



# Correlative Science and Tissue Banking Procedures

Canadian Cancer Trials Group

*March 11, 2019*

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## Our Policy

The Canadian Cancer Trials Group has established a Tumour Tissue Data Repository to ensure the careful collection of bio-specimens defined on a trial by trial basis, the storage, inventory management, quality assurance, tracking, access, and release of appropriate material to investigators to achieve the scientific objectives of correlative biology while safeguarding individual patient rights.

## Introduction and Scope

The Tumour Tissue Data Repository (TTDR) of the Canadian Cancer Trials Group was established in 1997 and is overseen by the Correlative Science Tumour Biology (CSTB) Committee in collaboration with the Tissue Bank Operational Committee (TBOC), an internal committee of the CTG central office. Specimens collected and banked include but are not limited to tumour tissue, whole blood, plasma, serum, urine, and bone marrow and derivatives made from these samples. The TTDR is housed within the Department of Pathology and Molecular Medicine at Queen's University.

Correlative biological questions are considered for inclusion in all Canadian Cancer Trials Group clinical trials either as:

- an integral component of the trial (for example: eligibility of participants based on a biomarker, or as a stratification factor)
- an integrated component of the trial such as correlative endpoints
- exploratory research questions asked on archival material collected and stored in the biobank of the Canadian Cancer Trials Group.

This document describes the process by which tissue banking is implemented in Canadian Cancer Trials Group clinical trials, including the scope, policies, procedures, assigned roles, responsibilities and accountability, study design, collection and storage, access to samples and governance.

## Governance and Compliance

### **Applicable Regulations and Guidance**

Our policies are compliant with:

- Canadian regulatory (Health Canada) and ethical (Tri-Council Policies) guidelines
- Canadian Tissue Repository Network (CTRNet)
- Best Practices as defined by the FDA and ISBER

The TTDR also functions as part of the NCI Group Banking Committee (GBC) as one of several co-operative group banks and participates in the process of creation and approval of GBC's policies, regulations and procedures. The TTDR has been involved in the development of the policies and procedures for tissue banking for CTRNet which are referenced by biobanks across Canada, and internationally.

Where possible, Canadian Cancer Trials Group uses laboratories which are GLP, CAP or CLIA certified for investigating protocol defined biomarkers, especially where these are planned as companion diagnostics.

### **Terms of Reference**

All committees involved in Correlative Science and Tissue Banking have Terms of Reference which detail membership, mandate, and meeting frequency. These committees provide input into potential trial related integral/integrated biological questions and serve as review committees for the approval of research proposals.

### **Research Ethics Board Approval**

The activities of the TTDR are covered by a general Research Ethics Board (REB) approval from Queen's University for all aspects of its work. REB approval is also required for individual research proposals using tissue accessed from TTDR at the institution at which the work is being done.

### **Structure and Committees**

The various committees and support services involved in the tissue banking activities of the Canadian Cancer Trials Group, both internal and external, and their relationships are indicated in figure 1 below. The TBOC is responsible for the internal policies and work instructions that relate to the operational aspects of the TTDR. The Operational Director, the Tissue Bank Manager, the Tissue Bank Coordinator, and the laboratory Scientific Advisor work with this committee and the support services to ensure that work instructions and policies are enacted. The Disease Site Group Correlative Sciences committees have a relationship with the TTDR through the central office faculty member on each committee as well as direct representation on the CSTB. The Tissue Bank Manager and Tissue Bank Coordinator liaise directly with trial teams as well as with the Operational Director of the TTDR.

