MANAGEMENT FRAMEWORK

BANQUE SIGNATURE

Medical/Psychosocial data and human biological materials bank

November 2022

Nom (Version)	Date Approbation	Étapes importantes
Version 1	23-10-2012	Résolution 2012023-6.2.
	26-09-2012	
Version 2	29-01-2013	Authorization to re-contact participants
Version 3.2	24-08-2016	Addition of a control group
Version 4	20-12-2022	Updated framework

Centre intégré universitaire de santé et de services sociaux de l'Est-de-l'Île-de-Montréal

Québec

MANAGEMENT FRAMEWORK
SIGNATURE BIOBANK

This management framework has been revised by the current members of the Management Committee:

Stéphane Guay, Signature Biobank Director, and director of Centre de recherche Fernand Séguin de l'Institut universitaire en santé mentale de Montréal.
Robert-Paul Juster, Adjunct Director of Siagnture Biobank, Centre de recherche Institut universitaire en santé mentale de Montréal.
Janick Boissoneau, Biospecimen manager, Biobanque Signature, Centre de recherche Institut universitaire en santé mentale de Montréal.
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Cécile Le Page, Coordonnator, Centre de recherche Institut universitaire en santé mentale de Montréal.

HISTORY OF CHANGES TO THE MANAGEMENT FRAMEWORK:

REVIEWS OF MODIFICATIONS OF THE ICF:

14-12-2012 : **Version 2.1**

29-05-2013 : page 40. Two new survey items; age of first menarche and date of last menarche.

20-05-2013 : pages 40 et 43: Authorization to re-contact participants

30-05-2014 : Retraction of SBQ-R questionnaire

09-09-2015 : Appointment of a new Director (Stéphane Guay)

30-06-2016 : Addition of a phone pre-interview questionnaire

30-08-2016 : **ICF version 3.**

- Addition of a control group (addendum of the protocol).
- Addition recruitment video for consent approval (GC mp4 version 1)

10-01-2017 : Addition of the SBQ-R questionnaire

17-08-2017 : Addition of new questionnaires.

- PSYRAT
- Modification of DAST-10 with type of substances use
- Hospitalisation history (HH)
- CEVQ questionnaire
- Familly income

03-07-2017 : Authorization to review medical files

07-08-2018 : **FIC Version 4.**

28-01-2019 : New questionnaire LGBT Status.

13-05-2019 : Modifications of AUDIT et DAST. Retraction of AUDIT-10-V1 retirées. Question T4 AUDIT-10-V2 removed.

09-08-2019 : Modification version 5

- New web address.
- Addition Question AUDIT-10 use of alcohol in the last 7 years.

- Addition of 5 Questions in DAST10C1 and modification of DAST-1C2-C10. (page 29-A1)
- Question on TABACCO (ESCC-2008) : Q3b : use of sur electronic cigarette
- Addition of 10 questions CAST (page 25-A1)
- Addition of questionnaire ASSIST (6 groups of questions)
- Authorization to collect urine

25-07-2022 : Addition of SIMPAQ at time A4

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LIST OF ABBREVIATIONS :

CAI	Commission de l'accès à l'information du Québec
REB	Research Ethics Board
FRQ	Fonds de recherche du Québec
RAMQ	Régie de l'assurance maladie du Québec
SIS	Système informatisé Signature
SSL	Secure Server Line
ICF	Informed consent form
IUSMM	Institut de Santé Mentale de Montréal
DERI	Direction de l'Enseignement, de la Recherche et de l'Innovation

1. Introduction

1.1. Objectives

The purpose of this management framework is to explain the rules and procedures for the operation of the Signature Biobank of medical, psychosocial and human biological material. It also sets out the principles that guide its use and presents the general orientation of the biobank towards the users of the Institut Universitaire en Santé Mentale de Montréal (IUSMM).

1.2. General definition

Biomarker :	Biomarkers are biological molecules found in blood, bodily fluids and organic tissue. Biomarkers may indicate normal or abnormal processes and the presence of a disorder or disease.
Biospécimen :	A sample of blood, bodily fluid or organic tissue.
Clinician :	In the following document, the term “clinician” includes all professional staff on treatment teams with access to users’ medical files.
Raw data :	*Raw data* represents the individual responses to each of the psychosocial signature questionnaires filled out by participants.
Aggregated data :	*Aggregate data* represents the average scores obtained by participants on the psychosocial signature’s various scales and subscales. This aggregate data may be presented in table or graphic form.
Participant :	In the following document, this term refers to users using Institut universitaire en santé mentale de Montréal’s health care services who have agreed to participate in the Signature Bank as a research subject.
Biobank :	A biobank is an administrative and technical structure in which human biological material, donors' personal and medical information are preserved, stored and managed.

2. General description of the data and human biological Materials Signature Biobank

2.1. Objectives of the Signature Biobank

On the other hand, the Biobank aims to collect *human biological materials* from the same Institut's participants (The list of requested human biological materials is detailed in Appendix B.)

The Biobank will enable greater use of medical and psychosocial data in combination with human biological materials for the following purposes:

- Developing mental health research in terms of its psychosocial and biological aspects as well as its medical aspects;
- Helping clinicians to improve the care provided to IUSMM's users as well as the care provided in the general mental health field;
- Facilitating IUSMM participants' involvement in their treatment and care—e.g., by making aggregate data available to the treatment team.
- Promoting knowledge transfer between clinicians and users. Encouraging collaboration with users based on the results of research derived from the Signature Biobank—e.g., through the use of innovative research tools such as the iPad.

