Office of Internal Audit

UT Southwestern Medical Center

Human Biospecimen Collection, Storage, Movement and Disposal Audit

Internal Audit Report 19:01

October 22, 2019

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Executive Summary

Background

The UT Southwestern Medical Center (UT Southwestern) mission statement highlights research as a key initiative in *"Research that solves for unmet needs by finding better treatments, cures, and prevention with a commitment to ensuring real world application."* Research activity is carried out in over 200 labs contributing to investigations from the microscopic level to the whole patient. Research studies performed by investigators range from basic and applied sciences to pre-clinical and clinical studies. Funding from federal and state agencies, commercial sponsors, foundations and other sponsors total over $470 million per year in support of approximately 5,800 research projects.

Human biospecimen refers to a quantity of tissue, blood, urine, or other human-derived material. A single biopsy may generate several biospecimens, including multiple paraffin blocks or frozen biospecimens. A biospecimen can comprise of subcellular structures, cells, tissue (e.g., bone, muscle, connective tissue, and skin), organs (e.g., liver, bladder, heart, and kidney), blood, gametes (sperm and ova), embryos, fetal tissue, and waste (urine, feces, sweat, hair and nail clippings, shed epithelial cells, and placenta). Use of human biospecimens is an integral part of research and provides an accurate representation of a patient's disease which can be utilized to study the response of biospecimens to a wide range of biological stresses. One of the most significant and increasing challenges in translational research is the limited availability of adequately annotated and appropriately collected biospecimens.

A biorepository collects, stores, moves and disposes biospecimens in support of various research studies. According to ISBER (International Society for Biological and Environmental Repositories), a biorepository is defined as *"an entity that receives, stores, processes, and/or distributes specimens, as needed. It encompasses the physical location as well as the full range of activities associated with its operation. It may also be referred as repository or biobank."*

UT Southwestern Medical Center has three large-sized biorepositories:

- Tissue Management Biorepository – Harold C. Simmons Comprehensive Cancer Center
- NTRC (Neuroscience Translational Research Center Biorepository) – O'Donnell Brain Institute
- Dallas Heart Study Biorepository – Center for Translational Medicine

In addition, there are smaller human biorepositories across the Institution collecting and storing biospecimens for research purposes within the departments. Individual Principal Investigators use human biospecimens obtained from biorepositories within UT Southwestern or from external sources on an as needed basis. Individual Principal Investigators rely on biorepositories to provide collection and storage services.

The Vice Provost and Dean of Research oversees research functions. The Associate Dean of Clinical Research serves as the Chair of the Biorepository Oversight Committee. In July 2018, UT Southwestern created the Biorepository Oversight Committee as an Institutional Standing Committee to increase a responsible and ethical environment and advance biomedical research.

Executive Summary

The committee's role is to ensure that biospecimens used for research are responsibly obtained, stored, and distributed, and to further ensure the necessary protections to the rights of individuals who have donated human biospecimens to UT Southwestern. The Principal Investigators have ultimate responsibilities to ensure compliance with the regulations and to have adequate safeguards in place to protect the integrity of the biospecimens.

Scope and Objectives

The Office of Internal Audit has completed its Human Biospecimen Collection, Storage, Movement, and Disposal audit. This was a risk based audit and part of the fiscal year 2019 Audit Plan. Audit procedures included data analytics; interviews with stakeholders; review of policies, procedures, and other relevant documents; physical walkthroughs of the laboratories and storage sites. The audit scope included active projects for fiscal year 2019.

The overall audit objectives were to assess the effectiveness and efficiency of processes and controls for human biospecimen collection, storage, movement and disposal. Specifically:

- Institution-wide governance and monitoring
- Safeguards for human biospecimen protection and storage
- Compliance with key regulations and institutional policies and procedures

During fiscal year, 2019 there were approximately 1,300 IRB approved studies identified as using human biospecimens. The audit excluded non-human biospecimens, cell lines, and specimens obtained prior to the implementation of the Institutional Review Board.

We conducted our examination according to guidelines set forth by the *Institute of Internal Auditors' International Standards for the Professional Practice of Internal Auditing*.

Conclusion

Due to the decentralized research activities at UT Southwestern and variability in methods used to track, compile and protect human biospecimens, a robust governance structure is needed to ensure human biospecimens are handled in a manner to protect the privacy of the donor, integrity of the research data and viability of the biospecimens. Developing policies and standardized guidelines, using a risk based approach, and establishing oversight for freezer management improves freezer inventory, tracking and preventative maintenance and ensures adequate back-up power support procedures. Establishment of a single point of accountability will ensure adequate monitoring, tracking, storage and security procedures are in place. In addition, evaluate the use of a comprehensive inventory tool for tracking human biospecimens across UT Southwestern to facilitate collaboration among researchers.

