1.0 PURPOSE

The purpose of this document is to describe the process to be followed when a donor, a donor's legally authorized representative, a deceased donor's next of kin, a Biospecimen Source Site (BSS), or any other authorized entity withdraws the consent for or recalls the specimens for any other reason for a GTEx case that was collected by the National Cancer Institute (NCI) for the Genotype Tissue Expression (GTEx) program, overseen by the Biorepositories and Biospecimen Research Branch (BBRB). This process will also be followed when specimens, slides, aliquots and derivatives, and data are recalled for other reasons.

2.0 SCOPE

This process is applicable to all case-specific materials collected for the GTEx program and must be followed by all project staff that are responsible for the performance and management of the project. The process should be adhered to by all entities to include BSSs, Comprehensive Biospecimen Resource (CBR), Pathology Resource Center (PRC), and associated collaborators, as specified within the withdrawal or recall request. Specimens and data that have already been distributed to approved third party investigators will not be withdrawn or recalled through this process.

3.0 RESPONSIBILITY

3.1 **BSS Principal Investigator (PI) or designee:** Responsible for requesting the initiation of a withdrawal or recall request on behalf of the donor, their next of kin, legally-authorized representative (LAR), or the Biospecimen Source Site.

3.2 **CBR Lead:** Responsible for acknowledging a withdrawal/recall request in the Comprehensive Data Resource (CDR) and managing the destruction (or return) of case-specific materials, sequestering of related data, verification of completion, and notification when all withdrawal/recall requirements are met. This Lead is a staff member at the CBR.

3.3 **CDR Lead:** Responsible for acknowledging each withdrawal/recall request in the CDR and managing the sequestering of the data, verification that appropriate data was sequestered, and notification when all withdrawal requirements are met.

3.4 **Data Manager (DM):** Responsible for acknowledging the approved withdrawal/recall request, assigning appropriate entities, and monitoring completion of the process in the CDR.

3.5 **Ethical, Legal and Regulatory Affairs (ELR) Manager:** Responsible for reviewing the ethical, legal, and/or regulatory impact of each withdrawal/recall request, approving the Withdrawal/Recall Request, investigating questions or issues, consulting with lead to resolve problems, and notifying the Requester when the process is complete. Member of the Withdrawal Approval Group.

3.6 **External Collaborating Entity:** Any organization, group, or analysis facility – such as the Laboratory, Data Analysis, and Coordinating Center (LDACC) and Brain Bank (BB) – associated with the GTEx program that receives case-specific material and associated data under an agreement.

3.7 **Project Manager:** Responsible for reviewing the operational impact of each withdrawal/recall request and approving associated actions. Member of the Withdrawal Approval Group.

3.8 **Quality Manager:** Responsible for reviewing the quality impact of each withdrawal/recall request and approving associated actions. Member of the Withdrawal Approval Group.

3.9 **Requester:** Responsible for initiating a withdrawal or recall request on behalf of a donor, their next of kin, the Biospecimen Source Site, or the GTEx program. Usually, the Requester is the BSS PI or designee.

3.10 **Technical Project Manager (TPM):** Responsible for fulfilling the specific tasks of the donor's, BSS's, or NOK's wishes for each withdrawal/recall request and approving associated actions. Member of the Withdrawal Approval Group.

3.11 **Withdrawal Approval Group (WAG):** Responsible for approving all withdrawal/recall requests, completing withdrawal activities in the CDR, and escalating any outstanding issues to appropriate parties. This group will consist of leads from the Quality Management, the ELR Manager, the Data Manager, and the TPM responsible for the BSS.

4.0 DEFINITIONS

4.1 **Case-specific materials:** All biospecimens, data, slides, digital images, aliquots, and derivatives currently being stored at the CBR, CDR, BSS, or External Collaborating entity that are associated with a specific case. This does not include materials released to the research community under an approved protocol, Material Transfer Agreement (MTA), or Data Use Agreement (DUA).

