Appendix 1 – NIH Intramural Research Program Human Biospecimen Guidelines

Purpose

The *NIH Intramural Research Program (IRP) Human Biospecimen Guidelines* are developed to assist NIH Institutes/Centers/Offices leadership (ICO), NIH Intramural Research Program (IRP) Principal Investigators (PIs) or stewards, Staff, or Contractors in the proper handling and oversight of human biospecimens maintained within IRP facilities or maintained on behalf of the IRP (referred to as "NIH maintained"), to include but not be limited to, their storage, tracking, and annual reporting requirement.

Acquiring, Sharing, or Transferring

Every ICO and their staff has the responsibility for stewardship and oversight of IRP human biospecimens maintained by NIH and for making these human biospecimens available to other researchers when feasible and appropriate. NIH investigators must abide by the highest scientific and ethical standards to preserve the public's trust and the substantial investment these valuable research resources represent.

- Oversight of Human Subjects Research

Generally, IRB review and approval is required for human subjects research using identifiable human biospecimens. Certain human subjects research with human biospecimens may be exempt from the requirement for IRB review and approval. The NIH Office of Institutional Review Board Operations (IRBO) is solely authorized to determine whether a human subjects research activity using human biospecimens is exempt or non-exempt from IRB review and approval. Other research with human biospecimens may not require any review by IRBO because it does not constitute human subjects research under the HHS Protection of Human Subjects, 45 C.F.R. 46, or equivalent FDA regulations. (See the Not Human Subjects Research page on the IRBO website for more information.) The NIH PI or steward using human biospecimens as exempt from the human subjects regulations must submit a request for an exemption to the IRBO by completing an application and submitting a protocol in the IRBO electronic IRB submission system. The protocol generally would be expected to explain the process for accepting or acquiring human biospecimens, all their intended use, and the research subject's data that will be kept with the human biospecimens, as well as the intended process for distributing or sharing human biospecimens and its data for research use.

- Institutional Biosafety Committee

NIH PIs must obtain IBC approval prior to performing research and storing human biospecimens. IBC registration and annual reviews are through their site-specific registration system; when applicable, project with possible dual use research of concern (DURC) or enhanced pathogen pandemic potential (ePPP) will be forwarded to the NIH DURC – Institutional Review Entity for further review.

- Human Biospecimen Sharing

NIH considers research tools to be a unique research resource that encompass full range of tools that scientists use in the laboratory, including cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry and DNA libraries, clones, and cloning tools (such as PCR), methods, laboratory equipment and machines. As stated in the NIH Research Tools Policy [https://sharing.nih.gov/other-sharing-policies/research-tools-policy], unique research resources arising from NIH-funded research are to be made available to the scientific research community consistent with

that policy and other rules and policies. Research tools obtained or derived from human tissues may warrant certain restrictions on the use and further dissemination of such tools to ensure consistency with donor consent and human subjects protection.

Human biospecimens maintained within NIH IRP facilities or maintained on behalf of the IRP must remain under the control of NIH unless disposal or transfer is approved through appropriate ICO channels.

- Human Biospecimen Transfer

Human biospecimens can only be transferred outside NIH via a specific written agreement approved by the IC – consistent with IRB approval, if required. Representative agreement types include Material Transfer Agreement (MTA), Clinical Trials Agreement (CTA), Research Collaboration Agreement (RCA)[1] or Cooperative Research and Development Agreement (CRADA)[2]. The NIH PI must follow the principles governing sharing of resources and comply with the relevant NIH material transfer policies.[3] For more information contact the respective ICO Technology Transfer Office.

When a PI departs NIH, unless the ICO has agreed to allow the investigator to properly transfer the human biospecimens to a receiving institution and a written agreement has been executed for this purpose, the PI must leave all human biospecimens and data at NIH. The ICO must assign another of its investigators to assume stewardship of the human biospecimens, in accordance with NIH Manual Chapter 2300-940, Clearance of Personnel for Separation or Transfer.

The departing/transferring investigator must follow policy requirements for handling the biospecimens and data as stated in NIH Manual Chapter 1743, Managing Federal Records, Appendix 5 to request copies of Federal records and biospecimens must additionally adhere to (if approved by ICO leadership), may only be transferred via a specific written agreement such as an MTA, CTA, RCA (PHS Policy 500, 2023), consistent with this policy within the NIH Intramural Research Program. Researchers may contact the Agency Intramural Research Integrity Officer (AIRIO) if they need additional information about biospecimens.

- Commercial Sources of Human Biospecimens for Acquisition

These Guidelines generally do not apply to tracking human biospecimens or biological materials that were obtained from commercial sources for use as reagents. For example, human cell lines or tissues purchased from American Type Culture Collection (ATCC) or other vendors for use as reagents are not tracked as human biospecimens. However, human biospecimens that are human fetal tissue (HFT), human embryonic stem cells (hESC), or induced pluripotent stems cells (iPSC), even from commercial sources, must be tracked.

- Disposal

[1] PHS, Public Health Service Technology Transfer Policy Manual, Policy 500, PHS Policy for Material Transfer Agreements (2023) https://www.techtransfer.nih.gov/policy/hhs-technology-transfer-policies

[2] PHS, Public Health Service Technology Transfer Policy Manual, Policy 400, PHS Cooperative Research and Development Agreement Policy, (2021) https://www.techtransfer.nih.gov/policy/hhs-technology-transfer-policies

[3] PHS, Public Health Service Technology Transfer Policy Manual, Policy 500, PHS Policy for Material Transfer Agreements (2023) https://www.techtransfer.nih.gov/policy/hhs-technology-transfer-policies

There are a variety of reasons that a collection may no longer be of scientific value and consequently, the cost of continued storage may no longer be justified. For example, disposal may be warranted if the human biospecimens have been compromised in some way or if data associated with the human biospecimens are no longer available. There may also be occasions when the custodianship of human biospecimens is evaluated, and the decision is made to transfer oversight to a PI or steward outside of the originating ICO. In either circumstance, the decision to dispose or transfer custodianship of NIH human biospecimens decision requires prior approval by the ICO, and in some cases, prior approval by the IRB. Written agreement may be required based on the circumstances. Additionally, the IBC and DOHS are to be notified, to update pathogen registrations and to obtain required permits.

Additionally, ICOs must adopt procedures to evaluate at least every two years when and how to dispose human biospecimens. IRB or IRBO approval may be needed for disposal of human biospecimens. For more information contact IRBO.

Storing

Each ICO in coordination with their PIs or stewards, must have the proper equipment for biorepositories to ensure that their human biospecimens are always stored in a safe and secure manner. The selection, purchase or lease, operation, and maintenance of this biorepository equipment must be in accordance with NIH Manual Chapter 26101-16, Management of Ultra-Low Temperature Freezers to Promote Energy Efficiency in Cold Storage for Biomedical Research, as well as with several Federal laws including the Energy Policy Act of 2005, the Energy Independence and Security Act of 2007, the Energy Act of 2020, and the Executive Order (EO) 14057 Catalyzing Clean Energy Industries and Jobs Through Federal Sustainability. Other NIH policies may be applicable.

