Compiled Public Comments on Request for Information on Developing Consent Language for Future Use of Data and Biospecimens

Guide Notice Number: NOT-OD-21-131

July 1, 2021 – September 29, 2021

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Submission ID: 1608

I am responding to this RFI: On behalf of myself

Name: Elizabeth J Kopras

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Rare diseases

1. **Utility and useability of this resource:**

I consent patients for biorepositories. Based on constant feedback, we should look to the Ireland model, which calls for a three page consent form. People don't want to read a bunch of legal crap. If they are willing to get stuck and have samples stored, they really don't care what we do with deidentified samples. If you bothered to ask the people who actually donate samples, you'd see this.

2. **Gaps or additional components that should be included:**

IRB requires us to keep language at 7th grade level, yet requires language at the 15th grade level.

3. **Specific language proposed in the informed consent sample language:**

Keep it simple. Record yourself reading this, and ask yourself if a ten year old could understand this?

4. **Hurdles or barriers to wider use of this resource by the community:**

My focus group participants feel that the consent form is designed to protect the scientists, not the participants. You need to change the language and the culture. Make it less legal.

5. **Other considerations relevant to this resource:**

Submission ID: 1609

I am responding to this RFI: On behalf of an organization

Name: Gamze Kilic-Berkmen

Name of Organization: EMORY UNIVERSITY

Type of Organization: EMORY UNIVERSITY

Type of Organization - Other: Academic Institution

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Neurology: Movement Disorders

1. **Utility and useability of this resource:**

Emory Admin Unit has developed this Bylaws document in collaboration with our NIH Program Officers and Liaisons, and the Emory Office of Sponsored Programs to serve as a guide and contract for each participating site. All centers receiving funding through our grant must sign this document. This document describes the DC infrastructure and projects and programs, data and resource sharing, publication and acknowledgment responsibilities and coordination, copyright and patent policy, financial responsibilities, and human subjects research and conflict of interest guidelines.

2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/MKKUuZJSXF.pdf

Attachment Description: Dystonia Coalition Bylaws including data share policy

Submission ID: 1611

I am responding to this RFI: On behalf of myself

Name: Gregory Simon

Name of Organization: Kaiser Permanente Washington Health Research Institute

Type of Organization: Non-Profit Research Organization

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

mental health services research

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

There is a need for understandable consent language regarding risk of re-identification, especially with respect to future data linkage. Even if data to be shared include no explicit identifiers, variables in data to be shared can still serve as keys enabling linkage to identifiable external data sources. It is probably misleading to offer complete assurances that data are de-identified, especially since we cannot anticipate external data sources that may become available.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1614

I am responding to this RFI: On behalf of myself

Name: Jennifer Lorvick

Name of Organization: RTI International

Type of Organization: Non-Profit Research Organization

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

health inequities

1. **Utility and useability of this resource:**

Will depend on the content

2. **Gaps or additional components that should be included:**

I strongly recommend using integrating 'teach to goal' methods. Also 5th grade reading level, short sentences and large type. The attached presentation has extremely useful for developing clear, comprehensible consent forms. I encourage you to contact Dr. Sudore about her work.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**

5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/uAZyOEPsvz.pdf

Attachment Description: great consent writing instructions

Submission ID: 1616

I am responding to this RFI: On behalf of myself

Name: Radwa Aly

Name of Organization: Medical FAculty Associates

Type of Organization: Academic Institution

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Neuroscience

1. **Utility and useability of this resource:**

This tool would be incredibly helpful to streamline the biorespository process and to serve as guidance or a kickstarter researchers on type of language that would be "Acceptable" and covers the basis in the even that they were interested in collecting biospecimens.

2. **Gaps or additional components that should be included:**

Some patients are concerned about DNA or insurance having access to this information. I'm wondering if some language describing that this information will not be shared with insurance/genetic testing will not be done outside of research and the collection of the specimens will not impact there care

3. **Specific language proposed in the informed consent sample language:**

N/A

4. **Hurdles or barriers to wider use of this resource by the community:**

The only hurdle I envision is dissimination and knowledge that it exists. The onus will be on organization leadership to be aware of the fact that it is exists and have the language available for researchers to use.

5. **Other considerations relevant to this resource:**

Submission ID: 1617

I am responding to this RFI: On behalf of myself

Name: Michael Hoffman

Name of Organization: University of Toronto

Type of Organization: Academic Institution

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Genomics

1. **Utility and useability of this resource:**

Thanks for assembling this useful resource which will prove helpful for a wide range of investigators.

2. **Gaps or additional components that should be included:**

The introduction should include more information about the importance of data and materials sharing for the robustness of scientific research and for the reduction of duplicated effort. I am concerned that the sample language only envisions controlled access to data and that this example will retrench a conservative approach to restrictive data sharing in cases when broader, unrestricted sharing would yield greater benefits with minimal potential for harm. Even in cases where individual-level raw data must be kept controlled access, either individual-level processed data or group-level summary data might be able be shared unrestricted. You should mention this in the sample language. The NHGRI data sharing resources provide much better sample language for broader sharing which should be included here for any relevant projects, not just genomics. Not including this language in the sample policy here creates a risk that investigators will inadvertently fail to comply with NHGRI and NIH-wide genomic data sharing policies.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**

When participants change their mind about participation I agree their materials should not be shared further by the investigators. The promise of best efforts to track down already-shared materials, however, is impractical. Subsequent inevitable failures to stop further research for already-shared materials will lead to disappointment for participants that will erode confidence in patient participation in research.

5. **Other considerations relevant to this resource:**

Submission ID: 1625

I am responding to this RFI: On behalf of myself

Name: Jeffrey Botkin

Name of Organization: University of Utah

Type of Organization: Academic Institution

Role: Bioethicist

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Genetic and genomic research

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

A substantial volume of research is conducted with data and biospecimens initially acquired for clinical purposes. Under the current federal regulations (45CFR46), these samples and data can be used for research if they are either anonymized or eligible for a waiver of consent. This approach has been controversial. Several state newborn screening programs have been sued by parents for the storage and research use of residual newborn screening bloodspots without parental approval. For a brief time, federal law required parental consent for storage and use of residual bloodspots and declared that residual bloodspots must still be considered human subjects research even if anonymized. These provisions were superseded by the 2018 changes in 45CFR46, nevertheless, the issue remains controversial and problematic for state programs. Further, in the 2016 NPRM, draft changes to the federal regulations proposed the possibility of requiring informed consent for the research use of clinically acquired specimens. Comments to OHRP demonstrated strong disapproval for this provision by academic and commercial research organizations but strong approval by the lay public. Some of the support for informed consent in this context has been driven by the popular book, The Immortal Life of Henrietta Lacks. The final changes to the regulations dropped this provision. Therefore, the status quo remains that data and biospecimens acquired for clinical purposes can be used for biomedical research without the knowledge or permission of the source individuals. I believe this is a tinderbox that risks high-profile controversy and substantial harm to the biomedical research enterprise. Accordingly, this NIH effort to address consent for use of data and biospecimens should address access and use of data and samples initially acquired for clinical purposes. SACHRP had the opportunity to address this issue when I chaired the committee. See: https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2016-january-5-recommendation-nprm-attachment-a/index.html It is my own opinion, and that of SACHRP at the time, that an opt-in consent approach, as proposed by the NPRM, was likely cumbersome and not likely to foster informed decision-making by patients seeking clinical care. A better approach, we proposed, is a notice and opt-out approach whereby patients are routinely notified in simple, effective terms that their data and biospecimens might be used for

research. If they object to this possibility, they can opt-out and future use of their data/biospecimens would be prohibited. This approach is unlikely to produce full awareness and a carefully considered response by many patients, but, at a minimum, research institutions would be providing information and permitting a choice. This would be a substantial improvement over current policies and procedures. The notice and opt-out approach also would require a rather complex tracking system such that investigators could determine what samples were available for research use. What language to use in this context, how to foster awareness and choice, and how institutions could administer a database of choices all could benefit from attention by this NIH initiative. I would argue that, because of the volume of research done with clinical data/biospecimens, the complete lack of public awareness of current practices, and the potential controversy surrounding this issue, that this is a more important set of issues than those surrounding informed consent for data/biospecimen use for individuals approached for research participation. Thanks for the opportunity to comment.