2.2. Purpose of the Signature Biobank

The Signature Biobank project follows the "decade of the brain" in Canadian mental health research. The development of basic research has paved the way for the treatment and prevention of mental illnesses that the Quebec and Canadian governments now want to prioritize. Mental illness is a major social problem: its prevalence rate affects over 50% of the Canadian population during their lifetime, and direct spending on mental health is set to double over the next 10 years. Now, the "decade of the patient" has begun with a focus on applied mental health research. The Signature Biobank is aligned with this vision. The project aims to build bridges between basic research and applied research on the one hand and between applied research and clinical practice on the other. The reason for this pooling of information is to better customize medication and intervention as well as to better document clinical decisions based on scientific data.

The Signature Biobank is therefore designed to systematically amass a vast collection of "signatures"—biological, psychosocial and clinical indicators—from volunteer participants who are users of IUSMM. The project involves collecting data each time a user is observed, at emergency service admission and after hospitalizations (including

management by outpatient clinics). All of this data can be used for research projects on the population as a whole or specific subgroup.

2.3. Population and selection criteria

The recruitment of participants with psychiatric disorders is done at the IUMMM mental health institute's emergency room, with patients able to give their consent. As of 2016, a so-called control cohort, without major psychiatric disorders, was also recruited.

In 2020, participant recruitment has been stopped. Should recruitment be reinstated, the ICF and recruitment protocols will be re-evaluated by the Management Committee to ensure that they are still appropriate. If major changes are required to meet the new recruitment requirements and/or procedures, the revised ICF and recruitment protocols will be submitted to the REB for approval prior to the resumption of recruitment.

In 2022, the biobank consisted of psychosocial and biological data from 2173 participants. Longitudinal follow-up of participants was done for 697 participants in the short term (named time T2), and for 473 in the long term (named time T4).

2.4. Data and biological material

The Signature Biobank consists of medical, psychosocial, and biological data, as well as plasma, serum, hair, blood cell, and saliva samples collected from participants who visited the IUSMM Emergency Department between 2012 and 2020. A second 'control' participant group, with no known psychiatric disorders, were also voluntarily enrolled between 2016 and 2020.

2.5. Ethical principles of the Signature Biobank

The first principle of the Signature Biobank is the principle of benefiting people—i.e., it aims to promote the health of Institut universitaire en santé mentale de Montréal's users. This principle impacts users through advances in research and prevention and the continuous improvement of care quality.

The second principle of the Signature Biobank is to encourage mental health research in the areas of care, prevention and basic research for the benefit of Institut universitaire en santé mentale de Montréal's users suffering from mental illness.

The third principle of the Signature Biobank is to serve as a tool that will enable clinicians to improve medical management, intervention and care for Institut universitaire en santé mentale de Montréal's users. The improved intervention and care may then serve as best practices for other psychiatric care environments.

3. Gouvernance mecanisms

3.1. Historic of the Signature Biobank

The Signature Biobank was an integral part of IUSMM's strategic planning in 2009.

Over the course of a lengthy process, a team of more than 80 people, comprising clinicians, researchers and international specialists, was consulted for the purpose of:

- **Determining the best biomarkers to study in order to understand the mechanisms at the root of human mental disorders.**
- **Identifying the best psychological and social measures to obtain in order to better understand the psychological and social aspects of mental illness.**

These measures can provide a comprehensive snapshot of the participant's emotional well-being and mental state, as well as capturing other characteristics related to mental health, such as lifestyle habits, sleep patterns and socio-demographic background.

- **Identifying the best methods for the tests to be conducted within IUSMM clinical populations (e.g., optimal moments for testing and taking samples, number of measures, etc.).**

This teamwork resulted in the engagement of the psychiatric community at Louis Hyppolite Lafontaine Hospital and the development of a list of questionnaires and selection of standard biomarkers, detailed in Appendices A and B. Updates to the Signature Biobank questionnaires were made following the recommendations of the Subcommittee, and approved by the Signature Biobank Coordinating Committee members.

3.2. Supervising organization and administrative structure

The Signature databank of biological material is managed by CIUSSS-EMTL.

The project was approved and ratified IUSMM's Board of Directors on October 23, 2012.

Responsibility for managing the Signature Biobank lies with the senior management of the IUSMM Research Center.

While the Signature Biobank is the institution's responsibility, the Institut's Research Centre's senior management (or designated representatives) and the REB must be formally consulted regarding any changes to the organizational structure, the cessation or resumption of activities, the preservation or destruction of data and any other ethics-related matters.

Any changes to the project's organizational structure must then be presented to the institution direction (DERI) for final approval.

Due to this administrative structure, all data and biological materials contained in the Signature Biobank belong to the institution, which ensures that the project is managed properly. In the event of a cessation in the Signature Data and Biological Materials Bank's activities, all its contents become the responsibility of the institution, which may then decide on the Biobank's future by choosing to resume its activities or to either preserve or destroy the data.

3.3. Funding

The creation of the biobank was made possible with the support of the IUSMM Foundation and *Bell pour la cause* funding.

The analytical laboratory and storage space at Biobanque Signature were financed by a grant from the Ministry of Higher Education, Research and Science.

