

Informed Consent Recommendations for Specimen Acquisition and Future Use

Guidance Document

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Biorepositories Task Force

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EXECUTIVE SUMMARY

In order to properly and fully utilize the valuable resource of banked specimens, PCORnet Networks must pay particular attention to how consent is obtained at the point of specimen collection. This document describes general elements to include in an informed consent document for the collection and use of specimens, as well as key points of consideration for the consenting process. Basic principles of consent to participate in research (i.e. benefits and risks, compensation, participation is voluntary) as set forth by federal regulations (e.g. 45 CFR part 46) are beyond the scope of this guidance. The importance of following plain language principles for informed consents applies as well, but will not be discussed in detail (see Group Health’s PRISM resources for more information). Furthermore, please be aware that institutional policies regarding informed consent requirements and formatting may supersede the recommendations put forth in this document.

ELEMENTS TO INCLUDE IN CONSENT FORM

A. DESCRIPTION OF RESEARCH

The Office of Human Research Protection (OHRP) states that informed consents should include a clear description of the specific types of research to be conducted; however, determining the specific purpose of future research is often a challenge. Importantly, will all future research with the specimens be limited to a specific disease or intervention? If so, that purpose must be clearly stated in the consent, and when these limits are declared, specimens can only be used for that purpose. If one wants to use the specimens for another purpose, participants must be re-consented. There are certain circumstances in which a waiver can be granted by an IRB to use the specimens for a purpose other than that to which the participant consented. Additional information on waivers can be found here: <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.111>.

Alternatively, when the exact nature and type of future research is unknown, general information about the possible future research must be provided, in accordance with applicable national or local regulations and policies. Using unspecified, future research language will allow for more collaboration amongst PCORnet colleagues and is recommended when possible.

Research Description Required Elements

1. Include the types and amounts of specimens to be collected and stored.
See Recommendations for Specimen Acquisition, Transport, Storage and Retrieval.
2. State the length of time specimens will be stored.
Recommendation: Unlimited storage time.
3. State the risks associated with the specimen collection process and risks associated with future results. For example, when the type of sample banked allows for genomic research, Genetic Information Nondiscrimination Act (GINA) language must be included (<http://www.genome.gov/10002328>).
4. State the governing body or board who has oversight for the use the specimens.
Recommendation: Develop a charter for a Biospecimen Oversight Committee that will have authority to decide future use of the specimens. Please consult *Procedures for Sample Use Permissions and Sample Allocations Recommendations* for additional details and examples.
5. State whether links between specimens and clinical data (identifiable or non-identifiable) exist. Most specimens can be linked to information about the participant. This information is described in the consent along with the person/entity who holds the link (e.g. an honest broker; entity that keeps sets of private information but distributes parts of those sets to other entities who should not have access to the entire set) and under what circumstances the link may be used (e.g. withdrawal, return of results, or for clinical updates).
6. State the potential for discovery of new information at any point and how such discoveries will be addressed. This will be discussed in more detail in the Section on Return of Results. As the storage time of specimens is unlimited, the timeframe in which the possibility for discovery of new information will occur cannot be anticipated at the time of consent. This needs to be made clear to the participant.
7. If viable cells (cryopreserved lymphocytes, PBMCs) are being stored and there is a chance they may be immortalized, language must be included that states this and for what purpose the cell lines will be used.

If any material will be available for commercial use and potential discovery of new tests, procedures or drugs that have a commercial value, the consent should state this as well as the fact that neither the subject nor their heirs will benefit financially from this discovery.

B. WITHDRAWAL

Language must be included as to what process should be followed to:

1. withdraw from future studies
2. request specimens be destroyed

Please note that withdrawing participation from a study does not mean that data and specimens must be destroyed (<http://www.hhs.gov/ohrp/policy/subjectwithdrawal.html>).

C. RETURN OF RESULTS

Some members of the PCORnet community commonly return results, at least at an aggregate level, and these practices will continue to be Network-specific. However, there is active discussion in the research community as to the researcher's responsibility to return medically actionable results to participants [1-5]. This conversation most often involves results from genomic studies performed on the specimens in which information about the participant or family members is discovered.

Multiple groups are putting forth recommendations as to how to handle incidental findings. A report by the Presidential Commission for the Study of Bioethical Issues [6] provides examples of different types of findings (e.g. primary, secondary, and discovery) and recommendations as to how to handle such findings. The American College of Medical Genetics and Genomics published a policy paper with recommendations on the return of incidental findings related to 56 genetic mutations to patients undergoing clinical genomic testing and directed attention as to what types of recommendations should be considered in the research community [7]. The Clinical Sequencing Exploratory Research (CSER) Consortium and the Electronic Medical Records and Genomics (eMERGE) Network published their recommendations regarding return of genomic results to research participants [2]. Their consensus is that medically actionable results should be returned to participants if he/she consented to return, with a referral for appropriate clinical follow-up offered. Importantly, they emphasized that participants should have the right to decline the return of results.