Submission ID: 1626

I am responding to this RFI: On behalf of myself

Name: Marta Wood

Name of Organization: University of KY

Type of Organization: Academic Institution

Role: Other

Role - Other: Clinical Research Project Manager

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Oncology

1. **Utility and useability of this resource:**

Very helpful. Great that it is concise and includes sample language with option to tailor as appropriate.

2. **Gaps or additional components that should be included:**

1. The consent document should include a statement indicating whether the biospecimens and/or data may be sold (vs. provided free of charge) to researchers. 2. Subjects should have the option of allowing access to data/specimens to specific groups, including (a) only at the institution/entity conducting the main study. (b) only non-profit entities (ie, excluding commercial entities), and/or (c) unrestricted access. Subjects have a legitimate right to restrict access to their data and/or specimens to specific types of researchers if they so desire.

3. **Specific language proposed in the informed consent sample language:**

"It is your decision whether or not to let researchers share your data and biospecimens for research in the future, and who they can share with. If you say “yes” now, you can change your mind later, but your data and biospecimens might still be used if they have already been shared. If you say “no

4. **Hurdles or barriers to wider use of this resource by the community:**

you can still fully participate in this study. Please initial next to your choice: My data and biospecimens can be used _____ in other research studies conducted by _____ (institution/practice/entity). _____ in other research studies conducted by _____ (institution/practice/entity) and other non-for-profit institutions. _____ in other research studies conducted by any/all institutions, including commercial/for-profit companies. (Institution/entity) may charge a fee to other institutions for using my data and/or specimens. _____ YES _____ NO _____NO, do NOT use my data and biospecimens in other research studies

5. **Other considerations relevant to this resource:**

Submission ID: 1627

I am responding to this RFI: On behalf of myself

Name: Shazia Ahmad

Type of Organization: Not Applicable

Role: Other

Role - Other: Rare Advoacy Professional

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

rare diseases, oncology, neurosicience

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

I think it's important to include a video on what is involved. I've spearheaded numerous programs where I've seen a gap in the Informed Consent process around biospecimen collection. I've supported this on a number of levels to create more education on the needs of the process so it is well undestood.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**

I think there could be challenges in understanding this piece by the community (patient/caregivers). A video explaining the process would add value.

5. **Other considerations relevant to this resource:**

current language: "The use of your data and biospecimens may lead to new tests, drugs, devices, or other products or services with commercial value. These products or services could be patented and licensed. There are no plans to provide any payment to you should this occur." This needs to also include details on what it means to be patented and licensed.

Submission ID: 1650

I am responding to this RFI: On behalf of myself

Name: Diane B Paul

Name of Organization: pair

Type of Organization: Other

Type of Organization - Other: patient advocacy

Role: Research Participant/Patient/Advocate

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

cancer

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

It would be useful for patients to get copies of any information that is gathered from them so that either they or their families could have this for their medical records. Language should be provided so that patients can consent to have the results from their samples, sent to their or their doctors. Patients should be able to decide for themselves if they want these records. (see word document for suggestions) With cyberattacks in the news, patients should be able to get a direct benefit for the risk they take in providing this information whether they can benefit clinically or not from the study,

3. **Specific language proposed in the informed consent sample language:**

Please see the attached word document.

4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Please see word document

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/uekpcPQdeF.pdf

Attachment Description: comments and suggested changes to the form

Submission ID: 1651

I am responding to this RFI: On behalf of myself

Name: Andrew Dwyer

Name of Organization: Boston College / Massachusetts General Hospital

Type of Organization: Academic Institution

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Genomics

1. **Utility and useability of this resource:**

It would be highly beneficial to have template language regarding use and access to samples that is in simple lay language - vetted by health literacy experts and readability algorithms. This should be concise and not be a lengthy legal add-on to informed consent documents

2. **Gaps or additional components that should be included:**

health literacy and genomic literacy barriers

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1658

I am responding to this RFI: On behalf of myself

Name: Paul Hewett-Marx

Name of Organization: NIH

Type of Organization: Government Agency

Role: Other

Role - Other: Scientific Review Officer

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Numerous health domains

1. Utility and useability of this resource:

This is a critically useful resource in concept and execution.

2. Gaps or additional components that should be included:

This guidance follows the traditional informed consent process regarding data collected and used and its de-identification "internally" or "within" the study. I think it is very important to convey information to the participant about how the data (even if de-identified) may be linked to non-study data by other researchers. There is a increasing risk that via integrating data and data science methods that leverage geographic and demographic data to potentially de-identify study data. I think advances in data aggregation and data science need to consider this potential reality under "considerations" and it should be incorporated in consent procedures and assurances as a potential risk to participants. I think it is important to add a consideration regarding appropriate procedures for translation and back translation and contextually specific local meanings of terms. It is important to point out the difficulties of conveying terms, concepts and meaning across languages and settings. Researchers should consider proper procedures for doing. Often in practice, informed consent forms are translated and back translated by laypersons and/or local investigators and important concepts and meanings mistranslated or not contextually accurate. This increases the potential for (non)informed consent and for increasing risks to participants.

3. Specific language proposed in the informed consent sample language:

1. Sample Language Intro: "This study is collecting data and biospecimens from you" implies that "data" is something physical that is taken. People who are not researchers (particularly with lower education) will not understand what "Data" means (or for that matter, what a "biospecimens" are). A more colloquial and appropriate term would be "information." As such, better wording for the sample language would be: "This study is asking you to provide information about yourself [and your family, children, spouse], and may include your [age, education, health status, attitudes]. The study is also asking you to provide [blood, mucous, semen]." A less optimal approach is to define terms for the participant: As in "The study is collecting data from you." Adding: "What we mean by data is [your age, education, etc.]. What we mean by biospecimens is [lblood, mucus, semen]. It is critical to think about

how the participant understands all the terms used in consent forms and how they might be translated into local languages. Currently, it is worded from the researchers perspective and assumes a common understanding of meaning, which is fraught; additionally, adding specificity is key to relevance to and understanding from the participant"s perspective. Note: sub-terms specifics may also need to be further explained (or as appropriate translated into local terminology). 2. Data sharing language:" While laudable, is it realistic that participants will have the ability to notify investigators and can investigators (on a case by case and continual basis update datasets, extracting individual cases?). Perhaps, if the request was made during the course of the study, but "at any time" makes the practicality of this not realistic and overly ambitious. Perhaps the time in which this is possible can be the active study period, set by the investigators, or set by the institutions IRB with the reasonable goal of accommodating the participants, but also what is realistic for the investigators. Note, the participants can opt out if they believe they are given too little time to change their minds. 3. I suggest that you add the term "de-identified" to the following sentence: "It is your choice whether or not to let researchers share your [de-identified] data and biospecimens." Also, as per above noted issue, this should be reworded altogether, e.g., "It is your choice whether or not we can share your information and [blood samples] with other researchers. Remember, no personal information that can identify you as an person/individual would be shared." I think you should go through all sample language with assessment of the language used throughout and simplify, e.g., "commercial value." Could be more simply worded, as in, "or other products that people could sell or services for which people may charge money."

4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1661

I am responding to this RFI: On behalf of myself

Role: Government Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**

Please change all sentences to active voice. Many readers will not understand sentences like, "...if some research with your data and biospecimens has already been done, the information from that research may still be used." That"s because it"s not clear who is doing what, and how information differs from research. Is this the right interpretation?... "if researchers have already used data from you or your biospecimens for a particular project, they may not be able to remove them." There are several other examples in which passive voice obscures meaning.

4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1662

I am responding to this RFI: On behalf of myself

Name: Melissa Riddle

Name of Organization: NIH

Type of Organization: Government Agency

Role: Government Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Behavioral and Social Sciences Research

1. **Utility and useability of this resource:**

This resource is a great idea. In the Program Officer role, applicants and grantees often ask if there are templates and/or sample text for important required documents. The suggested format--with sample standardized text, and prompts to fill in study-specific information--is similar to other templates we"ve used, and on which we"ve received positive feedback from users.