The NIH steward or staff must reach out to the ICO Cold Storage Coordinator to identify what biorepository equipment and locations are available for them to use for their human biospecimens. If new equipment is to be purchased, it must be consistent with all applicable Federal Acquisition Regulations (FAR), to include but not be limited to, FAR 23.103, which requires Federal agencies to purchase Energy Star or Federal Energy Management Program designated products. For more information contact the NIH Office of Management Assessment (OMA), Office of Research Facilities (ORF) Division of Environmental Protection (DEP), or the NIH Office of Research Services (ORS) Division of Scientific Equipment and Instrumentation Services (DSEIS).

- Physical standards

At NIH there is a diversity of equipment used for biorepositories. The common equipment is Laboratory Grade Freezers (LGF), Ultra-Low Temperature Freezers (ULTF), Laboratory Grade Refrigerators (LGR), or Liquid Nitrogen freezers (LN_2). Other equipment is possible as technology advances or through a variety of sources such as contracts or rentals in lieu of purchased.

The biorepository equipment should be operated using effective facility environments that include ambient temperature controls, good air circulation, lighting, oxygen or nitrogen monitoring for certain freezers, and backup emergency power. The biorepository equipment should be located in areas of low staff passage or controlled access. Systems should be in place to allow for local and remote temperature monitoring of freezers, refrigerators, and other temperature-controlled environments. Biorepositories should have emergency preparedness standard operating procedures (SOPs) that cover

equipment failures and power interruption that include back-up storage capacity and back-up power supplies such as generators.

- Best practices

All biorepositories, whether part of large, consolidated collections in freeze storage facilities or represented by individual freezers in laboratories, should follow best practices for specimen storage and retrieval.[4,5] For more information about biorepository equipment standards and its proper use or maintenance contact DEP.

- Quality management system

Each ICO must have a rigorous quality management system (QMS) implemented for their biorepositories as part of their stewardship of NIH human biospecimens. The purpose for a robust QMS is so that all biorepositories provide both high quality and consistently handled human biospecimens. Some aspects of the QMS will vary with the model and equipment under which the biorepository operates, individual ICO laboratory or as part of consolidated collections in a Freeze Storage Facility. All human biospecimen collections and biorepositories must have written SOPs detailing the policies and procedures used to appropriately store and handle human biospecimens. The International Society of Biological and Environmental Repositories (ISBER) has developed and published Best Practices[6] to aid those responsible of biorepositories so to improve the operations as well as the quality of the products and services. Another two sources are the NIH National Cancer Institute (NCI) guidelines[7] for human tissues biorepositories focused on primary human tissues for research and the Canadian Tissue Research Network (CTRNet) web site[8]. The CTRNet website offers a repository of SOPs that can be easily modified to meet the unique conditions to the PIs biorepository.

The steward, in coordination with the ICO Cold Storage Coordinator and DEP, should ensure that the biorepository equipment receives regular preventive maintenance and calibration in the proper frequency, which DEP has set at twice per year, at six-month intervals. These procedures should be written into a SOP to ensure consistency, accountability, and transparency. Deviations from the SOP must be documented for all events. Corrective action, if necessary, is recorded and follow-up monitoring is implemented to ensure that any incidents are not repeated. The SOP may need to be modified or updated to address such deviations. The SOPs must be reviewed as part of DEP inspections.

In the event that the management (i.e., storage, tracking, preventive maintenance, repairs) of the human biospecimens biorepository and its equipment has been contracted, the ICO Biospecimen Liaison and steward will coordinate with ICO Acquisition office or the NIH Office of Logistics and Acquisition Operations (OLAO) to ensure that the contract includes a robust and appropriate QMS program.

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[4] International Society for Biological and Environmental Repositories, Best Practices, Recommendations for Repositories (2018)https://www.isber.org/page/BPR

[5] NIH, National Cancer Institute, Division of Cancer Treatment and Diagnosis, Cancer Diagnosis Program, Biorepositories and Biospecimen Research Branch, Best Practices (2016) https://biospecimens.cancer.gov/bestpractices/

[6] International Society for Biological and Environmental Repositories, Best Practices, Recommendations for Repositories (2018) https://www.isber.org/page/BPR

[7] National Cancer Institute, Office of Biorepositories and Biospecimen Research: Best Practices for Biospecimen Resources https://biospecimens.cancer.gov/default.asp

[8] Canadian Tissue Repository Network (CTRNet) https://www.ctrnet.ca/en/home/

Tracking

Each ICO, in coordination with the steward of the human biospecimens, must have an in-house or contracted inventory and tracking electronic system for the entire human biospecimen life cycle, including receipt, assessment, storage, monitoring, use, transfer, and/or disposal. The use of SOPs that are detailed documented methods of each of the tracking procedures is necessary to ensure that all activities are performed uniformly. A SOP should be prepared in great detail so that trained personnel who have not performed any tracking procedure previously can perform consistently and accurately. Changes in SOPs should be documented and made only by authorized staff. ICOs should, on a regular basis or as-needed, distribute and educate stewards and appropriate staff regarding changes in SOPs. Previous dated version/s should be maintained as historical record in order to identify any differences in human biospecimens caused by changes in SOPs, especially in the collection, processing, storage, tracking, and/or distribution or sharing methods. Each SOP should be reviewed by the ICO at least annually and revised, as necessary.

- Inventory system requirements

NIH human biospecimens stored in biorepositories must be tracked using a computer-based inventory system. While there are a variety of computer-based inventory/tracking systems, the system used must be configurable, scalable, and that any NIH staff can accurately track the human biospecimen collections that they maintain, manage, or use.

Inventory systems must also have the capability to assign a unique identifier to each human biospecimen, document custodianship, link and track aliquots, and track significant events such as thaws, receipt and/or processing events, warnings, disposal, or transfers out of the biorepository.[9] Systems must be able to generate reports on each of these conditions and activities and must be able to link to detailed information on clinical and other variables (*e.g.,* participant information, protocol number, informed consent, clinical and epidemiological data) to facilitate research and serve as an archive so that the information remains available for future use. Inventory systems must meet federal requirements related to data privacy and security, such as those outlined in the Privacy Act of 1974.[10]

The inventory system must be able to assign a unique identifier to each human biospecimen, the human biospecimen container must have a printed label and should be either a one-dimensional (1D) or two-dimensional (2D) barcode that links it to electronic record documentation. The label must withstand all potential storage, handling, and transportation conditions.

If the human biospecimen is associated with Personally Identifiable Information (PII), the unique identifier must also enable the investigator to link the human biospecimen to clinical or research data about the subject or patient, the protocol, and informed consent under which the specimen was collected, as well as an NIH Clinical Center Biomedical and Translational Research Information System (BTRIS) patient identification number, as appropriate. The label must be able to withstand all potential transportation and storage conditions.

Human biospecimens with no PII associated with them (e.g., de-identified or those that are unlinked

[9] NIH, National Cancer Institute, Division of Cancer Treatment and Diagnosis, Cancer Diagnosis Program, Biorepositories and Biospecimen Research Branch, Best Practices (2016) https://biospecimens.cancer.gov/bestpractices/

[10] DOJ, Privacy Act 1974 (2015) https://www.justice.gov/opcl/privacy-act-1974

from a code that stores identifiable data, known as *coded* specimens) should be labeled in accordance with a SOP which must be developed for the laboratory or the biorepository. Minimum information should identify human biospecimen type and date of acquisition but information that is not identifying is permitted (e.g., disease or condition being studied).

