Standard Operating Procedure

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Supplementary Documents:	CSTB-WKI-0003 Correlative Sciences and Tissue Banking

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	Name	Signature	Date

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1 Policy

The Canadian Cancer Trials Group (CCTG) has established the Tumour Tissue Data Repository (TTDR) to ensure the structured and standardized collection, storage, inventory management, quality assurance, tracking, access, and release of tumour tissues and associated data. The repository operates in alignment with the scientific objectives of correlative biology while upholding the privacy and rights of individual patients. The TTDR supports trial-specific biospecimen collection, facilitates collaborative research, and enables access to high-quality biospecimens for investigators, ensuring that all processes comply with regulatory and ethical standards.

2 Introduction and Scope

Correlative biological questions are considered for inclusion in all Canadian Cancer Trials Group (CCTG) clinical trials in one of the following ways:

1. **Integral component**: As part of the trial design, such as participant eligibility based on biomarkers or use of biomarkers as stratification factors.
2. **Integrated component**: Included as correlative endpoints directly linked to trial outcomes.
3. **Exploratory research**: Addressed through the analysis of archival material stored in the CCTG biobank.

The **Tumour Tissue Data Repository (TTDR)** was established in 1997 and is overseen by the **Correlative Science Tumour Biology (CSTB) with the support of the Operations and Statistical Centre of the CCTG.**. The TTDR supports the collection and banking of various biospecimens, including but not limited to tumour tissue, whole blood, plasma, serum, urine, and bone marrow, ensuring high quality, and comprehensive sample availability for scientific investigation.

This Standard Operating Procedure (SOP) outlines the process by which tissue banking is integrated into CCTG clinical trials. It provides detailed guidance on the scope, policies, procedures, roles, and responsibilities, as well as study design considerations, specimen collection and storage, access to banked samples, and governance structures.

3 Definitions

3.1 Terms

Biobank: A collection of biological material and the associated data and information stored in an organized system for a population or a large subset of a population.

Repository: A Biorepository is a biological materials repository that collects, processes, stores, and distributes biospecimens to support future scientific investigation.

3.2 Acronyms

CS	Correlative Science
CSTB	Correlative Science Tumour Biology Committee
CTRNet	Canadian Tissue Repository Network
GBC	Group Banking Committee
HC	Health Canada
ISBER	International Society of Biological and Environmental Research
OBBR	Office of the Bureau of Biological Research
TBMMan	Tissue Bank Manager
REB	Research Ethics Board
SC	Study Coordinator
TB	Tissue Bank
TTDR	Tumour Tissue Data Repository

4 Governance and Compliance

4.1 Applicable Regulations and Guidance

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 the adult 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. The TTDR is an accredited biobank with the CTRNet certification program.

Where possible, CCTG uses laboratories which are GLP, CAP or CLIA approved for investigating protocol defined biomarkers, especially where these are planned as companion diagnostics.

4.2 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.

4.3 Research Ethics Board Approval

The activities of the TTDR are covered by a general 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.

4.4 Structure and Committees

The **Correlative Science Tumour Biology (CSTB) Committee of the CCTG**provides guidance, scientific leadership, and logistical support to the TTDR for the evolving translational biology program within CCTG trials. As a CCTG Endpoint Committee, the CSTB Committee does not generate or lead trials but has put in place relevant structures and processes that enable the best correlative biological questions to be incorporated, and to ensure the biospecimens collected for these studies are used in the best way possible for biomarker research. The TTDR is responsible for the operational aspects of biospecimen collection and ensures that the repository aligns with the objectives of CCTG trials.
The Operations and Statistical Centre provides regulatory and ethics guidance to the TTDR as well as the Information Technology support to ensure the appropriate collection, storage, inventory control, and quality assurance of the biospecimens received in the repository.The TTDR works closely with the Trial Management Group to ensure that trial-specific biospecimen banking is carried out efficiently, with clear processes for sample tracking, access, and release to qualified investigators. The leadership for the TTDR is provided by an Operational Director and a Tissue Bank Manager and is supported by a Tumour Bank Study Coordinator, biobank assistants and technical staff.
This governance structure ensures accountability, transparency, and consistency in all tissue banking activities across CCTG trials.

