



INTERNATIONAL CANCER GENOME CONSORTIUM

UPDATES TO GOALS, STRUCTURE POLICIES AND GUIDELINES

SECTION E.1 – INFORMED CONSENT, ACCESS AND ETHICAL OVERSIGHT

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E. 1. Informed Consent, Access and Ethical Oversight

1. Informed Consent

ICGC proposes that certain **Core Bioethical Elements** be respected by all members as a precondition of membership. These elements apply both to the prospective collection of cancer and other samples and to consent surrounding retrospective research using previously stored samples. Following these policies are guidelines that ICGC-member projects should consider in matters related to consent. ICGC-member projects will be responsible for carrying out these policies and guidelines. Nevertheless, ICGC acknowledges that the informed consent process used by ICGC members will necessarily differ according to local, socio-cultural and legal requirements.

POLICY: ICGC membership implies compliance with Core Bioethical Elements for samples used in ICGC Cancer Projects

1.1. Prospective Research

Core Bioethical Elements:

For prospective research, ICGC members should convey to potential participants, *that*:

- The ICGC is a coordinated effort among related scientific research projects being carried on around the world
- Participation in the ICGC and its component projects is voluntary
- Samples and data collected will be used for cancer research, which may include whole genome sequencing
- The patient's care will not be affected by their decision regarding participation
- The samples collected will be in limited quantities; access to them will be tightly controlled and will depend on the policy and practices of the ICGC-member project.
At least a small percentage of the samples may be shared with international laboratories for the purposes of performing quality control studies
- Data derived from the samples collected and data generated by the ICGC members will be made accessible to ICGC members and other international researchers through either an open or a controlled access database under terms and conditions that will maximize participant confidentiality
- Those accessing data and samples will be required to affirm that they will not attempt to re-identify participants
- There is a remote risk of being identified from data available on the databases
- Once data is placed in open databases, that data cannot be withdrawn later
- In controlled access databases the links to (local) data that can identify an individual will be destroyed upon withdrawal. Data previously distributed will continue to be used
- ICGC members agree not to make claims to possible IP derived from primary data
- No profit from eventual commercial products will be returned to subjects donating samples

Box 1. ICGC guidelines for information that should be provided to participants regarding prospective research (ICGC acknowledges that the informed consent process used by ICGC members will necessarily differ according to local, socio-cultural and legal requirements):

- ICGC administration, oversight, funding, duration, ethics and scientific approvals and contact persons;
- Who will be recruited and the approach;
- Procedures involved in participation, including any physical and psychological ‘risks’
- Information on the kinds of samples and data that will be collected;
- Protections in place ‘locally’ to ensure the confidentiality of samples and data;
- Research uses of data (ICGC members are encouraged to seek the broadest level of consent that is appropriate at the local level; e.g., “cancer and related research; cancer and other disease-related research”);
- Whether access to samples will be available for purposes such as validation, quality control, research, etc.;
- Whether access to medical/administrative health records will be sought;
- Whether information regarding participation will be included in medical records;
- Provided it is agreed at recruitment, if clinically important and validated findings emerge during the initial recruitment and screening phase, or in the early research, attempts will be made to pass this information back via the clinician, by whatever mechanism may be agreed at the local level;
- Information on whether or not compensation/reimbursement is available;
- Withdrawal procedures, such as sample retrieval and/or destruction and data coding and anonymization procedures;
- Ownership of samples;
- Prospects for third-party commercialization and intellectual property procedures;
- Purposes for which the uses of data and samples will not be allowed (if required to be named by country);
- How information on the general results of the research will be disseminated;
- Who participants can contact regarding their concerns.

1.1.1 Minors, Children and Newborns

ICGC projects that include pediatric populations should ensure respect for their rights and interests. In particular, their inclusion, the obtaining of consent or assent depending on their capacity and the protection of both their privacy and of the confidentiality of their personal and medical data are important.