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The following table summarizes of the observations, along with the respective disposition of these observations within UT Southwestern internal audit risk definition and classification process. See Appendix A for Risk Rating Classifications and Definitions.

Priority (0)	High (1)	Medium (2)	Low (0)	Total (3)

Key improvement opportunities are summarized below.

1. **Develop Standardized Guidelines and Establish Oversight for Freezer Management** – Adequate governance and oversight is not in place for freezer management which may result in a loss of valuable biospecimens and or delay in research. Additionally, formal biorepository freezer business continuity plans are not in place for identifying potential loss scenarios.
2. **Establish Clearly Defined Roles, Responsibilities, and a Single Point of Accountability –** Roles and responsibilities are not defined, published and made available to biorepositories and Principal Investigators across the institution. Additionally, responsibilities of human biospecimen repositories is decentralized increasing the risk of non-compliance with regulatory requirements and potential reputational risk.
3. **Establish Human Biospecimen Inventory Management Processes and Controls –** Biospecimen inventory management guidelines and controls have not been established increasing the risk of incomplete biospecimen records and/or delay in supporting research activities across the Institution.

Management has implemented or is implementing corrective action. Management responses are presented in the Detailed Observations and Action Plans Matrix section of this report.

We would like to take the opportunity to thank the various departments and individuals included in this audit for the courtesies extended to us and for their cooperation during our audit.

Sincerely,

Valla Wilson, Vice President for Internal Audit, Chief Audit Executive

Executive Summary

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Detailed Observations and Action Plans Matrix

Observation	Recommendation	Management Response
Risk Rating: High 1. **Develop Standardized Guidelines and Establish Oversight for Freezer Management** Institutional guidelines and adequate oversight are not in place to ensure appropriate freezer management and controls for protecting the integrity of biospecimens. There is no comprehensive inventory of all freezers and in many cases a lack of defined end of useful life and replacement procedures for freezers. This increases the risk of a loss of valuable biospecimens and loss in confidence for research outcomes. Additional freezer management control deficiencies include: • There are no preventive maintenance requirements to reduce the risk of freezer breakdown. Some freezers are under preventive contracts while others are not. • A standardized approval protocol, such as Facilities Department approval, for freezer acquisition is not in place to ensure freezers purchased can be stored in a proper area with appropriate power supply, adequate ventilation, and air conditioning (HVAC) and its impact on physical location of freezers.	1. Require the Biorepository committee to review and assess risks to determine the guidelines and oversight going forward for freezer management. 2. Update or create a policy for freezer management and monitoring requirements. 3. Conduct a comprehensive freezer inventory and determine appropriate function responsible for maintaining inventory. 4. Develop an approval protocol for all freezer purchases, determine method for systematically identifying these types of purchases across the institution and incorporate approval requirements into the approval matrix policy. 5. Coordinate with the Office of Safety and Business Continuity to identify methods for freezer tracking including verifying freezers location. 6. Revise biorepository business continuity plans to include preventative maintenance procedures, backup power resources and theft/loss procedures. 7. Ensure temperature fluctuation notification systems are in place for each freezer.	**Management Action Plans:** The Biorepository Oversight Committee will: 1. Develop the recommendation for oversight and obtain approval from the Vice Provost & Dean of Research and the Executive Vice President for Academic Affairs, Provost and Dean 2. Based on recommendation from leaders, develop freezer management and monitoring requirements. 3. Identify the Freezer population in major repositories across the institution. 4. In conjunction with Office of Clinical Research, draft the standard operating procedures (SOPs) for core-like freezer management and publish the final SOPs on the intranet for PIs access and reference. The SOPs will include guidelines for: a. (#4) determining acquisition protocol for new freezers, including feedback from Facilities Administration and Office of Safety and Business Continuity in the decision process. b. (#5) reporting updates to freezer locations. c. (#6) updating the business continuity plans to include plans for preventative maintenance, backup power sources coordinated with