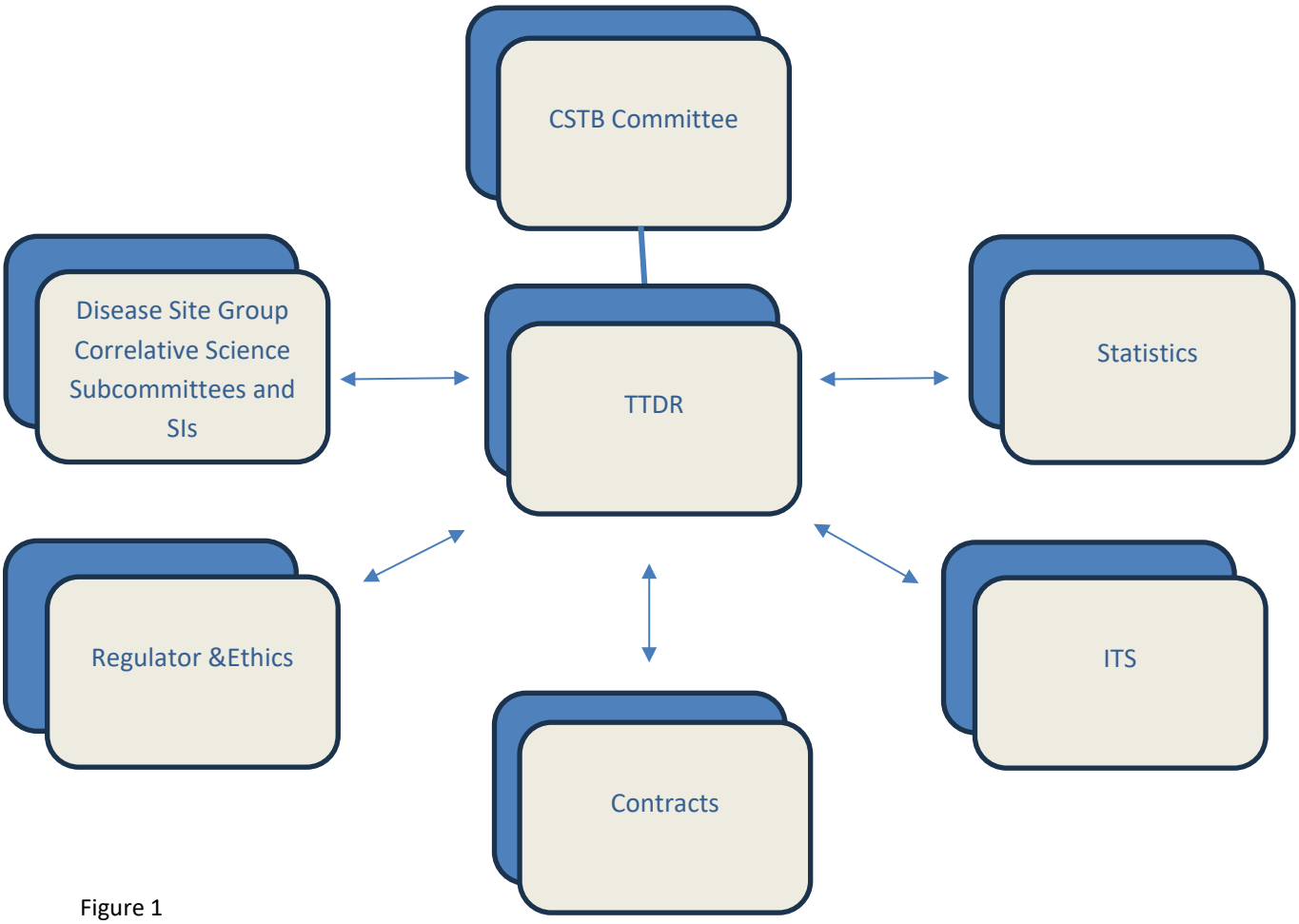


Figure 1

5 Protocol and Consent Development

5.1 Protocol

5.1.1 Templates

The OSCis responsible for ensuring that the generic protocol sections concerning tissue banking are current and compliant.

5.1.2 Development

Where applicable , correlative studies are always considered for a CCTG trial. It is the responsibility of the protocol authors, 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 Correlative Science (CS) section template. If

appropriate, information regarding the Correlative Science component must be included as follows:

- 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.

5.1.3 Review and Approval

In addition to the review and approval requirements detailed in the Protocol Development SOP, the CS component is also reviewed by the Director of Operations,CCTG Senior Investigator for the CSTB as well as the Disease Site Group Correlative Science Subcommittees.

5.1.4 Participation

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

5.2 Informed Consent

5.2.1 Templates

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

5.2.2 Mandatory vs. Optional Collection

If tissue collection is mandatory or optional, language addressing consent for collection or release of tissue will be included in the core consent.

5.2.3 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.