2. **Gaps or additional components that should be included:**

The actual sample text is probably general enough to cover future use of behavioral and social research data, but it might be useful to include specific information in the introduction or instructions for behavioral and social sciences researchers. One common situation in BSSR clinical trials is that recordings of participant-interventionist interactions may be recorded as part of quality assurance (e.g., tracking the fidelity of intervention delivery across interventionists or settings). These recordings have the potential to serve as rich datasets for secondary data analyses, especially about intervention process or mechanisms of action. Such projects might be well-suited for trainees and early-career investigators, making maximum use of existing data to provide opportunities for training and development of clinical investigators. My hope is that the consent process for relevant studies would plan for this sort of "future use" of study data.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**

The wide variability among IRBs about required language and formats of study documents may be a bit of a barrier to broad use of this resource. Would it make sense to engage IRB leaders to discuss the possibility of adopting this "future use" language broadly?

5. **Other considerations relevant to this resource:**

Submission ID: 1663

I am responding to this RFI: On behalf of myself

Name: Randolph Hall

Name of Organization: University of Southern California

Type of Organization: Academic Institution

Role: Other

Role - Other: Director

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Systems engineering

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

I encourage reference to the University of Southern California"s policy on biorepositories: https://policy.usc.edu/biorepositories/ We have established these elements for consent: Consent or waiver of consent is required for the storage and future use of data/human biospecimens entered into research repositories. Investigators conducting research that may later be of value for additional studies should address the possibility of submitting the data/human biospecimens to a repository in the initial consent. Re-contact of a donor for clinical studies separate from the research repository requires advanced consent from the donor. Return of medically relevant results should not be promised to donors in consent forms. However, it is permissible to disclose in the informed consent the possibility of returning medically relevant results. This should not be discussed as a benefit. Donors do not receive compensation for commercialized value of research that results from donated tissues or data. Donors should be informed of this fact. Donors must be allowed to withdraw their human data/biospecimens from a research repository. Donors should be informed that in the event they withdraw, it will not be possible to destroy human biospecimens and health information that have already been given to researchers. Donors must be informed of intended future use of data/human biospecimens. This statement may be specific or broad. If genetic analysis is planned, donors should be informed. However, the statement will dictate the limits on future uses. Donors must be informed of how release of data/human biospecimens will be controlled. All elements required by regulation under the circumstances of the proposed repository must be in place. For instance, extra protections required for children, pregnant women and fetuses, and prisoners must be used. A waiver of the requirement to obtain consent may be granted by the IRB if all of the requirements for waiver are met.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1664

I am responding to this RFI: On behalf of myself

Name: Roderick Corriveau

Type of Organization: Government Agency

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Neurodegeneration. Dementia research.

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

I suggest that language be included indicating the following: while knowledge generated using your de-identified samples and clinical data may be used to generate a product that could be sold for profit, your de-identified samples and clinical data themselves will be used for research only, and will never themselves be distributed for profit. At the least people should have the option to opt out of allowing their samples and clinical data be sold for a profit. (Re: Henrietta Lacks)

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1665

I am responding to this RFI: On behalf of myself

Name: Xiaohong Li

Name of Organization: Fred Hutchinson Cancer Center

Type of Organization: Academic Institution

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Cancer Biology, cancer genetics, cancer epidemology, population science

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**

Some data might be generated with older version of software and analysis methods (e.g. level 2, 3 data). Potential mistakes might exist in some mid-level analyzed data. Either users need to be careful and do validating when use some of the data, or users use the raw data and re-generate mid-higher level results.

5. **Other considerations relevant to this resource:**

Submission ID: 1666

I am responding to this RFI: On behalf of myself

Name: Natalia Gnatienko, Katherine Calver, Sally Bendiks

Name of Organization: Boston Medical Center

Type of Organization: Academic Institution

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Clinical HIV/substance use research, particularly in international settings

1. **Utility and useability of this resource:**

Our research team reviewed this resource and found it incredibly comprehensive and useable, as it allows for tailoring to unique contexts.

2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**

Introduction – Sample Language: it may be helpful to provide additional information as to what getting "approval" to use stored samples and data entails and who grants this approval. Consider including a plain language definition of "data and biospecimens" in sample language for study participants, as referenced in "II. Instructions for Use."that can be tailored to the specific study, based on data and specimens collected. Suggested edits below: "Data and biospecimens" are information collected from, or about, you during a research study. This may be survey results, medical images, health records, or wearable device information. It may also be human material, such as blood, tissue, urine, or DNA.

4. **Hurdles or barriers to wider use of this resource by the community:**

5. **Other considerations relevant to this resource:**

Submission ID: 1667

I am responding to this RFI: On behalf of myself

Name: Carl Simon

Name of Organization: National Institute of Standards & Technology

Type of Organization: Government Agency

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

regenerative medicine

1. **Utility and useability of this resource:**

1) I was looking for the ability to share specimens with outside investigators outside of the institution, and that was present. 2) I was looking for the ability to use specimens for future, unknown studies, and that was present.

2. **Gaps or additional components that should be included:**

Component 1, Option #1: You should add a statement to indicate the following: "The participant should be aware that no data is 100% safe, and a data breach or hack is always a possibility." Component 6: I think an additional Component #6 is needed to address dissemination. Possibly something like this: "Data from studies with your specimens may be disseminated publicly through mechanisms such as websites, publication in research journals, social media, data repositories, public lectures and other means. Results may be disseminated in aggregate form, such as averages and plots, or as raw data (so that others may analyze your data with different methods)." Component 7: I think an additional Component #7 is needed to address means of identification of the individual "Although we intend to keep your identity confidential, it may be possible for your identity to be discovered through research results. For instance, your specimens could be used in a study where DNA sequencing data are collected and published, and third parties may be able to identify you from the published DNA sequence data."

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1669

I am responding to this RFI: On behalf of myself

Name: Robert McLaughlin

Name of Organization: Public Health Institute

Type of Organization: Non-Profit Research Organization

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Epidemiology, Public Health/Disease Surveillance

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**

We have found that the right of withdrawal language in consent forms is particularly important for studies that collect specimens directly from research participants and that the following phrase captures what a participant can reasonably expect to be retrieved and destroyed in connection with the exercise of a right of withdrawal from a study: "the unused, identifiable portion of your specimen sample". We believe it is important to recognize that specimens exhausted through research, or de-identified and incorporated in analytic work through, for example, micro-arrays are feasibly within scope of the exercise of a right of study withdrawal.

4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1670

I am responding to this RFI: On behalf of myself

Name: Chuck Francis Lynch

Name of Organization: UNIVERSITY OF IOWA

Type of Organization: Academic Institution

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Cancer Surveillance

1. Utility and useability of this resource:

I am writing to request an exemption to population-based cancer registries for the need to have patient informed consent for tissue obtained after 2015 as part of the Genomic Data Sharing (GDS) Policy. For the past 30 years, I have been the Principal Investigator of the Iowa Cancer Registry, a member of the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Program since 1973. The NCI SEER Program collects population-based cancer data that extends well beyond academic health centers. For the past two decades, we have been obtaining tissue blocks for cancer patients that otherwise would be destroyed by their originating pathology laboratories. My institutional IRB has allowed this to occur without the need for patient informed consent. In addition, they have allowed us to use these tissue blocks in research projects so long as the tissue and its accompanied annotation data did not identify the patient. These research projects involve community-based specimens that reflect the general population and involve principal investigators who are not part of the Registry. Thus, the Registry has acted as an honest broker. Population-based cancer registries, such as the Iowa Cancer Registry, are considered Public Health Authorities under HIPAA, and not required to obtain patient informed consent for collection of their required cancer surveillance data. The GDS policy requiring patient informed consent for genomic-based research will severely hamper the tissue-based research that is being conducted through these population-based cancer registries. The revised common rule was designed to "…better protect human subjects involved in research, while facilitating valuable research and reducing burden, delay, and ambiguity for investigators". Obtaining patient informed consent for secondary use of de-identified tissue specimens accessed via SEER registries will represent unreasonable burden and delay to research. Requiring such consent will also decrease participation rates that lead to 1) bias toward inclusion of cases with better survival outcomes, 2) bias against inclusion of under-represented groups, and 3) mitigation of population representativeness by obtaining a sample of convenience. This will not serve science well. The GDS policy requiring patient informed consent has logistical implications for population-based cancer registries, where we are required to protect the confidentiality of the data we collect and provide for its security. If you require NIH-funded principal investigators to obtain patient informed consent, it will be impossible for them to do this because the registries will not release patient identifiers to them. If the population-based registries need to obtain the informed consent, we will 1) no longer be functioning as an honest broker, but rather as a research partner, 2) need financial support to cover the cost of obtaining informed consent, and 3) since years

may have passed since cancer diagnosis, the targeted patient may be deceased. In summary, requiring patient informed consent will 1) be a barrier to NIH-funded investigators to conduct population-based studies, 2) favor studying cancer patients with better outcomes resulting in survival bias, 3) minimize the opportunity for under-represented minorities to participate resulting in selection bias, and 4) lead to results with poor external validity. Overall, these problems will serve the veracity of science poorly.