Initial funding for the Signature Data and Biological Materials Biobank is provided by the IUSMM, the Fondation de l'Institut universitaire en santé mentale and the Research Centre of the IUSMM. Additional funding has been received from the RQSHA and other financial ressources are generated over time by the fees for accessing data and biological materials requested by researchers using the Biobank.

The management team must ensure that any income generated will first be used to create a reserve fund to ensure the long-term survival of the biobank. This reserve fund must help support management costs, the costs inherent in maintaining the Biobank and the purchase of new equipment.

The Signature Biobank therefore has no commercial or profit-making goals.

The Research Centre's senior management is committed to pursuing any possible grants that would increase the Signature Biobank's funding in order to support its ongoing management and the development of its infrastructure.

3.4. Structure of the Signature Biobank

3.4.1. History and change in gouvernance

Until early 2022, the Signature Biobank was managed by a Coordinating Committee. The Coordinating Committee worked with a Management Committee, which was responsible for managing the operation of the Biobank on the various hospital units targeted by the project for biological, psychosocial, and medical measurements.

In 2022, the Coordination and Management Committees merged. The Management Committee is now supervised by an Advisory Committee which is consulted on annual basis. The terms of reference for these two new Committees are appended to this management framework (Appendix H and I). The Management Committee is an integral part of the establishment's organizational chart. It reports to the Direction de

l'Enseignement, de la Recherche et de l'Innovation (DERI), which in turn reports to the Direction générale of CIUSSS-EMTL. The General Management is itself under the aegis of the CIUSSS-EMTL Board of Directors.

3.4.2. Biobank management

The Scientific Director of the IUSMM research center, automatically takes on the role of Director of the Signature Biobank. He is assisted by a researcher from CR-IUSMM, as deputy director to form the Steering Committee.

The Director oversees the biobank program and activities and ensures that they are conducted in accordance with the biobank's objectives. He/she must also ensure that the necessary infrastructure is in place for the proper management of the biobank, including the storage and protection of data and biological samples. He/she also ensures that the use of the material is respected and that confidentiality procedures are maintained according to the requirements of the REB.

The Director chairs the Management Committee of the Signature Biobank acts as the Management Committee's representative on the IUSMM Research Centre's Executive Committee, the IUSMM's Executive Committee and the IUSMM's Board of Directors (Quebec). He/she receives reports from the Management Committee through the Biobank Coordinator and approves the agenda for meetings to address issues raised by the Management Committee. The Director of the CR-IUSMM can exercise a veto on Management Committee votes if he/she feels that the Committee's decisions are not consistent with the mission of the Biobank and its management framework. He also has the responsibility to ask the REB and the Scientific Evaluation Committee to set up an ad hoc committee to deal with any dispute or complaint that could not be handled and resolved by the Management Committee to the satisfaction of all parties concerned.

Figure 2

Organigram of the Signature Biobank

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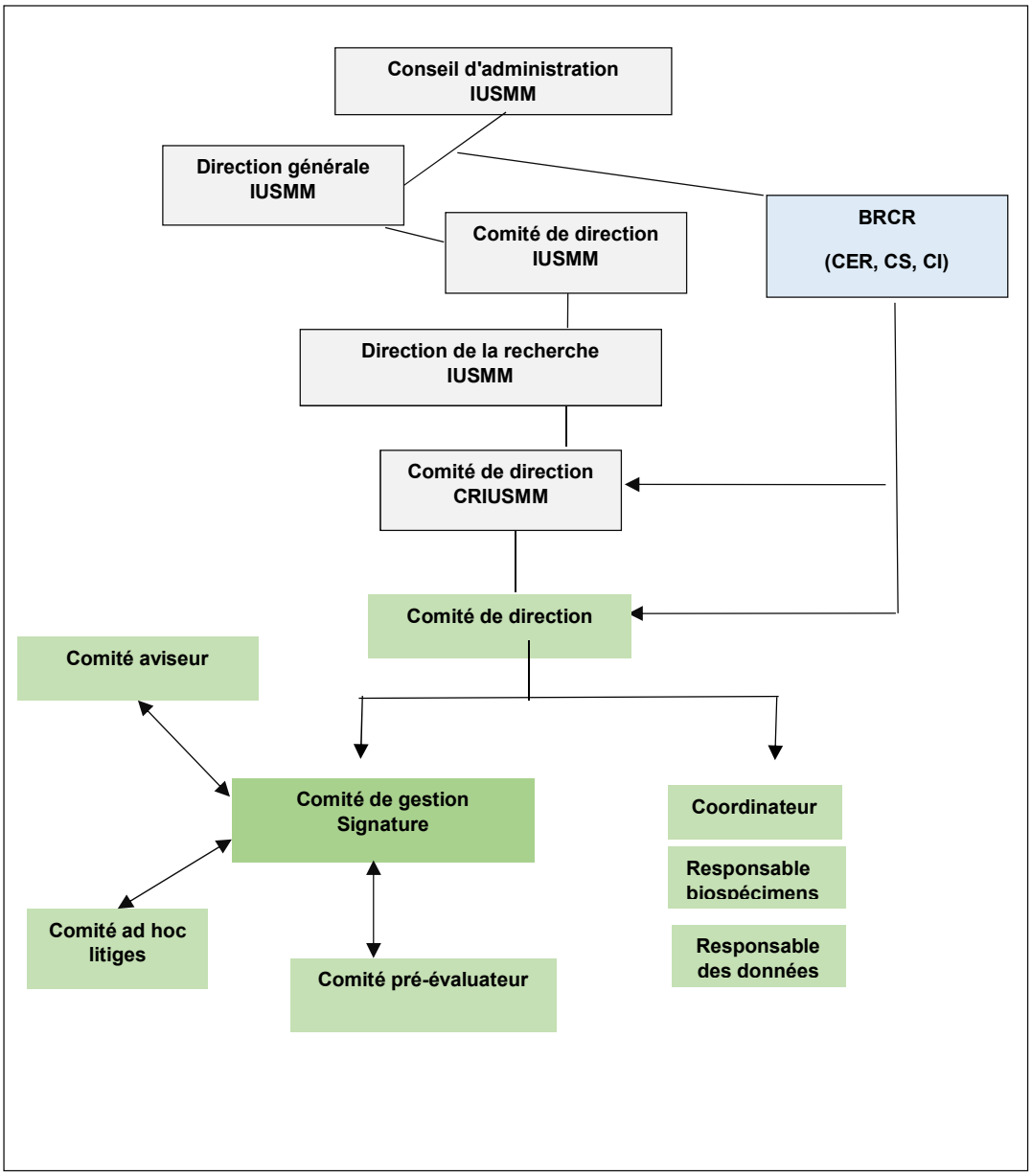