6 Tissue Acquisition, Storage and Tracking

6.1 Facility

The TTDR is governed by the policies and procedures of the 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, CCTG SOPs are applicable.

6.2 Logistics

In CCTG led trials banking of biospecimens occurs at the TTDR. In exceptional circumstances (for example: special facilities are not available at the TTDR), off site banking may be considered

providing that this SOP and associated WKIs are used.

For trials led by other cooperative group(s) CCTG may collect and either temporarily or

permanently store specimens at the TTDR from the Canadian cohort of patients.

Remuneration is paid to Canadian institutions/pathology departments on receipt of blocks/slides, for administrative, retrieval and shipping costs. If a contract for a specific study has negotiated a higher amount for tissue acquisition this will be outlined in the letter of centre activation and passed on to the referring institution. (TTDR SOPs). Depending on the trial and the sources of funding, remuneration may also be paid for the collection of liquid samples.

6.3 Laboratory Manuals

A Correlative Science laboratory manual will be drafted by the trial SC and reviewed by theTTDR staff using a standard template.
This manual serves as a comprehensive guide to ensure consistency, accuracy, and reproducibility in the collection, handling, processing, storage and shipping of biospecimens across all participating centers

6.4 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. This is done as part of the randomization process. In some trials, sample submission will be requested at the time of randomization.The specifics for each trial will be outlined in the protocol.

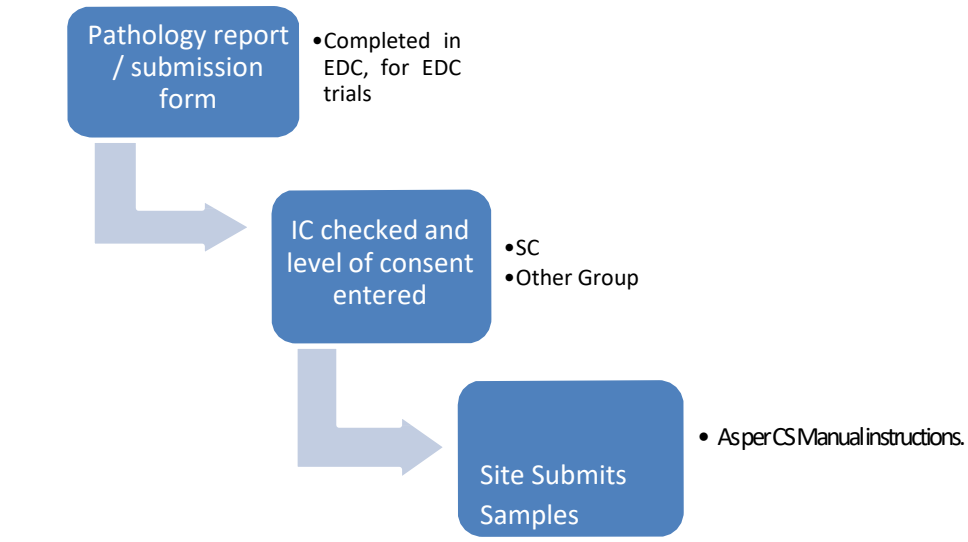
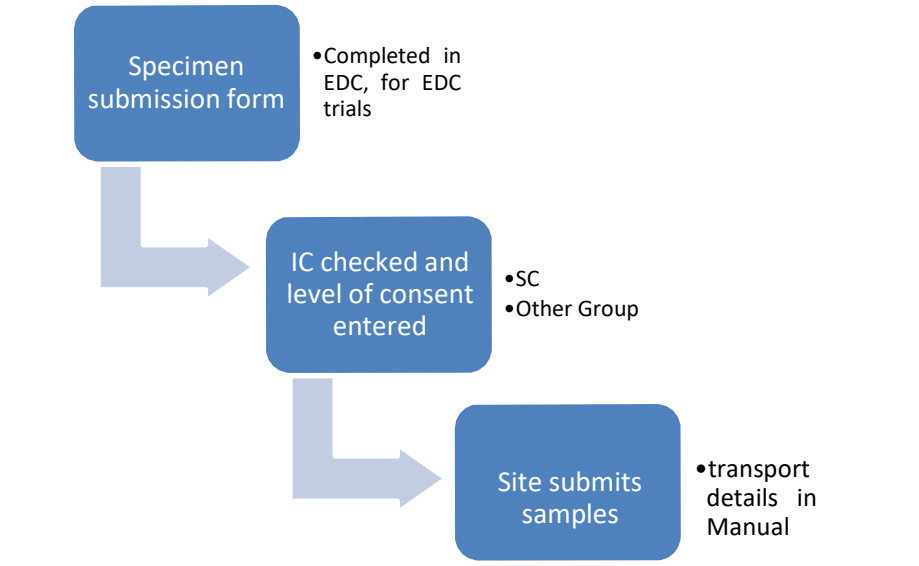


Figure 2

6.5 Liquid samples

The collection of liquid samples follows 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.