The inventory system must be able to provide data for the annual NIH-wide assessment of storage and tracking practices known as the NIH Human Biospecimen Storage and Tracking Report to U.S. Congress, as required by the NIH Reform Act of 2006.[11] Stewards who indicate in their NIDB Annual Report that they work with human biospecimens must report the type of human biospecimens currently stored, along with information about labels and tracking systems.

The tracking of historical collections of human biospecimens obtained before guidelines were first issued in 2008 should be upgraded to meet these revised guidelines when feasible, with some IC and BL approved exceptions. Historical collections (collections acquired prior to 2008) that may not have unique identifiers on every vial/tube, may be exempted and counted as a single collection. Proper documentation of this exemption to include when and who made the determination must be part of the biorepository and inventory system files as overseen by the steward or those maintaining the repository.

The final disposition of each human biospecimen, whether it be exhaustion, sharing, transfer, or disposal, must be documented by the inventory system.

The ICO or delegee should perform an annual audit of the inventory system and biorepository following a written SOP. A random sampling of the human biospecimens location and information is reviewed to confirm that the human biospecimens are in the correct location, as indicated by the inventory system. The audit must also provide records on changes to human biospecimen information and subject records, such as who made changes, when the changes were made, and the old value versus the new value. The results of the audit must be documented, particularly any discrepancies, and the report must be stored as part of the biorepository files. Additional corrective or investigational steps may be needed and should be anticipated in the audit SOP.

Reporting

At each ICO there is an ICO appointed Biospecimens Liaison that serves as a resource for IRP stewards regarding Manual Chapter 3008 and these Guidelines. The Liaison should train stewards on their human biospecimen reporting requirements and provide support and guidance about the handling of and reporting for human biospecimen collections.

- NIH Biospecimen Report

The annual NIH Biospecimen Report completed by NIH stewards and extracted from the NIDB Annual Report, is an internal information-collection tool and further supports the NIH Annual Report to Congress regarding how NIH stores and tracks NIH maintained human biospecimens[12]. The NIH Biospecimen Report also facilitates the IRP community's sharing of information, which may facilitate

[11] H.R. 6614, 109th U.S. Congress NIH Reform, Public Law 109-482, Title 1 (2017) https://www.congress.gov/bill/109th-congress/house-bill/6164

[12] Manual Chapter 3008 – NIH Human Biospecimen Program https://policymanual.nih.gov/ 3008

scientific collaboration. Each NIH PI that serves as a steward of NIH maintained human biospecimens is required to report on their human biospecimen collections annually, through a process managed by the Office of Intramural Research (OIR). The first report is the NIDB Annual Report.

The NIH Biospecimen Report is rolled out 1-2 weeks after the NIDB Annual Report filing closes in NIH Intramural Data Base (NIDB). The NIH Biospecimen Report is completed by each NIH steward through the NIDB portal, under the Biospecimen Reports section. The reporting process is initiated by an email from the Deputy Director of Intramural Research (DDIR) embedded in the NIDB system, triggered by each ICO Biospecimen Liaison. Each steward will enter the types of human biospecimens (see List of Human Biospecimens in the Supplemental Information section of these Guidelines) they were maintaining in their biorepositories on a specific date which is mentioned in the process initiation email from the DDIR. Once the NIH Biospecimen Report closes, the data is compiled, validated, and integrated for OIR.

The OIR publishes Frequently Asked Questions on the Biospecimen Reporting Process (FAQs) to assist and guide stewards during the process of reporting and to elaborate on issues or concerns by stewards and NIH staff, such as providing examples on specific topics. For additional information and details contact the NIH Agency Intramural Research Integrity Officer (ARIO).

Human Fetal Tissue and Human Stem Cells

Each NIH PI who acquires, uses, and/or stores human embryonic stem cells (hESCs), induced pluripotent stem cells (hiPSCs), or human fetal tissue (HFT) must keep accurate and current information on the storage and tracking of these human biospecimens. This requirement applies also to commercially acquired HFT, hESC, and hiPSC biospecimens. Each NIH steward must provide this information into the annual NIH Biospecimen Report.

- Use considerations

The use of HFT for research is sensitive and researchers must be mindful of its ethical implications. Researchers must ensure that allowable uses of HFT is in accordance with all applicable federal, state, and local laws or regulations, and NIH policies. This includes the need for NIH approval prior to acquiring HFT (see the OIR Sourcebook for further information), the expectation to maintain appropriate documentation that informed consent was obtained at the time of tissue collection, IBC registration and approval, as well as the need for continuous oversight review during the performance of the research.

Safety and Shipping

Human biospecimens must be handled safely in accordance with the U.S. Occupational Safety and Health Administration (OSHA) regulations[13] and recommendations for labeling, handling, and storage of human biospecimens. NIH PI and staff handling human biospecimens must complete the "Introduction to Laboratory Safety" and "Blood Borne Pathogen" training and complete the refreshers annually.[14] For more information about human biospecimen safety standards contact the Division of Occupational Health and Safety (DOHS).

- DOHS requirements

[13] OSHA, Standards Booklet 3186-06R, Model Plans and Programs for the OSHA Bloodborne Pathogens and HazardCommunications Standards (2003): https://www.osha.gov/Publications/osha3186.pdf
[14] NIH Safety Training: https://www.safetytraining.nih.gov/default.aspx?m=Please-Log-In

When biospecimens are being collected from humans, the collection and storage process must adhere to and follow procedures appropriate for the type of human biospecimen being collected and its intended uses. For example, human biospecimens must be handled in accordance with NIH Manual Chapter 3035-Working Safely with Potentially Hazardous Biological Materials.

It is critical that when collections are disposed or transferred that the ICO, IRBO, IBC, and DOHS are aware of and approve the request, if necessary, to transfer or dispose the human biospecimens. Prior to the disposal of human biospecimens, the NIH PI or delegated staff must consult and coordinate with DEP to ensure that the process is in compliance with NIH Waste Disposal Guide policies.[15]

Packing and shipping of human biospecimens must conform to all applicable regulations and standard, including but not be limited to, the U.S. Department of Transportation (DOT) regulations[16] and the International Air Transport Association (IATA) standards[17] and guidelines[18].

Additional restriction may apply for sharing or transferring of biospecimens that contain select agents, such as 9 CFR 121[19] and 42 CFR 73[20]. For more information about select agents and toxins contact DOHS.

Human Data Sharing

Considerations

- Sharing scientific data accelerates biomedical research discovery, in part, by enabling validation of research results, providing accessibility to high-value datasets, and promoting data reuse for future research studies. To further facilitate peer-review and scientific collaboration, any data derived from the use of human biospecimens must be collected in a manner that allows sharing for secondary research purposes following the NIH Manual Chapter 3016, Intramural Research Program Human Data Sharing (HDS) Policy, the NIH Data Management and Sharing Policy, and the NIH Genomic Data Sharing Policy. Each NIH PI or staff handling data derived from human biospecimens must complete the "Information Security and Management Training".[21]
- As a PI responsibility, human data can only be transferred outside NIH via a written agreement approved by the ICO; such transfers may also require IRB approval.
- The appropriate sharing of data derived from human biospecimens must be consistent with human subject permissions in, as applicable, the signed informed consent and IRB-approved protocol.
- If collaborations involve the transfer of NIH maintained biospecimens to third parties that will impose restrictions on the use of data generated from biospecimens that are incompatible with NIH