3.4.3. Other members

The biobank coordonnitor

Under the supervision of the biobank management team, the Biobank Manager is responsible for managing the Signature Bank's data and biological materials, as well as requests for access to data and biological materials. He/she acts as a resource person and intermediary between the various players (researchers, clinician-users, research management, members of the REB, data and biological material management technicians).

With the data biobank manager., he/she is also responsible for keeping track of the history of collected specimens, from the collection, conservation, distribution and destruction stages as required. A summary of the data inventory is available on the Signature biobank dashboard website (https://signature.shinyapps.io/tableau/).

The coordinator is also responsible for keeping a log of access requests. The register will enable each access request to be tracked and managed.

The biobank coordinator keeps the Management Committee informed of the progress of the biobank's activities, on a regular monthly or fortnightly basis, at Management Committee meetings.

An annual report is produced by the biobank coordinator at the beginning of the calendar year, and is validated by the Management Committee before being forwarded to Executive Management, which submits it to the CIUSSS-EMTL Board of Directors. This report describes the progress of data collection, where applicable, the number of access requests and publications or communications resulting from research associated with the Signature Biobank.

He/she will produce communication documents (newsletter, social media, etc.).

Once a year, the coordinator is responsible for renewing Signature Biobank's ethics certificate.

Data biobank manager

The database managemer is appointed by the Scientific Director of the research centre and reports to the Biobank coordinator and the direction committee of the research centre.

His role is now primarily to ensure the confidentiality of data stored in the Signature database. He works in tandem with the Biobank coordinator and informs him of the available data when data access requests are received. He is the only person (other than the Biobank coordinator) with access to the source code linking study participants' demographic information to their depersonalized code.

Biospecimen manager

The biospecimen manager is appointed by the Scientific Director of the research centre and reports to the Biobank coordinator and the Direction committee of the research centre. Initially, he/she was in charge of the technical team that collects and stores the biospecimens. Now he/she mainly oversees the appropriate management and preservation of biospecimens and liaises between the various parties (research nurses, clinical nurses, research technicians) involved in the biospecimen collection process. He works in tandem with the biobank coordinator to inform him of the available biospecimens when biospecimen access requests are received. He /she is also in charge of the infrastructure, and space allocated for the biospecimens storage and the proper functioning of the storage devices (fridges, freezers…). He/she supply specimens to researcher whose research projects have been approved by the REB.

3.4.4. Management committee

The Signature Biobank Management Committee is responsible for seeing to the proper day-to-day functioning of the Signature Biobank with respect to the taking of biological, psychosocial and medical measurements and the management of data and biological materials. It ensures the proper functioning of the Signature Biobank in the various hospital units where measurements are taken and resolves internal Signature Biobank management issues at the operational level.

The Management Committee is responsible for coordinating the various resources of the biobank and ensures the smooth operation of the Signature Biobank by ensuring cohesion between the various players involved. It is also the body designated to receive, process and attempt to resolve, in the first instance, any dispute or complaint concerning requests for access to data or biological material.

The Management Committee validates the annual report produced by the Biobank coordinator before forwarding it to the scientific Director, who submits it to the Board of Directors of the University Institute of Mental Health in Montreal. The annual report presents the progress of data collection, the number of requests for access and any publications resulting from research associated with the Signature Biobank.

The management Committee evaluates any requests for changes to the Signature Biobank (modifying the Biobank's structure, expanding its operations to include other programs or institutions, adopting new directions arising, for example, from recent scientific discoveries, etc.) proposed by the IUSMM Research Centre's senior management. When the requested change is deemed beneficial by the Management Committee, it must then, if necessary, be presented to the Scientific Evaluation Committee and REB before being presented to the institution for final evaluation and approval.

In its most recent mandate, the Management Committee is also responsible for developing relevant collaborations and partnerships to ensure the development of the biobank. It ensures that knowledge is disseminated to the external community of

stakeholders and other biobanks. The Management Committee meets bi-monthly to discuss the management of the Signature Biobank.