2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:** UNIVERSITY OF IOWA

Submission ID: 1673

I am responding to this RFI: On behalf of myself

Role: Member of the Public

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**

Useful resource but assumes some basic understanding. Reading level may be simple but what is inferred by the technical terms used is less than clear.

2. **Gaps or additional components that should be included:**

Need to define what "data" are - asking for consent on DATA and/or specimens will be aided by clarifying what is meant by Data vs. personally identifiable information. For the lay person, data is a vague word and should be explained for each trial.

3. **Specific language proposed in the informed consent sample language:**

See above - specify what data are and specify again what samples are collected that may be used. Needs to be tailored to each protocol rather than generic language.

4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Should look at informed consent process and documents from the perspective of the general public and go beyond reading level. Many terms in these documents are technical and have implications. This is not obvious to a non-scientific person. Examples - use of your Data… what data exactly are you going to use and what will be done with them? Use of your bio specimens - what is collected and what of these are you going to share and for what purpose? Use of your data or specimens for non-related research - what does this mean? Informed consent should include an understanding of the processes and all implications and not just readability of forms. Volunteers should have a change to fully understand what it means to have their data and samples shared. Also explain what "deriving benefit, or lack thereof" means. The intent is to avoid coercion but the moment the work "benefit" shows up, it should come with an explanation.

Submission ID: 1678

I am responding to this RFI: On behalf of myself

Role: Bioethicist

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

International research

1. **Utility and useability of this resource:**

Thank you for putting this together. It provides very helpful sample language.

2. **Gaps or additional components that should be included:**

Please add language for explaining to participants the sort of information that could be gleaned from their biospecimens and the sorts of research that could be conducted on them. Please consider adding language regarding whether data and biospecimens will be sent and/or stored in another country. This is a big issue for the collection of biospecimens in many low- and middle-income countries.

3. **Specific language proposed in the informed consent sample language:**

"going forward" is corporate-speak. Try: "after that."

4. **Hurdles or barriers to wider use of this resource by the community:**

It is only in English. Please consider developing resources in other languages.

5. **Other considerations relevant to this resource:**

Submission ID: 1679

I am responding to this RFI: On behalf of an organization

Name: Shannon Swiatkowski

Name of Organization: CWRU Clinical and Translational Science Collaborative of Cleveland

Type of Organization: CWRU Clinical and Translational Science Collaborative of Cleveland

Type of Organization - Other: Academic Institution

Role: Other

Role - Other: Research Administrator

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology): Translational Research

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Genetic information, cell lines derived from samples, etc, are confusing to manage and guidance is sorely needed in this area related to research regulations. This is currently listed as a point to consider, but no real guidance, best practices, or sample language is included. Would suggest that this is a highly important area to consider and should be explicitly addressed. Sharing data with international companies or companies and institutions outside of your state is becoming more common. As different countries and states adopt different rules and regulations, we should consider a blanket statement related to data receiving different protections in other countries or states.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Component 2 Voluntary participation, para 1 - I'm unsure about distinguishing between allowing opt in/out for studies with direct benefit vs. no direct benefit. In accord with the principles of autonomy and respect for individuals, I feel that participants should be asked about opting in/opting out for use of their data and samples for all except for explicitly designated biobank/repository/registry studies where the purpose of the research is to collect, store and share the data and samples. Empiric international research has shown that most participants are willing to give consent to use their samples (and most would give broad consent) for future research, but they want to be asked for their permission to do so. The document states that participants should be given the option to agree to or opt out of having data or biospecimens stored and shared for future research. This is true for identifiable data, but having options in the consent form introduce a lot of additional potential for consenting mistakes, so should be done carefully. In addition, when related to completely deidentified data and biospecimens, providing options may introduce burden when truly deidentified information is currently generally considered not to be Human Subjects Research.

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/CqYhTNTwyY.pdf

Submission ID: 1680

I am responding to this RFI: On behalf of an organization

Name: Marc Tunzi, MD, MA

Name of Organization: Society of Teachers of Family Medicine

Type of Organization: Society of Teachers of Family Medicine

Type of Organization - Other: Professional Organization/Association

Role: Bioethicist

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

clinical research

1. **Utility and useability of this resource:**

please see letter, attached

2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/WMdvulZmEV.pdf

Attachment Description: response letter

Submission ID: 1681

I am responding to this RFI: On behalf of myself

Role: Research Participant/Patient/Advocate

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Pediatric patients

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

As the parent of/advocate for a child with a severe and chronic medical condition, I have concerns regarding future use of children's biospecimens and data after they are 18. Approval that parents may give on behalf of minor children should be limited in scope and only be valid until the children are 18. Although it will definitely add administrative burden to researchers to track "expiration dates" for pediatric consent, I believe that if they are divided into age cohorts it can be done and should be done. Pediatric research is critical and has been life-changing for my own child's well-being. However for patients that survive into adulthood, they should be able to control their own participation in research and should not be bound to approvals that were made on their behalf - and for them, probably in a blur of extensive hospital care and general childhood. I've heard IRB panelists' arguments that unique cohorts' data should be preserved for future use, but if it is that important then please follow-through on securing consent for the participants after they are no longer children - or if the pediatric participants have died, then from their next of kin. Being reluctant to follow-up with individuals or families to gain (or be denied) additional consent after the patient is/would have been 18 is not a valid justification if the ongoing research is important enough to continue using their data. People have told me they are being compassionate in not contacting next of kin, but I call that being squeamish and not wanting to lose access to their data. Ask the hard questions. Imagine if you yourself realized, in your 20s or 30s, that your own biospecimens and medical data were still being as authorized for ongoing use by a consent form that your parents signed when you were three or nine or even twelve. Perhaps you would authorize it, or perhaps you would withdraw - I think the option is a basic right of research participation. In addition, in the age of genetic databases reliably de-identifying genetic data has its limits, and the privacy of patients' data is even less protected once they are no longer of an age within a "protected population." This already has ramifications for medical insurance coverage - insurance companies have, even under the current legal protections, very publicly outed families with rare genetic disorders as a reason to defund medical insurance. It's easy to find someone, even "de-identified", if you are the one person in that age range/demographic in your county or state who has a condition that requires specialized care. On a personal level, ethical level, and on a practical level, I strongly believe we should limit the scope of approval for use of pediatric participants' biospecimens and data. Thank you for your consideration.

Submission ID: 1682

I am responding to this RFI: On behalf of an organization

Name: Amanda Cashen, MD

Name of Organization: Washington University in St Louis

Type of Organization: Washington University in St Louis

Type of Organization - Other: Academic Institution

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Biomedical research

1. Utility and useability of this resource:

This resource could be useful to researchers and IRBs by providing template language that (1) is comprehensible to research participants and (2) covers all the possible future uses of the data and specimens.

2. Gaps or additional components that should be included:

At our institution, we include in the future use section of the consent form the statement, "By allowing us to use your tissue/data you give up any property rights you may have in the tissue/data." We added this language in response to past experiences with research participants.

