E1. Ethics and Informed Consent

E.1.1 Core Bioethical Elements for Participation in ICGC ARGO

ICGC ARGO follows the Global Alliance for Genomics and Health's (GA4GH) Framework for Responsible Sharing of Genomic and Health-Related Data[1] which is founded on the belief that everyone should benefit from scientific advances and that data producers should receive proper attribution. ICGC ARGO is also mindful that local cultural and regulatory practices, including ethical review, will differ across its member projects and their individual research studies. In order to support the aims of ICGC ARGO while respecting differences between members, core bioethical principles will be adopted to help enable the gathering and translating of cancer genomics data into more effective prevention strategies and therapies, to provide better outcomes for patients and their families.

As with the early stages of ICGC, it was decided that a set of core ethical elements were needed for participation, as it is stated broadly across the Policies that ICGC membership implies compliance with a set of Core Bioethical Elements. In addition, because this is an international consortium, it was also recognized that there would be some issues around consent, data access and ethical oversight that could not be harmonized across member projects. For prospective research, a set of flexible guidelines were drawn up on additional points of information, such as administrative details, that should be provided to participants, with the acknowledgement that the informed consent process used by ICGC programs will necessarily differ according to local, socio-cultural and legal requirements.

Given the structure and objectives of ICGC ARGO the focus initially is on ethical elements informing prospective research. Table 1 below outlines elements ICGC ARGO members should convey to potential participants:

1	The ICGC ARGO is a coordinated research effort among related scientific and clinical projects carried out around the world.
2	Participation in ICGC ARGO and its projects is voluntary.
3	Data derived from samples and associated health records and data generated by ICGC ARGO members will be made accessible to ICGC ARGO members and other international researchers through an open, registered, or controlled access database under terms and conditions that maximize participant confidentiality. Researchers accessing data under these terms and conditions may link it to other databases for study purposes.
4	Unless foreseen otherwise in the consent, those accessing data will be required to attest that they will not attempt to re-identify participants and use data only for the purposes described.
5	There is always a remote risk of being identified from data available on the databases.
6	Local sites will hold the key enabling the re-identification of participants. Prior to inclusion in ICGC ARGO, a second system generated code unique will be attributed to each donor and sample before data processing. This allows for further safeguards in the data access environment.
7	There are practical limitations to withdrawing data. Once data has been distributed or placed in publicly accessible databases it cannot be readily retrieved from aggregate analysis or published data and cannot be withdrawn.
8	ICGC ARGO members agree not to make Intellectual Property claims on ICGC ARGO raw data.
9	No profit from any eventual commercial products will be returned to participants.

10	Member projects should confirm with ICGC ARGO whether or not they will be returning individual research results to participants, that this decision has received formal approval (where applicable), and is addressed in any consent materials for ICGC ARGO participation.

E.1.2 Informed Consent

Because of the differing regulatory requirements and cultural norms held by differing countries, harmonization of consent across ICGC ARGO is not possible. However, for the science to move forward, a core set of elements is needed to ensure the ethical use of patient and participant data.

ICGC ARGO Programs are asked if their data is consented for:

- Any approved future biomedical research?
- Deposit of open access fields/datasets in open access databases?
- Deposit of controlled fields/datasets in controlled access databases?
- Linkage with other research datasets?
- International data sharing?
- Sharing for widespread use without specific restrictions?

E1.2.1 ICGC ARGO Assessment Tool for Participation

This tool aims to provide guidance on determining whether datasets which include genomic data, are suitable for inclusion in ICGC ARGO. It does not apply to samples and data that have not been consented for genomic research.

We recognize that consent materials may have used different language reflecting requirements from another time and may be ambiguous, or be silent, as to data sharing and potential uses of the data. To help you determine whether your data can be used for ICGC ARGO, the ICGC Ethics and Governance Committee has drawn up the following tool based on the principles found in the Global Alliance for Genomics and Health's Consent Policy[1] and other best practice documents[2].

Step 1: Please answer the following questions[3]:

Is your data consented for:	**Yes**	**No**
1. Any approved future biomedical research?		
2. Deposit of open access fields datasets in open access databases?		
3. Deposit of controlled fields in controlled access databases?		
4. Linkage with other research datasets?		
5. International data sharing?		
6. Use by bonafide researchers including not-for-profit and commercial?		

Step 2: If the answers to all the above are **Yes**, your data can be used for ICGC ARGO.
If any were **No**, please answer the following questions:

	Yes	No
1. Does your consent allow for re-contact of participants?		
2. Is it feasible for you to re-contact and re-consent your participants for inclusion in ICGC ARGO?		

Step 3: If both answers to the above are **Yes**, please re-contact and re-consent.
If either or both are **No**, please answer the following:

	Yes	No
1. Is it possible for you to apply to an authorized local committee to obtain an ethics waiver of the re-consent requirement for participation in ICGC ARGO?		

