APPROUVÉ – CÉR CHUM

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BIOBANQUE QUÉBÉCOISE DE LA COVID-19

MANAGEMENT FRAMEWORK OF THE QUEBEC COVID-19 BIOBANK (BQC19)

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- Simon Rousseau, PhD, McGill University Health Centre - co-Director of the Biobank

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- CIUSSS de l'Estrie- CHU de Sherbrooke: Alain Piché, MD, M. Sc., FRCPC
- Montreal Clinical Research Institute (IRCM), Emilia Liana Falcone, MD, PhD

The REB reviewer is the Research Ethics Board of the CHUM

Business address of the BQC19
THE ROYAL INSTITUTION FOR THE ADVANCEMENT OF LEARNING (RIAL)/ MCGILL UNIVERSITY, having its head office is located on 845 Sherbrooke W street, Montreal, Quebec, Canada.

VERSIONS HISTORY

Date DD/MM/YYYY	Version	Page	Description of the modification
03/06/2020	03	20	Approved version by the BQC19 Governing Committee
11/09/2020	04	30*	Revision of sections 8 and 9 (addition of roles of the BQC19 staff and detailed description of the sample and data access process) Approved version by the BQC19 Governing Committee Precision on the hosting of biological data and Material, the security of data transfer, the centralized data processing system and the intellectual property and marketing.
09/10/2020	05	29	Removal of problematic sentence with the inter-institutional agreement (section 9.5). Modification of the affiliation of Catherine Laprise, PhD, Karine Tremblay, PhD and Luigi Bouchard, T.M/R.T., PhD
05/11/2020	06	29	Remove problematic sentence with the inter-institutional agreement (section 9.5) and restate the previously removed sentence that was not problematic with the inter-institutional agreement.
24/11/2020	07	32	Insertion of an advertisement in the participant recruitment process (Section 5.1.3). Inclusion of a section on the core analyses to be performed by the BQC19 (section 7). Inclusion of a section on data sharing with the partnerships initiatives (section 10.8) : Sharing of data collected by the BQC19 through partnerships (section 10.8.1) and the CGEN HostSeq (section 10.8.2)
18/12/2020	08	32	Inclusion of the IRCM site and Emilia Liana Falcone, MD, Ph D. to the BQC19. Corrections typos in text. In 5.3.1, replace the terms « T » with « J » and months by days in order to standardize the information in the Management Framework and the EII (budget). In the Core Analyses table, row « basic laboratory for non-hospitalized patients, the sentence « on the non-hospitalized patients (cohort 2) » has been removed.

*excluding appendices

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PREAMBLE

This Management Framework contains the operating rules and procedures of the Quebec COVID-19 Biobank (BQC19). The BQC19 was established following an emergency mandate received from the *Fonds de recherche du Québec - Santé* (FRQS) and Génome Québec (GQ) to provide Québec with a provincial infrastructure for the banking of samples and data that can be used by the scientific and medical community to better understand, fight, and ultimately limit the impact of COVID-19.

This Management Framework was drafted during the public health emergency declared on March 14, 2020, in order to rapidly put in place an infrastructure efficient in mobilizing samples and data from people infected with COVID-19 during the pandemic. Given the urgency of the situation and the challenge of undertaking such an exercise, this Management Framework is being developed and approved in several distinct phases to both address the urgent need to start the operations, while respecting the core values of ethics and transparency. This procedure will enable the BQC19 to be receptive to the realities on the ground, both scientifically and ethically, and will enable the Management Framework to adapt quickly to reflect these realities while remaining innovative, anticipatory and forward-looking.

1. OBJECTIVES AND DESCRIPTION OF THE BQC19

Research is essential to better understand the evolution and determinants of the SARS-CoV-2 infection responsible for the COVID-19, to identify those at risk and take appropriate measures to protect them, to help the government take social measures to control the spread of the infection, and to anticipate and be better equipped for future pandemics.

Access to high-quality biological Material and data from SARS-CoV-2 infected and uninfected patients is absolutely essential. The urgency and the magnitude of pandemics, as well as a proper resource management and the protection of personnel, dictate immediate action and coordination of efforts at the local, regional, national and international levels.

Following the initiatives put forward to find a solution to the COVID-19 pandemic, the FRQS and Génome Québec have mandated a group of researchers to establish the BQC19.

This decentralized infrastructure will align the research efforts of all research institutions in Quebec and facilitate national and international research collaborations.

The mission of the BQC19 is to support the institutions of the health and social services network (HSSN) by facilitating the supervision and common resource management of the unique biological Material and data stored in the BQC19 in order to make them accessible for research on COVID-19 and related diseases. To this end, the academic partners of the HSSN also play an integral role.

The BQC19 ensures provincial coordination and identification of the expected standards of various banking infrastructures established in the HSSN institutions and federated to constitute the BQC19. The notion of sharing research results is at the heart of the BQC19 mission. More precisely, the BQC19 will support efforts to discover and develop new biomarkers of disease sensitivity and progression, therapies and vaccines that are new or re-directed to address COVID-19, as well as any research effort related to the prevention, treatment and epidemiological and population management of COVID-19. Finally, the BQC19 will encourage health research and precision medicine on COVID-19.

2. OWNERSHIP OF THE BQC19 INFRASTRUCTURE

The infrastructure required for the BQC19 is owned by the participating institutions.

The BQC19 includes several participating institutions of the health and social services network (HSSN), and each institution acts as a trustee with regards to the stored data and biological Material. A researcher is responsible for the BQC19 in each participating institution. The Lead Researcher is nominated by the participating institution. Every institution has the infrastructure necessary for the operation of the BQC19 and may use it for the hosting of the BQC biological Material and data as directed by the BQC19. A list of the infrastructure at each participating institution is available in Appendix 1.

BQC19 Participating Institution	Lead Researcher for the BQC19
Centre hospitalier de l'Université de Montréal (CHUM)	Daniel Kaufmann, MD
Institut universitaire de cardiologie et de pneumologie de Québec (IUCPQ)	François Maltais, MD, FRCPC
CIUSSS du Saguenay-Lac-Saint-Jean	Karine Tremblay, PhD
CHU de Québec- Université Laval	Alexis Turgeon, MD
CHU Ste-Justine	Tse Sze Man, MD, FRCPC
CIUSSS du Centre-Ouest-de-l'Ile-de-Montréal (Jewish General Hospital)	Brent Richard, MD, M. Sc.
McGill University Health Centre (MUHC)	Donald Vinh, MD, FRCPC, FACP
CIUSSS de l'Ouest-de-l'Ile-de-Montréal (Douglas Mental Health University Institute)	Gustavo Turecki, MD, Ph. D
CIUSSS de l'Estrie- CHU de Sherbrooke	Alain Piché, MD, M. Sc., FRCPC
CIUSSS du Nord-de-l'Ile-de-Montréal (Hôpital Sacré-Cœur)	Nicolas Gauthier, PhD, CSPQ, FCACB
CIUSSS de l'Est-de-l'Ile-de-Montréal (Hôpital Maisonneuve-Rosemont)	Han Ting Wang, MD, FRCPC
Montreal Clinical Research Institute (IRCM)	Emilia Liana Falcone, MD, PhD

Other institutions may join the BQC19 in the future. Institutions wishing to join the BQC to recruit adult populations must submit an application to the Director of the BQC19. Applications to add new institutions to recruit pediatric populations must be made to Dr. Sze Man Tse. The required procedures to regulate the participation and ensure the safety of the pediatric populations are provided in Dr. Sze Man Tse study entitled « Biobank of samples and data for pediatric respiratory disease research » (Appendix 2 – approved documents of the CHU Sainte-Justine). Applications for the addition of new institutions will be forwarded to the BQC19 Governing Committee (see sections 3 and 9 of this Management Framework) for final decision.

2.1 BQC19: PROVINCIAL ET LOCAL COLLECTIONS

Each participating institution of the BQC19 is committed to collect a minimum set of data and samples, as described in section 5.