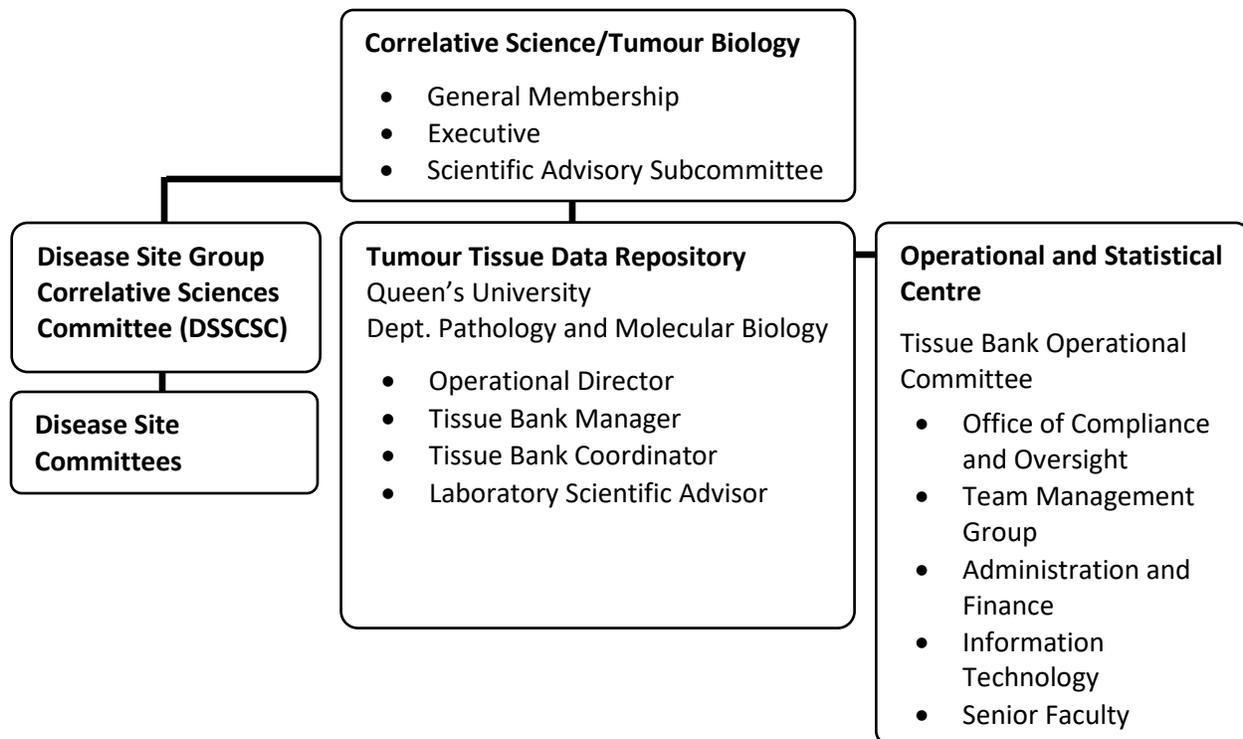


Figure 1

## Protocol and Consent Development

### Protocol

#### *Templates*

The Tissue Bank Manager and TBOC are responsible for ensuring that the generic protocol sections concerning tissue banking are current and compliant with applicable regulations.

#### *Development*

Where applicable, correlative studies are considered for all new CCTG trials. It is the responsibility of the protocol authors, often with a Correlative Science Chair for the trial, and in collaboration with the Tissue Bank Manager, to coordinate the development of the CS component, using the generic protocol and CS template. If appropriate, information regarding the CS component must be included as follows for embedded questions:

- Background information and the rationale supporting the research question(s)
- Objectives
- Statistical considerations (sample size, power, planned analyses, etc.) which the trial statistician views as appropriate for the trial
- Logistical considerations

A Chair for the Correlative Science component of a trial should be appointed and a subcommittee for CS may be named.

### ***Review and Approval***

The CS component is reviewed by the Tissue Bank Manager, Tissue Bank Coordinator with input from the Director of Operations, the Scientific Advisor for Translational Work, and the Disease Site Group Correlative Science Committee as needed.

### ***Participation***

All participating centres are required to take part in the specimen collection and banking in Canadian Cancer Trials Group led trials which include a correlative science component, although an individual patient makes his or her own decision to participate in the trial (when banking is mandatory) and to allow (when banking is optional) specimen banking.

### **Informed Consent**

#### ***Templates***

Generic tissue banking informed consent forms are available and must be used to develop the sample informed consent.

#### ***Mandatory vs. Optional Collection***

If tissue collection is mandatory, language addressing consent for collection or release of tissue will be included in the core consent. For optional collection, a separate tissue banking sample informed consent is developed.

