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1.0 PURPOSE


- 1.1 The purpose of this standard operating procedure (SOP) is to provide guidance on the processes used to continuously track the chain of custody (COC) for tissues collected at the biospecimen source sites (BSS) or processed and stored at the Comprehensive Biospecimen Resource (CBR) for projects under the National Cancer Institute (NCI).
- 1.2 Specifically, this SOP will establish COC procedures and control what actions and materials are tracked for each sample within the project workflow.

2.0 SCOPE

- 2.1 The COC is defined as the documentation of the chronological movement of samples from the time of collection through shipment, receipt, possession, handling, processing, analysis and final storage. In addition, the COC is also documentation for the return shipment of samples which are no longer valid due to recall or donor consent withdrawal.
- 2.2 This COC SOP encompasses all objectives required to adequately and accurately track the COC of biospecimen samples and related data.
- 2.3 Tracking COC is an essential part of any operational and analytical process of a research project to ensure the identity and integrity of the sample from collection through data reporting and provide the necessary accountability for procured specimens.
- 2.4 Establishing a COC is essential in an effort to remove doubt regarding the identity and integrity of samples collected, processed, and submitted for analysis and allows the project to defend the findings.
- 2.5 COC implements the process necessary for statistical procedure control and root cause analysis, a manufacturing discipline used to produce outputs (in this case, biospecimens) within required quality and tolerance limits.

3.0 RESPONSIBILITY

- 3.1 It is the responsibility of all project staff to ensure that all the biospecimen shipment COC's are documented.
- 3.2 BSS: It is the responsibility of each principal investigator to ensure that members of their project team appropriately document the collection, handling, processing, storage (if any), and shipment of samples to ensure proper COC (see OP-0011-F1 GTEx Chain of Custody Form). The BSS should also accurately capture the appropriate data in the CDR (Comprehensive Data Resource) and/or BRIMS (Biorepository Information Management System) per the SOPs.

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4.0 Receiving entities: It is the responsibility of each receiving entity to both document its role within the sample’s COC and to adhere to their local COC SOP. Any additional data collected in laboratory notebooks (or by other means) may be extracted and included on the COC or for verification of process adherence or data queries. This includes but is not limited to: data received, initials of custodian, initials of analytic technician, parameters analyzed, results, disposal of samples, amounts remaining (if any), and training of staff on procedures.

5.0 DEFINITIONS & ACRONYMS

- 5.1 **BB** – Brain Bank. The receiving and processing facility for the brain, brain structures, and hair biospecimens collected for the GTEx project.
- 5.2 **BRIMS** – Biorepository Information Management System. Advanced biospecimens inventory management system provided and administered by the CBR and designed to track the lifecycle of biospecimens, as defined by the projects’ objectives from preparation of the collection kit, through the point of collection to delivery, receipt, storage, processing and distribution to various receiving entities.
- 5.3 **BSS** – Biospecimen Source Site. Hospitals and/or research facilities tasked to collect, process, store, and ship clinically-annotated biospecimens and associated data in accordance with program-developed SOPs and protocols.
- 5.4 **Case ID** – Unique alpha-numeric identification of a case. This coded ID is assigned by the BSS to all of the components of a collection kit at the time that a consented donor is identified. This ID subsequently identifies the project, genealogy of all specimens, and data collected and/or aliquots derived from that case.
- 5.5 **CBR** - Comprehensive Biospecimen Resource. Centralized entity responsible for creating and managing the kit components shipped to the source sites. Also responsible for informatics support with the CDR, storage and processing all designated biospecimens (and associated inventory data) collected, creation of slides and digital images, and maintenance of the image management system, as well as quality checks on collected and processed specimens. The CBR serves as the re-distribution biorepository.
- 5.6 **CDR** - Comprehensive Data Resource. Centralized custom-made informatics system that stores and reports all collection, handling, and processing data for biospecimens and annotations collected for use by this program. The system provides secure, role-based access for BSSs to input data related to each case collected that is associated with a limited data set related to the donor. Interfaces are provided to other systems that contain related case data (e.g., inventory data at the CBR, molecular data at the molecular analysis facility, research data in dbGaP at the LDACC, etc.).