3. Specific language proposed in the informed consent sample language:

We recommend the following modification to the proposed language. Component 1: We do not support inclusion of specific details about the site of storage, biobanks used, and timeframe data/specimens will be held. These details unnecessarily limit the future use of the data and specimens. It is more important for participants to know that their data and specimens may be broadly shared with various entities, for instance, researchers at this institution, at other research centers or institutions, industry sponsors of research, or large data repositories. Similarly, the entity that controls access to the data/specimens may change, especially if data is shared with a large repository. Rather than specifying which entity has control, we recommend a general statement indicating that there is an approval process for researchers to access the stored data/specimens. We think the statement that data and biospecimens maybe be shared "around the world" could be unnecessarily alarming to participants. (Under Option #1) The statement "Your name and other identifying information will not be on any data and biospecimens you provide" is probably false. Identifying information may remain on the data/specimens before they are shared. With IRB approval, patient identifiers may be shared for other research projects, which is not unusual if those projects are happening within the original institution. More accurate statements are "your name and other identifying information will be removed before your data and biospecimens are shared" or "data and specimens linked to your identifying information will not be shared without additional oversight and research approval." Component 3: We have received feedback from researchers that retrieving data and specimens that have already been shared is nearly impossible. The

statement in Component 2 that "your data and biospecimens might still be used if they have already been shared" is accurate, and we think that is sufficient information for a participant. The text in Component 3 could be deleted. Component 4: We are concerned that re-identification from genetic data may become easier in the future. We recommend specifically addressing the risk of re-identification from genetic data.

4. Hurdles or barriers to wider use of this resource by the community:

This resource will only be helpful if researchers find it. Institutions and IRBs should be notified when the guidance is complete. Also, a link on the OHRP website could be helpful.

5. Other considerations relevant to this resource:

Submission ID: 1683

I am responding to this RFI: On behalf of myself

Name: Becky Fillingham

Role: Member of the Public

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Oncology

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**

Concerned with connecting "data" and "biospecimens" together. People tend to view "data" as the clinical data, for which the rules are different. In general, once data is generated, it (both clinical research and research data generated from specimen analyses) will continued to be used for research (current and future) regardless of the revision/permission from a patient for the use of biospecimens, for which future use can be addressed. Such permissions are generally only utilized for specimen use. I have always found the combination misleading for trial participants.

4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1686

I am responding to this RFI: On behalf of myself

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

molecular biology

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Regarding the following sample language in Component 1: "The code key will be kept in a locked location separate from your information. The code key can only be accessed by people who have permission." It is very ambiguous. It is totally unclear how safe or secure the "locked location" is, what is its nature (a box with a key? a wall safe? a computer file with a password) and how far apart it needs to be from the other sensitive information. This needs to be expressed in much more detail to be useful at all. ---------- Regarding this sample language in Component 4: [Risks] When we share your data and biospecimens, there is a small risk that people may get access to it who are not supposed to. We will protect your data and biospecimens as much as possible during storage and when they are shared. However, there is a small chance your identity could be discovered. The word "small" gives a sens of security that may be misleading to the individual giving consent in an age where most systems claimed to be secure are being hacked fairly easily. Life sciences researchers in academic institutions are likely to not have the appropriate sense of how secure their system is. Instead of "small risk" it should read "risk". Instead of "small chance" it should read "chance".

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1687

I am responding to this RFI: On behalf of an organization

Name: Linda Ehler

Name of Organization: NIAID/DAIDS/OPCRO/ProPEP

Type of Organization: NIAID/DAIDS/OPCRO/ProPEP

Type of Organization - Other: Government Agency

Role: Government Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

HIV/AIDS and related coinfections and comorbidities as well as SARS-CoV-2

1. **Utility and useability of this resource:**

The guidance document and sample ICF language will be helpful because it addresses areas that me be overlooked when drafting ICFs and provides points to consider. It is also helpful since the sample ICF language is not mandated and can be revised as necessary.

2. **Gaps or additional components that should be included:**

The current document seems to focus only on domestic research/ and does not address international data-sharing and biospecimens issues that may occur at ex-US sites. In general, we recommend adding reminders for investigators to address local, national, and other international requirements, as appropriate.

3. **Specific language proposed in the informed consent sample language:**

The term "biospecimens" is at a high language level. We recommend considering using the term "samples" instead to lower the level.

4. **Hurdles or barriers to wider use of this resource by the community:**

It may be difficult to include information in a general use ICF to address all of the points to consider. The addition of this information may increase the length of the ICF, especially in those ex-US/international areas where describing the topic/concept of data-sharing and biospecimens may be difficult to do based on local languages, customs, etc. Also, many international sites require a separate biospecimens ICF.

5. **Other considerations relevant to this resource:**

Please see the attached document for our detailed comments for each of the above sections.

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/vLgHglJmOd.pdf

Attachment Description: NOT-OD-21-131_ RFI_ Developing Consent Language for Future Use of Data and Biospecimens_ProPEP_final

Submission ID: 1688

I am responding to this RFI: On behalf of an organization

Name: Rafael Santos

Name of Organization: The Pennsylvania State University

Type of Organization: The Pennsylvania State University

Type of Organization - Other: Academic Institution

Role: Institutional Research Oversight Committee Member

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Human Research Protections

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

NIH Genomic Data Sharing Policy Investigators that intend on storing specimens should be made aware of any policy/regulation that may apply to their future work. This can be difficult when the specimens are being stored for future unspecified work. IRBs and investigators often encounter this difficulty when reviewing consent forms to ensure adherence to the NIH Genomic Data Sharing Policy. While this policy is referenced under section III of this notice, the reference instructs researchers to incorporate any "additional considerations" needed by the policy. It would be helpful if section III either confirms that the suggested language meets the requirements of the policy or that the suggested language in section IV is updated to incorporate any missing policy elements. Ensuring that the suggested language meets the requirements of the NIH GDS Policy is especially important due to the limitations on use of the data that would be required if the policy elements are not met. Investigators are often uncertain whether future analysis on the specimens they collect will be NIH funded and are often unaware that this policy could affect their future work. Incorporating compliance with the policy within this suggested language would help to facilitate IRB review and approval of research that falls under this NIH policy. 2018 Common Rule The 2018 Common Rule incorporated three additional elements of informed consent under 45 CFR 46.116(b)(c) that directly applies to the collection and use of specimens in research: (7) A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit; (8) A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and (9) For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen). The sample language proposed in this notice does address the requirement under 46.116(b)(c)(7) in regard to commercial profit; however, the language does not address the requirements under 46.116(b)(c)(8) and (9). It is suggested that the sample language be updated to meet these requirements in order to facilitate adherence to the regulations governing use of specimens in research.

Submission ID: 1689

I am responding to this RFI: On behalf of an organization

Name: Jeri Burr

Name of Organization: Trial Innovation Network (TIN)

Type of Organization: Trial Innovation Network (TIN)

Type of Organization - Other: Other

Role: Other

Role - Other: See attached letter

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

See attached letter

1. **Utility and useability of this resource:**

See attached letter

2. **Gaps or additional components that should be included:**

See attached letter

3. **Specific language proposed in the informed consent sample language:**

See attached letter

4. **Hurdles or barriers to wider use of this resource by the community:**

See attached letter

5. **Other considerations relevant to this resource:**

See attached letter

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/OoLajyGrWg.pdf

Attachment Description: Trial Innovation Network Single IRB Response to ROI Future Use of Biospecimens Language

Submission ID: 1690

I am responding to this RFI: On behalf of an organization

Name: Timothy Badmington

Name of Organization: Public Responsibility in Medicine and Research

Type of Organization: Public Responsibility in Medicine and Research

Type of Organization - Other: Professional Organization/Association

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/bmOFWSiWdI.pdf

Submission ID: 1691

I am responding to this RFI: On behalf of myself

Name: LAURIE A SKOKAN

Name of Organization: Providence St. Joseph Health

Type of Organization: Other

Type of Organization - Other: Non-profit health system

Role: Institutional Research Oversight Committee Member

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

All types of clinical research

1. Utility and useability of this resource:

I very much appreciate the NIH's effort to assist investigators and IRBs with developing informed consent materials for data and biospecimen sharing. As data and biospecimen sharing become the norm, institutions, investigators, and IRBs may benefit from having access to sample consent language that is simple and comprehensive. The proposed language is a great start. The CIRB of the National Cancer Institute has provided template consent language to member institutions. I think making standard consent language available to all researchers, institution and IRBs will help further the research endeavor while also protecting the rights and privacy of individuals who are willing to share their biospecimens and data. In short, the utility of this resource is invaluable to stakeholders, and will lead to the ability to obtain better informed consent from research volunteers, and do so in a way that enhances efficiency for researchers, study teams, and IRBs.