Detailed Observations and Action Plans Matrix

Observation	Recommendation	Management Response
• Freezer temperature fluctuation notification system vary such as the internally hosted Facilities Administration Central Data Acquisition System services, outside vendors and/or they maintain empty back-up freezers for use in case of freezer malfunction. • Freezers, which are located in various places across campus, may not have adequate back-up power sources in the event of power failure or may not have adequate backup freezer to relocate biospecimens. • Business Continuity plans may not be adequate to ensure the safety of biospecimens.	8. Revise institutional business continuity plans to include back up plans for large scale biorepository power outages to ensure uninterrupted power supply is available to protect specimens.	Facilities Administration and theft/loss. d. (#7) And options for temperature fluctuation management systems for the freezers. 8. Coordinate with the Facilities Administration team to identify back up plans for large scale biorepository power outages. **<u>Action Plan Owners</u>:** Biorepository Oversight Committee Chair and members Assistant Director, Clinical Research, Office of Clinical Research **<u>Target Completion Date</u>:** December 31, 2019 - Recommendation to leaders April 30, 2020 - Draft SOPs May 31, 2020 - Finalize the SOPs June 30, 2020 - Publish the SOPs

Detailed Observations and Action Plans Matrix

Observation	Recommendation	Management Response
Risk Rating: Medium **2. Establish Overall Accountability and Clearly Define Roles and Responsibilities for Managing Biospecimens** Roles and responsibilities are not clearly defined and published to make available to Principal Investigators across the institution as required by the RES-155 Biorepository Oversight Committee policy. It is not clear as to who is accountable for ensuring policies and standard operating procedures are followed and appropriate monitoring procedures are in place. Without an assigned person for oversight and established monitoring procedures there is increased risk of non-compliance with regulatory requirements, loss of funding and potential reputational risk.	1. Define roles and responsibilities as required by the RES-155 Biorepository Oversight Committee policy. 2. Identify a single point of accountability to provide oversight and monitoring. 3. Implement standard operating procedures to be followed as defined in the Biorepository Oversight Committee policy. 4. Define and publish institution-wide best practice guidelines for biospecimen collection, storage, transfers, inventory, and disposal in alignment with defined guidelines with leading source(s) such as the *ISBER*. Communicate the available institution-wide best practice guidelines to biorepositories and Principal Investigators (PIs).	**Management Action Plans:** 1. Biorepository Oversight Committee in conjunction with Office of Clinical Research will draft the standard guidelines/operating procedures (SOPs) for management of key biorepository activities. 2. The Biorepository Oversight Committee is the responsible party for oversight and guidelines and will develop monitoring procedures to ensure expected procedures are occurring as intended. 3. Guidelines developed will be based on the best practices compiled from ISBER and other sources as deemed appropriate by the Biorepository Oversight Committee. 4. Biorepository Oversight Committee will publish the final SOPs on the intranet for PIs access and reference. **Action Plan Owners:** Biorepository Oversight Committee Chair and Committee members Assistant Director, Clinical Research, Office of Clinical Research **Target Completion Date:** April 30, 2020 - Draft SOPs May 31, 2020 - Finalize the SOPs June 30, 2020 - Publish the SOPs

Detailed Observations and Action Plans Matrix

Observation	Recommendation	Management Response
Risk Rating: Medium ● **3. Establish Human Biospecimen Inventory Management Processes and Control Guidelines** Biospecimen inventory management guidelines, procedures and controls have not been established increasing the risk of incomplete biospecimen records and/or delay in supporting research activities across the institution. Each biorepository chooses to use OpenSpecimen, Freezerworks, and Microsoft Excel, relational databases or other inventory systems based on budget constraints.	1. Evaluate the feasibility of using a sustainable institution-wide inventory tool for biospecimen tracking and monitoring. 2. For centralized inventory tracking, provide training on how to populate and maintain inventory using the system-wide inventory tool. 3. For decentralized inventory tracking methods, implement increased requirements for monitoring and tracking accurate inventory records including periodic reconciliation of biospecimen inventory records to specimens on hand.	**Management Action Plans:** 1. Office of Clinical Research is evaluating OpenSpecimen site wide license option and will work with Biorepository Oversight Committee in evaluating the cost allocation and personnel requirements for implementation. 2. Biorepository Committee Oversight Committee will also review the acceptance level of requiring migration to OpenSpecimen across campus and will determine the appropriate decentralized options for PIs. 3. Develop monitoring processes to ensure accurate tracking procedures are in place. **Action Plan Owners:** Biorepository Oversight Committee Chair and Committee members Assistant Director, Clinical Research, Office of Clinical Research

Detailed Observations and Action Plans Matrix

Observation	Recommendation	Management Response
		Target Completion Date: December 31, 2019 - Recommendation to leaders April 30, 2020 - Draft SOPs May 31, 2020 - Finalize the SOPs June 30, 2020 - Publish the SOPs Publish the SOPs by June 30, 2020