In the minimal sample set, a fraction of the collected samples will be labeled for the « local biobank » by the centres responsible of collecting for the BQC19.

- For the nucleic acids extracted from blood (DNA and RNA), the distribution between the BQC19 and the local biobanks is 80%:20%;
- For plasma, it is 70%:30%;

- For PBMCs, it is 50%:50%. [(1)]

The first tube of plasma or PBMC (*Peripheral blood mononuclear cells*) will always be prioritized for the local biobank, and the second tube will always be for the BQC19.

The institutions are authorized/encouraged to collect beyond the minimal set, in order to respond to the local projects. These collections are also referred to as « local biobanks ». Their Management Framework is, to date, integrated with that of the BQC19, in the absence of other frameworks.

[(1)] For the pediatric PBMC, see Appendix 2.

3. MANAGEMENT OF THE BQC19

The Steering Committee is responsible for the administration of the BQC19. It reports to the BQC19 Governing Committee, chaired by representatives of the granting agencies and which includes leaders of the participating institutions and other experts, in particular experts in legal matters and in patient-partner relationships.

The BQC19 Access Committee is responsible for authorizing access to the biological material and associated data for studies involving more than one site. Access to the data and material of one site is made through the local Access Committee or through the BQC19 Access Committee if desired by the local institution. The composition and operation of these committees is detailed in sections 8 and 9 of this Management Framework.

4. FUNDING

The BQC19 is funded by the FRQS, GQ and the Public Health Agency of Canada (PHAC).

5. RECRUITMENT

5.1 RECRUITED POPULATION

5.1.1 INCLUSION AND EXCLUSION CRITERIA

- Inclusion:
    - Patients who were tested for COVID-19 at one of the participating institutions of the BQC19;
    - Adults capable of consent to research;
    - Adults rendered incapable of consent to research due to COVID-19 (sudden and temporary incapacity);
    - Adults incapable of consent to research due to a condition other than COVID-19, if represented by an agent, guardian or curator;
    - Children under the criteria outlined in Dr Sze Man Tse's study « Biobank of samples and data for pediatric respiratory disease research » (Appendix 2);
    - A targeted percentage of 50% of the BQC19 participants will have tested negative for COVID-19.

5.1.2 PLACE OF RECRUITMENT

Participants will be recruited from the HSSN institutions participating in the BQC19.

5.1.3 IDENTIFICATION OF POTENTIAL PARTICIPANTS

The Lead Researcher for the BQC19 at each participating institution shall ensure that potential participants to the BQC19 are identified for recruitment in accordance with this Management Framework and the applicable laws and regulations at their institution.

The approval of the institutional Director of professional services is required when the identification of potential participants is achieved through medical records.

In certain institutions, the attending physician may be involved in the identification of potential participants.

Recruitment of participants may be achieved through the posting of advertisements at the participating institutions and through the dissemination of such advertising on the websites of the BQC19, the participating institutions, and in selected targeted social medias. Individuals interested in participating in the BQC19 will contact the research teams. The advertising poster was requested and approved by the CIUSSS-SLSJ. This advertisement was approved by the BQC19 Communications sub-committee and by the CHUM Research Ethics Board as the REB reviewer for the HSSN institutions. This advertisement may be used by all participating institutions and is available upon request.

5.2. OBTAINING CONSENT

5.2.1 WHO MAY CONSENT

- A competent adult may consent to his/her participation in the BQC19 for him/herself;
- The consent of an incapacitated adult shall be given by a representative legally authorized to consent to the care required by their state of health;
- The consent of a minor is outlined in Dr Sze Man Tse's study « Biobank of samples and data for pediatric respiratory disease research » (Appendix 2).

5.2.2 RECRUITMENT AND CONSENTMENT PROCESS

Given the high risk of infection of the COVID 19 clinical and research staff, and the unique clinical context of each participating institution, acquiring and documenting consent will be modulated with respect to the usual standards that normally require a face to face meeting and obtaining a written consent using an Informed Consent form (ICF). In addition, the consent process should be adaptable, taking into account the patient's state of health.

Each institution shall establish its unique consent process and reflect it in the Manuals of Operating Procedures (MOP) (Appendix 1). The MOPs should specifically address the following points: 1) The time and place where the patient is approached; 2) the procedure to follow when a patient is diagnosed as SARS-CoV-2 positive or SARS-CoV-2 negative; 3) the timetable and the nature of sampling (including the data) depending on whether the patient is diagnosed as SARS-CoV-2 positive or SARS-CoV-2 negative; 4) the time period over which the recruitment will be conducted. Appendix 3 provides the detailed description of the above-mentioned points per institution, in addition to the overall procedure according to local specifics, taking into account the procedures and regulations in effect. In order to ensure consistency across the BQC19 and harmonization of existing procedures, any consent process established by a participating institution of the BQC19, must respect the following two principles:

1. The autonomy of the participants (taking into account their state of health) must be respected at all times.
2. Recruitment into the BQC19 must be achieved safely for all involved participants.

More specifically, if the participant is capable to consent to the BQC19 and their state of health, according to the clinical staff, allows them to begin the consent process:

- The research staff verbally present (by telephone or other electronic tool available in the participant's room) the BQC19 and answer any question the participant may have.
- The research staff record and document the participant's verbal consent (electronic or other) in the ICF (electronic version);
- The research staff forward a copy of the ICF confirming the participant's consent to the participant via email or by regular mail;
- The participant reply to this exchange (electronically or by mail) including the text designated to the ICF in order to document the consent;
- If the participant dies before responding or if the research staff receive no response after a follow-up, the recorded and documented verbal consent is valid.

If the participant is incapable of consenting to the BQC19 or becomes incapacitated due to illness:

- The BQC19 lead research staff at the institution contact by phone the legal representative (mandatary, curator or guardian for the incapable adult and spouse, close parent or interested person in case of sudden incapacity) and present the BQC19;
- If the legal representative demonstrates an interest in the participation of the person represented, a copy of the ICF shall be sent to them by email;
- A phone conversation or videoconference shall be scheduled to answer questions from the legal representative, if any;
- Verbal consent is recorded and documented in the ICF (electronic version);
- A copy of the ICF certifying the consent is forwarded to the legal representative by email;
- The legal representative responds to the latter email with the text designated to the ICF in order to document the consent;
- If the participant dies before the legal representative responds or if the research staff receive no response after a follow-up, the recorded and documented verbal consent is valid.

If the participant regains his/her capacities (in case of sudden incapacity) and must confirm his participation in to the BQC19:

- Procedures for obtaining the consent of the capable participant to the BQC19 are followed.

If the participant is a minor:

- The process is outlined in Dr Sze Man Tse's study «Biobank of samples and data for pediatric respiratory disease research » (Appendix 2).

5.3 COLLECTED MATERIAL AND DATA

Biological material shall be collected by the clinical staff, or any other person according to institutions guidelines in effect, as part as the participant's standard care.

All collected biological material shall be processed at one of the participating institutions of the BQC19 in accordance with the institution's Standard operating procedures in order to ensure optimal storage. These procedures also entail that the required clinical data are electronically linked to the samples in the BTRSRV2 data management application and that the management and inventory is kept updated in BTRSRV2.

Each participating institution of the BQC19 will have its own MOP to ensure that the collection process and tracking of the biological Material are in accordance with local realities. In order to facilitate and promote cohesion within the

BQC19, a common core document is provided. These MOPs are appended to this Management Framework and are available to other BQC19 member institutions (Appendix 3, specific to each institution).