2. Gaps or additional components that should be included:

I believe the proposed resource would be more useful to relevant stakeholders if it was a bit more clear in its scope and force, and if it provided additional language explaining the broader context for data sharing. For example, there seems to be some contradictory information, making it unclear whether the proposed sample consent language is intended to apply only to deidentified information and biospecimens, or to include identifiable information and biospecimens. From the perspective of protecting the rights, privacy, and information of research participants, it is considered best practice not to keep key codes with stored biospecimens or data; rather, if recontact with participants is necessary, secondary researchers should contact the researchers who collected the materials or data and have access to the code, and have them reach out to participants. Obviously this involves additional effort and collaboration, but could also be detailed in the ICF so as to provide clear information to research participants. Additionally, it is not clear how how the recommendations in this document relate to the provisions of the Common Rule, particularly the idea of broad consent. Connecting these would be especially helpful to IRBs. The Common Rule allows researchers to strip identifiers from data and biospecimens collected during a primary research study and make them available for future research without seeking informed consent, since research with such data and specimens is not considered human subjects research. The Common Rule requires only that potential participants be informed about

this possibility. In this document, NIH seems to be recommending that participants be given the opportunity to provide their informed consent for any scenario in which their data or biospecimens might be stored or shared for future research, even if identifiers will be stripped before doing so. If NIH considers seeking informed consent in all cases a best practice—even though it goes beyond regulatory requirements—then it should make that explicit, and, furthermore, should initiate a conversation with the stakeholder community about why this is a best ethical practice. Lastly, I wonder if this resource would be more useful to the community if it included general language providing the context for the request to share data, for instance, why data sharing is valuable, how it contributes to science and knowledge, why participants are asked to share their data, etc. As it is currently written, whether participants allow their data or biospecimens to be shared is set up as a purely "neutral" choice with little explanation of how contributing information for future use can advance science. As a leading proponent of responsible data sharing and its value to the scientific enterprise and the public, it seems that the NIH has an opportunity to shape how data sharing is introduced and presented to potential research participants across a wide range of studies.

3. Specific language proposed in the informed consent sample language:

Introduction: The current statement, "These studies may be done by researchers at other institutions, including commercial entities." Given that the Common Rule calls out whether research participants will financially benefit from participation, a more nuanced reference and definition of "commercial entities" would be consistent with the Common Rule. Component 1: Introduction-Description, Option #1: The sample language here should make clear that the code is not shared along with the biospecimens, and is safeguarded by the original researchers who have obtained consent. Component 1: Introduction-Description, Option #2: The sample language should be written to make it clear that, even when all reasonable steps are taken to remove identifying information, deidentification cannot be guaranteed, given advances in technology and the ways in which various set of "deidentified" data can now be combined. Understanding this risk is a critical component of informed consent to participate in the main study. Component 3: Discontinuation/Withdrawal states that, in the case of discontinuation or withdrawal, "We will do our best to retrieve all your data and biospecimens that have already been shared, but it may not be possible." This language runs the risk of overpromising the retrieval efforts that study teams are not prepared or equipped to make. I suggest instead that the default here be a statement that if participants request that their date no longer be shared, researchers will not keep sharing their data and biospecimens, but that data and biospecimens that have already been shared cannot be withdrawn.

4. Hurdles or barriers to wider use of this resource by the community:

Obtaining consensus on ICF language is always a herculean task. However, the NIH, as a respected institution, should leverage its position to strongly advocate that research institutions adopt some template language. As an HRPP administrator, it would be exceedingly helpful to have the weight of the NIH more strongly behind the language. I also see this as an opportunity to "sell" the value of biospecimen research to the patient community. Accomplishing this will take some additional explanation in the ICF.

5. Other considerations relevant to this resource:

In the era of the single IRB, having acceptable language around biospecimens and data for researchers, regulatory staff, and IRBs is invaluable. It will standardize the information provided to research participants and create efficiencies in preparing documents for review, as well as the review itself. I do think it would be important to stay away from check boxes if possible, which may mean the future use of biospecimens and data is not optional. Tracking the various responses when check boxes are present can be challenging and lead to potential errors. All studies and all institutions will have different requirements, but the more broadly the consent can be written initially, the more flexibility there will be in the future.

Submission ID: 1692

I am responding to this RFI: On behalf of myself

Name: Selenia E Wohlslagel

Type of Organization: Not Applicable

Type of Organization - Other:

Role: Research Participant/Patient/Advocate

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Neuroscience

1. **Utility and useability of this resource:**

I have MS. I'm white female. I agree to sharing of data.i have had MS for at least 39 years and I am 73 years old.

2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**

I need to be close in order to participate. I live in Ft Myers Florida not far from Naples Florida Mayo Clinic

5. **Other considerations relevant to this resource:**

I am fully vaccated with Moderna vaccine for COVID-19. It caused no problems with the MS.

Attachment Description: FDA clinical research

Submission ID: 1694

I am responding to this RFI: On behalf of myself

Name: Paul Macey

Name of Organization: UCLA

Type of Organization: Academic Institution

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

neuroimaging and behavioral interventions

1. **Utility and useability of this resource:**

Thank you, this will be invaluable. I will look to change all my consents to use this standard language.

2. **Gaps or additional components that should be included:**

We have something about being contacted to participate in other studies (opt-in check box). Passing on potential participants to other studies (my own or my colleagues) can be very helpful for recruitment.

3. **Specific language proposed in the informed consent sample language:**

Contact for future research studies: [] I agree to be contacted for future research studies []I do not want to be contacted for future research studies Minor change for consistency: This study is collecting ... > This study involves collecting... (Since the language uses "we" for other actions, it's weird to have "the study" do this one action)

4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1695

I am responding to this RFI: On behalf of myself

Name: Dorcus Johnson

Name of Organization: Kent State University i-School

Type of Organization: Academic Institution

Role: Member of the Public

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Library and Information Science (LIS) & Archival Studies

1. **Utility and useability of this resource:**

This resource has utility and useability across the information society and library and information professionals may encounter instances of reading and assisting with language interpreation for the target audiences noted with 8th grade educational level attainment or below across diverse cultures and etnicities in their fields of practice. Make sure there is connection to health literacy best practices by incorporating transrelational interdisciplinary learning exchanges/ opportunities at the master's level to ensure diversity, equity, and inclusion (DEI) with health majors of all sorts and practice to ensure the public is truly informed and giving full consent amongst vulnerable communities.

2. **Gaps or additional components that should be included:**

The information society has technology as a foci in pandemic, so plrsse add accessibility for voice, and other alternative communication methods in conveying the information in the consent. Apply all open source and legacy technologies in this aspect. Possibly include a means for option for a librarian or other information professional to assist in this process from the patient end to the legacy technology creators, et al.

3. **Specific language proposed in the informed consent sample language:**

In-field best practices finds an 8th grade level of education and reading comprehension is high when encountering people across the information landscape in commumities of need seeking help with consent of any sort/kind. This preemptively calls for reading assistance for comprehension and understanding; library and information profrssionals assist, but many do not truly comprehend documents of consent due to lamguage. Information and library profrssionals as students could be used more widely on teams where lamguage help is needed in consents like these of high importance. Also patients need the same help with understanding data consent.