[15] NIH Waste Disposal Guide: https://orf.od.nih.gov/EnvironmentalProtection/WasteDisposal/Pages/default.aspx
[16] DOT, Pipeline and Hazardous Materials Safety Administration, Office of Hazardous Materials Safety, PHH50-0079, Regulations and Compliance (2006) https://www.phmsa.dot.gov/
[17] International Air Transport Association, 62nd edition, Dangerous Goods Regulations (2021) https://www.iata.org/publications/dgr/pages/index.aspx
[18] International Air Transport Association, Infectious Substances Shipping Guidelines (2021) https://www.iata.org/publications/store/Pages/infectious-substances-shipping-guidelines.aspx
[19] 9 CFR 121, (2022) Animals and Animal Products: https://www.govinfo.gov/content/pkg/CFR-2021-title9-vol1/pdf/CFR-2021-title9-vol1-part121.pdf
[20] 42 CFR 73, (2022) Select Agents and Toxins: https://www.govinfo.gov/content/pkg/CFR-2021-title42-vol1/pdf/CFR-2021-title42-vol1-part73.pdf
[21] NIH Information Security and Information Management Training Courses: https://irtsectraining.nih.gov/publicuser.aspx

data sharing policies, PIs should contact their respective ICO Technology Transfer Office before entering into such collaborations.

Records Retention and Disposal

- All records that pertain to this chapter must be retained and disposed of under the authority of NIH Manual 1743, "Managing Federal Records".
- As a PI responsibility, records must be maintained in full compliance with current NIH Records Retentions and Disposal guidelines. If necessary, backup file capability should be created for this purpose.
- Records to include NIH e-mail and Text messages, including attachments that are created and/or received on Government furnished accounts / equipment, NIH computer systems or transmitted over NIH networks that are evidence of the activities of the agency or have informational value are considered Federal records. These records must be maintained in accordance with current NIH Records Management guidelines.
- Contact the appropriate Records Liaison within the NIH Institute, Center, or Office (ICO) for additional information.

Supplemental information

- **Definitions**

  Biorepository: An organization, place, room, or container (a physical entity) in which biospecimens are stored.

  Coded: human biospecimen, often called linked samples, are those for which the identifiers have been replaced with a numerical code that provides a link between the identifiable information and a specific person. An example of biospecimens of this type are materials provide by the NIH Department of Transfusion Medicine, where additional materials can be requested, but have no PII directly available to the researcher.

  Collection: A set of similar types of human biospecimens taken from a human patient or research subject (such as blood samples, liver biopsy material, sputum samples), which are stored, tracked, and reported on together as like material.

  De-identified: Biospecimens from which identifiable information has been removed. If there is a secure and controlled way to link back to the identifiable information of origin, the investigator using the biospecimen must not have access to that linkage in order for the biospecimens to be considered de-identified.

  Human Biospecimens: A quantity of tissue, blood, urine, or other human-derived material. A single biopsy may generate several human biospecimens, including multiple paraffin blocks or frozen sample. A human biospecimen can comprise 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).

  Human Induced Pluripotent Stem Cells (hiPSCs; Stem Cell Basics): Mature human adult cells reprogrammed into an embryonic stem cell-like state.

Human Fetal Tissue (HFT; NIH Grants Policy Statement 4.1.14 Human Fetal Tissue Research**):** Tissue or cells obtained from a dead human embryo or fetus after a spontaneous or induced abortion or stillbirth. This definition does not include established human fetal cell lines acquired from a vendor or through an MTA.

Human Embryonic Stem Cells (hESCs; NIH Guidelines for Human Stem Cell Research**):** Cells that are derived from the inner cell mass of blastocyst stage human embryos, are capable of dividing without differentiating for a prolonged period in culture, and are known to develop into cells and tissues of the three primary germ layers.

Human Subject, for the purpose of MC 3008 (2018 Common Rule definition, see 45 CFR 46.102(e) for the complete definition)**:** A living individual about whom an investigator (whether professional or student) conducting research: (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Identifiable Biospecimen (2018 Common Rule definition, 45 CFR 46.102(e)(6))**:** A biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.[22]

NIH Core Facility: For purposes of this manual chapter, a NIH Core Facility is a facility generating data/reagents for multiple investigators and projects. Each Core Facility should have its own NIH annual report in NIDB. The text should describe the scientific area and list the projects being supported. Each Core Facility has its own assigned ZIC number.

Principal Investigator (PI, NIH Manual Chapter 3014-001**)** – The investigator with the overall responsibility for the design, conduct, and reporting of the research, and must assure both the protocol and the research team's actions are compliant with applicable law, regulation, and NIH policy, even when certain aspects of the research are delegated to other investigators.

Reports: This policy refers to three types of reports.

- NIDB Annual Report - NIH investigators that have a ZIA or ZIC number covering their research, will report annually details of their research.
- NIH Biospecimen Report - NIH investigators that submit data to the NIDB are asked if they maintain (storage/use/acquisition) NIH Human Biospecimens, if so, they report additional details. Those investigators that do not have NIH Human Biospecimens can opt out within the reporting system.
- NIH Human Biospecimen Storage and Tracking Report to U.S. Congress (aka "NIH Annual Report to Congress) - is based on the data from the NIH Biospecimen Report submitted by NIH investigators.

[22] 45 CFR § 46.102(e)(6), Protection of Human Subjects https://www.govinfo.gov/content/pkg/CFR-2021-title45-vol1/pdf/CFR-2021-title45-vol1-sec46-102.pdf

Steward: A steward is a Principal Investigator or Lead Investigator (reporting to a PI) that files an annual report in NIDB ("NIDB Annual Report") based on their assigned ZIA or ZIC project number and subsequently reports the storage/use/acquisition of human biospecimens associated with their NIH annual report in NIDB ("NIH Biospecimen Report"). PIs or stewards may delegate some biospecimen collection reporting activities to others (including contractors) but are ultimately responsible for annual human biospecimen reporting of collections under their control.

Unique Identifier: A set of characters used as a code that is unique in the context of the system for which it is created. It serves as a means of identification and reference (often instead of a name) for an entity, person, thing, function, procedure, activity, variable, or body of data (NCI Thesaurus).

Unlinked: meaning that the biospecimens were initially collected with identifiers but, before the research use, have been irreversibly stripped of all identifiers by use of an arbitrary or random alphanumeric code and the key to the code is destroyed, thus making it unlikely for anyone to link the biospecimens to the sources. This does not preclude linkage with existing clinical, pathological, and demographic information so long as all individual identifiers are removed.[23] Biospecimens provided through collaborations may fall into this category, where they were originally collected with PII, which has been stripped.[24]

[23] NIH, Intramural Research Program, Policy 3016 (2015) https://policymanual.nih.gov/3016

[24] HHS, Public Health Service Technology Transfer Policy Manual, Policy 500, Policy for the transfer of materials from NIH Intramural laboratories (2012)https://www.ott.nih.gov/policy/hhs-technology-transfer-policies

- **List of Human Biospecimens**

Blood or Blood Components

Blood	Blood Clot
Buffy Coat	Menstrual Blood
White Blood Cells	Red Blood Cells
Serum	Plasma
Umbilical Cord Blood	Peripheral Blood Mononuclear Cells
Platelets	