The term of reference of the Management Committee is provided as annexe H. Decisions and discussions are recorded in the meeting minutes by the biobank coordinator.

The Management Committee includes:

- Biobank director
- Adjunct biobank director
- Biobank coordinator
- Data biobank manager
- Biospecimen manager
- A clinician-researcher
- A student from University of Montreal, department of Psychology

3.4.5. Advisory Committee

To ensure optimal execution of Signature Biobank development, an Advisory Committee, comprised of experts in the field, was appointed in April 2022 to:

a. Advise on annual program progress.

b. Provide strategic advice to Biobank Management Committee members on initiatives and projects to maximize impact on transdiagnostic and clinical mental health research.

c. Advise on knowledge translation.

d. Advise the Management Committee on the relevance of current collaborations and partnerships, and on future opportunities for such partnerships and collaborations.

e. Promote the dissemination of knowledge to the external community of relevant stakeholders and other biobanks.

The advisory committee members include :

- A psychiatrist-clinician
- a representative of other clinical professionals
- one or more neuroscience researchers

The various representatives on the Coordinating Committee are appointed for an initial term of two (2) years. The Advisory Committee may also request on an ad hoc basis the

presence of other resource persons, when required for the examination of any particular issue related to its mandate.

The mandate of the advisory committee is presented in the terms od reference sin Appendix I.

4. Consent

4.1. Consent and the specific context of a psychiatric institute

In the psychiatric field, obtaining user consent for a research project is a process that must be handled in a balanced way. Some users are incapable of providing consent due to the stage of their illness while some are perfectly capable of providing consent despite their mental illness; in others, the capacity to consent varies depending on their current state. The capacity to consent is a continuum rather than a black-or-white scenario. The users treated in a psychiatric hospital have differing degrees of risk based on their mental illness; any research project must therefore take this into account both in its eligibility criteria and its implementation.

In the case of an incapable person of full age under protective supervision, the proxy, guardian or trustee named for him by the court may represent the user (legal representation) and provide substitute consent. In the case of incapable individuals without legal protective supervision (i.e., assigned by the court), they may be represented by a civil union or de facto spouse or, if there is no spouse and/or there are impediments to obtaining the latter’s consent, by a close relative or other individual with a special interest in the user, in accordance with the conditions for substitute consent to care stipulated in the Civil Code of Quebec (Article 21, Alinéa 1).

Although this only concerned a few rare cases, minors were recruited by Signature Biobank only if they were aged 16 or over.

It was up to the research nurse to attest to the user's capacity for free and informed consent, after presenting the biobank project and answering any questions. At each new measurement cycle, to ensure the continuity of the user's consent, the research nurse verbally verified that the user still agreed to participate in the project, and reiterated that he or she could withdraw consent at any time.

The most recent CIF, was approved on July 8, 2019 by the REB (Appendix C). This form explains the objectives and operation of the Signature Biobank, as well as the practicalities of participation. This information was also available in a video format that could be viewed on a tablet (i.e., iPad) to promote informed decision-making and facilitate user understanding.

4.2. Withdrawal of consent from users as research subjects

Participants may withdraw from the Signature Biobank at any time simply by giving verbal notice. They may also request in writing that data and biological materials pertaining to them be destroyed. The biobank undertakes not to contact participants for the completion or updating of questionnaires.

A withdrawal procedure will be initiated, including:

- When such a request is made, the database management technician must place the participant's data and and notify the participant in writing that the process has been carried out. Date of withdraw and date of specimen destruction will be recorded in the database.
- The person in charge of the biological material will physically destroy the samples and record the date of destruction in the computerized sample directory..
- The coordinator will complete a paper withdrawal of consent form, which will be attached to the participant's ICF, and will inform the participant in writing that this destruction procedure has been applied.

However, participants' right of withdrawal includes the following limitation: once their denominalized data has been aggregated with other data and provided to one or more researchers for an analysis or publication, it is impossible to withdraw the data from that particular analysis or publication, since it has already been pseudonymisated.

5. Collect of data and biospecimens

5.1. Recruitment and eligibility requirements

It is possible for any user of IUSMM's clinical services (including the hospital's outpatient clinics) to participate in the Signature Data and Biological Materials Biobank. Biobank participants were recruited when they are admitted to IUSMM's emergency department or inpatient unit, when they are transferred to a hospital outpatient clinic or when they present directly at an outpatient clinic from the evaluation-liaison module (MEL).

As part of the Signature Biobank's implementation, participants used an iPad to watch a video explaining the project as a whole and the terms of their involvement. They were then able to sign a consent form, following which they will complete a series of self-assessments with the research nurse (Appendix A).

As of August 2016, a so-called 'control' cohort was also assembled. A consent form specific to this cohort was developed and endorsed by the REB (August 24, 2016). Prior to recruitment, a participant's eligibility is assessed using a recruitment form, to verify that the person meets the selection criteria for the control cohort. If the participant is deemed suitable for recruitment, explicit consent is submitted for signature for official approval to participate in the biobank. In case of non-eligibility in the case of an incidental finding during the blood sample analysis, the participant will be invited to consult his/her family physician as detail in the Biobank protocol (verson 4).