Due to the lack of consensus from the community, it is recommended that the decision regarding return of results be decided as each study is designed and the consent form developed. However, many institutions are making policies around this issue, so please be sure to consult your local policies for requirements. If it is decided to return results, one must explicitly state:

1. Under what circumstance results will be returned (i.e. only for life-threatening conditions, clinically-actionable conditions).
 - a. What results can be returned? Is it only results from assays performed in a CLIA lab (i.e. a lab certified to perform clinical testing) or can research results be shared? What are the implications of the type of results shared and how are these discussed with the participant?
2. How the contact process will occur and what specific types of information will be conveyed.

D. SHARING

Specimens and Specimen-Associated Data

PCORnet is founded on the notion that sharing amongst Networks will advance research more rapidly than entities working in isolation. As such, your consent forms should explicitly state that the participant's specimens and data associated with their specimens may be shared outside of your Institution. Ideally, the sharing statement should be as broad as possible, for example, "your specimens and data may be shared with other investigators" (and any necessary governmental or funding agencies as required). If there is a possibility that specimens may be shared with commercial entities, this should be specified. You may also want to obtain a Certificate of Confidentiality to provide an added layer of privacy protection for your participants (<http://www.hhs.gov/ohrp/policy/certconf.html>).

Providing examples of sharing scenarios can be helpful for the participant to better understand this concept. The Biorepositories Task Force guidance entitled *Procedures for Sample Use Permissions and Sample Allocations Recommendations* will address processes for governing and oversight of specimens.

Data Generated from Specimens

Consent forms also need to specify with whom data generated from a specimen will be shared. For example, all genome-wide association data from studies that receive NIH funds must be submitted to a database per NIH regulations (http://gds.nih.gov/PDF/NIH_GDS_Policy.pdf). NIH expects investigators to obtain participants' consent for their genomic and phenotypic data to be used for future research purposes and to be shared broadly. The consent should include an explanation about whether participants' individual-level data will be shared through unrestricted- or controlled-access repositories.

Recommendation: At a minimum, consent forms should state that all specimens, specimen-associated data and data generated from specimens may be shared with PCORI and PCORnet partners. When possible, a broad statement such as "Specimens and data will be shared with other investigators" is preferred.

PEDIATRIC-SPECIFIC CONSIDERATIONS

Specimens collected from pediatric participants follow the same federal regulations as other research performed in this population. Specifically, if the collection and storage of the pediatric specimens meets the definition of human subjects research according to 45 CFR part 46 then certain additional procedures must be followed above and beyond that of research with adults:

1. When collecting specimens for storage and future research use, parental/guardian permission is required and participant assent may also be required for those considered appropriately mature.
2. Once the participant matures, parental permission no longer applies and the overseeing IRB must ensure that informed consent is obtained from the now-adult participants unless the IRB determines that informed consent can be waived (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.111>)

STRATEGIES FOR CONSENT

What the participant consents to directly dictates what the specimens can be used for in the future. As discussed above, some consents limit the use of the specimens to very specific research studies whereas other consents are very open – leaving the specimens to be used for unspecified, future use. Consent strategies fall into five main categories:

1. *Specific consent*: Consent is obtained for a very specific research purpose. Participants will need to be re-contacted and asked to consent for each new use of their specimens.
2. *Tiered consent*: Participants are presented with many options for what their specimens can be used. These may include broad, future use; future use related only to the original study topic; or a need to contact the participant for any future use. An example of a tier consent approach is provided below:

With your permission, we would like to store your blood sample for use in future research.

You do not have to agree to this in order to be in the study, and your decision will not affect the care you receive from the study doctors.

Please pick one of the choices below:

- My blood may be kept and used in research to learn about, prevent, or treat diabetes.
- My blood may be kept and used in research to learn about, prevent, or treat diabetes or other health problems (e.g., heart disease and mental illness).
- My blood may not be used in future research unless researchers contact me to tell me about the study and ask my permission.
- My blood may not be used in future research. I do not want researchers to contact me about future studies.