Appendix A – Risk Classifications and Definitions

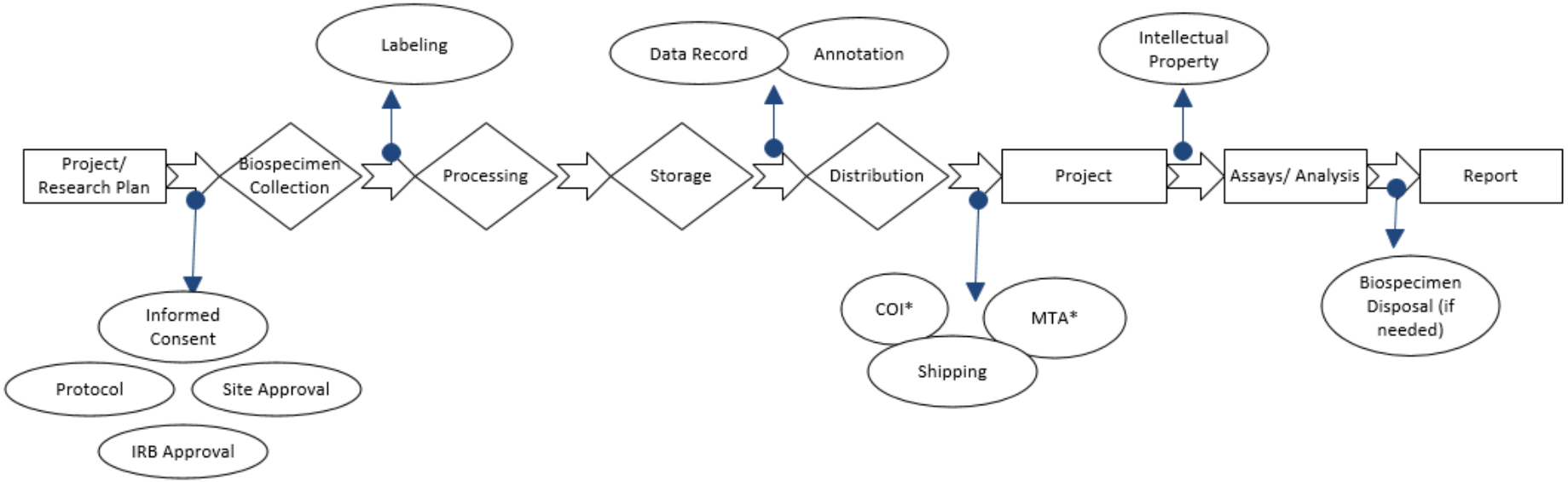
As you review each observation within the Detailed Observations and Action Plans Matrix of this report, please note that we have included a color-coded depiction as to the perceived degree of risk represented by each of the observations identified during our review. The following chart is intended to provide information with respect to the applicable definitions and terms utilized as part of our risk ranking process:

	Degree of Risk and Priority of Action	
Risk Definition- The degree of risk that exists based upon the identified deficiency combined with the subsequent priority of action to be undertaken by management.	**Priority**	An issue identified by Internal Audit that, if not addressed immediately, has a high probability to directly impact achievement of a strategic or important operational objective of a UT institution or the UT System as a whole.
	High	A finding identified by Internal Audit that is considered to have a high probability of adverse effects to the UT institution either as a whole or to a significant college/school/unit level. As such, immediate action is required by management in order to address the noted concern and reduce risks to the organization.
	Medium	A finding identified by Internal Audit that is considered to have a medium probability of adverse effects to the UT institution either as a whole or to a college/school/unit level. As such, action is needed by management in order to address the noted concern and reduce the risk to a more desirable level.
	Low	A finding identified by Internal Audit that is considered to have minimal probability of adverse effects to the UT institution either as a whole or to a college/school/unit level. As such, action should be taken by management to address the noted concern and reduce risks to the organization.

It is important to note that considerable professional judgment is required in determining the overall ratings presented on the subsequent pages of this report. Accordingly, others could evaluate the results differently and draw different conclusions. It is also important to note that this report provides management with information about the condition of risks and internal controls at one point in time. Future changes in environmental factors and actions by personnel may significantly and adversely impact these risks and controls in ways that this report did not and cannot anticipate.

Appendix B – Biospecimen Process Map

Following is an overview of the human biospecimen collection, annotation, storage, sharing/ transport, associated analysis and derived results:



* COI – Conflict of Interest
MTA – Material Transfer Agreement