5.2. Collect and data storage

This kind of project is not possible without the active participation of clinicians and, most importantly, patients. In order to promote research subjects' active participation in the project, a customized iPad application was developed. It was tested by means of a pilot project in 2010 with 120 patients in order to ensure its technical viability and suitable conditions for obtaining consent from patients asked to participate in the research (e.g., informing them via video).

The collected psychosocial signature data were then be transferred in anonymized form to a centralized database. Researchers and clinicians interested in accessing the database for research purposes will submit a data access request, which will be reviewed by the REB.

Participants diagnostics :

While self-reported questionnaires have indisputable benefits with respect to the various psychological dimensions experienced by participants, users are clearly not in a position to self-report their psychiatric diagnosis and may not always be able to adequately report the various medications prescribed to them. What's more, a large number of people suffering from psychiatric disorders have other chronic disorders as well, and it may be difficult for some users to recall all of the medical conditions with which they have been diagnosed during previous years.

For the purpose of obtaining this key information, it is therefore appropriate to use additional methods that make it possible to validate information via multiple sources. On the one hand, the Signature Biobank will obtain information relating to participants' diagnosis and psychiatric medication from their attending psychiatrist. Meanwhile, a request has been initiated in 2018 to the Commission d'Accès à l'Information du Québec (CAI) and the Régie de l'Assurance Maladie du Québec (RAMQ) each year for all participants who took part in the Signature project. The following information will be requested for the preceding two-year period with the aim of fully understanding all the chronic diseases from which participants are suffering: past and present mental and physical illnesses; medications prescribed for past and present mental and physical illnesses; medical complications; and causes of death. This information request will serve to confirm the diagnoses obtained from participating psychiatrists at the IUSMM while also contributing to making better diagnostic assessments based on all available medical information and to identifying physical disorders whose presence may be linked to mental disorders.

5.3. Biospecimen collection

Once the consent to participate in the Signature Biobank is signed by the participant, blood, hair and saliva samples are collected according to the procedure described in Appendix H (Protocol version 4). Before the samples are processed, they are denominated according to the procedure described in paragraph 6.1.

A portion of the samples are sent to the Louis-Hyppolite Lafontaine Hospital laboratory and to the Optilab laboratory of HMR for analysis. The remaining samples are transferred to the Signature laboratory of the Research Center where they are either analyzed immediately or stored for further use. Les données biologiques recueillies sont énumérées à l'Annexe B and in protocole version 4. In addition to the data listed in Appendix B, the Biobank may consult the medical records of IUSMM participants. Biological data collected are listed in Appendix B and in protocol version 4. In addition to the data listed in Appendix B, the Biobank may consult the medical records of IUSMM participants.

5.4. Use of biobank data

The data obtained also has the potential to provide direct clinical benefits: psychiatrists (and other clinicians) will have access to a summary of participants' scores on the various psychosocial questionnaires. Based on their clinical judgment, psychiatrists will therefore be able to use participants' aggregate data to complete their clinical evaluation or discuss it with them. For example, once several signatures have been collected, they will be able to visually portray participants' clinical evolution. Aggregate data reports kept in a participant's medical file will also include the following official disclaimers:

1) *In accordance with existing professional codes of ethics, under no circumstances whatsoever may data from the Signature Biobank be used or interpreted for diagnostic or therapeutic purposes except by those with the necessary professional qualifications. These assessment tools are not a valid substitute for a clinician's judgment. They represent one source of information among many that may offer avenues for reflection and observation or enable the validation of hypotheses over time.*

2) *Research data has no legal bearing on clinical practice.*

6. Mode of régulation

6.1. Denominalization du matériel collecté

Participants' biological material samples and medical/psychosocial data will be stored in a strictly confidential manner. To this end, data will be denominalized.

The denominalization process involves replacing identified, personal information—e.g., surname, given name, alphanumerical coordinates or ID such as medicare number comprised of the patient's initials and date of birth—using a simple algorithm. All data and biological material in the Biobank can be transmitted to user-researchers in their denominalized form.

For the collection of biospecimens, the nurses' office received a unique code generated following entry of the participant's demographic data. This unique code was used to print barcodes for the biospecimen containers. The biospecimens obtained were aliquoted and placed in specific cryotubes. Biospecimen data were therefore denominated as soon as the sample was taken.

Once the biospecimens had been analyzed, the biological data were integrated into the central database using the same method as for the transfer of medical and psychosocial data.

6.2. Data retention and traceability

Collected information will be stored in a secure, computerized database SQL, located on the CR-IUSMM Est-de-l-ile servers, in accordance with the document storage regulations governing health and social services institutions in Quebec.

The biobank's data manager keeps the list confidential and has secure access (with coding key and computer passwords) to the coded file containing the pairing between the nominal information and the associated code. This list will never be passed on to the user-researchers.

A copy of the scripts and analysis data prepared by the data manager is stored on another IUSMM server.

Only the data manager has access to the denominalized database. Access to this database is password-protected.

6.3. Mesures de sécurité physique et informatique

Les données psychosociales et médicales autorapportées par les participants

In order to ensure the confidentiality of data, all psychosocial and medical data will be obtained by means of an IT tool, the Système Informatisé Signature (SIS). Participants had access to a secure SIS website containing the questionnaires via which they inputted their data.

To reach the questionnaire website, they had to identify themselves to the system by using an access code and personal password. Other security measures, such as regular updating of passwords and locking of the system when not in use, have also been put in place.

