

## Repository Protocols

### Structure and Function of a Repository

Research repositories (e.g., registries, data repositories/banks, tissue repositories/banks) should be designed for three distinct purposes only:

1. Collect data/research materials for *future* research use(s)
2. Store and manage the data/research materials
3. Distribute the data/research materials for use in research activities

Repository protocols are specifically not to be used to obtain IRB approval to conduct analyses, answer research questions, or test hypotheses. A separate IRB protocol, typically called a secondary use protocol, must be submitted by any investigator who wishes to *use* the data/research materials stored in the repository protocol to *conduct research* (e.g., testing hypotheses, conducting analyses to answer specific research questions, etc.). This principle applies even to the investigators who are listed as study team members on the repository protocol, who wish to use the data/research materials in a particular analysis or investigation.

Note that funding linked to a repository protocol should be used only for the management of that repository protocol. Funding that supports secondary use protocols should be linked only to the relevant separate secondary use protocols.

Table 1: Purpose of repository protocols vs. secondary use protocols

	Collect, store, and manage data/research materials for future research	Collect, store, and manage data/research materials for a specific research study/analysis	Have specific research questions to answer	May be hypothesis-driven
<b>Repository Protocols</b>	<b>YES</b>	<b>NO</b>	<b>NO</b>	<b>NO</b>
<b>Secondary Use Protocols</b>	<b>NO</b>	<b>YES</b>	<b>YES</b>	<b>YES</b>

Research repositories that hold individually identifiable data/research materials are subject to IRB oversight and require prospective IRB review and approval prior to initiating any activities pertaining to the repository protocol. When data/research materials with no identifiers will be obtained from the repository protocol, a [Not Human Research Subjects \(NHRSR\) determination](#) can be made by the IRB. If, however, the investigators requesting the data/research materials are already listed on the repository protocol from which the data/research materials are requested, a human research protocol must be submitted to the IRB for review and approval because the investigators on the repository protocol have access to identifiable data/research materials at the source level.

## **Repository Study Staff**

The study staff on the repository protocol should be limited to only those who are directly working on the repository protocol to collect, manage, and distribute the data/research materials for the repository protocol. Investigators who are only conducting research using the data/research materials obtained from the repository protocol should not be added to the repository protocol as study staff.

Before proposing the establishment of a repository, an investigator should consider whether the data/research materials they plan to collect would be readily available from already established repositories (either one that already exists within Mass General Brigham or is accessible to the investigator by another means).

## **Establishing Repositories for Future Research Use**

Principal Investigators wishing to create a repository are responsible for establishing and managing the collection, storage, access, and distribution of data/research materials collected under the repository. Therefore, they need to ensure that access to the banked data/research materials is only granted for the appropriate use conducted by the qualified individual/entity.

The primary research mission of the repository protocol, operational scope, and objectives should be well defined and include who will have access to the data/research materials, coding of data/research materials, and the process to ensure that future research projects involving identifiable data/research materials are not conducted without prior IRB approval. The repository protocol should have an established governance structure, as well as policies, best practices, and regulatory and procedural standards that are described in the IRB-approved protocol. Please refer to the [Repository Protocol Template](#) for elements that should be included.

## **Obtaining Informed Consent and HIPAA Authorization**

When obtaining data/research materials directly from participants under a repository protocol, written informed consent and HIPAA authorization for research purposes should be obtained to allow the collection of data/research materials to be used for future research. Obtaining consent for broad sharing for future research maximizes the potential downstream use of the data/research materials collected and ensures that future use aligns with established ethical principles relevant to use of research materials. The IRB will consider the acceptability of data/research materials obtained without consent for secondary use on a case-by-case basis. For example, The IRB may consider the following circumstances to allow the use/collection of data/research materials that were obtained without consent/HIPAA authorization:

- Grandfathered collections obtained in research studies conducted prior to 2006, where storage in a repository protocol was not mentioned specifically, may be included under a waiver of consent/HIPAA authorization at the IRB's discretion.
- Completely anonymized data/research materials (i.e., no code nor key to re-identify individuals exists) obtained from clinical procedures, or data/research materials obtained with IRB approval, may be included under a waiver of consent/HIPAA authorization at the IRB's discretion. Contact the IRB to discuss this option before submitting a request for a waiver of consent/HIPAA authorization.

Ensuring that the appropriate consent has been obtained can be done by prospectively obtaining consent from participants for the repository protocol and/or obtaining consented materials from other sources (e.g., participants provided consent for future use under different research studies, sometimes called “feeder” studies). Consent and HIPAA authorization may be obtained in a paper format or electronically (e.g., via REDCap with an electronic signature). The content of the consent/authorization form depends on the purpose of the repository and the permitted future use of the data/research materials.

