope of the CHSS Biobank Registry project itself.

IV. Data Collection and Withdrawal Mechanisms:

Each CHSS institution will participate in the CHSS Registry by agreeing to and securely supplying to the CHSS Data Center, located at The Hospital for Sick Children (SickKids), Toronto, Ontario, Canada, a coded list of specimens held in its Biobank. Some of the initial data sets will be available from feasibility testing. It is important to emphasize that at no point will tissue specimens within any institution be sent to the CHSS Data Center.

The data supplied from each Biobank to the CHSS Data Center includes the institution's name, a primary and secondary diagnosis for each patient who provided the tissue or fluids and that Biobank's unique patient ID code #. (see Figure 1)

The Data Center will create a **diagnostic category** from the institutional diagnoses supplied. The category is necessary to collapse the various institutional diagnostic terms into a consistent format. For example, a defect in the inter-ventricular septum (a VSD) is coded by these 8 institutions in many different text formats, all indicating the same basic diagnostic category of ventricular septal defect.

The Data Center will double code each Biobank's patient ID code # as CHSS #, and only the latter will be held in the registry database. Obtaining the patient ID code # is necessary so that specimens no longer available can be deleted from the registry and to avoid duplication in subsequent data imports. The link between CHSS # and patient ID # will be securely

maintained separately by the CHSS Data Center. The CHSS # and patient ID # will be accessible only to the Project Team, Project Governance Committee and authorized staff of the CHSS Data Center, as needed. Only each individual Biobank will be able to identify its own specific patients. These biobanks will maintain any links to the patient's identity, as per their own institutional requirements. Searching the CHSS Registry will identify in aggregate, non-identifying format, the number of specimens held within each Biobank but not who those patients are.

Methods used to ensure accuracy of classifications and data entry will include quality control checks by the Project Team and appointed CHSS Data Center staff. These data, as outlined in Figure 1 will be entered into a REDCap database. Data queries will be formatted to identify, in aggregate, non-identifying format, the diagnostic categories and within each category, the primary and secondary diagnosis, as supplied by each institution and the number of specified specimens within each Biobank.

Each institution's Biobank has its own individual consent process for obtaining Biobank tissue and accompanying data, and its own governance process for managing its Biobank data, and will only provide coded data for use in the CHSS Biobank Registry in accordance with these processes and institutional requirements. Any and all research studies arising from the CHSS registry will require their own individual IRB/REB review and approval, as appropriate. The CHSS may or may not be involved in these studies.

V. Registry Database, Confidentiality, Security and Data Retention:

The registry will use Research Electronic Data Capture (REDCap), open source research software by Vanderbilt University with over 1,500 active institutional partners in over 90 countries. REDCap is capable of importing from and exporting into various types of data management software such as SAS, SPSS, and Microsoft Office tools like MS Excel. More information about the application can be found at http://project-redcap.org .

Each CHSS institutional Biobank contributor and each CHSS institutional member surgeon will have access to the REDCap CHSS Biobank Registry by centrally assigned password. These individuals (the registry users) will be able to search the data file to identify the number of specimens available by diagnostic category, primary and secondary diagnosis and institution. No other parties will have access to the data, unless required by law. No analyses of data will be derived from the CHSS Biobank Registry per se apart from a simple table or graph of numbers. These reports of aggregate, non-identifying data will be available to the password-protected users and generated by the REDCap system or add-in software, on a read only basis.

Data updates will be done on a regular basis (approximately yearly) by the CHSS Data Center and with the cooperation and agreement of the individual participating Biobank institutions.

The data collected from each Biobank contributor, the data compiled and housed at SickKids and the registry data housed in the REDCap file will be securely retained on an ongoing basis for as long as required and then securely destroyed according to the institutional policy effective at that time.

VI. Research Projects:

Research projects facilitated by the CHSS Registry will be of 2 types.

1. Biobank members may propose genomic studies based upon knowing how many specimens are available and where they are held. These studies may or may not involve the CHSS.