Questionnaire responses are denominalized, meaning that a code is used to identify the participant. This ensures that data transferred to the server does not contain any identifying information.

Once questionnaires have been filled out on the secure website, the data is encrypted (as a series of random symbols), making it completely non-identifiable if intercepted while being transferred to the server.

To ensure the security of data during transfer from a computer to the server, the standard method of Secure Sockets Layer (SSL) technology is used. SSL technology is used by banks to ensure complete confidentiality for data transferred during online banking transactions.

Data collection was carried out in two (2) stages: demographic information, then questionnaire responses.

- Demographic data (name, age, gender, etc.) is the first information provided by participants. This data was be immediately encrypted and sent to the server. Personal demographic data and the code that identify the participant henceforth are stored in an encrypted table separate from the data table containing the questionnaire responses. This process prevents any connection being made between the demographic data and questionnaire responses.

- The system then generated a unique, temporary access code that allowed the participant to begin filling out questionnaires on an iPad. The entered data is denominalized, encrypted and sent to the server to be stored in the database.

Biospecimens

Biospecimens that will be analyzed later after collection are stored in the Signature Center, located in the IUSMM Research Center. Access to the Signature Centre is available to authorized personnel only. The freezers are connected to emergency outlets and monitored remotely under the direction of the Biospecimen Manager.

6.4. Time of storage of data and biospecimen

The data of the biobank will be kept for the duration of the biobank's existence. Only participants who wish to withdraw their consent will have their data destroyed, provided that it has not yet been used in a research project.

Depending on the nature of the biological material, its intended applications and the means of storage, the biospeciemn may have a limited life span.

7. Managing access request and database

7.1. Définitions: Types of data and biospécimens

There are two types of data in the Signature Biobank database: raw data and aggregate data. ***Raw data*** refers to the individual responses to each of the questions on the psychosocial signature-related questionnaires filled out by participants. It also covers data on individual concentrations of specific biomarkers based on the results of biospecimen analysis.

Aggregate data refers to the average scores obtained by each participant on the various psychosocial signature scales and subscales. This aggregate data may be represented in table or graphic form.

There will be two types of biospecimen available in the Signature Biobank's biospecimen bank: primary biospecimens and secondary biospecimens:

Priselected biomarkers refer to biospecimens that may only be used for analyzing the biomarkers described in Appendix B of this document.

Emerging biomarkers are biomarkers that may become of interest in mental health research based on new research data that appears in the coming years. Part of the biobank's biospecimens are reserved for analysis of emerging biomarkers. To gain access and proceed with their analysis, researchers must apply for access to the biobank, providing a scientific rationale for the measurement of these emerging biomarkers, which will be approved by the access committee and, if necessary, the management committee. In order to access and analyze these emerging biomarkers, researchers will have to submit a request to the Management Committee which provides a scientific basis for measuring them.

7.2. Use of data

Only researchers (including clinician-researchers) making a written request for data access will be able to obtain raw data from the Biobank, subject to endorsement of the management framework, REB approval and a signed researcher commitment form (Appendix E). Researchers requesting data access will only receive denominalized data (Figure 2).

Data from the biochemical analysis of metabolic markers were also transmitted to the participant's clinical file once the biochemical analyses had been completed. Only metabolic data are transmitted to clinicians.

7.3. Managing data and biospecimen access requests

The procedures for accessing raw data, aggregate data and biospecimens are explained in detail in Appendix G. A guide detailing the steps to be followed to obtain access to the material has been developed and made available on the biobank website. Some aspects of these procedures may eventually be modified over time. The various procedures and required forms will also be available on the Signature Biobank website (www.banquesignature.ca).

7.4. Process to access the biobank material:

The Biobank receives the access requests from researchers through the Biobank coordinator who forwards them to the members of the Access Committee. The coordinator must record the access requests in the appropriate log.

The Access Committee evaluates:

- The alignment of the study project with the biobank's objectives
- The feasibility of the project with the material that the biobank can make available for the project under study, according to the selection criteria of the participants
- The cost of access to the samples
- The level of risk (assessment of statistical power, potential existence of similar requests).

To requests access to un-analyzed biological material, the Access Committee will ensure that the request is for the preferred biomarkers described in Appendix B of this document. When the Committee notices that a study overlaps with another study, it will inform the Management Committee and notify the researchers involved in order to allow them to collaborate.

The quorum of the Data Access Committee is 3 members, including the Biobank Coordinator, the Data Manager who also acts as a biostatistician, and the Biospecimen Manager. The Committee meets when a written request for access is made to the biobank.

In all cases, any researcher wishing to access the biobank's data and/or samples must submit a copy of the approval of his or her study project by his or her institution's REB. This approval must be kept by the Biobank coordinator in the Biobank access request files. The researcher must also approve and sign the commitment form (Appendix E).

The researcher agrees to abide by the ethical rules of his or her institution and those of CIUSSS. The researcher undertakes to respect the confidentiality of data and not to attempt to identify participants. It is also the researcher's responsibility to obtain any additional approvals required by the organization or institution with which he or she is affiliated. The use of data and biological samples must also comply with Signature Bank's objectives and the rules of the management framework.

External researchers must also obtain a signed Material Transfer Agreement (MTA) between their institution and IUSMM.

Requests for access to data and biological material are subject to cost recovery. Costs are re-evaluated annually.