In this situation, the Core **Bioethical Elements** and the guidelines in Box 1 will remain the same as for adults involved in prospective research. In addition, where scientifically validated information of clinical significance emerges that reveals conditions that are preventable or treatable during childhood, the health interests of the child or minor concerned are the primary consideration in the communication of such results.¹

¹United Nations. 1989. Convention on the Rights of the Child. Available at: <http://treaties.un.org/doc/Publication/MTDSG/Volume%20I/Chapter%20IV/IV-11.en.pdf>.

1.2. Retrospective Research

1.2.1. Living Individuals

When conducting research involving samples or data collected previously and the individuals are still living, if existing consents are already in place that will allow ICGC research, the research should proceed without re-contacting those individuals. If appropriate consents are not in place, these individuals should be re-contacted for their consent to participate in the ICGC.

In this situation, the **Core Bioethical Elements** and the guidelines in Box 1 will remain the same as for prospective research, with the exception that where the individual is no longer a patient, there will not be a concern that their care could be affected by participation.

1.2.2. Deceased Individuals and Anonymized Collections

Retrospective research can also be carried out using other sources of samples and data such as: samples and data from the deceased and anonymized collections. Using these sources raises different issues regarding consent; guidelines are provided in Box 2.

The **Core Bioethical Elements** for research involving samples and data from deceased individuals are *that*:

- Where required by law or ethics, consent should always be obtained from the families of a deceased individual if their samples and data are to be used; if re-consent is not required, however, ethics review is sufficient
- Ethics committee review should be sought for all research proposing the use of existing sample and data collections
- Existing collections are a limited and valuable resource; access to them will be tightly controlled.

Anonymized samples cannot at this time be used to retrace individuals or their families.

The **Core Bioethical Element** is that such samples can be used, subject to the removal of any identification or possible combination of factors allowing re-identification and ethics review.

Box 2. ICGC guidelines for retrospective research using existing collections of samples and data (ICGC acknowledges that the informed consent process used by ICGC members will necessarily differ according to local, socio-cultural and legal requirements)

For retrospective research using identifiable collections from the living:

- If existing consent allows for ICGC research, samples and data may be used without further consent;
- If consents are not in place, re-consenting should be pursued (see Box 1);
- If seeking consent is judged by the researchers to be impractical or likely to cause distress to individuals, ethics committee approval may be sought to waive consent requirements.

Criteria for a waiver may include that the research:

- Poses minimal risk to the individuals;
- Does not violate individuals' rights;
- Has privacy and confidentiality protections in place;
- Is important and cannot be conducted in any other manner.

For research using identifiable collections from the deceased:

- The wishes of the deceased regarding the use of their coded samples and data should be taken into consideration;
- Relatives of the deceased, if known, may be consulted regarding the wishes of the deceased;
- Research may proceed without consent if a waiver is provided by an ethics committee or if permitted by national legislation and policies;
- If samples and data are anonymized, research may proceed without consent.

1.3. Access

In addition, the nature of the data produced by ICGC members, including prospective cohorts of cancer patients, substantial clinical annotation and extensive genomic data, raises important human subject privacy protection issues. The patient/individual protection policies developed for ICGC are designed to balance two important goals: to facilitate investigations of genomic changes related to cancer and, at the same time, to respect and protect the patients/individuals whose data and materials have been or will contribute to ICGC-member projects. It is technically possible that genomic information (DNA sequence, genotype) generated by the projects comprising the ICGC could lead to identification of an individual if similar specimen data from that person (or a blood relative) were obtained from a third-party database and correlated. There is also a risk of individual identification by computer-based analysis of the clinical data in conjunction with, for example, third-party demographic and healthcare management databases. This potential identification could then publicly link the individual to his/her clinical information collected by the participating projects, and could lead to social risks such as discrimination or loss of privacy.

POLICY: To minimize the risk of patient/individual identification, the ICGC has established the policy that datasets be organized into two categories, open and controlled-access.