Body Fluid or Substances

Amniotic Fluid	Nipple Aspirate
Ascites or Peritoneal Cavity Fluid	Pericardial Fluid
Bile	Prostatic Fluid
Breast Milk	Rectal Secretions
Bronchial or Pleural Fluids	Saliva/Buccal Cells
Cerebrospinal Fluid	Sebum
Cerumen	Semen
Cervical Secretions	Sputum
Colostrum	Stool
Eggs/Oocytes	Swabs (any)
Eye Fluids	Sweat
Gallstones	Tears
Gastric Secretions	Urine
Kidney Stones	Vaginal Secretions
Miscellaneous Body Fluids	

Human Cell Lines (Derived at NIH or by Collaborators)

Immortalized/transformed human cell lines from healthy tissue or tumors, tumorigenic,diseased tissue

Human Stem Cells (Acquired from NIH Core Facility or NIHcollaborators)

Human Induced Pluripotent Stem Cells	Human Embryonic Stem Cells Lines
Other Human Stem Cell Lines	

Human Fetal Tissue/Human Fetal Cells

Tissues

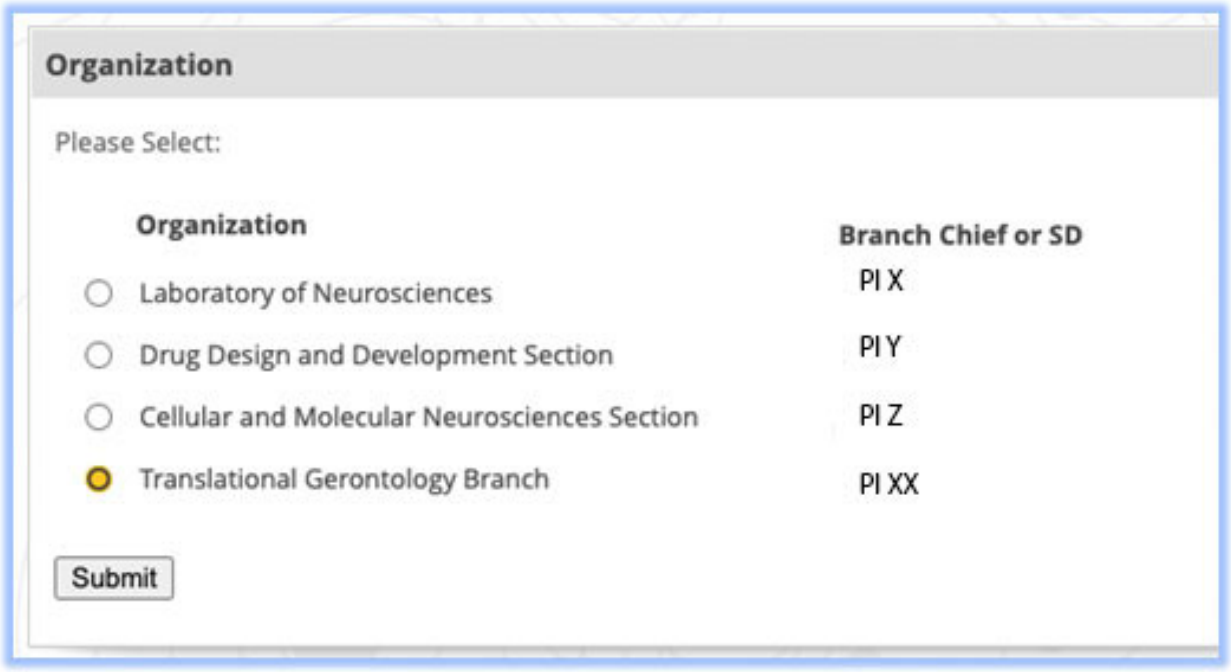
Adipose	Nail Specimen
Adrenal Gland Specimen	Nasopharynx Specimen
Artery Tissue Specimen	Nerve Specimen
Bile Duct Tissue Specimen	Nose Specimen
Bladder Tissue Specimen	Oral Cavity

Bone Marrow Specimen
Bone Specimen
Brain Tissue Specimen
Breast Tissue Specimen
Bronchial Tissue Specimen
Cartilage Specimen
Cataract Specimen
Central Nervous System Tissue
Colon Tissue Specimen
Duodenal Tissue Specimen
Embryonic Tissue Specimen
Endocervical Specimen
Endometrium Specimen
Esophageal Tissue Specimen
Eye Tissue Specimen
Fallopian Tube Specimen
Gallbladder Tissue Specimen
Gastric Tissue Specimen
Hair Specimen
Heart Tissue Specimen
Histopathology Slides
Human Fetal Tissue
Ileal Tissue Specimen
Jejunal Tissue Specimen
Kidney Tissue Specimen
Liver Tissue Specimen
Lung Tissue Specimen
Lymph Node Specimen
Middle Ear Tissue Specimen
Miscellaneous Tissue Specimens
Muscle Specimen
Tumors
Malignant/Benign Tumors
Ovary Specimen
Pancreas Specimen
Paraffin Tissue Blocks
Parathyroid Gland Specimen
Pericardial Tissue Specimen
Peritoneal Tissue Specimen
Pharynx Specimen
Placenta Specimen
Pleura Specimen
Prostate Tissue Specimen
Rectal Tissue Specimen
Skin Specimen
Small Intestine Tissue Specimen
Soft Tissue Specimen
Specimen from Non-Specified Site
Specimen of Product of Conception
Stoma Specimen
Teeth
Tendon Specimen
Testes Specimen
Thymus Specimen
Thyroid Gland Specimen
Tongue Specimen
Tonsil Specimen
Trachea Specimen
Ureter Tissue Specimen
Urethra Tissue Specimen
Uterine Cervix Specimen
Uterus Specimen
Vaginal Tissue Specimen
Vocal Cord Specimen
Vulva Specimen