For a tissue repository, informed consent may be obtained in writing using the Mass General Brigham Research Tissue Bank Consent Form template. For a data repository, informed consent may be obtained in writing using the Mass General Brigham General Research Consent Form template. If the repository is for both tissue and data, use the Mass General Brigham Research Tissue Bank Consent Form template and modify the template language as needed.

If a research study has two components, one to answer research questions and another to collect and store data/research materials for the current research study as well as for future research studies, there are two methods to obtain consent from participants for the repository protocol (see the bullet points below). Regardless of which method of obtaining consent is being used, participation in the repository protocol (i.e., data/research materials collected under the research study become a part of the repository protocol) should be presented as an option, not a required component of the research study.

- One method of obtaining consent for the repository protocol is to use two separate study-specific consent forms for the research study and the repository protocol, respectively.
  - When this method is used, the consent form for the research study should explain that the data/research materials collected under the research study will become a part of the repository protocol if a participant agrees via a separate consent document.
  - Once a participant agrees, then obtain consent from the participant for the repository protocol using the repository protocol consent form.
- The second method is to prepare one combined consent form under the research study.
  - If the combined method is used, the consent form should provide an option for participants to select whether or not their data/research materials collected under the research study will also become part of the separate repository protocol for future use.
  - When using the combined consent form, this consent form must describe both the research study as well as the repository protocol to the same extent. That is, the descriptions of the repository protocol should include all elements/information that would be required for a stand-alone consent form for a repository protocol.
  - When using a combined consent form, a [certified copy](#) of the informed consent for the combined protocol should be placed in the repository records.

Investigators who will use data/research materials obtained from a repository protocol, as well as investigators releasing data/research materials from a repository protocol, must be cognizant that the proposed research must be consistent with the scope and terms described in the original informed consent document which was used to collect the data/research materials. Any consent terms for future use must be honored, even if the data are de-identified. For example, if the consent form states only de-identified data/research materials will be shared, this **MUST** be

honored in all future uses and cannot be waived by the IRB nor any other entity for downstream use of data/research materials. Note that a Limited Data Set includes certain identifiers (e.g., dates) and is not considered de-identified data. If consent was not obtained for research purposes (e.g., data/research materials obtained for clinical purposes) or the original consent does not adequately include the proposed secondary use, specific informed consent for the new research protocol may be required. If the source consent includes any restrictions (e.g., cancer research only), they must be honored. Aggregating or de-identifying data/research materials does not release the requirement to adhere to the conditions described in the source consent document.

Neither the hospital HIPAA notification nor any clinical procedural consent form replaces the research consent form. Those forms notify patients that their data/materials may be used in research; however, they do not include all the elements/information required by the regulations that must be provided to participants to consent for research purposes.

HIPAA-related language included in the research consent form (i.e., language in the consent form to obtain HIPAA authorization) does not replace information that should be included in the consent form regarding accessing identifiable information or sharing data/research materials for research purposes outside the primary study. That is, HIPAA-related language in the consent form itself is not sufficient to allow sharing of data/research materials for future research.

### **Re-Consenting Minors or Individuals with Impaired Decision-Making Capacity Who Regain Their Capacity**

Minors whose identifiable data/research materials are stored in the repository protocol should be re-consented when they reach age of majority. Information regarding the re-consent process should be included in the protocol and consent form. A typical plan might include language that explains that an attempt, or attempts, will be made to contact the participants after they become an adult for re-consent and will describe the process if contact cannot be made. It is acceptable to include in the plan that either data/research materials will be destroyed if contact cannot be made, or data/research materials will be anonymized (i.e., destroying the code and the key to re-identify participants) at that point. Data/research materials that have already been distributed do not need to be destroyed.

When data/research materials are collected from individuals with impaired decision-making capacity through surrogate consent, investigators should consider whether they will re-consent these individuals if they regain the capacity to consent for themselves, and, if so, the process of obtaining re-consent should be described in the protocol. This population may include participants who were enrolled post-anesthesia, in an ICU, in the ER, or post neurological injury.

### **Creating a Recruitment Registry**

A Recruitment Registry is a special type of repository that is set up for the purpose of collecting and maintaining participants' information for recruitment into ongoing/future research studies. Recruitment Registries are particularly useful in keeping track of participants with an ongoing/long-term medical condition who may be interested in participating in multiple research

studies (e.g., migraines, IBS, HIV, hepatitis infections, etc.) within a department or center or for those who are willing to serve as healthy controls in research. Formally consenting participants into a Recruitment Registry allows the retention of participants' contact information even if they do not, at that moment, consent into any other study. The retention of participants' contact information should be compliant with Mass General Brigham IRB Pre-Screening Guidance.