5.3.1 BIOLOGICAL MATERIAL

Adult participants who had have a negative or positive diagnostic test of SARS-CoV-2 and have been hospitalized:

- One to five additional blood samples, 48 ml each, up to a maximum of 240 ml, will be drawn when sampling is required as part of the participant's standard care. No blood samples will be drawn solely for the BQC19 during hospitalization on D0, D2, and D7. However, samples may be drawn exclusively for the BQC19 even if not clinically indicated on D14 and/or D30.
- Blood samples should ideally be collected five times (during hospitalization):
    - Recruitment Day (D0)
    - On day 2 (D2)
    - On day 7 (D7)
    - On day 14 (D14)
    - On day 30 (D30)

Participants who had have a negative or positive diagnostic test of SARS-CoV-2 during their hospitalization but were discharged from hospital:

- During medical follow-up visits associated with the SARS-CoV-2 and for up to two years, 60 ml of additional blood will be drawn at each scheduled visit on approximately Day 30, 90, 180, 365, 540 and 760 following hospital discharge (in an outpatient clinic or at home). Blood will be collected at a maximum of 200 ml per month and it will not necessarily be collected as part of the participant's standard care.

Participants who had have a negative or positive diagnostic test of SARS-CoV-2 and have not been hospitalized:

- During medical follow-up visits associated with the SARS-CoV-2 and for up to two years, 60 ml of additional blood will be drawn at each scheduled visit on approximately Day 30, 90, 180, 365, 540 and 760 following original diagnosis (in an outpatient clinic or at home). Blood will be collected at a maximum of 200 ml per month and it will not necessarily be collected as part of the participant's standard care.

Minor participants with a positive or negative diagnosis of SARS-CoV-2:

- Samples collection is processed as outlined in Dr Sze Man Tse's study « Biobank of samples and data for research in pediatric respiratory disease » (Appendix 2).

Pregnant adult participants with a positive or negative diagnosis of SARS-CoV-2:

- The following additional samples will be processed to be stored and used for research purposes:
    - Vaginal swabs (two swabs) on admission and delivery (if the period between admission and delivery exceeds 7 days), with the possibility of self-sampling.
    - Collection of amniotic fluid (10 ml) in case of caesarean delivery (C-section).
    - Collection of cord blood (25 ml).
    - Collection of breast milk (maximum 5 ml): within 24 hours and between 24 and 48 hours after delivery, then once a week if mother or child is hospitalized or seen in an outpatient clinic.
- Any remaining portion of post-natal biological Material related to pregnancy (in particular placenta samples) will be sent to the biobank.

In order to ensure the integrity of the BQC19, the date and time of any sampling will be documented.

5.3.2 BIOLOGICAL MATERIAL AND DATA ALREADY COLLECTED

Additional biological material collected as part of any COVID-19 research that would otherwise be destroyed may be stored in the biobank if deemed relevant by the Lead Researcher at the participating institution where they were collected.

In addition, the BQC19 is developing strategic partnerships with the population database CARTaGENE and the Canadian Longitudinal Study on Aging (CLSA) in order to enhance epidemiological studies on COVID-19 at a population level. The process of importing these data will be done within a framework that minimizes the risk of re-identification. To that end, some variables may not be imported if the importation will compromise this fundamental principle. The ELSI sub-committee (ethical, legal and social implications) of the BQC19 will ensure compliance with this principle.

5.3.3 DERIVATIVES OF BIOLOGICAL MATERIAL

DNA, RNA, proteins, lipids, metabolites and primary cells may be isolated from the BQC19 biological material. In order to support its objectives and those of the researchers seeking access to biological Material, the BQC19 and the HSSN banks may develop cell lines, organoid, xenografts, as well as genetic analyses related to COVID-19 or any other relevant research process.

5.3.4 CLINICAL DATA

Clinical data relevant to research on COVID-19 will be stored in the BQC19. This includes pertinent medical information of the participant, including medical records, X-rays and imaging. The physical evaluation of the participant, as well as his/her general state of health are recorded in the Case Report Form/CRF approved by the Steering Committee.

Participant's consent to the BQC19 is obtained for the following reasons:

1- Allow to collect and use the information, in their medical record at the hospital, pertinent to the BQC19 objectives.
2- Allow access to data from the *Institut de la statistique du Québec*, to access, among other things, the database for death records.
3- Allow access to data from the *Laboratoire de Santé Publique du Québec (LSPQ)*, to access, among other things, the data on the isolated and tested virus from BQC19 participants.

5.3.5 RESEARCH DATA GENERATED FROM BQC19 RESOURCES

The BQC19 recognizes the importance of developing its database. Researchers accessing BQC19 samples and data must provide a copy of their derived data to the BQC19, in accordance to the Transfer Agreement in force. The exact nature of the derived data and the timeframe within which they must be provided will be determined during the evaluation process and will be included in the Transfer Agreement. These derived data are an integral part of the BQC19 research data, and will be available to other researchers who may, in the future, have access to this enhanced data.

6. STORAGE OF BIOLOGICAL MATERIAL AND DATA

6.1 STORAGE METHODS OF BIOLOGICAL MATERIAL AND DATA

6.1.1 HOSTING STRUCTURE OF BIOLOGICAL MATERIAL AND DATA

The BQC19 processes data from participating institutions. Data processing occurs at several levels. The first level starts at each institution and includes participants' identifiable data. The second level consists of collecting data in a

centralized location. At this level, each patient is assigned a unique code. These two levels are managed by the network database located at the Biomedical Telematics Laboratory (LTB) at the Research Centre Étienne Lebel of the *CIUSSS de l'Estrie (Centre Hospitalier Universitaire de Sherbrooke (CHUS)* (see section 6.2.). Once the data is compiled, de-identified and processed for quality, clinical data will be transferred to a secured and centralized processing system. This is where all data from the BQC19 are stored (including data from the processing of collected samples). The association between the clinical data and the BQC19 sample data is achieved through the unique code assigned to each participant. Scientific analyses performed on the collected data will be made possible by the computing power of this system. Data extraction and secure data transfer required to share data with third parties will also be done via this centralized processing system.

Protection of participant identifiable information

Each site acts as the custodian of the identifiable information of the BQC19 participants. Identifiable information is any data that can provide information to track the participant directly or indirectly. This data is stored in a local database located on a secure server in each participating institution.

The only link between the identifiable information and the clinical data stored in the BQC19 is the five (5) digit (code) number that the application assigns to the participant in the identifiable (and therefore local) part of the BTRSRV2 computer application. The coded data is imported and stored on the network side of the BTRSRV2 database. Therefore, the ability to obtain participant identifiable information by consulting only the shared section of BTRSRV2 is unlikely.

Biological material

Each sample is identified by a numbering system generated automatically by the central server via the network side of the BTRSRV2 application, available in each participation institution. By this unique identification, which links each sample to a site and to a given participant, it is possible to manage the inventory and be informed on the exact location of each sample.

Information on biological material (location, quantity, availability, etc.) is also stored on the network of the BTRSRV2 database. Depending on the type of banked samples, the information collected directly about the sample is of major importance as it defines the exact nature of the biological material and its storage method.

Data derived from processing biological Material (including genetic data)

All analyses results on biological Material (including genetic data), whether from the BQC19 or from external partners, must be returned to the BQC19. These data will be transferred directly to the centralized data processing system in a coded form.

6.1.2 BIOLOGICAL MATERIAL AND DATA « PATHWAY »

See Appendix 1 for the details at each participating site.

6.2 BTRSRV2 DATABASE

6.2.1 STRUCTURE AND PRINCIPLES

The BQC19 uses a computer application (BTRSRV2) to store, organize and present biological Material and data collected from various participating institutions. It is a so called hybrid application that merges the power of modern programming languages with the flexibility of the Internet.

The application is described in more details in Appendix 4.

6.2.2 USER LEVELS, ACCESS CONTROL, USERS

The local section of the BTRSRV2 is a computer application that includes participant' personal data. Therefore, its use is reserved to persons who have received (with the authorization of the BQC19 Director or his delegate) a personal user ID and password.

In order to meet administrative, usage and consultation needs of the BTRSRV2, five levels of users have been created:

1. Super administrator :
   a. Has all rights (creation of subject (participant with a unique identifier code, or visits leading to the storage of samples and/or data for a participant));
   b. Has rights to all apps;
   c. Has rights to manage users for all participating institutions;
   d. Has rights to manage the lists of variables;
   e. Has rights to access information of participants and visits of his/her institution only.