Step 4: If the answer to the above is **Yes**, please request a waiver per your local procedures.
If the answer is **No**, your data cannot be used for ICGC ARGO.

References:

[1] www.genomicsandhealth.org

[2] In the case of uncertainty regarding the interpretation of steps or questions listed, please contact: secretariat@icgc-argo.org

[3] For an explanation of terms, please refer to the Global Alliance for Genomics and Health's Data Sharing Lexicon, available online at: https://www.ga4gh.org/ga4ghtoolkit/regulatoryandethics/

E1.3: Withdrawal of Consent

Participants have the right to withdraw from a research study at any time and without having to give a reason. The ability of research participants to stop their involvement in research is important to ensure they feel that their involvement is voluntary, and that their decision to participate or not is respected.

ICGC ARGO involves processing and storage of individual-level genomic and clinical data in open (publicly accessible) or controlled-access databases, so there are practical limits on the ability to withdraw some of this data. Given the structure of ICGC ARGO there are two areas these practical limitations are relevant: 1) ICGC ARGO members have an exclusive membership level-dependent period of accessing data (commonly known as the "embargo period"), and 2) ICGC ARGO is managed by a federated data model, which involves many steps of data processing and exchange across various different systems. Hence, ***when*** a participant decides to withdraw from the study, there can be potential difficulties in withdrawing that data, depending on the stage of processing their data is at. The limitations can be summarized as:

1) The data has already been distributed or used in a research project and cannot be readily retrieved from aggregate analysis or published data, and
2) The data must be kept for regulatory purposes as well as institutional policies to comply with data integrity obligations.

These limitations should be discussed in the consent form and as part of the consent process, including a full explanation of the extent to which withdrawal of data is possible or not possible and what the process is.

POLICY:

- If consent is withdrawn ***prior*** to public data release (release to the external research community), data (clinical and molecular) will be deleted from systems and no longer available or used in the project. There are limitations to deleting or withdrawing data fully, and these are explained further below in Point 3.
- If consent is withdrawn ***after*** data has been publicly released data is not possible to delete.
- Once data is removed from systems this cannot be undone.

Process of Removing data Following Withdrawal:

1. Participant requests withdrawal of consent for research via local program guidelines and processes.
2. Program Principal Investigator (PI) notifies the Data Coordination Center (DCC) via the Contact Form with details of the request to withdraw.
3. DCC determines the *stage of data processing,* and the following limitations and exceptions apply to data sets:
    a. Data that remains in an unprocessed state at submission phase will be deleted from systems and no longer available or used in the project.
    b. Data that has been processed and released but remains under member embargo will be removed from further use in line with Point 1 of the policy. However, data may already have been distributed, shared and downloaded internally amongst member programs as part of their research. To facilitate removal, programs with this level of data access will be requested by the DCC to delete copies of data sets they hold, along with communicating to their members and collaborators to delete the data that has already been downloaded.
    c. Data that is released publicly (externally available- Step 3 of Data Flow) after the embargo period (24 months) is not possible to withdraw. While data will be removed from live systems, data previously distributed may continue to be used. Data that has been downloaded and previously used by researchers through public, open databases is not tracked and will not be possible to locate and remove.
4. The DCC will delete data from the system in line with the above policy and remove the data from the live databases and file systems in these steps:
    a. Files will be suppressed immediately so they are no longer downloadable.
    b. A thorough audit will be undertaken to confirm accuracy and completeness.
    c. Once confirmation takes place after the above deletion will occur.
5. Data will remain in a Backup environment (Step 4 of Data Flow) either for a defined period of time, or permanently, depending on the stage of data exchange and data type.
    a. Unprocessed data or data handled between steps 1 and 2 of the Data flow will remain in backup for 90 days, then be deleted according to an established schedule.

   b. Data that has been released and refined (for example indexed data) will remain in backup permanently as it is technically not feasible to delete all data from backup systems. Data in backup is not used for any other purpose and it is not accessed by any other organization. Backup data is also surrounded with appropriate technical and organizational security.
6. Data will be deleted from systems as described above within 28 days. Once the removal of data is complete, the DCC will confirm in writing to the Program PI of this action.
7. It is recommended that PI's then communicate to the individual requesting withdrawal of the actions taken.
8. All requests for withdrawal and the detailed steps of removal are recorded within DCC systems.

References:

[1] GA4GH Consent Clauses for Genomic Research, July 2020

[2] NHGRI- Special Considerations for Genomics Research: https://www.genome.gov/about-genomics/policy-issues/Informed-Consent-for-Genomics-Research/Special-Considerations-for-Genome-Research

[3] Genomics England, Informed Consent Policies: https://www.genomicsengland.co.uk/information-for-participants/participant-forms/

E.1.4 Return of Results

Decisions regarding returning individual results will be the responsibility of the member projects. All member projects should notify ICGC ARGO if they will be returning individual results to participants and confirm that this decision has received approval from a responsible body, according to applicable regulations and policies. This policy will be kept under review.