4.2 **Legally-Authorized Representative (LAR)**: An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

4.3 **Recall** - An activity referring to case-specific materials that needs to be removed from the biorepository for various reasons including: donor was found to be ineligible after the case was already shipped; deviations related to the case were found to be unacceptable to the project; or biospecimens being returned to source site for other reasons.

4.4 **Withdrawal of consent** - When the donor or Next of Kin or other approved entity requests the withdrawal of their original consent to participate in GTEx or related projects.

5.0 ENVIRONMENTAL HEALTH & SAFETY

N/A

6.0 MATERIALS/EQUIPMENT

Please note that it is preferred that all requests are initiated in the CDR. However, in exceptional circumstances, requesters may email the TPM to initiate a request.

6.1 Computer

6.2 Internet connection and approved CDR access

7.0 PROCEDURE

Initiate Withdrawal/Recall Request

7.1 The Requester initiates each request to withdraw or recall a specific donor's specimens by logging into the CDR and following the instructions.

7.1.1 For any withdrawal of consent, the Requester is usually the BSS PI.

7.1.2 For biospecimens that have been recalled for any reason, the Requester might be at the BSS or GTEx staff.

7.2 The ELR Manager acknowledges the withdrawal/recall request in the CDR and reviews the specific case to verify that all the essential information is provided for processing. *Must acknowledge or respond within 5 business days from receipt.*

7.2.1 After verifying that all the necessary information is complete, the ELR Manager completes a **Withdrawal or Recall Request Approval Form, ER-0005-F1**, and uploads it to the QM Approval folder in SharePoint. This form is routed by the ELR Manager or QM for approval. Proceed to Step 7.3.

7.2.2 The ELR Manager will notify BBRB of the withdrawal/recall request via email within this timeframe.

7.2.3 If the ELR Manager determines that additional information is required, proceed to Step 7.4.

7.3 The WAG reviews the **Withdrawal or Recall Request Approval Form, ER-0005-F1**, and determines the appropriate action. *Must approve or respond within 10 business days from receipt.*

7.3.1 If the withdrawal/recall request is approved as documented by completion of the signature block on ER-0005-F1, proceed to Step 7.5.

7.3.2 If the withdrawal/recall request is not approved or the WAG requests additional information, proceed to Step 7.4.

7.4 The ELR Manager or WAG will communicate need for clarifications or additional information via the TPM. The TPM will consult with the Requester to resolve issues and questions.

7.4.1 Once questions or issues are resolved, repeat steps 7.2 and 7.3.

7.5 The Data Manager reviews and acknowledges receipt of the approved form, ER-0005-F1, and notates the case record in CDR. *Must acknowledge within 5 business days from receipt.*

7.5.1 All forms will be stored in the appropriate QM folder in SharePoint.

7.5.2 The Data Manager will assign the appropriate External Collaborating Entities to receive and process the request. Each Entity Lead will be officially notified via the appropriate communication channel and copies of communications will be uploaded to the CDR.

Complete and Verify the Request in the CDR

Note: The steps for completion of the request must be completed within 5 working days of the acknowledgement of this request.

7.6 The Data Manager initiates the automated sequester of data associated with the donor's case by selecting that action in the CDR. Once initiated and saved, the case status is permanently changed, and as a result, the case is removed from all lists and APIs and the case data is no longer available for research use.

7.7 The Data Manager or designee verifies that the data has been completely and appropriately sequestered for the requested case, and acknowledges completion in the CDR form.

7.7.1 Query the CDR to verify that the case data is no longer accessible

7.7.2 Verify data for that case is absent from LDACC API

7.7.3 Verify that all data and specimens, except case status, are absent from CDR-AR

7.7.4 Verify PRC reports for that case are unavailable

7.8 The Data Manager notifies the Withdrawal Approval Group of the completion of this sequester by following the withdrawal/recall workflow in the CDR.

Complete and Verify the Request at CBR

Note: The steps for completion of the request must be completed within 10 working days of the acknowledgement of this request.

7.9 The CBR Lead acknowledges the withdrawal/recall request in the CDR.

7.10 The CBR Lead oversees the withdrawal or recall of the donor's case-specific materials using documented and approved procedures.