#### ***Content***

Patients will be made aware through the informed consent process as to whether their specimens will be used in predefined research, or stored for future research. Elements included in the tissue consent are in compliance with Canadian Tri-Council Policy Statements. The issues around the use of tissue for genetic research are addressed in the generic tissue consent. Patients will be given the option of explicitly agreeing to varying aspects and levels of consent in the use of their tissue.

## **Tissue Acquisition, Storage and Tracking**

### **Facility**

The TTDR is governed by the policies and procedures of Department of Pathology and Molecular Medicine at Queen's University regarding security, infrastructure, emergency response and disaster planning. For all other considerations, including the database and IT, Canadian Cancer Trials Group SOPs are applicable.

### **Logistics**

In Canadian Cancer Trials Group led trials banking of bio-specimens occurs at the TTDR. In exceptional circumstances (for example: special facilities are not available at the TTDR), off site banking may be considered for individual trials provided that procedures and work instructions consistent with this document and the Correlative Study Laboratory Manuals are used.

For trials led by other cooperative group(s) Canadian Cancer Trials Group may collect and either temporarily or permanently store specimens at the TTDR from the Canadian

cohort of patients. In most cases, samples are sent directly to the coordinating group's biorepository.

A standard or negotiated fee is paid to institutions/pathology departments on receipt of bio-specimens or administrative, retrieval and shipping costs.

Standardized and trial specific bio-specimen collection kits may be provided to assure the quality of the samples obtained. In some cases there may be additional funding available for the collection of liquid samples.

### **Laboratory Manuals**

A Correlative Science Laboratory Manual will be drafted by the trial team with input from the Tissue Bank Manager, Tissue Bank Coordinator, and the TTDR staff according to a standard template. Trial specific laboratory manuals may not be required.

### **Blocks, Slides and Cellular Material**

The usual process for requesting blocks, slides, or cellular material is documented in Figure 2. The receipt and review of a diagnostic pathology report or pathology submission form and the verification of the level of informed consent will initiate a request to the site to submit the material required for the trial. In many situations which are trial specific, the blocks, slides, or cellular material may be sent directly to the TTDR as part of the randomization process. The specifics for each trial are outlined in the protocol.

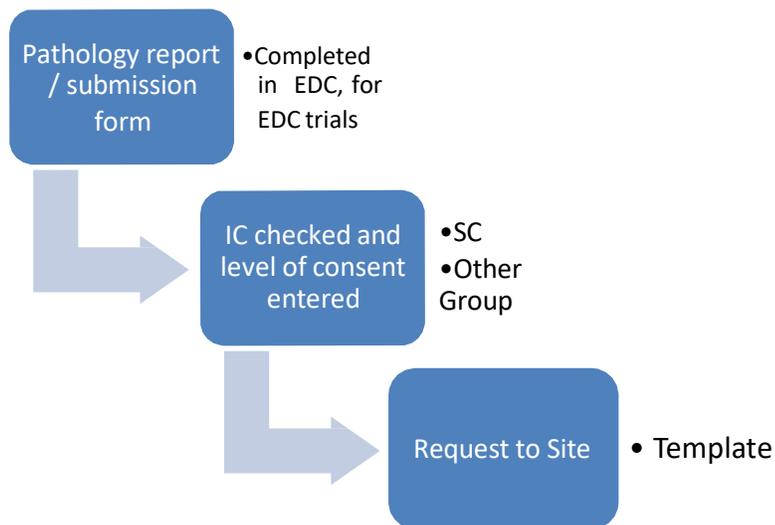


Figure 2

## **Liquid samples**

The collection of liquid samples will be described in the laboratory manual and will follow the process indicated in Figure 3. In contrast to the collection of blocks, slides, or cellular components, samples are sent directly to the TTDR as per the protocol specific instructions and not as a result of a direct request from the TTDR. Individual trials will specify whether samples must be sent to the TTDR in real time or whether they can be batched and sent at pre-specified time points. Details as to the correct local storage procedures will be outlined in the Correlative Study Laboratory Manuals.