- **Steward Reporting of Human Biospecimen in NIDB: NIH Biospecimen Report**

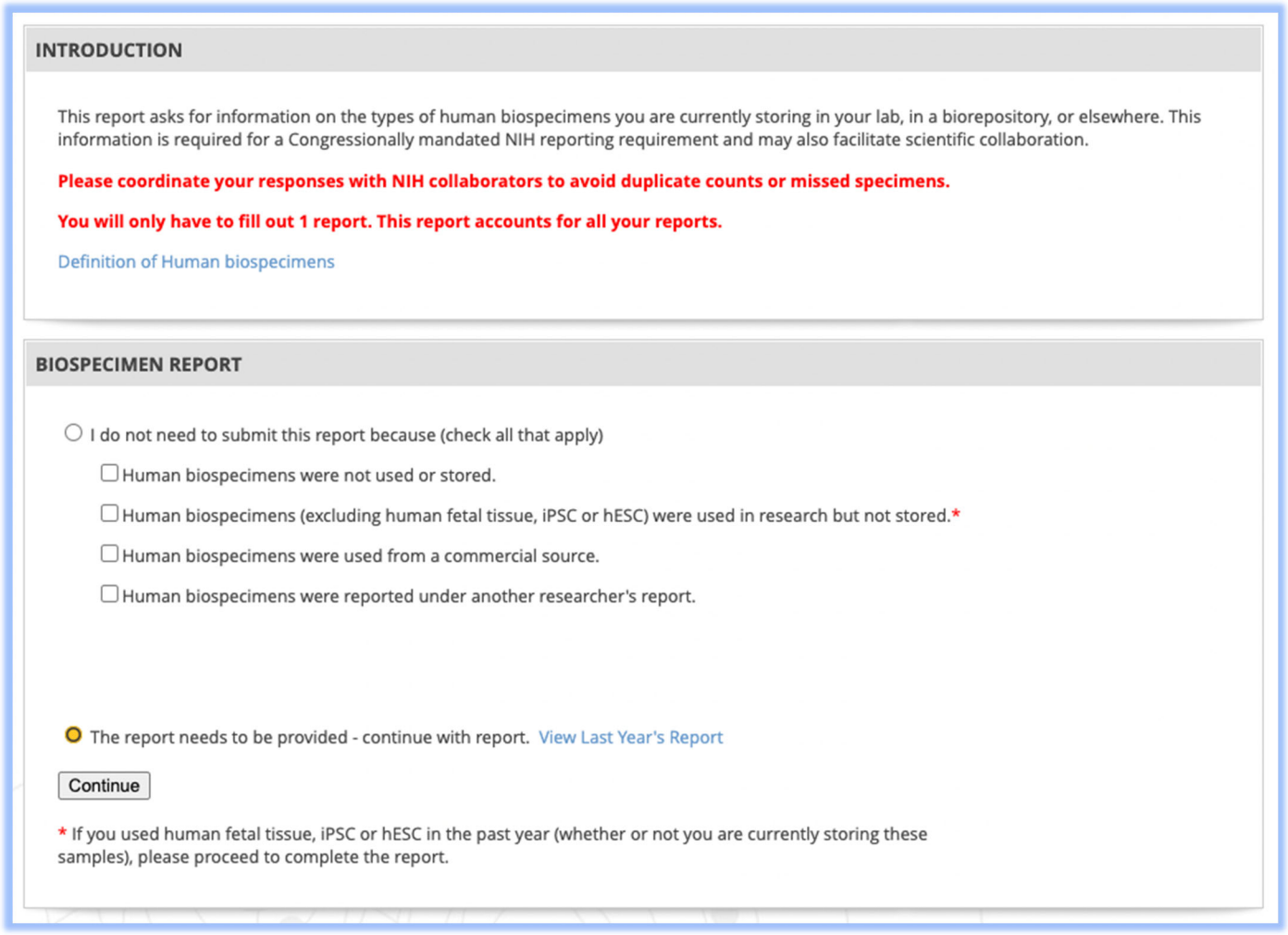
First, if you work in more than one lab, select the one under which you are reporting the human biospecimens, or which lab accounts for the majority of your work involving human biospecimens. This step is for purpose of NIH Biospecimen Report approval workflow.

Image 1



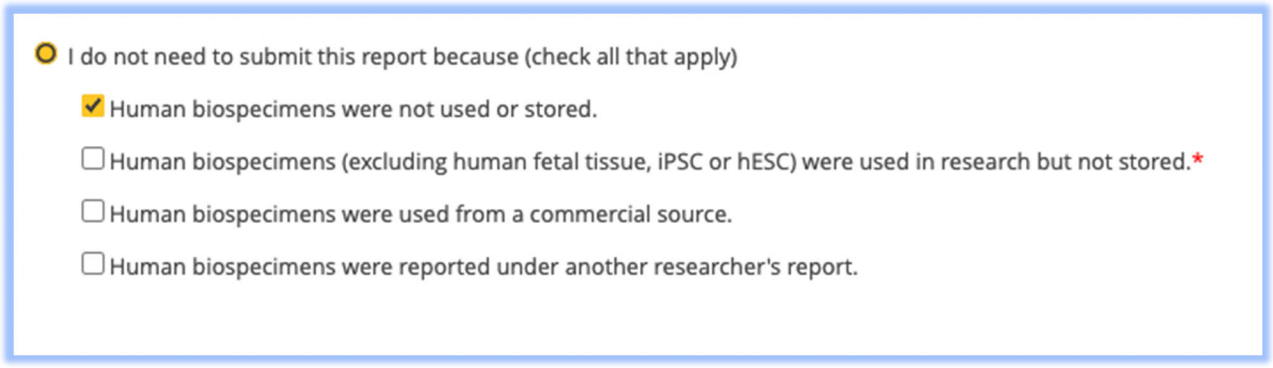
Next, you will see a page, shown in image 2, that allows you to either continue with the NIH Biospecimen Report or to "opt out", in the case where you do not have any human biospecimens to report, for any of the reasons shown:

Image 2



If you have nothing to report and thus choose to opt out, select at least one reason shown in image 3:

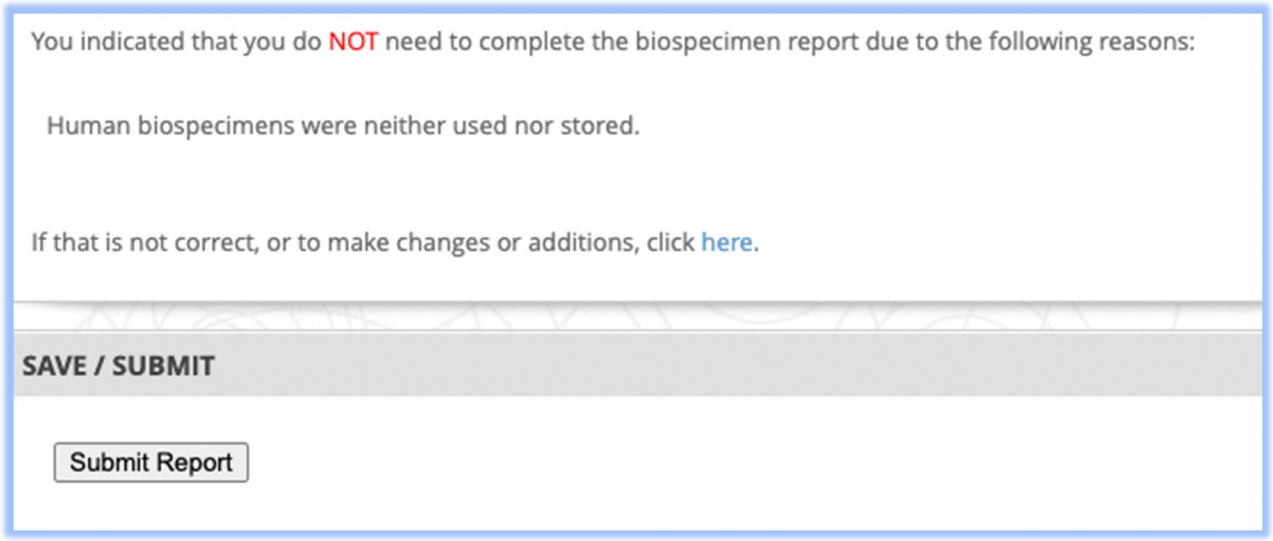
Image 3



And then choose “Continue”.