* Adapted from the National Cancer Institute's informed consent template for cancer treatment

Considerations for the tiered approach, as detailed by the National Human Genome Research Institute [8] are:

- i. The consent form should be designed in a way that does not allow research participants to make conflicting choices within the same consent form.
 - ii. If a study investigator provides research participants with a set of choices or levels of participation in the research project, then it is important that the investigator, and, as appropriate, the data repository have the appropriate mechanisms in place to track the individual choices and to ensure that the data are used in a manner consistent with those choices.
3. *General permission (broad consent)*: Participants are asked to consent to all future use of their specimens for purposes that an ethical review board determines to be scientifically meritorious and ethically permissible.
 4. *Presumed consent*: Participants are informed that their specimens will be used in future research unless they expressly deny permission.
 5. *Dynamic consent*: Participants are more actively involved in the consenting of downstream research projects. This may take the form of the participant receiving information (generally through a website) for proposed projects and opting-in to ones of interest, or participants may change their consent preferences for data and specimen sharing over time (often facilitated by web portals)[9-11]. An example of a PPRN using this approach is the Platform for Engaging Everyone Responsibly (PEER) from the CENA PPRN. View a presentation on this tool here: <https://www.nihcollaboratory.org/Pages/Grand-Rounds-02-21-14.aspx>. This option requires the researcher to carefully track changes in participants' preferences and ensure that the specimens are used in a manner consistent with those preferences.

E. CHOOSING A CONSENT STRATEGY

1. Consider your participants' preference. Studies have shown that the majority of the participants surveyed found general permission acceptable [12, 13]. However, there are subpopulations and substudies in which this is not the case (e.g. obtaining genomic information). Additionally, with the growing technological capacities for dynamic consent, others have found that participants want to have more direct control over the use of their samples [9, 11].
2. When possible, try to consent to unspecified, future research (i.e., stay away from words such as "only used for"). This will allow the greatest collaboration with other researchers.
3. A tiered consent offers a good compromise between respect for the participant and the ability for future research. However, if you do a tiered consent you must be able to track participants' responses and appropriately and ensure specimens are used in a manner consistent with the consent selections.

SUMMARY OF CONSENT EXPECTATIONS FOR PCORNET

The Biorepositories Task Force sets forth the following expectations related to informed consent for specimen acquisition and future use. We acknowledge that there may be rare exceptions to implementing these expectations, but in general these should be minimum requirements for PCORnet biorepository activities.

1. Participants should be asked to consent to future, unspecified research to allow for optimal collaboration amongst PCORnet investigators.
2. At a minimum, consent forms should state that all specimens, specimen-associated data and data generated from specimens may be shared with PCORI and PCORnet partners.
3. Specimens should be stored for an indefinite amount of time.
4. A process should be described for providing results that are medically actionable, when possible.

RESOURCES

Below are links to website that provide supporting information and documents for biorepository consents.

F. GENERAL INFORMATION

- Office for Human Research Protection: <http://www.hhs.gov/ohrp/>
SACHRP's FAQs terms and recommendations on informed consent and research use of biospecimens:
<http://www.hhs.gov/ohrp/sachrp/commsec/attachmentdfaq%27stermsandrecommendations.pdf.pdf>
- Cooperative Group Banks: Biorepositories for NCI-Sponsored Cancer Clinical Trials:
<http://cgb.cancer.gov/>
- Tailored language for genomics research: <http://www.genome.gov/27026589>
- Genetic Information Nondiscrimination Act (GINA): <http://www.genome.gov/10002328>
- NIH Genomic Data Sharing Policy: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-124.html>

- Group Health’s Program for Readability Science & Medicine (PRISM):
http://www.grouphealthresearch.org/capabilities/readability/readability_home.html
- Group Health’s Program for Readability Science & Medicine (PRISM) Readability Toolkit:
http://www.grouphealthresearch.org/capabilities/readability/ghchs_readability_toolkit.pdf

G. BEST PRACTICES

- International Society for Biological and Environmental Repositories Best Practices:
<http://www.isber.org/?page=BPR>
- National Cancer Institute Biorepositories and Biospecimens Research Branch Best Practices:
<http://biospecimens.cancer.gov/practices/>

H. MODEL CONSENT FORMS

- National Human Genome Research Institute; Consent form examples and model consent language: <http://www.genome.gov/27526660>
- National Cancer Institute: Section II. Sample Informed Consent Documents:
<http://specimens.cancer.gov/bestpractices/ap2/>
- National Cancer Institute: Simplification of informed consents:
<http://www.cancer.gov/clinicaltrials/conducting/simplification-of-informed-consent-docs/page2>
- Supplemental Material from Beskow et al. 2010 [14]
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3250643/#!po=73.5294>
- Supplemental Material from Beskow et al. 2010 [15]
<http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0013302#pone.0013302.s001>
- For sample consent forms, please see Appendix A.

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APPENDIX A – SAMPLE CONSENT FORMS

1. Personalized Medicine Research Project (PMPR)
2. Registry and Biorepository Study
3. University of Iowa Tissue Procurement Core (TPC)
4. University of Iowa Biobank
5. Framingham main consent with blood draw
6. Framingham consent for cell lines
7. Example of re-consent for use of existing samples

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