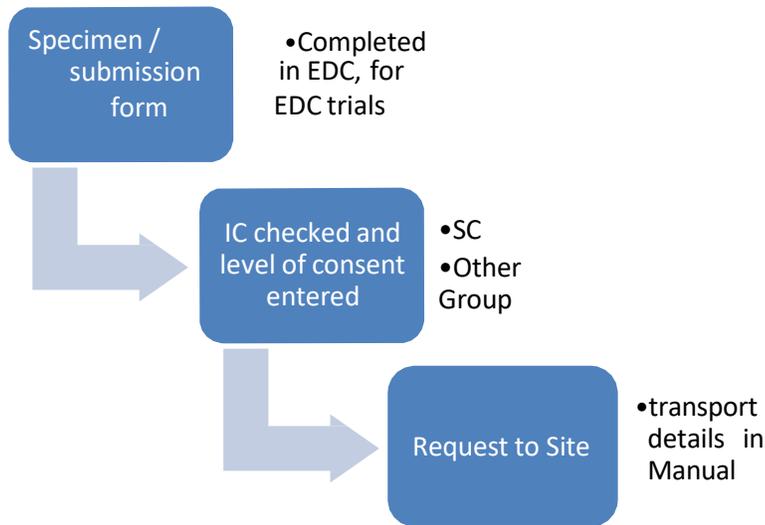


Figure 3

## **Identification and Storage**

- Specimens received at the TTDR from the originating institution are labeled with a pathology accession number (if applicable), other local identifiers and (usually) a Canadian Cancer Trials Group patient ID.
- Upon receipt, the sample is logged into the TTDR Database and assigned a unique tumour bank ID number (de-identification).
- The TTDR maintains a database with patient information such as Canadian Cancer Trials Group ID number, patient initials, pathology accession number (to ensure blocks can be returned on request) and tumour bank ID number.
- In order to preserve patient confidentiality, patient identifiers are not provided to researchers accessing the material.
- As derivatives are made from samples received (tissue microarrays, DNA, RNA, serum and plasma aliquots) unique identifiers are attached.

### **Returns and Consent Withdrawal**

Blocks and slides may be returned upon request by overnight courier for urgent clinical patient management, or at pre-specified times if mandated by local requirements. Blocks and slides will not be destroyed by the TTDR.

Liquid samples are generally destroyed rather than returned.

Destruction of any tissue is compliant with Canadian regulations and guidelines and Queen's University policies and procedures.

If consent is withdrawn, and tissue has not been used, the same principles will be followed to return or destroy samples.

Documentation of destruction or return is maintained at TTDR.

### **Samples Received in Error**

Although blocks and slides are called in following verification of patient consent, liquid samples may be submitted prior to receipt of the informed consent. On occasion, samples may be submitted from patients who have not consented, or who have withdrawn consent. In such instances the following process is followed:

- The sample is immediately 'quarantined'.
- The site is asked to document the error in writing, and notify the patient and their REB, and to submit a corrective action plan.
- The site and TTDR retain a copy.
- The sample is destroyed or returned and documentation provided to the site and filed at TTDR.

### **Databases and Tracking**

The TTDR database links with individual trial databases as appropriate. Inventories are available to the trial team as well as on the Canadian Cancer Trials Group web site, and are reported to the CSTB committee regularly.

## **Access to Tissue**

### **Approval and Oversight**

Disease Site Group Correlative Science Committees are responsible for:

- Ensuring appropriate CS sections are developed for protocols, and reviewing those plans prior to the actual release of tissue, to ensure that the plans are consistent with current knowledge and technology.
- Reviewing applications for access to tissue for research not planned in the protocol.

Template request forms for access to specimens, evaluation forms for the Correlative Science Review Committee and tissue release forms are in place.

Approval for use of specimens for NCI US affiliated trials will need to be sought from appropriate US Committees; however, applicants are encouraged to first submit to Canadian Cancer Trials Group for constructive input, and support in US application.

