



Canadian Longitudinal Study on Aging (CLSA)

Biospecimen Access Guidelines

This guideline is specific to biospecimens and supplementary to the application documents. Please read all associated documents (click on the links) in their entirety before proceeding with an application submission.

1.0. INTRODUCTION

The Canadian Longitudinal Study on Aging (CLSA) collects blood and urine from consenting participants and stores the biospecimens in a biorepository (BBC) at McMaster University in Hamilton for future use. The sample types ([Types of Biological Samples Collected at Baseline](#)) have been selected to cover a wide range of scientific questions that may be asked throughout the life of the CLSA and beyond.

Biospecimens collected with the consent of the participants are valuable and finite resources. The CLSA has the authority and the duty to responsibly manage biospecimens collected as part of the CLSA and to make sure the best possible scientific value is derived from these samples. To achieve this objective, the Scientific Management Team (SMT) will facilitate the widest possible use of the biospecimens collected as part of the CLSA. The SMT will also ensure that approved applications to use this resource will be of highest scientific quality that will result in reliable, valid, informative, and novel set of biomarkers to advance the health and well-being of Canadians.

Information in this guideline is intended to facilitate the application process ([Data Access Application Process](#)) by providing a framework for addressing and determining access issues; it does not prescribe rigid criteria as it is impossible to predict how the biospecimens will be used and for what type of scientific questions. However, the applications submitted to access CLSA biospecimens will have to demonstrate that their research questions reflect the integrity of the CLSA design (e.g., longitudinal design or national generalizable selection of the sample).

2.0. REQUESTS FOR BIOSPECIMENS

Calls for proposals to access biospecimens will be issued once a year. Biospecimens from baseline and subsequent follow-up collections of the CLSA will be made available to the research community. The type and number of biospecimens released will be such that a sufficient number are retained to allow for future longitudinal analyses.

The CLSA recognizes that funders may require evidence that applicants will be able to access the necessary biospecimens prior to committing funding. The CLSA will review requests to provide a letter of support for grant applications to CIHR or other funding agencies describing the potential feasibility of the proposal using the CLSA samples. The letter of support will be provided after the preliminary review of the grant proposal no less than 6 weeks prior to the grant deadline to the applicant for submission to granting agencies. However, final approval of the biospecimen application is contingent on the full review (as listed in Section 3) by the CLSA Data and Biospecimen Access Committee (DSAC). The DSAC is comprised of health experts, and, if required, ad hoc member(s) to ensure there is appropriate expertise available to review the proposal.

Specifically, you may submit an application under any of these three conditions:

- a) You have secured funding to execute your proposed plan;
- b) You have applied for funding but funding has not been confirmed;
- c) You have not applied for funding because you need provisional letter of support to submit a grant or application.

To apply for access a completed [CLSA Data and Biospecimen Request Application](#) is required.

3.0. REVIEW PROCESS

The process for review will be similar to alphanumeric data requests (see [Data Access Application Process](#)). That is, if an application meets the requirements of the administrative review, feasibility assessment and statistical review (described below), it will be sent for review and consideration by the CLSA DSAC. This Committee will assess proposals based on their suitability with the CLSA objectives and priorities.

Part 1: Administrative Review

The CLSA National Coordinating Centre will review the application for completeness, including but not limited to, ethics status, proof of peer review, proof of funding to analyze samples, applicants and co-applicants from Canadian Institutions (for sharing data), keywords, project timeline, and signatures.

Part 2: Feasibility Assessment

Upon receipt of a completed application, a feasibility assessment will be conducted by the BBC to ensure the requested biospecimens are available. All alphanumeric data (data from questionnaires and physical assessments) required along with the biospecimens should be requested using the [CLSA Data Access Application Documents](#).

Part 3: Statistical Review

The CLSA Statistical Analysis Centre (SAC) will review the alphanumeric component of the data request application for completeness and feasibility, including but not limited to ensuring the project description includes variables that were collected in the CLSA, project description includes variables that were collected but are not yet released, analyses proposed are feasible from the point of view of availability of data and sample size. In addition, the statistical review will evaluate any requests for additional data and linked data.