On the confirmation page, select “Submit Report”, shown in image 4:

Image 4

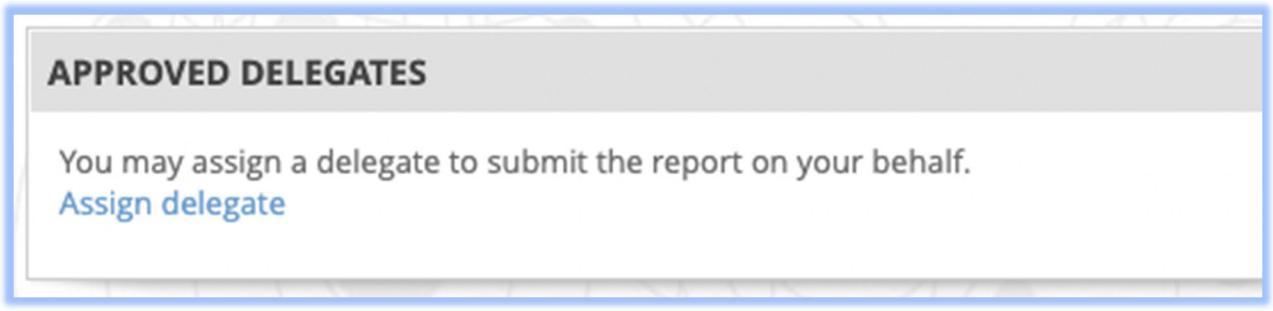


This will be the end of your reporting requirement for the current year if you have nothing to report.

If you DO have biospecimens to report, select the button, “The report needs to be provided…” on Image 2, above.

This introductory page also provides a link to assign a Delegate to complete the report on your behalf, shown below in image 5.

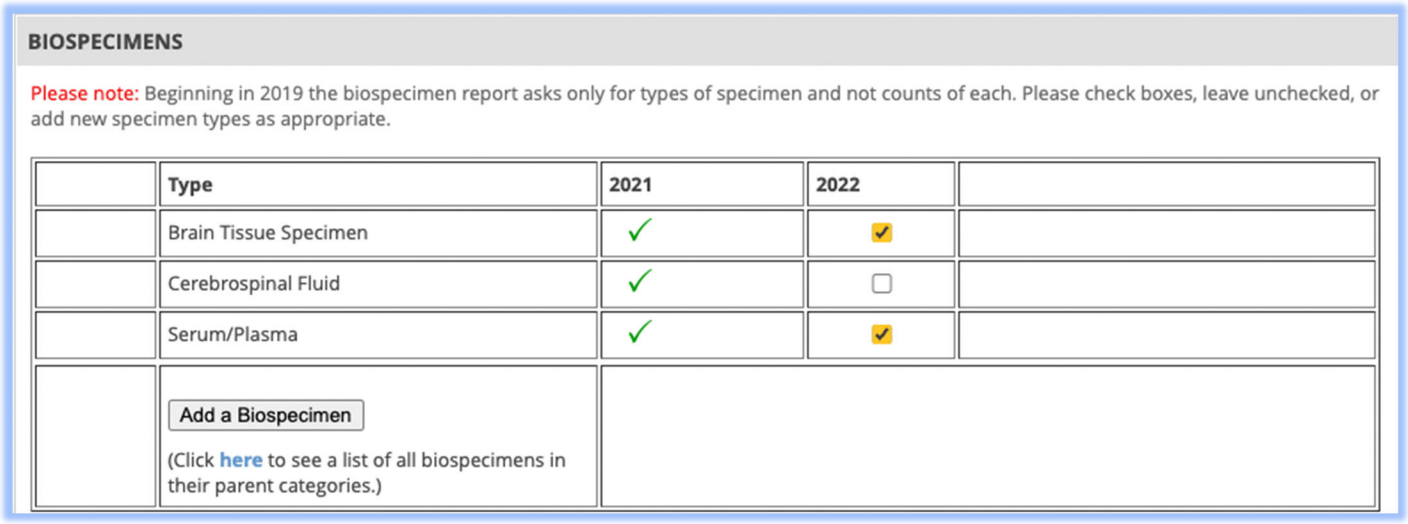
Image 5



On the next page, shown in image 6, the top section will present any biospecimens that you recorded the previous year and allows you to select these again, or simply not check any that you no longer

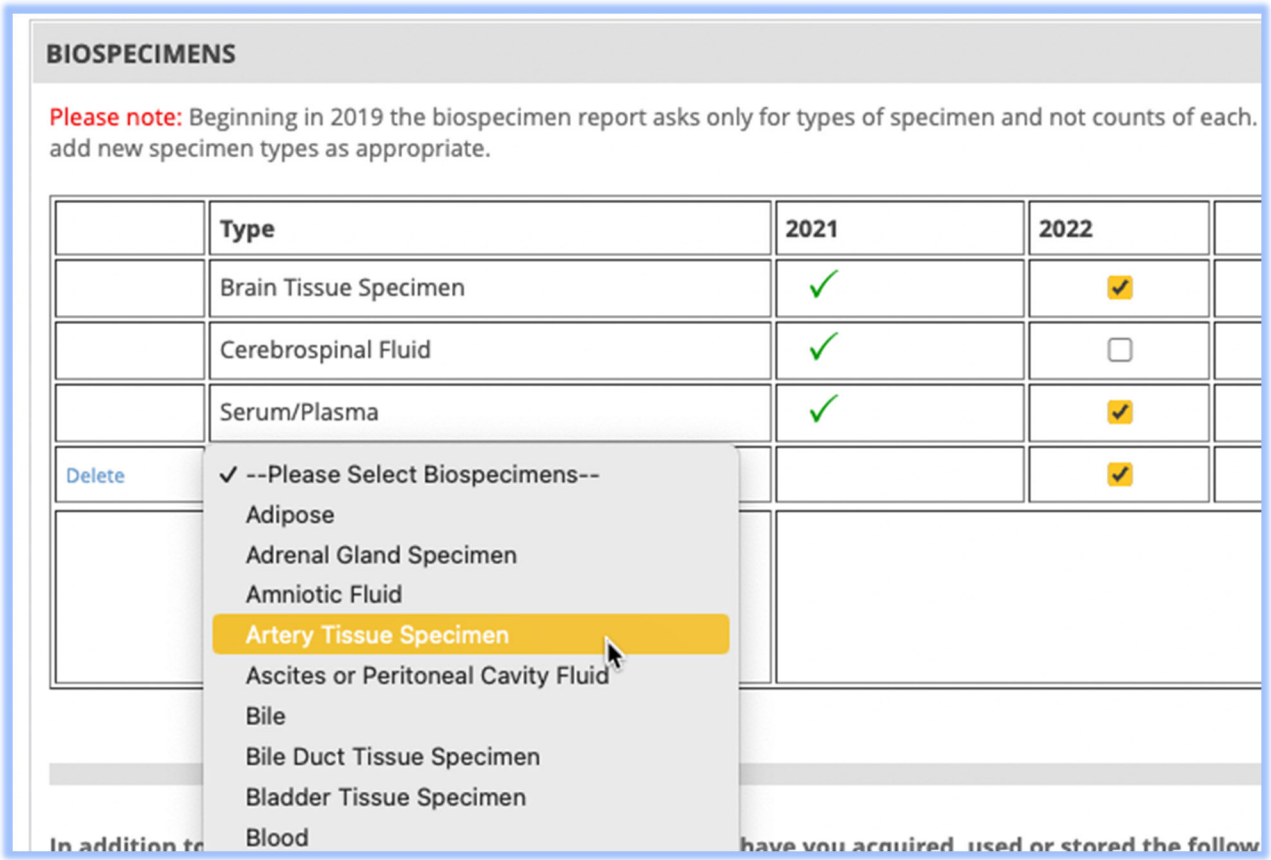
stored for the current reporting period. In the example below, the investigator is indicating that they store Brain Tissue Specimen and Serum/Plasma for the current year.