### **Logistics**

Samples released to researchers are identified by a Tumour Bank Identification Number (TBID). Results of investigative work are returned to the central office of the Canadian Cancer Trials Group according to pre-specified arrangements between the trial specific senior biostatistician and the investigator. All analyses are conducted by the central office of the Canadian Cancer Trials Group unless alternative arrangements have been made and approved by the central office biostatistician. The linking of the TBID and the clinical information is done by the Tissue Bank Manager or by the Oracle programming team in the central office.

### **Project Tracking**

The distribution of any banked specimens for approved correlative science projects, project status, progress, and subsequent data submission and statistical analyses are monitored through the Correlative Science Project Tracking Database (CSPTD).

### **Requirements for Access and Release of Tissue**

The following must be in place (including for protocol defined research):

- REB approval for the research project filed at Canadian Cancer Trials Group (may not be required if the research done is for eligibility or a specific endpoint of the trial).
- A Tissue Bank contract, Material Transfer Agreement or Sample Release Agreement must be executed prior to tissue release. The contract addresses:
  - Confidentiality
  - Use of tissue including return upon request or upon completion of project
  - Intellectual property
  - Publication and review requirements
  - Arrangements regarding analyses
  - Compliance with any specific contractual obligations that Canadian Cancer Trials Group may have with regards to the tissue or trial

- Appropriate funding to conduct the research and complete the analysis must be in place.
- Curriculum Vitae of the PI conducting the research must be approved and filed at the Canadian Cancer Trials Group.

Specimens will be used only for the pre-planned purpose(s) and those not fully used will be returned to the Canadian Cancer Trials Group or destroyed.

### **Request for Access to banked samples**

A web based application form is available on the external web site of the Canadian Cancer Trials Group and information required and the process to be followed is outlined in detail, including:

- A brief description of the project
- A well described hypothesis
- A 2-3 page outline of the proposal which will include background information and the rationale for the proposal, appropriate references, and a rationale for the need for clinical trial related material
- A description of the nature and amount of material required
- A well-developed statistical analysis plan to support the hypothesis and the sample size ( developed in collaboration with the trial specific Study Chair and /or the trial biostatistician)
- An indication of funding support and REB approval should have been obtained or indicated that it is being sought

## **Statistical Analysis**

A statistical analysis plan (SAP) will be developed for all projects, either as part of the trial SAP, or as a separate SAP (if CS are being conducted after the primary trial analysis, or in the case of research not planned in the protocol). All results from completed CS projects will be sent back to the Canadian Cancer Trials Group for statistical analyses, unless alternative arrangements have been made and approved by the Disease Site Group Correlative Science Committees.

Results linked to de-identified samples sent to researchers will be decoded by the TTDR or through the Oracle programmers and linked to patient information in the Canadian Cancer Trials Group database.

## **Quality Control and Assurance**

All aspects of this document are subject to Canadian Cancer Trials Group processes regarding audits, including:

- Laboratories (Audit of a Vendor)
- TTDR and processes (Central Office Quality Measures and Audits).

## References

### Links

Canadian Tri-Council Guidelines

<https://www.homelesshub.ca/resource/tri-council-policy-statement-ethical-conduct-research-involving-humans-tcps>

ISBER

<https://www.isber.org/default.aspx>

Canadian Tissue Repository Network: Policies and Procedures.

[www.CTRNet.org](http://www.CTRNet.org)

### Acronyms

<b>CS</b>	Correlative Science
<b>CSTB</b>	Correlative Science Tumour Biology Committee
<b>CTRNet</b>	Canadian Tissue Repository Network
<b>GBC</b>	Group Banking Committee
<b>HC</b>	Health Canada
<b>ISBER</b>	International Society of Biological and Environmental Research
<b>OBBR</b>	Office of the Bureau of Biological Research
<b>OTBC</b>	Operational Tissue Banking Committee
<b>REB</b>	Research Ethics Board
<b>SC</b>	Study Coordinator
<b>SI</b>	Senior Investigator
<b>TB</b>	Tissue Bank
<b>TBC</b>	Tissue Bank Coordinator
<b>TBM</b>	Tissue Bank Manager
<b>TTDR</b>	Tumour Tissue Data Repository