Table 1 includes a list of data elements and the data access category within which they will be available.

The first category, Open Access Datasets, will be publicly accessible and contain only data that cannot be aggregated to generate a dataset unique to an individual. The second category, Controlled Access Datasets, will contain composite genomic and clinical data that are associated to a unique, but not directly identified, person.

ICGC Open Access Datasets	ICGC Controlled Access Datasets
<ul style="list-style-type: none"> • Cancer Pathology <ul style="list-style-type: none"> ○ Histologic type or subtype ○ Histologic nuclear grade • Patient/Person <ul style="list-style-type: none"> ○ Gender ○ Age range • Gene Expression (normalized) • DNA methylation • Genotype frequencies • Computed Copy Number and Loss of Heterozygosity • Newly discovered somatic variants 	<ul style="list-style-type: none"> • Detailed Phenotype and Outcome Data <ul style="list-style-type: none"> ○ Patient demography ○ Risk factors ○ Examination ○ Surgery ○ Drugs ○ Radiation ○ Sample ○ Slide ○ Specific histological features ○ Protocol ○ Analyte ○ Aliquot • Gene Expression (probe-level data) • Raw genotype calls • Gene-sample identifier links • Genome sequence files

Table 1. Listing of data categories and level of access restriction on those data.

An International Data Access Committee (IDAC) will be established as a policy-making group. It will develop the additional policies by which investigators can obtain access to controlled data, provide oversight to any ICGC member projects that will have the responsibility to review requests for such data, and monitor compliance by bodies that are authorized to distribute ICGC data, and users of the controlled data. The IDAC will have broad geographic representation (of whom 50% will be non-ICGC members) and will include individuals representing the ICGC Executive, experts in ethics, databases and international law, cancer survivors, potential users of the data, and other independent lay persons. The IDAC will ideally have fewer than 20 members.

As proposed in Box 8 of this document (Additional guidelines for ICGC data management and security), authorizations to access controlled data will be broad, so that authenticated users will get permission to obtain access to controlled data generated from all samples studied by any participating cancer genome project (as the feasibility of providing permissions to datasets originating from single or partial subsets of participating centers has been determined to be unworkable in the context of the ICGC).

The IDAC will also develop guidelines for practical approaches to providing qualified investigators with access to controlled data. In doing so, it will consider mechanisms and tools that have been already in use by other organizations that distribute controlled datasets to international scientists (for example, the U.S. TCGA project or the Wellcome Trust Case Control Consortium). Potential users and their institutions will be required to submit Assurance Agreement forms that include:

- a written description of the purpose of the research to be done;
- an agreement to not to try to identify or contact the donor subjects;
- agreements not to redistribute controlled access data; and
- plans to destroy controlled access datasets once they are no longer being used.

Interested users and institutional officials who are authorized to make legally binding agreements for the institution will have to provide a signed statement agreeing to adhere to the conditions that will be recommended by the IDAC. Investigators will need to agree to regular review and renewal requested by the IDAC for such authorization and in cases when they move to new institutions. No authorization will be granted to scientists or other individuals that are not supported by an institution that assumes responsibility to fulfill the terms of the Assurance Agreement.

The implementation of a data access process will be the responsibility of ICGC Funding Members, i.e., the ICGC Executive Committee, who will establish policies and processes based on the policies and guidelines developed by the IDAC for the Consortium. The management, i.e., receipt, review and approval, of requests for data produced by ICGC members, whether directly or through third-party data repositories wishing to redistribute cancer genome Controlled Access Data ideally will be determined after further consultations. It is anticipated that permissions will be obtained across all jurisdictions to allow establishment of a centralized authentication mechanism at ICGC franchise databases. Delegated organizations will maintain records of all requests for controlled data, authentication procedures, authorizations or denials, and report these semi-annually to the IDAC. Unusual requests or unexpected issues will be referred to the IDAC as they arise.