Part 4: Data and Biospecimen Access Committee Review

Completed submissions passing the feasibility assessment and statistical reviews, will be reviewed by the CLSA DSAC. Proposals will need to provide the scientific justification for the proposed analysis of biomarkers and clearly demonstrate why a population based platform is critical to answer their proposed research question(s). The proposal should clearly articulate what is known about the biomarker to date with regards to physiological relevance and analytical measurement of it.

The proposal should ask a meaningful question that requires measurement of the biomarker(s) from a longitudinal study. Questions most meaningful in biomarker studies are those that are likely to benefit the health of older Canadians by improvements to clinical practice guidelines or providing an important public health message (e.g., faster and accurate diagnosis of a disease, better risk stratification approaches, clearer understanding of disease pathogenesis, or

improved therapeutic stratification based on phenotype). Biomarker and -Omics that provide high dimensional data on large number of the CLSA participants are encouraged (e.g., metabolomics, lipidomics and proteomics).

Although only baseline biospecimens are currently available the study design should be such that the biomarker data can be used to answer prospective study questions when the follow-up (FUP) data and biospecimen are available (FUP-1, 2018; FUP-2, 2021, etc.).

Criteria that will be used to assess applications requesting biospecimens include:

- Number of Biospecimens: larger sample sizes provide greater data consistency for the cohort and broader use of the data to cover a wide range of research questions.
- Type of Biospecimen required: there are variable quantities of the different biospecimens types. Requests for sample types that have more aliquots (e.g., serum, plasma, dried blood spots) will be easier to obtain than biospecimen types with fewer aliquots (e.g., whole blood).
- Volume of Sample required: maximal use of the aliquot limits wastage. More biomarkers tested will increase use of the sample volume. Biospecimens are not returned to the biorepository for reuse. This practice eliminates potential loss of sample integrity.
- Laboratory Measurement: most error in test results occur prior to the analytical phase. A system to minimize this variation is needed. Assays with high accuracy and precision will provide high-quality results. Monitoring of the testing method using both internal and external quality control will ensure timely detection of errors and minimize analytical variation.

Part 5: Analytical Method Assessment

After the recommendations for approval by the DSAC, the applicants will be contacted by the CLSA Biorepository and Bioanalysis Centre (BBC) to ensure that all standardized procedures exist to receive biospecimens, handling processes (e.g., thaw procedure, mixing) and tracking of the samples and associated data.

It is critical that applications provide information about the analytic methods to be used including justification for the method chosen and method details, i.e., method principle, sample type, sample volume, accuracy and imprecision, limit of detection. Method validation or verification documents will be reviewed to assess the quality of the method.

It is essential to assess whether all the quality control procedures are in place to minimize variation in the data and ultimately in the applicability of the study results. This necessitates thorough knowledge of the testing methodology and a mechanism to anchor a past test result with a future test result. This effort will enable test results from past time-points to be combined with future time-points without the need for reanalysis, thus reducing cost in reanalysis and wastage of this precious resource, or requiring statistical manipulation. The CLSA will include longitudinal quality control (LQC) samples to monitor the consistency of the analytical method. Linkage of the alphanumeric data will be done once all the derived biomarker data has been returned to the SAC and upon successful review of the LQC data.

Part 6: Final Approval

Once a proposal has met the requirements of all the previous five steps, the final approval for specimen access will be made by the SMT based on the recommendations of the DSAC, SAC and BBC.

4.0. HANDLING OF COMPETING APPLICATIONS

As the amount of material is limited, the CLSA may suggest that applicants proposing similar studies collaborate. By encouraging the collaboration between prospective researchers, the biospecimens can be used more efficiently. If the applicants are not willing to collaborate, their applications will be considered separately.

5.0. RESUBMISSION

If access to the biospecimens is refused, the applicant has the right to submit a new application at the next submission date for proposals to access biospecimens and address issues presented during the review process. There will be no appeals considered by the CLSA Scientific Management Team.

6.0. CONDITIONS OF ACCESS

Once an application has been approved, the following conditions of transfer of data and biospecimens apply.

6.1. Evidence of Funding

The CLSA will only release biospecimens to projects with funding or evidence of institutional support and resources. Applicants will need to supply written evidence (e.g., a letter from the funding body or the financial officer of the institution indicating that application will be supported by internal funds) that the research is sufficiently funded before biospecimens are released.