4. **Hurdles or barriers to wider use of this resource by the community:**

Hurdles and barriers to wider use of this resource are inclusive of educational level of the documents and lack of comprehension of the same and the correlating data consent as well. Lack of funding to expand library and information professionals and master's level students of the academy to be included more widely into interdisciplinary and traslational teams for higher adoptability and usage attached.

5. Other considerations relevant to this resource:

Fund more library and information professionals to help with this problem for information seeking and searching for user needs and greater user experience towards knowledge gain to increase teams for interdisciplinary and translation outreach success.

Submission ID: 1696

I am responding to this RFI: On behalf of myself

Name: Lawal Hassan

Name of Organization: Hassan Institute Of Technology Nigeria

Type of Organization: Research Participant/Patient Advocacy Organization

Role: Institutional Research Oversight Committee Member

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Health Sectors

1. **Utility and useability of this resource:**

I Lawal Hassan From Nigeria I want to partnership with your Organizations

2. **Gaps or additional components that should be included:**

Health Products, Medical Products, Medicine Gynecologist,

3. **Specific language proposed in the informed consent sample language:**

English Language,

4. **Hurdles or barriers to wider use of this resource by the community:**

We want to help our youths and society

5. **Other considerations relevant to this resource:**

Site and locations

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/xcqeZMfUWy.pdf

Attachment Description: Attachment

Submission ID: 1700

I am responding to this RFI: On behalf of an organization

Name: Hannah Gunderman

Name of Organization: Carnegie Mellon University Libraries

Type of Organization: Carnegie Mellon University Libraries

Type of Organization - Other: Academic Institution

Role: Other

Role - Other: Librarian

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Any domains within STEM disciplines present at CMU which may use human subjects and collect human data.

1. **Utility and useability of this resource:**

We thank the NIH for giving us the opportunity to respond to this Request for Information. At CMU Libraries, we often work with researchers who are putting together informed consent documents in preparation for review through CMU's Institutional Review Board, so it is incredibly important that we understand the informed consent guidance shared through various funding agencies.

2. **Gaps or additional components that should be included:**

We appreciate that the proposed consent language for future use of data and biospecimens is clear and uses plain language (free of jargon and unclear prose) in regards to the risks and possible benefits of the data producer. Overall, we feel this language is highly effective in conveying the rights of the individual taking part in a study, and we only have minor thoughts for revision to share:

3. **Specific language proposed in the informed consent sample language:**

Under Component 2, Option 1, we would suggest adding the language "If you say 'yes' you can change your mind later (at no consequence to you)" to mirror the language used in informed consent documents approved through an institutional IRB. It may also be useful to explain that if an individual decides to not share their data, does it jeopardize the individual from taking part in future studies. Under Component 4, Risks and Benefits, we suggest adding language that says what actions, if any, the participants have the right to pursue if their data falls into the wrong hands and/or is used in an unintended way, including any legal actions or if legal liability is waived when the participant consents to share their data. We also suggest adding information that describes how the participant will be notified in the instance of their data being misused.

4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/ICAfTSYiiN.pdf

Attachment Description: A written version in letter form of our comments.

Submission ID: 1701

I am responding to this RFI: On behalf of myself

Name: Thomas C. Tucker, PhD, MPH

Name of Organization: University of Kentucky

Type of Organization: Academic Institution

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Cancer Epidemiology

1. **Utility and useability of this resource:**

Requiring informed consent is problematic when using archival tissue (tissue taken in the form of a biopsy or as part of a surgical resection). Requiring informed consent for using these tissues in research projects is not a requirement under the common rule. In fact, under the revised "Common Rule" studies using archival FFPE tissue blocks for research with no patient identifying information is considered exempt or not human subjects research. Drafters of the revised "Common Rule" understood that requiring informed consent will bias the results making the study results unusable and the cost would be so expensive that it could not be done in many situations. Finally, in terms of protecting patients "from undue risk", using archival tissue is very low risk with the potential for significant scientific findings that will help to prevent cancer, find it at an early stage when our treatments are most effective, or lead to new treatments. Requiring informed consent is very short sighted and highly counter productive. Rather than protecting patients, It can easily have the opposite effect by preventing findings that will save lives.

2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**

Requiring informed consent is problematic when using archival tissue (tissue taken in the form of a biopsy or as part of a surgical resection). Requiring informed consent for using these tissues in research projects is not a requirement under the common rule. In fact, under the revised "Common Rule" studies using archival FFPE tissue blocks for research with no patient identifying information is considered exempt or not human subjects research. Drafters of the revised "Common Rule" understood that requiring informed consent will bias the results making the study results unusable and the cost would be so expensive that it could not be done in many situations. Finally, in terms of protecting patients "from undue risk", using archival tissue is very low risk with the potential for significant scientific findings that will help to prevent cancer, find it at an early stage when our treatments are most effective, or lead to new treatments. Requiring informed consent is very short sighted and highly counter productive. Rather than protecting patients, It can easily have the opposite effect by preventing findings that will save lives.

5. **Other considerations relevant to this resource:**

Requiring informed consent is problematic when using archival tissue (tissue taken in the form of a biopsy or as part of a surgical resection). Requiring informed consent for using these tissues in research projects is not a requirement under the common rule. In fact, under the revised "Common Rule" studies using archival FFPE tissue blocks for research with no patient identifying information is considered exempt or not human subjects research. Drafters of the revised "Common Rule" understood that requiring informed consent will bias the results making the study results unusable and the cost would be so expensive that it could not be done in many situations. Finally, in terms of protecting patients "from undue risk", using archival tissue is very low risk with the potential for significant scientific findings that will help to prevent cancer, find it at an early stage when our treatments are most effective, or lead to new treatments. Requiring informed consent is very short sighted and highly counter productive. Rather than protecting patients, It can easily have the opposite effect by preventing findings that will save lives.

Submission ID: 1702

I am responding to this RFI: On behalf of an organization

Name: John J Graff, PhD, MS

Name of Organization: Arbor Research Collaborative for Health

Type of Organization: Arbor Research Collaborative for Health

Type of Organization - Other: Non-Profit Research Organization

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Population-based research in quality of care and outcomes

1. **Utility and useability of this resource:**

We find this resource very helpful and straight forward.

2. **Gaps or additional components that should be included:**

In Component 2 of the resource document, "Voluntary Participation", where it is stated that “If the protocol is a repository with the sole intent of collecting data and/or biospecimens for future use no opt out mechanism is necessary.” We actually recommend still offering the opt out mechanism as a quality assurance practice in our consenting process, so that the prospective participant is given a “second chance” to opt out, if they did not quite, at first review of the consent form, understand that the sharing of data and/or biospecimens were a requirement for participation – therefore making them ineligible.

3. **Specific language proposed in the informed consent sample language:**

We find the specific language to be very helpful.

4. **Hurdles or barriers to wider use of this resource by the community:**

N/A

5. **Other considerations relevant to this resource:**

N/A

Submission ID: 1703

I am responding to this RFI: On behalf of an organization

Name: Bernard Lo and Joshua R. Sanes

Name of Organization: National Academies of Science, Engineering, and Medicine's Committee on Ethical, Legal, and Regulatory Issues Associated with Neural Chimeras and Organoids

Type of Organization: National Academies of Science, Engineering, and Medicine's Committee on Ethical, Legal, and Regulatory Issues Associated with Neural Chimeras and Organoids

Type of Organization - Other: Professional Organization/Association

Role: Other

Role - Other: Committee Co-chairs

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Neural organoids, chimeras, and transplants