2. Institutional administrator :
   a. Has all rights (creation of subjects and visits) ;
   b. Has rights to all apps;
   c. Has rights to manage users for his/her institution.

3. User:
   a. Has same rights as the institutional administrator except for user management.

4. Restricted User:
   a. Has same rights as a user but his rights are granted on a case-by-case basis;
   b. May have rights to one or more apps.

5. Read only :
   a. Has same rights as a user but they are not entitled to create subjects, nor visits, and are not able to save and backup data;
   b. May have rights to statistical apps (by institution only) and to generate reports on a case-by-case basis.

6.2.3 DATA SECURITY AND DURABILITY

Private database (local)
Periodic and automatic data backup is crucial to prevent data loss. The security and protection of data contained in the private database are the sole responsibility of the Lead Researcher in an institution, and as such, he/she shall make arrangements with the IT department of his/her institution in order to ensure security. Information on private database (local) is included in Appendix 1.

Shared database (network)
Mechanisms have been put in place to ensure the availability of data from the BTRSRV2:

I- Site Security:
The LTB is located in an environment controlled by a card access system. The BQC19 server is installed under lock inside the Research Centre Étienne Lebel.

II- IT security:
Access to the server is password protected and restricted to LTB administrators. In addition to its own security system, the server also benefits from a firewall security system set up by the IT department at the CHUS.

III- Data security and availability:
The LTB ensures the integrity of the data collected. The server that hosts the BQC19 data has an auxiliary power supply in case of power failure and is available 24 hours a day, every day of the year. The data is backed up to a hard drive and the server operating system simultaneously maintains a block-level striping with distributed parity (RAID level 5). A full backup copy of the data is retrieved daily according to a two-week schedule. A weekly backup of the data is also carried out and placed in a secure location to counter the effects of a major disaster.

Destruction of biological material and associated data

Biological material has a limited lifespan depending on its nature and mode of storage. A data destruction mechanism has been introduced to address ethical requirements. In BTRSRV2, once a sample reaches its storage limit, it is automatically labelled as expired; as a result, the process of sample withdrawal is initiated.

Sample withdrawal process includes physical destruction of the biological material as well as the associated data (see section 6.6 – Right of withdrawal). With respect to the data, the BQC19 Coordinator at the participating institution is notified by BTRSRV2 that a sample has now expired. This notification is in the form of an email sent directly to the BQC19 Coordinator at the institution advising of expired material. In addition, an alert message will be displayed on the home screen of the Coordinator at his/her next connection to BTRSRV2.

The BQC19 Coordinator at the institution must login to the management screen to view the sample identified as expired. He/she has a choice to remove the expiry attribute or to proceed with the deletion of the data. If they choose to remove the expiry attribute, they must support their decision. However, if they decide to delete the data, they must re-enter their user ID and password and answer in the affirmative on two alert messages indicating that the data associated to this tissue will be irretrievably deleted.

The BTRSRV2 application then proceeds to completely delete the data related to that sample in the shared and associated tables. The database management system is equipped with mechanisms that prevent the recovery of deleted data, in whole or in part.

6.2.4 DATA TRANSFER SECURITY

The Biobank site uses a data encryption protocol (128 bit SSL connection) that ensures the security of transmission between the site that enters the data and the server that receives it.

6.2.5 UPDATES

The BTRSRV2 application undergoes regular updates. These updates are to address a new function addition, settings modifications or application correction. During an update, a test is initially performed on a twin and independent application which is a true copy of BTRSRV2. Once the programmers have received assurance that the update is working properly, it is applied to the official version.

Updates rarely affect the normal operation of BTRSRV2. Otherwise, a message will be sent to users beforehand indicating that there will be an interruption of service, including the reason and the duration of this interruption.

6.2.6 TRAINING

Any person entering data into the BTRSRV2 must be trained beforehand by the BQC19 Coordinator or a member of the BQC19 team.

6.3 CENTRALIZED DATA PROCESSING SYSTEM

Data from BTRSRV2 as well as results from analyses performed on the samples as described above, shall be transferred, validated and stored in a centralized data processing system. At this moment, the data remain in the system where it was generated. The centralized data processing system is under development and will be described in details in the next version of this Management Framework. This system will meet all necessary security, confidentiality and quality requirements. The next version of this Management Framework will include at the very least, the information on the system, its structure and principles, users levels, access control and users; as well as data security and durability, update process and required training.

6.4 PHYSICAL SECURITY MEASURES

In accordance with the policies in force at each participating institution that govern the occupational health and safety components, physical security measures shall be implemented to ensure the security of staff as well as the biological Material and data for which the BQC19 is the custodian.

Physical access of the BQC19 sites at the participating institutions must be controlled on both sides, the biological Material and the BQC19 records. The same applies to the electronic data. Only those authorized by the BQC19 Lead Researcher at each participant institution must have access to biological Material and BQC19 records.

6.4.1 SECURITY MEASURES FOR STAFF

Anyone handling BQC19 biological Material must ensure that it is handled safely and optimally while eliminating loss and contamination risk. Internal policies at each participating institution must be followed with respect to the management of biological Material and to the procedures regarding internal transfer for samples and specimens.

Each of the participating institution is subject to internal policies for handling infectious and hazardous Material. Staff who will handle human samples shall complete laboratory biosafety training at a containment level 2 or 3 depending on the types of the processed biological samples.

6.4.2 SECURITY MEASURES FOR THE BQC19 BIOLOGICAL MATERIAL AND DATA

Biological samples shall be kept in places where access is restricted to authorized persons. A mechanism to control access at the secured premises shall be introduced and documented. It is recommended that the control mechanism is based on a card access system that documents all card activities and use, if possible. Paper documents must be stored in secured locations and physical access to the BQC19 records must be controlled by the use of locked filing cabinets.

Biological Material must be centrally stored within each participating institution. This consolidation of biological Material enables a better quality and inventory control. Samples are stored according to the type of storage required: room temperature, frozen in -20 °C or -80 °C freezers, or stored in liquid nitrogen.

Freezers and refrigerators must be connected to red emergency sockets, i.e., a generator is activated within a short period of time allowing ideal temperature maintenance for adequate storage of biological samples. They are to be

located in a room with appropriate air conditioning system. An emergency freezer must also be available if necessary. In the event of power outage or a technical problem, the internal temperature of a -80 °C freezer begins to drop and takes approximately 4 hours to reach a critical temperature of -65 °C.

The level of liquid nitrogen in the tanks in which the samples are stored must be checked twice a week.

6.5 PRIVACY AND CONFIDENTIALITY

The minimum precautions taken by various BQC19 participating institutions to protect confidentiality are as follows:

- Coding;
- Data under lock;
- Appointment of a BQC19 Lead Coordinator at each participating institution.

Furthermore, data stored on the BTRSRV2 server and the centralized data processing system do not contain any information that can be traced to the participant. The only potential identifying element is the unique code associated to each participant (coded data). Identifiable information are stored solely on the local server of a BQC19 participating institution (see section 6.1).

As above-mentioned, the protection of privacy and confidentiality is a core value of the BQC19. This must manifest in practical measures. For example, given the dynamic nature of the tools for dataset analysis, the ELSI sub-committee (ethical, legal and social implications) and the Clinical data sub-committee shall be responsible for periodically evaluating the nature of the risk of re-identification with respect to these tools in order to take all necessary measures to minimize this risk.

6.6 SHELF LIFE

BQC19 biological material and data will be retained as long as their scientific interest and applicable ethical rules warrant.

6.7 RIGHT OF WITHDRAWAL

BQC19 participants have the right to withdraw their consent verbally or in writing, without explanation and without consequences on the quality of care and services they are entitled to receive. BQC19 agrees to no longer contact these participants, to no longer use and to destroy their biological material and data, as well as any associated identifiers, if possible.