If access is approved "subject to funding" the biospecimens requested will be reserved. The biospecimens will be reserved for a specified time and, if funders require significant changes to the proposed study or its protocol these changes will require a new review by the DSAC. An applicant will have one year after the approval to secure funding and ethics approval. If this time period is insufficient, the applicant will be required to provide justification for additional time. The requested biospecimens will be held for the applicant during the designated time required to obtain funding and ethics approval. However, if a competing application measuring the same biomarker or group of biomarkers is accepted, funded and approved by ethics, during this year, the original applicant will be given a period of time to try to generate a collaboration with the competing application. The applicants will have to provide the justification why this collaboration may or may not be possible before the biospecimens are released.

6.2. Documentation

To meet data quality standards set by the CLSA, documentation pertaining to biospecimen handling and analysis will be required from each applicant. This includes the method description, instrumentation used, criteria for monitoring variation, statistical analyses and other associated information to understand and assess the quality of the data. Data support documentation will be available on the CLSA website for use by research community accessing the new biomarker data.

6.3. Costs

The applicant will have to pay for access to the biospecimens on a cost-recovery basis and these costs are used to sustain the CLSA platform. For publically funded projects, the CLSA has a fixed cost for each biospecimen regardless of type (e.g. Serum, PBMC, Urine). These costs include administration, IT, retrieval, and consumables. The cost is \$5.00 per aliquot and is subject to change. The cost for shipping is additional and will vary depending on the destination's distance from Hamilton, Ontario.

The associated alphanumeric data checklist is provided at a fixed cost of \$3,000. However, access to any complex data that requires special data manipulation by the SAC or NCC will require additional resources and the costs to access complex data will be assessed on a case by case basis.

A detailed cost-estimate review will be done as part of the feasibility assessment and no samples will be released prior to the finalized CLSA Access agreement and payment being in place at McMaster University.

6.4. Usage Limitation

Biospecimens from the CLSA biorepository must only be used for the purposes stipulated in the CLSA Access Agreement. If the researcher would like to perform additional biomarker analysis outside the original agreement, an amendment to the original application will be required. The CLSA SMT will conduct initial review of the amendment and determine if it requires full review by DSAC.

Biospecimens supplied from the CLSA biorepository may only be transferred to researchers or laboratories named at the time of the original application or in subsequent applications/amendments and specified in the [CLSA Access Agreement](#).

6.5. Privacy and Confidentiality

Researchers cannot link the anonymous biospecimens with any other datasets.

Researchers must not attempt to identify any individuals from the biospecimens provided.

Should researchers believe that they have inadvertently identified any individuals, they must inform the CLSA and provide details of the circumstances under which the identification occurred. Information related to the identification of an individual must not be shared and researchers must not attempt to contact the individual.

Further information can be found in the [CLSA Longitudinal Study on Aging – Privacy Policy](#).

6.6. Intellectual Property Rights

Inventions and data arising from research using CLSA biospecimens may have commercial value. The CLSA will have no claims over inventions (and any resulting patents, etc.) that are developed by researchers as a result of using biospecimens from the CLSA. All data arising

from research using CLSA biospecimens will be returned to the CLSA with exclusive use by the researcher who paid for the analyses lasting for a period of one year after which the data will be made available to all researchers, subject to section 3.2.3 of the CLSA IP policy, as applicable. Further information can be found on the CLSA website, at www.clsa-elcv.ca (see Data Access Intellectual Property Statement).

6.7. Shipping and Receiving Requirements

Biospecimens will be shipped to the laboratory indicated in the CLSA Access Agreement within an agreed upon time-frame to the researcher receiving final approval and signed CLSA Access Agreement.

A shipping and receiving protocol form will be sent to the laboratory to complete prior to shipping the biospecimens. All biospecimens are shipped in cryoshippers. A procedure outlining the handling and method for returning the cryoshipper will be provided.

Sources for document development: *Statistics Canada*; Access Requirements and Protocols for the Canadian Health Measures Survey Biobank <http://www.statcan.gc.ca/eng/survey/household/5071y#appa> and from the *National Child Development Study*; Policy for use and oversight of samples and data arising from the Biomedical Resource of the 1958 Birth Cohort (National Child Development Study) https://www2.le.ac.uk/projects/birthcohort/copy_of_document-downloads/application-docs/POLICY.DOCUMENT.120609.pdf