6.6 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 CCTG 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 CCTG 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 without approval from the trial Senior Investigator.
- As derivatives are made from samples received (tissue microarrays, DNA, RNA, serum and plasma aliquots) unique identifiers are attached

6.7 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 regulations. Blocks and slides will not be destroyed by the TTDR unless specifically requested by sites or trial SI.

Liquid samples are generally destroyed rather than returned.

Destruction of any tissue is compliant with Canadian regulations and guidelines and Queen's University Environmental Health & Safety 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.

6.8 Samples Received in Error

Although blocks and slides are called in, liquid samples may be submitted prior to receipt of the informed consent. On occasion, samples may be submitted from patients who have not consented, were deemed ineligible, or who have already 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

6.9 Databases and Tracking

The TTDR database is oracle based and links with individual trial databases as appropriate. Inventories are available to the trial team as well as on the CCTG web site, and are reported to the CSTB committee regularly.

Centre specific problems are identified by the Tissue Bank Manager and resolved in collaboration with the Operational Director of the TTDR and the trial team.

7 Access to Tissue

7.1 Approval and Oversight

Disease Site Group Correlative Science subcommittees 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 be sought from appropriate US Committees; however, applicants are encouraged to first submit to CCTG for constructive input, and support in US application.

7.2 Logistics

Samples released to researchers are identified only by a TB ID. Results of investigative work are returned to the central office of the CCTG according to pre-specified arrangements between the trial specific senior biostatistician and the investigator. All analyses are conducted by the central office of the CCTG unless alternative arrangements have been made and approved by the Disease Site CSC. The linking of the TBID and the clinical information is done by the Tissue Bank Managerr or by theOracle programming team in the central office.

7.3 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).

7.4 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 CCTG (may not be required if the research done is for eligibility or a specific endpoint of the trial)
- ATumour 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
    - Intellectual property
    - Publication and review requirements
    - Arrangements regarding analyses
    - Compliance with any specific contractual obligations that CCTG 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 Qualified Investigator conducting the research must be approved and filed at the CCTG

Specimens will be used only for the pre-planned purpose(s) and those not fully used will be returned to the CCTG.

7.5 Protocol Defined Research

Protocol development and review are detailed in section 5. The Disease Site Group CSsubcommittee re-reviews the proposals prior to tissue dispatch to ensure the plans are correct and appropriate.

7.6 Other research

A web based application form is available on the external web site of the CCTG 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, REB approval, and a signed Tumour Bank Contract/MTA oSample Release Agreement

8 Statistical Analysis

A statistical analysis plan 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 CCTG for statistical analyses.

Results linked to coded samples sent to researchers will be decoded by the TTDR or through the Oracle programmers and linked to patient information in the CCTG database.

9 Quality Control and Assurance

All aspects of this SOP are subject to CCTG SOPs regarding audits, including

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

In addition, each office, including the TTDR is responsible for ensuring SOPs, WKIs and a Quality Control process is in place.

10 Roles and Responsibilities

Role	Responsibility
Correlative Science Tumor Biology Committee (CSTB)	See CSTB terms of reference
Tissue Bank Manager	Oversight of TTDR operations
Disease site CS sub committee	Trial specific protocol content review (as applicable) Access to tissue; approval and oversight

	Ensure conduct of protocol defined research
CCTG	SAP and analysis (unless otherwise agreed/documented)
AMG	Vendor Audit/Internal Audit

11 Appendix

N/A

12 References

Canadian Tri-Council Guidelines: Revised 2010

ISBER

Canadian Tumour Repository Network: Policies and Procedures. **www.CTRNet.org**

13 Revision History

Version Number	Version Date	Brief Description of Revision(s)
V001	2010-Jun-23	Initial Release
V002	2012-Jul-06	The TTDR is a registered biobank with the CTRNet certification program statement was added at the time of 2 year review.
V003	2014-Sep-02	Administrative changes to remove references to TB Study Coordinator and change PI to QI.
V004	2017-Feb-27	2 year review and approval.
V005	2020-Jan-23	Update ICH to International Council for Harmonisation
V006	2024-Oct-25	Clarifications and reflection of new personnel
V007	2026-Jun-03	Updated document status to public.