Image 6



You can also add new biospecimens by selecting that "Add a Biospecimen" button. This will present a list of all biospecimens, as shown in image 7:

Image 7



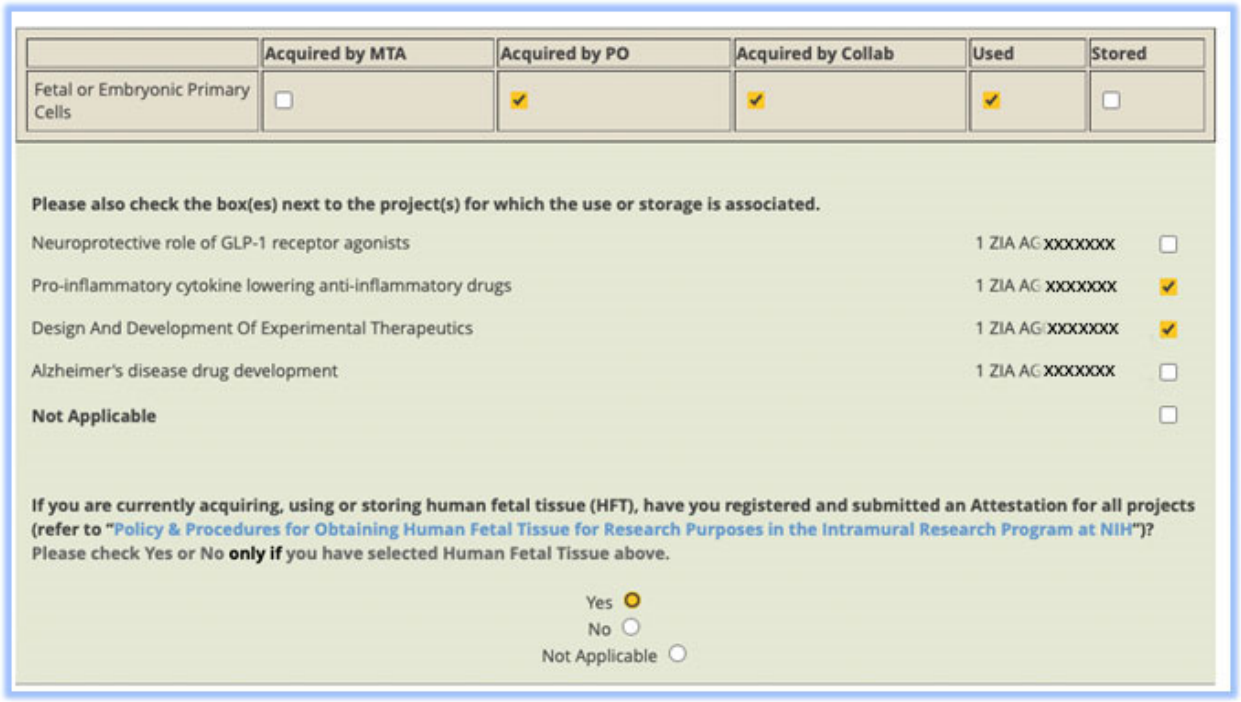
There is a second section, shown in image 8, which applies **only** to investigators who **use or store** any of four specific "regulated tissues":

- Human Fetal Tissue (HFT)
- Human Fetal Cells or Human Embryonic Stem Cells
- Human Embryonic Stem Cell Lines (hESC)
- Human induced Pluripotent Stem Cells (hiPSC)

For these biospecimens you will need to answer a few further questions regarding:

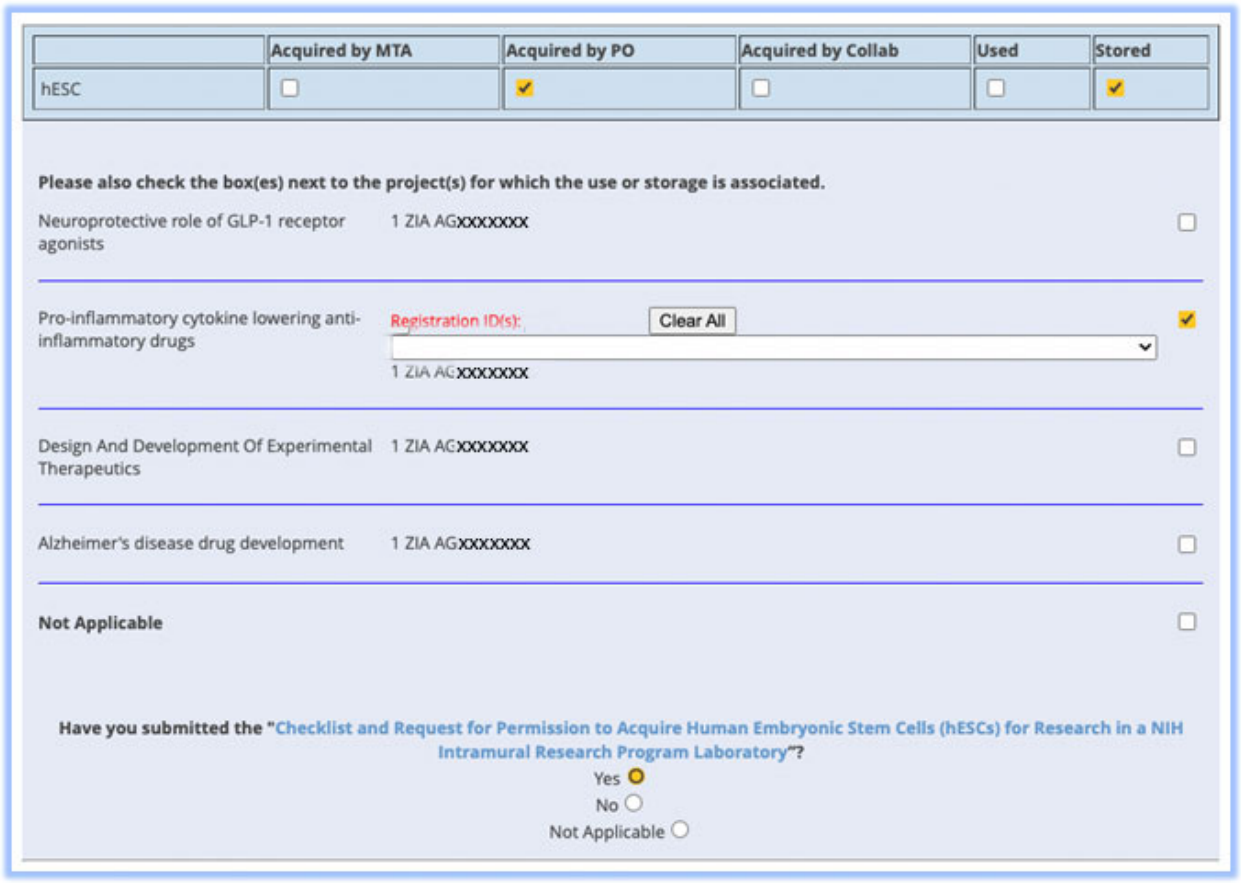
- The means of Acquisition/Use/Storage,
- The projects with which these regulated tissues are associated, and
- Whether you have submitted the applicable Attestation, Registration, or Checklist (depending on the tissue type).

Image 8



In addition, for hESC, you will also need to indicate one or more Registration IDs, as shown in image 9:

Image 9



Once you have addressed these two sections of the NIH Biospecimen Report you are finished. You can either save and resume later, or save and submit, as shown in image 10:

Image 10