2. Genomic studies that may, in future, include one or more of our (at present 11) CHSS cohort studies will require approval by the CHSS Research Committee. These proposals must follow approved CHSS guidelines for undertaking a research project. [2]

IRB/REB approval must be obtained, as appropriate, prior to study initiation.

VII. Project Team Member Roles, Contracts, Communications and Conflicts of Interest:

The data contained within the CHSS Registry will be controlled by the CHSS Data Center, as the data trustee, under the leadership of the Data Center's Executive Director and Managing Director, with data withdrawal rights given to the institutions contributing Biobank data, as applicable. Except in the case of a disagreement, the Executive Director will have ultimate decision making responsibility for the CHSS Biobank Registry. Any contract requirements for the CHSS Biobank Registry project, such as Data Sharing Agreements, will be facilitated through the SickKids legal services department, as appropriate. In the event that the Executive Director or CHSS Data Center is no longer at SickKids, the data housed at SickKids and managed by the Project Team would then be managed by the Executive Director's appointed successor and/or securely transferred to the new CHSS Data Center, as applicable. The CHSS Project Team members have no conflicts of interest associated with the CHSS Biobank Registry. If any conflicts of interest are identified in the future, these will be communicated to the appropriate individuals, including at SickKids, the institutions contributing Biobank data to the CHSS Biobank Registry, the CHSS institutional member surgeons and the Governance Committee for the CHSS Biobank Registry, in a timely fashion. The Data Center website (www.chsssdc.org) is used to disseminate information to member institutions.

VIII. Funding, Fees and Commercialization:

The CHSS Biobank Registry is not commercially funded. It is supported by CHSS surgeon members by an annual contribution from each CHSS institution to the Data Center, by the

Gruber lab at the University of Iowa and also through SickKids' support of the CHSS Data Center. There will be no user fees charged for the CHSS Biobank Registry. Although it is possible that future studies arising from the CHSS Biobank Registry may include commercial research, the CHSS Biobank Registry itself is a non-profit, non-commercial venture.

IX. Governance Structure:

A Project Governance Committee, including the Project Lead as Committee Chair, and the Project Team members will be established for the CHSS Biobank Registry to ensure there is oversight for the future uses of the CHSS Biobank Registry data. The appointment and appointment term of additional committee members, which may include some public/participant advisory role, will be determined by the core Project Governance Committee members in consultation with the CHSS Research Committee. Project Governance Committee members will attend regularly scheduled meetings (approximately quarterly) and review documents or discuss issues on an ad-hoc basis. Any disagreements will be handled and resolved through the Project Governance Committee. CHSS Biobank Registry general progress updates (e.g., number of participating Biobank contributors, number of samples available) will be provided to the Project Governance Committee, as well as to the institutional Biobank contributors and CHSS member surgeons on a regular basis.

X. References:

1. A User's Guide, Third Edition, Volume 1, Agency for Healthcare Research and Quality, AHRQ Publication No. 13(14)-EHC111, April 2014. Definition of a patient registry: An organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes.

2. Congenital Heart Surgeons' Society Research Policies 2015 (www.CHSS.org)

XI. Legend:

Figure 1. Each institutional Biobank (A, B, C, & D in Figure 1) provides to the CHSS Data Center the institution's name, patient ID code # and primary and secondary diagnosis for that patient. Consent and tissue specimens remain within the individual Biobanks.

The Data Center will create a unique CHSS # to double code each Biobank's patient ID code #. Only the CHSS # will be held in the registry database. Obtaining the patient ID code # is necessary so that specimens no longer available can be deleted from the registry and to avoid duplication in subsequent data imports. The link between CHSS # and patient ID # will be securely maintained separately by the CHSS Data Center. The CHSS # and the patient ID # will be accessible only to the Project Team, Project Governance Committee and authorized staff of the CHSS Data Center, as needed. The CHSS #s, although contained in the registry database, will not be accessible to the registry users. Searching the CHSS Registry will identify the number of specimens held within each Biobank in aggregate, non-identifying format, but not who those patients are.

The Data Center will create a **diagnostic category** from the institutional diagnoses supplied in order to collapse the various institutional diagnostic terms to a consistent format.

Figure 1. Schema of CHSS Biobank Registry