7.10.1 The CBR's procedures for the destruction (or return) of biospecimens and sequestering of associated data must be approved by the GTEx program.

7.11 The CBR Lead uploads the supporting documentation to the CDR, as applicable (e.g., autoclave log, data log, or other supporting documentation, according to approved SOPs) verifying that CBR systems have been appropriately updated to reflect the withdrawal or recall of biospecimens/data.

7.12 The CBR Lead notifies the Withdrawal Approval Group of the completion of the process by following the withdrawal/recall workflow in the CDR.

Complete and Verify the Request at External Collaborative Entity

Note: The steps for completion of the request must be completed within 10 working days of the acknowledgement of this request.

7.13 The External Collaborating Entity Lead acknowledges the withdrawal/recall request.

7.13.1 If the External Collaborating Entity does not have access to the CDR, notify the appropriate TPM via email.

7.13.2 The TPM will enter the appropriate information on behalf of the external entity.

7.14 The External Collaborating Entity Lead oversees the withdrawal or recall request of the donor's case-specific materials using the External Entity's procedures.

7.15 The External Collaborating Entity Lead uploads the verification files to the CDR, as applicable (e.g., autoclave log, data log, shipping log, or other supporting documentation), indicating that the associated specimen data has been completely processed and/or appropriately sequestered in the entity's systems as requested.

7.16 The External Collaborating Entity Lead notifies the TPM that the specimens have been appropriately destroyed (or returned) and associated case data has been sequestered, as requested. The TPM notifies that WAG that completion has occurred.

7.16.1 Notification must be via email, fax, or other documented form signed by the External Collaborating Entity Lead.

7.16.2 ELR Manager may consult with appropriate Entity Leads to request additional information, as necessary, to complete the request within a reasonable and previously agreed upon time frame.

7.16.3 Once all the necessary supporting documentation is received from the entity or entities, the ELR Lead will record the information in the CDR.

Withdrawal/Recall Request Closure

7.17 The Data Manager monitors the completion of all tasks for each case listed in steps 7.6 through 7.16. Once all tasks have been completed and verified by the Data Manager, the WAG is automatically notified by CDR. *Must notify WAG within 5 business days from receipt.*

7.18 The WAG reviews all tasks related to the request, confirms the completion of the request, and notifies TPM. *Must approve or communicate issues/questions within 5 business days from receipt.*

7.18.1 When all actions are taken to the WAG's satisfaction, each WAG member must submit approval in the CDR in the following order:

7.18.1.1 ELR
7.18.1.2 TPM
7.18.1.3 DM
7.18.1.4 QM
7.18.1.5 GTEx Program Director

7.18.2 If the closure activities are approved, proceed to Step 7.20.

7.18.3 If the WAG requests additional information (i.e., closure activities are not approved), the Data Manager will communicate issues/questions to the TPM via email. Proceed to Step 7.19.

7.19 If the WAG requires additional information, the TPM consults with the appropriate leads, resolves any issues or questions, and communicates all information back to the WAG.

7.20 The TPM will notify the Requester and BBRB that the request has been completed and will record the date of reporting in the CDR.

7.21 The Requester may provide information back to the TPM that all associated case paperwork has been destroyed and that the Donor, NOK, or legally-authorized representative (LAR) was notified. If this information is available, the TPM records this in the CDR.

8.0 TIMELINES

All of the timelines in this SOP will be monitored by QM. If any timeline is missed, the incident will be entered in the Issue Register and managed using the appropriate SOP.

9.0 METRICS

The CDR will provide the metrics to measure this process, including (at a minimum):

9.1 Number of cases withdrawn or recalled (e.g., by project, source site, and type)

9.2 Number of tissue types withdrawn or recalled (e.g., by project, source site, and tissue type)

10.0 REFERENCES

10.1 NCI Best Practices for Biospecimen Resources: http://biospecimens.cancer.gov/bestpractices.

10.2 HHS Guidance on Withdrawal of Subjects from: Data Retention and Other Related Issues: http://www.hhs.gov/ohrp/policy/subjectwithdrawal.html