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- 5.7 **COC** – Chain of Custody. Documentation of the chronological movement and operational steps for each sample and annotations throughout their receipt, handling, and processing lifecycle from the time of collection through inventory, processing, distribution, analysis, and final storage.
- 5.8 **Kit ID** – A human-readable combination of alpha-numeric characters that identifies a kit or combination of tissue collection components within a specified project.
- 5.9 **LDACC** - Laboratory Data Analysis and Coordinating Center. Research institute responsible for the overall coordination of GTEx activities and molecular and statistical analysis.
- 5.10 **MAF** - Molecular Analysis Facility. Organizations that perform specific molecular analyses on biospecimens using defined platforms in which they have expertise.
- 5.11 **NCI** – National Cancer Institute. The National Cancer Institute (NCI) is part of the National Institutes of Health (NIH), which is one of 11 agencies that compose the Department of Health and Human Services (HHS). The NCI is the Federal Government's principal agency for cancer research and training.
- 5.12 **PRC** - Pathology Resource Center. Centralized resource consisting primarily of expert pathologists whose function is to review biospecimens (either slides or images) collected for the program and assess their quality and fitness for use by researchers.
- 5.13 **Sample ID / Specimen ID** – A machine or human-readable combination of alpha-numeric characters that identifies the sample or case. In the following example, GTEX-000002, the 4 alphas (e.g., GTEX) identify the study/project for which specimens are collected. The subsequent six numerals (e.g., 000002) identify the donor or case. This ID is associated with all of the specimens collected from one donor at a specific time/visit (donation).
- 5.14 **SOP** – Standard Operating Procedure. An established procedure to be followed in carrying out a given operation or in a given situation.
- 5.15 **TPM** – Technical Project Manager. The individual responsible for direct communications with those involved with deliverables, submitted SOPs, other documents, as well as ensuring that relevant procedures and documents are assessed and controlled.

6.0 ENVIRONMENTAL HEALTH & SAFETY

Not applicable

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7.0 MATERIALS/EQUIPMENT

7.1 The *required COC* form, whether filled out in BRIMS or paper form OP-0011-F1, will be utilized to ensure that the COC process is adequately documented. In addition to the required COC form, each BSS and receiving entity may also utilize additional COC procedures, per their local SOPs, as additional documentation of the process. ***This shall not replace the required COC form.***

8.0 PROCEDURE

8.1 Sample Collection:

8.1.1 The sample must be collected under the conditions detailed per the specified sample/specimen collection approved SOP.

8.2 Sample Handling:

8.2.1 It is imperative that the samples are properly handled as specified in all project related SOPs. This is to maintain sample identification and ensure that there is no contamination during collection. Any deviation from the specified project sample/specimen handling SOPs should be documented by the BSS or other research entity.

8.3 Sample Labeling:

8.3.1 The labeling or proper marking of samples will help to ensure positive identification throughout the handling and analysis process.

8.3.2 All labeling should be conducted per the applicable project specific SOP. In most instances pre-labeling by the CBR is utilized and provided to the BSS.

8.3.2.1 If ink is being used for the marking, then it must be indelible and unaffected by the products and temperatures to which it will be subjected.

8.3.2.2 Other methods such as barcode identification can be used as long as they are placed along the flat edge and/or do not impair the saturation capacity of the cassette.

8.3.3 If kit specific IDs are utilized (project specific), all kit containers must have a unique identification (kit ID#) to exclude the possibility of interchange. The kit ID # is located on the outside of the kit box.

8.4 Sample Transportation:

8.4.1 All transported samples must be accompanied by an appropriately populated **GTE_x Chain of Custody Form (OP-0011-F1)** and **Shipping Manifest (OP-0011-F2)**. These forms are either entered in BRIMS or completed on a paper form.

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8.4.1.1 The COC form includes the following information, as applicable: name of project, case ID, kit ID, origination of sample, collection date, shipper and receiver information based on user login (signatures if on paper), and sampling conditions. The Shipping Manifest will be provided to detail what biospecimens are included within a shipment. This may include use of approved:

- Electronic forms: For example, the CBR's BRIMS will be utilized to complete and print the shipping manifest and COC from the system. Once data is entered in the system, this will mark the status of the shipment as "in progress".
- Paper forms: shall be used only in the event BRIMS cannot be accessed, e.g. BRIMS error, computer malfunction, etc. The forms are OP-0011-F1 and OP-0011-F2 that are similar to the BRIMS forms of the COC and Shipping Manifest, respectively. These forms are not provided by the CBR; these forms are associated with the specific SOP.