A withdrawal procedure is initiated as soon as the participant requests it.

Steps of withdrawal:

a. Verification of the identity of the applicant participant.
b. Verification of the availability of the biological material:
    - If the biological material is available for use, proceed to step c;
    - If the biological material has been partially distributed, proceed to step c. for the portion still unused by the BQC19;
    - If the biological material has been distributed, inform the participant of the date the data were destroyed and that the destruction of the material must be completed by the end of the study for which the biological material was shared. A letter will be sent to the User-Researcher advising him/her of the date of destruction of the data

relating to the sample in question. The User-Researcher will thus have the opportunity to obtain the information relevant to his research prior to that date.

c. An information letter from the BQC19 Coordinator at the institution involved in the withdrawal request (Appendix 5) stating the facts is sent to:
   - The Director of the BQC19;
   - The Coordinator of the BQC19;
   - The Lead Researcher of the BQC19 at the involved institution;
   - The Director of the LTB;
   - The IT Coordinator of the LTB.
d. Physical destruction of samples, computer data and paper documents are to be completed in accordance with the procedures in force at the involved participating institution.
e. Certificates of destruction are issued by the BQC19 Coordinator at the involved institution and by the IT Coordinator of the LTB (Appendix 6). These certificates shall be kept locally at the involved institution.
f. A copy of the information letter and a copy of the Certificates of Destruction are sent to the participant. The withdrawal is reported to the Research Ethics Board at the annual renewal.

The reference to this withdrawal is automatically included in the annual report prepared by the site.

6.8 RECONTACTING PARTICIPANTS

Participants who have consented may be recontacted by the BQC19 Lead Researcher at the institution where they were recruited.

6.9 ACCESS TO BQC19 FOR AUDIT PURPOSES

For the purposes of surveillance and control, protection and security, the records of BQC19 participants as well as their medical records may be accessed by a person mandated by regulatory bodies, in Canada or abroad, such as Health Canada, and representatives of the institution or the Research Ethics Board. These individuals and organizations adhere to a privacy policy. No photocopies or copies of BQC19 documents may be made during audits.

Participants have the right to consult their research records to verify the information collected, and to have them corrected if necessary.

6.10 RETURN OF RESULTS TO PARTICIPANTS

When the research results in validated scientific outcomes, the latter will be available to participants via the scientific publications.

Information resulting from research on BQC19 samples is used only for scientific purposes. This information shall not be entered in the participant's medical record or communicated to the participant or to unauthorized third parties.

BQC19 participants will have the opportunity to view the list of projects using biobank data and biological Material, including a summary of the project in lay language on the BQC19 website.

6.11 INCIDENTAL FINDINGS

For adult participants, incidental research findings shall not be shared with the participant nor their physician, as they will not be of clinical quality. As a result, they cannot be used for clinical decision-making. If this reality changes, the Management Framework as well as the consent shall be amended accordingly. For pediatric participants, the required procedures are as outlined in Dr Sze Man Tse's study « Biobank of samples and data for research in pediatric respiratory disease » (Appendix 2 - (Appendix 2 – approved documents of the CHU Sainte-Justine).

7. CORE ANALYSES

In order to provide a timely response to the pandemic, while optimizing the use of samples collected by the BQC19 that are particularly valuable and unique, to ensure return on investment and in response to:

- The recent development of the global pandemic (2nd wave);
- The ongoing changes in patient management; and
- The recent announcement related to the COVID-19 vaccine development.

The BQC19 Governing Committee has approved on November 18, 2020 that a series of core analyses may be performed on these samples, the results of which will be provided to the scientific community as soon as possible.

These core analyses are summarized in the table below.

Type of Analysis	Objective
Whole Genome Sequencing and Genotyping (GWAS) of the host genome	Identification of all genetic variants of the host genome as well as genetic variations such as changes in the number of copies of certain genes (whole-genome sequencing) as well as common genetic variations across the genome (genotyping GWAS) associated with COVID-19. These results will enable studies on susceptibility and response to the disease and the risks of developing a severe form of the disease.
Virus Genome Sequencing	Provide a better understanding of the infection trajectory and the different identified strains of the virus. These data along with the whole-genome sequencing may also be correlated with the severity of the disease and the immune response.
Proteomics (1) SomaScan	The simultaneous measurement of 5000 proteins in the collected samples will make more data available to predict the risk of the disease progression in several areas, i.e. cardiovascular. This technology was chosen because of the large number of proteins measured in a single sample.
Proteomics (2) Immuno-inflamatory markers	This approach, which is complementary to the SomaScan above, will measure identified immuno-inflammatory markers using a very specific and sensitive technique. These data will provide a better understanding of this important aspect of patients' response to the disease and possibly guide future treatments.
Basic laboratory test for non-hospitalized patients	Enable basic blood tests and provide important data for research on participants in both cohorts. This includes basic values for liver, cardiac and renal damages, as well as standard inflammatory parameters.
Metabolomics	Enable measurement of metabolites in COVID-19 which may lead to research on the identification of individuals that are likely to develop a severe disease and on the understanding of the molecular pathways that may explain this susceptibility as well as the spectrum of severity and diversity of clinical manifestations.

Type of Analysis	Objective
Immunoserology	Enable a very detailed and quantitative measurement of specific antibodies against-SARS-COV-2 virus in the infected patients, well beyond the standard serological tests, as well as the ability of these antibodies to neutralize the virus. This will guide research on patients' immune response to the COVID-19, a key element in the disease management.
Transcriptomics	Transcriptomics signatures have been associated in other viral diseases, with cellular and immune response, disease pathogenesis, and infection trajectory beyond the initial phase. Transcriptomics analyses performed on the participants' RNA will generate important data in this area in the case of COVID-19

While optimizing the use of samples, this systematic approach should rapidly contribute to the generation of data to identify molecular signatures for the stratification of the risk of severe disease and to develop a better understanding of the pathogenesis of the disease and its long-term side effects, in particular to patients with comorbidities. In addition, there are significant synergies in studies integrating different types of data.

8. BQC19 RETURNS

8.1 INTELLECTUAL PROPERTY AND COMMERCIALIZATION

The BQC19 considers its mission accomplished when the data derived are made available to the scientific community under the terms of the Material and/or Data Transfer Agreements and in accordance to the terms stated in the Wellcome Trust Foundation declaration.

Accordingly, the BQC19 and its participating institutions waive any intellectual property rights resulting from the use of the material and data by a material/data User

No intellectual property can be claimed on the initial material and data. Intellectual property rights obtained from the research derived data shall not prevent the broad use of the data by the research community.

Participants shall not financially benefit from their participation and/or the invention of a commercial product created in whole or in part from their biological material and/or data stored in the biobank.

8.2 DISSEMINATION OF RESULTS AND PUBLICATIONS

Scientific data and knowledge are common property and must be shared in an appropriate framework. The BQC19 commits fully to the Wellcome Trust Foundation declaration on "Sharing research data and findings relevant to the novel coronavirus (COVID-19) outbreak" available at: https://wellcome.ac.uk/press-release/sharing-research-data-and-findings-relevant-novel-coronavirus-covid-19-outbreak. As COVID-19 represents a significant and urgent threat to global health, the BQC19 is committed to ensuring that research results and data related to this outbreak are shared quickly and openly to guide and inform public health and help save lives (see section 9.3.2.).

The User-Researchers shall mention in their scientific publications and communications (written and oral) that the material and data used were obtained from the BQC19. They will also mention the financial contribution of PHAC, the FRQS and GQ. When a publication is accepted, the User-Researcher will transmit to the BQC19 Manager a copy of the publication, communication and documents mentioning the BQC19 (see section 9.3.2.). Any biological Material or Data Transfer Agreement shall include the necessary provisions to that effect.

A sample text on how to acknowledge and cite the BQC19 and the financial support of its granting agencies is available on the BQC19 website.