In addition to providing informed consent for the collection and retention of their contact information, registry participants would also typically provide information that could inform future recruitment, such as health conditions or diagnoses, medications, allergies, study visit availability, etc. Such questions should address the common entry inclusion/exclusion criteria of studies which will draw participants from the Recruitment Registry.

Studies wishing to recruit from the Recruitment Registry should specify the Recruitment Registry protocol number in the recruitment section of their study protocols. Study teams who wish to obtain informed consent and/or collect registry data electronically (i.e., using REDCap) should specify their electronic methods in the protocol and submit any participant-facing data collection instruments to the IRB for review and approval.

### Appendix: When to Establish a Repository Protocol

Event	Submit Repository Protocol?	Process
<p>You would like to collect and retain contact information and additional demographic and/or health information for the purpose of setting up a registry from which you will recruit participants for future studies.</p>	<p>Yes</p>	<ul style="list-style-type: none"> <li>• Establish a repository protocol (e.g., recruitment registry) and store the information in the repository. You can open a repository protocol in parallel to a research study or it may stand on its own.               <ul style="list-style-type: none"> <li>○ Best practice: set up a recruitment registry from the beginning so consent can be obtained upfront.</li> </ul> </li> <li>• Participants may be asked to sign two separate consent forms for the two protocols or one combined consent form which presents as an option for the collected data/research materials to become a part of the recruitment registry.</li> <li>• When using one combined consent form, the consent form must describe both the research study as well as the recruitment registry. The descriptions of the recruitment registry should include all elements that would be required for a stand-alone consent form for a recruitment registry.               <ul style="list-style-type: none"> <li>○ A <a href="#">certified copy</a> of the combined informed consent should be placed in the repository's records.</li> </ul> </li> </ul>
<p>You would like to answer a research question but also retain the collected research materials (e.g., biospecimens, images, etc.) for potential downstream research.</p>	<p>Yes</p>	<ul style="list-style-type: none"> <li>• Establish two protocols – one to answer the research question, and another (a repository) to store collected research materials for potential downstream research.</li> <li>• Participants may be asked to sign two separate consent forms for the two protocols or one combined consent form which presents as an option for the collected research materials to become a part of the repository.</li> <li>• When using one combined consent form, the consent form must describe both the research study as well as the repository protocol. The descriptions of the repository protocol should include all elements that would be required for a</li> </ul>

		<p>stand-alone consent form for a repository protocol.</p> <ul style="list-style-type: none"> <li>○ A <a href="#">certified copy</a> of the combined informed consent should be placed in the repository's records.</li> </ul>
<p>You would like to have a centralized location for storage of department-wide data/research materials.</p>	<p>Yes</p>	<ul style="list-style-type: none"> <li>• Establish a repository protocol; present in “feeder” study consent forms as an option for data/research materials collected as part of the research study to become a part of the repository protocol.</li> <li>• If a participant agrees to have their data/research materials to become a part of the repository protocol, obtain separate consent form for the repository protocol using the repository protocol consent form.</li> <li>• If using a combined consent form for the feeder study, the combined consent form must describe both the feeder study as well as the repository protocol. The descriptions of the repository protocol should include all elements that would be required for a stand-alone consent form for a repository protocol. <ul style="list-style-type: none"> <li>○ A <a href="#">certified copy</a> of the combined informed consent should be placed in the repository's records.</li> </ul> </li> <li>• Note that funding linked to a repository protocol should be funding only for the management of that repository protocol.</li> </ul>
<p>You would like to access data/research materials which have been collected as part of a repository.</p>	<p>No</p>	<ul style="list-style-type: none"> <li>• Establish a secondary use protocol; scope should be consistent with what the participants agreed to in the consent form of the repository protocol. <ul style="list-style-type: none"> <li>○ Once the secondary use protocol is approved by the IRB, submit a request/application to the repository operators to receive data/research materials.</li> </ul> </li> <li>• Note that funding linked to a secondary use protocol should be funding only for the completion of that specific project</li> <li>• <b>DO NOT</b> add study staff members from the secondary use protocol to the repository protocol solely because they will use the data/research materials from the repository protocol. <ul style="list-style-type: none"> <li>○ The study staff on the repository protocol should be limited to those</li> </ul> </li> </ul>



		who are directly operating and managing the repository protocol.
--	--	--

**Resources:**

[Real-World Data: Assessing Registries To Support Regulatory Decision-Making for Drug and Biological Products | FDA](#)

[Open Domain-Specific Data Sharing Repositories \(nih.gov\)](#)

[NIH Common Data Elements \(CDE\) Repository](#)