7.4.1. Return of data

The Access Committee will also be responsible for following up study projects, including the return of results obtained by researchers from the use of biobank data and biospecimens. Once a study project has been completed, the researchers' results must be returned to Signature Biobank before the end of the funding period, in the form of a

report or scientific article. Analytical results obtained on biospecimens must be returned as raw data with a detailed protocol.

7.5. Handling of complaints or disputes concerning access

All complaints from researchers or clinicians concerning a problem with accessing data or biological materials must first be submitted in writing to the Biobank coordinator, who will inform the Coordinating Committee. If a complaint is maintained or a dispute is not resolved, despite being reviewed and handled by the Coordinating Committee, it must then be addressed in writing to the senior management of the IUSMM Research Centre, which will then ask the REB appoint the members of the Ad Hoc Committee that will be tasked with reviewing and handling the dispute or complaint (see Section 3.4.8, The Ad Hoc Dispute Resolution Committee).

The ad hoc Litigation Committee is a structure that will be set up if and whenever required.

Depending on the specific content of the complaint or dispute, the ad hoc committee should be made up of 4 or 5 members, including a representative of the Signature Bank Management Committee, a representative of the REB, a representative of the Scientific Research Assessment Committee and any other internal and/or external expertise deemed relevant by the REB and the SRC to ensure an objective and neutral analysis and handling of the complaint or dispute.

The ad hoc Committee will be chaired by the representative of the REB. The ad hoc Committee must have been set up, and must have analyzed the complaint and/or dispute and then rendered its decision (in the case of a dispute), or issued its recommendations (in the case of a complaint), in writing within a maximum period of three months.

The data or biological material concerned by the complaint will be placed in quarantine during this period, i.e. it may not be the subject of further access requests while the complaint or dispute is under consideration.

8. Biobank users

8.1. Rules relating to intellectual property and researchers' and clinicians' authorship rights

The Signature Biobank is the product of efforts undertaken by a large group of people, especially the researchers and clinicians involved in its creation. In this regard, the Signature Biobank is similar to major international projects that use collective names to identify the group of contributors involved in their development. For the Signature Biobank, this group is collectively referred to as the "***Signature***

Consortium." Appendix F provides a complete list of everyone included in the ***Signature Consortium***.

Members of the ***Signature Consortium*** who have contributed to the implementation of the project, the development of psychosocial or biological signatures or the Signature Biobank research protocols do not have individual authorship rights for research publications resulting from psychosocial data or biological materials accessed through the Signature Biobank.

All researchers and clinicians who access data from the Biobank agree to credit the ***Signature Consortium*** as an author in scientific papers, book chapters, scientific reports, popular science publications and knowledge transfer documents resulting from analysis based on Signature Biobank data.

With regard to psychosocial data, there is no authorship condition attached to publications resulting from access to Signature Biobank data.

In all publications, authors should acknowledge the biobank in the Materials and Methods section and thank the funding agencies as follows:

> *The Signature Consortium acknowledges contributions to the Biobank Signature of the Centre de recherche de l'institut de santé Mentale de Montréal (www.banquesignature.ca). The Biobank Signature received funding from the Fondation de l'Institut Universitaire de Santé Mentale de Montréal and Bell pour la cause*.

8.2. Private partners

Private partners such as pharmaceutical companies are not excluded from accessing the Signature Bank, but requests must be made by means of research projects with at least one lead researcher or clinician who is affiliated with IUSMM. These research projects must be evaluated and approved by the Scientific Evaluation Committee and REB. The private partner shall agree in writing to comply with the management framework's rules and must sign a contract, whose terms will be discussed and ratified by the Managing Committee and the CIUSSS_CEMTL management.

8.3. User requests to modify the biobank operation

All requests to modify the Signature Biobank or its operation must be made by the Scientific Director of the CR-IUSMM, who will ensure that the various concerned parties (if necessary, the Scientific Evaluation Committee and REB) are consulted and provide their opinion on the proposed change. If these parties' opinions are favourable, the Management Committee will submit the proposed change to the hospital's Executive Management for ratification by the institution.

8.4. Using the website to interact with Signature Biobank users

A website (www.banquesignature.ca) was created to make forms, procedures, scientific papers published by researchers and other relevant information accessible to anyone interested in becoming involved in the Signature Biobank as a participant (IUSMM patient), attending clinician or researcher.

This website is also used to inform researchers and clinicians about the number of participants who have been tested on each medical, psychosocial and biological measure, with the aim of better managing access requests for data and biological materials.

9. End of Biobank

The Signature Biobank has been established for an unlimited period of time. If it were to cease operations, everything in it would be the responsibility of the facility (IUSMM), i.e DERI, which reports to the CEMTL and which can then decide on the future of the biobank, either by restarting its activities or by retaining the data or destroying it.

10. Management framework modification

The Management Framework, excluding appendices, must be approved by the REB of the CIUSSS de l'Est-de-l'ile de Montréal, as well as any amendments. The follow-up of modifications is summarized at the end of the management framework.

The content of the annexes may be amended at any time by the Biobank directors, without formal notification to the REB or the Legal Services Office, to ensure the smooth operation of the biobank. However, to the extent that the directors determins that the amendment could have a significant impact on the scope of the Management Framework or on the objectives of the biobank, the directors will seek the approval of the REB prior to making the amendment.

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