9. GOVERNANCE OF THE BQC19

The BQC19 is under the direction of Vincent Mooser. Michaël Chassé and Simon Rousseau act as co-Directors.

Three persons shall be hired by the BQC19, a Manager, a Coordinator and an Access Officer, to provide, among other things, strategic, operations and administrative support, and to ensure communication among the various participating institutions (see section 9.3).
The organization chart of the BQC19 is available in Appendix 7.

9.1 GOVERNING COMMITTEE OF THE BQC19

The role of the Governing Committee is to:

- Approve the specific rules to access data and biological material as well as related procedures.
- Approve the expertise profiles required for the members of the Access Committee.
- Ensure the implementation of rules and procedures stated by the Québec COVID-Pandemic Network (QCPN) and by the Steering Committee of the BQC19.
- Promptly approve access to data and biological Material based on the recommendations of the Access Committee.
- Make the final decision in the event of a dispute over access to data and biological Material

9.2 STEERING COMMITTE OF THE BQC19

The BQC19 has a Steering Committee, mandated to evaluate the progress of the BQC19 and the participating institutions, to take scientific decisions, to review the timeline and finances of the BQC19, to make modifications to the latter if necessary and to identify solutions to potential issues along the way. The Steering Committee is also responsible to approve the content of this Management Framework and to ensure it remains up to date.

Furthermore, the Steering Committee is responsible for:

- Maintenance of the BQC19 biological material and data inventory;
- Communications, such as the distribution of the information related to the BQC19 (including the BQC19 website);
- Tracking research data returned to the BQC19, in accordance with the principles of *FAIR* (*Findable, Accessible, Interoperable, Reusable*).

The current members of the Steering Committee are listed below. The Steering Committee aims to include one representative from each participating institution. When a new institution is added a representative from that institution will be invited to join the Steering Committee

9.2.1 MEMBERS OF THE BQC19 STEERING COMMITTEE

Name	Institution
Vincent Mooser	McGill University
Michaël Chassé	CHUM
Simon Rousseau	IR-CUSM
Daniel Kaufmann	CHUM
Brent Richards	Jewish General hospital

Daniel Auld	McGill University
Ma'n H. Zawati	McGill University
Sze Man Tse	CHUSJ
Karine Tremblay	Université de Sherbrooke/CIUSS du SLSJ
Alain Piché	CIUSSS de l'Estrie- CHU de Sherbrooke
Alexandre Montpetit	Génome Québec
Emilia Liana Falcone	IRCM

The Manager, the Coordinator and the Access Officer of the BQC19 shall also be ex-officio members of the Steering Committee. They will be non-voting members.

In order to support the Steering Committee in its decision-making, several sub-committees will be created. These will include a Population sub-committee, a Scientific sub-committee, an ELSI sub-committee (ethical, legal and social implications) and a Communication sub-committee. The chair of each of the sub-committees will also sit on the Steering Committee to regularly update the members on the latest developments.

9.3 BQC19 MANAGER

The duties and responsibilities of the BQC19 Manager, who reports directly to the BQC19 Director, include in particular:

- Support the BQC19 Director and the Steering Committee on governance, strategic planning, communications, finances, reporting, alignment with the COVID-19 immunity taskforce and partnerships with other Canadian COVID-19 Biobanks;
- Provide professional expertise to the Steering Committee on governance, logistics and communications;
- Work closely with the departments within McGill University to implement and manage collaborative agreements, Material and Data Transfer Agreements and Service Agreements etc.;
- In collaboration with the Deputy Director of the McGill Genome Centre, monitor the BQC19 budget and gather necessary information to prepare financial and budgetary analyses and projections for the BQC19 to enhance strategic planning;
- Research: Gather necessary information and provide advice to the BQC19 Director and Steering Committee based on research data, bibliometrics and research funding statistics;
- Manage interactions between the BQC19 and other key players in the scientific community, in particular the COVID-19 immunity taskforce and CanCOGeN/CGEN;
- Liaise between the BQC19 and the Canada Excellence Research Chair (CERC) team working on genomic medicine at McGill University in order to optimize interactions between these major research initiatives;
- Work closely with the BQC19 Director on the medium- and long-term planning of the BQC19, especially in terms of funding.

9.4 BQC19 COORDINATOR

The duties and responsibilities of the BQC19 Coordinator, who reports directly to the BQC19 co-Directors, include in particular:

- Act as resource person for the participating sites with regards to the BQC19, especially on samples information, laboratory protocols implementation, data entry and management in the BTRSRV2 as well as access management to the secured centralized data processing system;
- Provide training for the BTRSRV2 users in each site and liaise between users and the Telematics Laboratory responsible for programming;

- Ensure communications between the BQC19 Director and the participating institutions, and confirm coordination with operations;
- Manage all aspects related to institutional feasibility review of sites and to multicentric ethics approval, including preparing and filing the required documentation for the Nagano platform;
- Prepare and maintain the Standard Operating Procedures manuals (SOP) detailing the BQC19 procedures;
- Monitor clinical activities in sites using the BTRSRV2 database and focus on acquiring current understanding on patient recruitment/retention in accordance with the competitive recruitment protocol;
- Organize transfer of funds and/or payment of invoices to sites based on their needs and the pre-determined budget, and maintain a record of all documentation pertinent to the BQC19 financial management;
- Provide regular reporting to BQC19 management on patient recruitment and retention, both actual and planned, with a focus on budget compliance;
- Provide regular reporting to the BQC19 management on actual and planned expenditures related to BQC19 funds;
- Prepare an annual report for the BQC19 Governing Committee and Steering Committee on the distributed data/biological Material and the list of research projects derived from the Biobank. The report shall also include the number of recruited persons, the number of complaints filed by participants and the number of participants who withdrew from the BQC19. This report will be forwarded to the REB reviewer at the annual renewal.

9.5 BQC19 ACCESS OFFICER

The Access Officer is mandated to manage the access requests submitted to the BQC19. To that end, he/she will:

- Receive requests from researchers and ensure the file is complete and compliant with the process requirements;
- Identify whether the request is for the provincial collection or a local collection; direct (if applicable) the request to the appropriate resource and follow up and coordinate with the BQC19;
- Organize and coordinate the Access Committee meetings in preparation for final assessments;
- Ensure communication between the Québec COVID-Pandemic Network for all inquiries related to the BQC19 samples and data access;
- Assess and determine the amount of compensation requested from the user-researcher based on the content of the application;
- Prepare meetings minutes of the Access Committee;
- Communicate the outcome of access requests to researchers and to the BQC19 Coordinator.

The Access Officer is also responsible of answering the different researchers' inquiries, regarding access to BQC19 samples and data. To that end, the Access Officer will :

- Receive, acknowledge and respond to requests from researchers;
- Liaise with the BQC19 Coordinator or the Steering Committee as required;
- Receive, acknowledge and evaluate requests for letters of support before sending recommendations to the BQC19 Director.

9.6 PATIENT-PARTNER COMMITTEE OF THE BQC19

A patient-partner committee will be established within the BQC19 to enable community representatives of adults and pediatric patients (in this case, a parent) to play an integral part in the durability of these resources. Committee members will act as partners and advise the Governing Committee on how best to integrate the voice of patients into

the BQC19 infrastructure. Mores specifically, members of this committee will advise the BQC19 on future biobank plans, research tools and communications.

10. ACCESS COMMITTEE OF THE BQC19

The project must be submitted on the BQC19 website access portal. The Access Officer will receive these requests and conduct an administrative analysis of the submissions to ensure that all fields have been completed by the User-Researcher and that all documents associated with the request have been attached (see section 9.5). Thereafter, if the submission is only for samples and/or data from the local collection, the evaluation and access process will be the responsibility of the Access Committee at the participating institution, unless the institution wishes that the BQC19 Access Committee complete the evaluation. In the absence of a local Access Committee that adheres to the access principles of the BQC19, the evaluation will be conducted by the BQC19 Access Committee. In the event that the evaluation is completed by a local Access Committee, decisions will need to be communicated to the BQC19 Access Committee in order to maintain a log of use.