8.4.1.2 ***The COC form (whether electronic or paper) should be filled out by the shipping entity at the time of shipment and by the receiving entity as soon as samples or materials are received and evaluated.***

8.4.2 One COC form can travel with a batch or list of samples provided all samples have gone through the identical COC.

8.4.3 It is important to minimize the number of staff/entities handling the samples to ensure comprehensive documentation and sufficient specimen tracking.

8.4.4 A reputable courier service should be approved and managed by the CBR as outlined in the project specific SOP or as instructed by the project management team and/or the CBR.

8.4.5 At the time of transfer to a courier, all kits or shipping materials must be packaged according to project specific shipping SOPs.

8.5 Sample Receipt:

8.5.1 Since the potential exists during transportation for tampering, accidental destruction, and/or physical or chemical action to occur within the sample container or kit, an inspection upon receipt will be performed.

8.5.2 Once the samples have been delivered to the receiving entity, the addressee must complete the following steps:

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- 8.5.2.1 The package should be checked for tampering.
- 8.5.2.2 The package should be opened to verify its contents against the Shipping Manifest included in the shipment.
- 8.5.2.3 Relevant fields of the accompanying COC form should be completed in BRIMS (the paper form should be signed by responsible personnel).
- 8.5.2.4 While the receiving entity is processing the receipt of the package, i.e. verifying and documenting multiple parameters in the shipment, the samples should be logged as 'received' in BRIMS and according to approved SOPs.
- 8.5.2.5 Custody of a specimen is considered at the time of shipment and when the shipment is opened and inspected. Any staff member who takes receipt and custody of a specimen must complete relevant portions of the COC form.

8.5.3 The receiving entity is responsible for obtaining temperature readings of the shipments. This can be accomplished by using a NIST-calibrated thermometer or utilizing a data logger within the shipment. Sufficient dry ice, if used, upon receipt may also be recorded in lieu of a temperature recording. This information should be recorded on the COC form. This will provide further support that the package has been shipped within the targeted temperature range for kit and/or biospecimens.

8.6 Sample Custody:

- 8.6.1 A sample should only be in the possession of identified project personnel or an identified approved courier. A sample is considered under a staff member's custody if any of the following apply:
 - 8.6.1.1 The sample is in the physical possession of the staff.
 - 8.6.1.2 The sample has been secured or stored to ensure no one can tamper with the sample.
 - 8.6.1.3 The sample has been secured in an area to which access is restricted to authorized personnel only.

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8.7 Chain of Custody Form Completion

8.7.1 The COC form should be completed by all entities interacting with the samples.

8.7.2 All sections should be completed or identified as N/A, if applicable.

8.8 Continuous Monitoring:

8.8.1 A combination of paper and electronic systems may be utilized to track sample(s). Refer to Section 7.4.1 as to when paper forms may be used.

8.8.2 Each sending or receiving entity is responsible for maintaining its own COC procedures for referencing and auditing purposes.

8.8.3 Each step of the completed COC should be completed in BRIMS.

8.8.4 If paper forms are used, forward the paperwork to the appropriate individuals. In addition, the COC should be generated by the shipping entity in BRIMS as soon as access is available.

8.9 Sample Transfer:

8.9.1 Any entity which transfers possession to another entity must provide two copies of the COC: (a) a copy of the COC form for their records, and (b) a copy to be placed within the box for shipment.

8.10 Resolving Discrepancies:

8.10.1 If a discrepancy is recorded, for example the number of samples shipped does not match the number received, the shipping party and receiving party will notify the TPM and will work to resolve the discrepancy and document the resolution.

8.10.2 Any discrepancy resolution request should be addressed within 24 hours of receipt. Specimen(s) will remain in quarantine until issues are resolved pertaining to biospecimen identification, labeling or related issue.

8.11 Storage of COC Forms:

8.11.1 The COC form should be stored at the BSS for a minimum of 10 years from close of the project as per the document retention policy.

8.11.2 The electronic COC is saved within BRIMS and can be printed at any time. All completed COC paper forms will be collated and an audit log will be retained to include the kit content chronological history and current specimen location.