If the submission is for samples and/or data from the provincial collection, it will be evaluated by the BQC19 Access Committee under the supervision of the QCPN. The roles of the QCPN and the Access Committee are defined hereinafter.

10.1. ROLE OF THE QUÉBEC COVID-PANDEMIC NETWORK

The QCPN is the organization identified to ensure impartiality throughout the access process. The QCPN ensures that the chair, members of the Access Committee and the access process are not subject to a conflict of interest. The QCPN guaranties the latter by providing documentation that will include a declaration of conflict of interest signed by each participant, well-defined and publicly available access procedures, and minutes. The QCPN is responsible and accountable for the integrity of the process.

The QCPN is responsible for establishing an impartial and independent Access Committee (the chair and voting members of the Access Committee will not have any affiliation with the BQC19 Steering Committee and will not be involved in the collection of samples and data).

The QCPN enforces the rules and criteria for access to the BQC19 as approved by the Governing Committee.

The QCPN maintains an overall vision at the provincial level to encourage consolidating samples. It supervises the Access Officer who is the person in charge of the administrative/operational access process, as described above, for the BQC19 data and biological samples. The Access Officer may redirect requests to local biobanks when appropriate.

The QCPN ensures the confidentiality of access requests as well as that of documents related to their evaluation.

10.2 ROLE OF THE ACCESS COMMITTEE

The Access Committee is responsible for:

- Analyzing requests submitted by the Access Officer in accordance with the access rules and criteria and as approved by the Governing Committee;
- Analyzing requests according to a schedule created by the QCPN;
- Providing, through the Access Officer, the results of the assessments to the Governing Committee;
- Ensuring that the Access Officer prepares and forwards minutes of the Access Committee meetings to the QCPN.

10.2.1 MEMBERS OF THE BQC19 ACCESS COMMITTEE

Composition of the Access Committee – required expertise:

- Immunology/vaccinology, virology/infectious diseases/systems biology (-omics), pharmacology/pharmacy, statistics, epidemiology, biobank expert, ethics, patient partner;
- One member should be able to identify the risks of re-identification of participants. Depending on the projects submitted, additional expertise may be required for an appropriate assessment. The Access Committee will engage external experts on an ad hoc basis. In particular, if projects involve pediatric population samples, a pediatric expert will be called in to the committee;
- Non-voting members: Access Officer and a representative of the BQC19 Steering Committee approved by the QCPN;
- Regional representation (regardless of the size of the contribution of the participating institutions to the BQC19). Representatives from outside Quebec will be accepted;
- At least two potential members will be identified by expertise (management of conflict of interest/attendance management, etc.);
- The chair and members of the Access Committee are not in any conflict of interest situation with respect to the evaluated applications.

10.3 MEETINGS AND MINUTES OF THE BQC19 ACCESS COMMITTEE

The Access Committee shall meet if necessary on a regular basis, by any appropriate means (e.g., in person, via teleconference, shared files) to review access requests depending on their frequency. Access decisions shall be taken by a majority of votes. Discussions and decisions of the Access Committee will be documented in the minutes by the Access Officer sitting as an observer.

10.4 PROCEDURES FOR ACCESSING BQC19 BIOLOGICAL MATERIAL AND DATA

10.4.1 FREE ACCESS

Data with a very low risk of re-identification and no particular vulnerability (“open access data”), such as metadata and aggregated patient cohorts, etc. will be made public online on the BQC19 website without formalities.

10.4.2 CONTROLLED ACCESS

Biological material and data with a direct or higher risk of re-identification and/or special vulnerability will always be considered as controlled access data. These data shall remain within the network side of the data management application, whose access is strictly controlled. These data will follow the processing procedures listed in Section 6.

10.5. GUIDING PRINCIPLES TO ACCESS BQC19 DATA AND BIOLOGICAL MATERIAL

Eligibility criteria for submitting an access request:

- Academic Researcher in Canada;
- Academic Researcher outside of Canada;
- Researcher in the private sector.

Access will be allocated in a fair, non-discriminatory, objective and transparent manner to all researchers, regardless of their research discipline:

- Well-defined and publicly available rules of access conditions and priorities;
- Adherence to the access processes, rules and criteria of all involved;
- Data may be accessible by everyone, subject to authorizations, legal frameworks and regulations, and depending on the nature of data.

Access to data and biological material shall be subject to an access fee.

The use of data must be consistent with consents given by the participants: Access must respect the rights, interests and expectations of the BQC19 participants and must support initially consented research by the participants, in line with the BQC19 mission.

Data access, a renewable resource, will be provided to enable rapid use of data by all requesters in order to meet the urgent needs for research n COVID-19. Data access applications must demonstrate that the use will minimize the risk of re-identification, and they shall include a section describing the measures taken to that purpose, if necessary. An expedited evaluation process will be available for data only access requests.

Access to biological Material, a limited resource, must be completed responsibly and with sufficient justification.

Applications will be evaluated according to the defined criteria including, but not limited to, the value of the data returned to the BQC19, the scientific contribution of the research project and the potential impact of the access to the samples on the risk of depletion. The evaluation shall also respect *FAIR* principles (*Findable, Accessible, Interoperable, Reusable*) (https://www.nature.com/articles/sdata201618)

Samples use limitation criteria:

- Demonstrated scientific validity, consistent with the BQC19 mission: The use of the Biobank resources must help to maximize scientific, clinical and social advantages.

Independent peer review will be recognized and used by the Access Committee:

- The access process must demonstrate and continuously enhance the value, utility and sustainability of the BQC19. It shall also maintain the reputation of the BQC19, the participating institutions and the granting agencies.

Any experimental data made possible by the access must be communicated to the BQC19, and must become accessible to third parties (adoption of FAIR principles, Open Access/Wellcome Chart COVID)

Maintaining a registry of all projects benefiting from access to the BQC19 biological Material and data. This registry will be made available to the research communities in whole and the general public.

Recipients of data and biological Material shall complete all training required as stipulated by the rules and regulations on the use of human biological data and specimens in research. Special attention shall be paid to the expertise of the teams manipulating the data, without risk of re-identification, in particular in projects involving artificial intelligence approaches.

Various research projects may benefit from the use of BQC19 biological Material and data. Given the objectives of the BQC19, academic researchers, HSSN and private sector researchers, in Canada and worldwide, may access the BQC19 biological material and data if their research projects meet appropriate scientific and ethical standards and are approved by the duly constituted REB.

The process to allow controlled access to the biological material and data is initiated by an application submission via the access portal on the BQC19 website.

1. The researcher must submit an access request that includes a summary of the research project, a justification of the types and quantities of the requested biological material and data, as well as a proof or availability of funding required to carry out the project.
2. The BQC19 Access Officer shall verify the availability of the Material with the BQC19 Coordinator and determine in which participating institutions the appropriate biological Material are located.

3. A cost recovery will be calculated and requested from the researcher for every use of samples and data. (see section 9.6).
4. The Access Officer shall initiate an administrative review of the submitted application. Following this review, the project shall be subjected to an evaluation by a feasibility sub-committee as well as the BQC19 Access Committee.

Access to the BQC19 data and samples shall solely be granted by the BQC19 Access Committee for provincial projects and by the Access Committee at the participating institution for local projects. The access request shall be considered only if the research projects meet the following conditions:

- The research project must respect the objectives of the BQC19 and the scope of the participant' consent;
- The research project must have a scientific value and be scientifically sound;
- The research project must be submitted and performed by qualified researchers;
- The research project must be approved by the duly constituted REB at the latest following the approval of the Access Committee, and prior to signing the biological Material and Data Transfer Agreements, namely:
  - The REB that would be competent to review and approve the project (i.e., the REB that is competent to review the studies of the requesting researcher); or
  - The REB of the CHUM, in the event that the REB is not competent to review and approve the project; or
  - If the applicant researcher is from a jurisdiction where non-identifiable research data and biological material are exempt from ethics review, the REB of the CHUM shall undertake the project ethics review.

5. Once access is approved and the ethics approval is provided, a biological Material and Data Transfer Agreement must be signed. This agreement shall be signed by the User-Researcher of the biological material/data and their institution prior to sending the Material and data. This agreement shall include, in particular, provisions related to the following conditions:

   - Cost recovery measures for the data, biological material and services, as applicable;
   - Measures in effect to ensure confidentiality;
   - The fact that data and biological material shall not be used to create a new biobank;
   - The fact that data and biological material shall not be shared with an unapproved third party and must be returned to the BQC19 or destroyed at the end of the project;
   - Acknowledgement in the publication and communication of the research results of the financial support of the FRQS, GQ and PHAC as well as the contribution of the BQC19 and the local infrastructures of the participating institutions;
   - The fact that raw data shall be shared with the BQC19 in order to be incorporated to the BQC19 database.
6. Preparation and sending of biological Material and associated coded data.
7. Sending the request for compensation.
8. Follow-up on publications with the User-Researcher.

10.6 COST RECOVERY

The BQC19 was formed during a public health emergency, and its establishment was supported by public funds. In order to ensure its durability, a mechanism of cost recovery shall be implemented to enablle its growth and partial self-funding in the long term. This request of compensation shall consider the number of variables used, the number of participants included in the study and the number of hours required for the preparation of the data export file.

The following principals must be respected in cost recovery:

- The BQC19 shall allocate a cost recovery, calculated and defined before the distribution of the material/data to the academic researchers, the HSSN and the industry as determined by the BQC19 Governing Committee;
- The BQC19 shall operate on a mixed cost method (cost per project and cost for the infrastructure maintenance). The latter must take into account the BQC19 operating cost in the short and long term;
- Access fees will be determined by the Governing Committee and be reflected in the access agreement. The biobank determines the cost by using an agreed-upon method, as suggested by the Canadian Tissue Repository, to calculate costs and determine user fees to be invoiced to researchers for services related to accessing the biobank.

10.7 SHIPPING OF THE BQC19 BIOLOGICAL MATERIAL AND DATA

The BQC19 biological material must be considered potentially infectious. Therefore, it must be handled, packaged, labelled and accompanied by documents required by the different regulatory agencies, when shipped. In Canada, the transportation of infectious Material is governed by the Transportation of Dangerous Goods Act, 1992 (TDGA), the *Transportation of Dangerous Goods Regulations* (TDGR) and the International Air Transport Association (IATA) *Dangerous Goods Regulations* (DGR).

In the event of international shipping, the shipper must be informed on the rules and regulations of the receiving country in order to combine them of those in Canada. All packages shall be sent with a certainty that they will not be delayed by the authorities.

10.8 DATA SHARING WITH PARTNERSHIPS INITIATIVES

Partnering with national and international initiatives that can be mutually beneficial is one of the expected objectives of the BQC19, especially by PHAC.

10.8.1 SHARING OF DATA COLLECTED BY THE BQC19 WITHIN THE FRAMEWORK OF PARTNERSHIPS

The data collected by the BQC19 may, under the conditions stated hereinafter, be shared through a contract and upon the approval of the Steering Committee and the Governing Committee. Data must be shared in a non-identifiable form and these partners shall become custodians of these data. Therefore, they shall not be subject to the process detailed in section 10.4 and 10.6. The principles governing these partnerships are as follows:

- The vision and the mission of the partnership initiative must align with those of the BQC19, in particular to the adoption of the principles outlined in the Declaration of the Wellcome Trust Foundation;
- The data access and sharing processes of the partnership initiative should be governed by the same principles as those of BQC19;
- The processes in place by the partnership initiative for access and sharing of data received from the BQC19 shall be subject to the conditions outlined in the Consent Form signed by BQC19 participants;
- Only non-identifiable data from the BQC19 shall be shared with the partnership initiative;
- Although shared with the partnership initiative, these data shall remain available to the scientific community through the channels specifics to the BQC19 which are detailed in sections 10.4 and 10.6;
- The participant identifiable information shall be managed only by the BQC19.

The development of these partnerships must be the subject of a prior amendment of this Management Framework and be approved by the CHUM REB acting as REB reviewer on behalf of the HSSN institutions.

10.8.2 CGEN HOSTSEQ: PARTNERSHIP INITIATIVE OF THE BQC19

CGEn HostSeq is a joint research program of the *Hospital for Sick Children*, McGill University and the *University of British Columbia*, funded by the Government of Canada and administered by Genome Canada. As part of this program, 10,000

genomes will be sequenced (whole-genome sequencing) from the DNA extracted from the blood of SARS-CoV-2 infected patients, with the goal of accelerating COVID-19 research by sharing these data with the scientific community, through a rigorous and independent access process.

Given that the principles set forth in section 10.8.1 are being met, a partnership between the BQC19 and HostSeq shall be formed to share with the latter the whole-genome sequencing data derived from the BQC19 samples as well as the data collected in the CRF of the BQC19.

The Governing Committee has approved, in its meeting on June 15, 2020, the principle of a collaboration agreement with CGEn HostSeq for the whole-genome sequencing of the BQC19 samples. This sequencing shall be performed at the McGill Genome Centre at McGill University and sequencing data shall be made available to the scientific committee as detailed in section 10.8.1.

11. CONTINUITY OF THE BQC19

If the BQC19 Lead Researcher at the participating institution is no longer qualified to manage the BQC19, another investigator may be appointed for that institution. In the event that no researcher has expressed an interest in joining the BQC19, the direction of academic research of the CISSS and the CIUSSS, or the CHU research centre Director shall appoint a new lead researcher.

If no Lead Researcher has been identified, or if the Director of research decides that the BQC19 is no longer an essential infrastructure for the institution, the process of dissolving this BQC19 site by the institution's decision is initiated.

In this case, the biological material may:

1. Remain in site and be managed by the BQC19 staff on the premises.

   If the BQC19 Lead Researcher at the closed institution wishes to keep the BQC19 biological material and data at the institution:
   - Data extraction is done to remove the biological material data and samples from the management. application BTRSRV2;
   - The data is deposited in a raw database that is made available to the researcher;
   - The researcher retains the local database as well as the raw database. The BTRSRV2 application is removed;
   - The institution is removed from the BTRSRV2 network database.

2. Be transferred to another participating site.

   The biobank is closed at the institution and samples are transferred to another site.

   - Data extraction is done to build a list of inventory of the biological material;
   - Information related to biological samples missing from the physical inventory are deleted from the network database. Participants are checked against the local database to eliminate those who do not match any sample;
   - The biological material is transported physically to the new site;
   - All biological Material are assigned to the new institution database. The former biobank in the closed institution is deleted from the database;
   - Local database is retrieved by the new institution. The LTB shall assist to recode the participants in the retrieved local database in order to ensure the integrity;
   - The hosting institution must modify the location and number of participants of all biological material transferred into the network database.

3. Be destroyed, as a last resort option.
   The institution's biobank is closed and it is not possible to retrieve the biological material:

   - The biological material is destroyed ;
   - Data extraction is done to remove from the BTRSRV2 ann data related to the biological material in question;
   - The institution is removed from the network database;
   - The information in the local database is deleted.

12. ETHICS FOLLOW UP

The CHUM REB has approved this Management Framework through a multi-centric review and shall provide a follow up for the participating institutions of the HSSN. Given the current health emergency situation at the time of the creation of the BQC19, this Management Framework will require revisions. During the health emergency situation, any amendment in procedures required to ensure the security of the participants or of the research staff shall not require any ethics approval prior to its implementation. The REB must be involved at the earliest possible time in order to share the risk reduction measures with other institutions.

13. REVISION

A thorough revision of this Management Framework shall be undertaken every five (5) years. Failing a revision within the five (5) year time limit, the latest version of the REB approved Management Framework shall remain in force.

List of Appendices