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

On behalf of the National Academies of Science, Engineering, and Medicine's Committee on Ethical, Legal, and Regulatory Issues Associated with Neural Chimeras and Organoids, we wish to respond to the Request for Information: Developing Consent Language for Future Use of Data and Biospecimens. Earlier this year Committee issued the consensus peer-reviewed report "The Emerging Field of Human Neural Organoids, Transplants, and Chimeras: Science, Ethics, and Governance" (https://www.nap.edu/read/26078/chapter/1). The study was sponsored by the National Institutes of Health and the Dana Foundation. The Committee found that new models for studying the human brain — human neural organoids, transplants, and chimeras — show promise for advancing understanding of the brain and laying the groundwork for new therapeutic approaches to brain diseases that have so far proved hard to treat. However, this promise must be carefully weighed against the ethical concerns such models may raise. The committee then considered these concerns and made several findings that NIH might consider as it addresses informed consent for data and biospecimen sharing. First, one ethical concern the report identified is whether previously collected and deidentified biological materials should be used for this type of research without the specific consent of the people who originally donated the tissues. Finding III.3: Under Subpart A of the Federal Policy for the Protection of Human Subjects, often called the Common Rule, existing biological materials that have been collected with appropriate consent and deidentified may be used in future research projects. However, provisions of the Common Rule are seen by some as a minimal standard for meeting ethical requirements in this area. For biological materials collected in the past, specific consent for human neural organoid, transplant, and chimera research was generally not obtained. There is active discussion regarding the advantages and disadvantages of obtaining specific consent going forward for the collection of fresh tissue for such research. As a practical matter, recontacting donors to obtain specific consent is sometimes impossible. Moreover, many induced pluripotent stem cell (iPSC) lines obtained from donor tissue have been

extensively characterized or were derived from patients with very rare diseases, and deriving new lines would be extremely difficult in these cases. On the other hand, most donors were not aware that their tissues would be used for neural organoid, cell transplant, or chimera research, and some might have objected if directly asked for their consent for such uses. Past ethics violations during research with African American and Native American participants make this a sensitive topic for these populations. Second, the report found that engaging the public regarding emerging areas of research, such as neural organoid, chimera and transplant research, has several benefits. Finding VI.1: Calls have been increasing for greater public engagement in assessing the value of emerging areas of biomedical research. Such engagement has several benefits, including helping the public understand the research, identifying public concerns, facilitating informed public discussion, and influencing science policy. However, the United States currently lacks robust mechanisms for facilitating this public engagement. Analysis of lessons learned from efforts on related topics could support the design of effective strategies for engaging the public in discussion of human neural organoids, transplants, and chimeras. Finding VI.3: During its meetings and deliberations, the committee appreciated hearing the perspectives of religious scholars of several faith traditions and engaging in discussions with experts in medicine, biology, philosophy, law, theology, religious studies, and other disciplines. These discussions were mutually enlightening and should be continued. Because of the plurality of religious and secular views in the United States, ongoing dialogues between religious and secular perspectives and among different viewpoints are important. There are currently few if any established forums for fostering this exchange. Respectfully submitted, Bernard Lo, M.D. University of California San Francisco Joshua R. Sanes, Ph.D. Harvard University Co-Chairs Committee on Ethical, Legal, and Regulatory Issues Associated with Neural Chimeras and Organoids National Academies of Science, Engineering, and Medicine

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/hhOuiBDcpN.pdf

Attachment Description: Summary of Committee Report

Submission ID: 1704

I am responding to this RFI: On behalf of an organization

Name: Amy Yarnell

Name of Organization: Data Discovery Collaboration

Type of Organization: Data Discovery Collaboration

Type of Organization - Other: Other

Role: Other

Role - Other: Librarian

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Health Sciences, Library and Information Science

1. Utility and useability of this resource:

As members of the Data Discovery Collaboration, we applaud this effort to support researchers in crafting informed consent language that takes data and biospecimen sharing into account. Too often researchers do not start thinking about data sharing until after the informed consent process. This kind of sample language is also requested frequently from libraries and research support offices. The language will be most helpful if coordinating language is developed to meet other NIH requirements, like the upcoming NIH Data Management and Sharing requirements. Having easily accessible language for researchers to reuse about consent in those required Data Management and Sharing Plans would help facilitate use of this informed consent language. It would be helpful to add very clear labeling of each "chunk" of sample language provided in the final resource so that researchers can select the sample language that most closely matches the methods of their study. For example, ideally, sample language that describes the potential risk should be as close to the real risk of the study and not an over- or under-estimate.

2. Gaps or additional components that should be included:

Regarding the recommendation to consider readability of informed consent documents, researchers may want to look to their institutional library, writing center, or related office. These offices may offer services or provide expertise to help edit informed consent documents for clarity and reading level appropriateness. Component 1 indicates a space in the sample language to provide a name for where data or biospecimens are stored, but if it can be done briefly and clearly, the language may also want to indicate the nature of the facility or platform (physical or virtual), and some indication of security measures taken by them.

3. Specific language proposed in the informed consent sample language:

Because research study participants may have different comfort levels with sharing their data as compared to sharing their biospecimens, we propose that these be split apart to empower participants to consent to different practices for each. In addition, sample language should define what is meant by

data and biospecimens. Specifically, we suggest that the sample language be expanded to include definitions for each with space for studies to customize the specific types of data and the specific types of biospecimens that will be collected.

4. Hurdles or barriers to wider use of this resource by the community:

As a means to help the community learn about and use this resource, the NIH should consider integrating it with other NIH resources (e.g., guidance on compliance with the new NIH Data Sharing or Management plans). Additionally, the NIH should consider working with funded coordinating clinical or data centers (e.g., the clinical coordinating center for the PASC study) to help disseminate this suggested language. As these centers coordinate many study sites, they are a resource for disseminating important tools and information. Finally to ensure that the language can be used in all communities, the NIH should provide the language in translation and in ADA compliant formats. As the document and language evolves develop mechanisms to manage and monitor document translations and general accessibility in cases where visual or non-textual tools may be used.

5. Other considerations relevant to this resource:

Document translation & accessibility - Look for ways to automate informed consent documents and integrate with other technologies to simplify access to the information.

Submission ID: 1705

I am responding to this RFI: On behalf of an organization

Name: Anna Shirley

Name of Organization: University of Utah IRB

Type of Organization: University of Utah IRB

Type of Organization - Other: Institutional Research Oversight Committees (e.g. IRB, IBC, IACUC)

Role: Other

Role - Other: IRB Administrator

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/GprwMfhhVl.pdf
Attachment Description: UUIRB Response to NIH Request for Information in Developing Consent Language for Future use of Data and Biospecimens

Submission ID: 1706

I am responding to this RFI: On behalf of myself

Name: Vicki Holmes

Type of Organization: Not Applicable

Role: Member of the Public

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

I would like to know why you do not list Orthostatic Tremor as a disorder in your list . Those of us that have it are desperate for research and information. When the NIH does not list it, it is discouraging.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1707

I am responding to this RFI: On behalf of myself

Type of Organization: Non-Profit Research Organization

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

population genomics

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

If renewable biospecimens will be created such as immortalized cell lines, this information should be specified clearly in the consent language - If induced pluripotent stem cells will be created with the potential to differentiate into a variety of downstream cell types (such as neurons or organoids), this information should be specified clearly in the consent language - If biospecimens and/or data may be shared for research purposes that are more general than the described research study (i.e., general research use), this information should be specified clearly in the consent language

Submission ID: 1708

I am responding to this RFI: On behalf of an organization

Name: Emma A. Meagher, MD

Name of Organization: University of Pennsylvania

Type of Organization: University of Pennsylvania

Type of Organization - Other: Academic Institution

Role: Other

Role - Other: Chief Clinical Research Officer

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/POVHCZZVXk.pdf

Submission ID: 1709

I am responding to this RFI: On behalf of an organization

Name: Kristin H West

Name of Organization: COGR (Council on Governmental Relations)

Type of Organization: COGR (Council on Governmental Relations)

Type of Organization - Other: Industry (Trade Association)

Role: Other

Role - Other: Director, Research Ethics & Compliance

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Academic research

1. **Utility and useability of this resource:**

Please see attached letter for comments.

2. **Gaps or additional components that should be included:**

Please see attached letter for comments.

3. **Specific language proposed in the informed consent sample language:**

Please see attached letter for comments.

4. **Hurdles or barriers to wider use of this resource by the community:**

Please see attached letter for comments.

5. **Other considerations relevant to this resource:**

Please see attached letter for comments.

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/IctyhMNnbe.pdf

Attachment Description: Letter containing comments re. NOT-OD-21-131

Submission ID: 1710

I am responding to this RFI: On behalf of an organization

Name: Marilyn M. Li

Name of Organization: The Children's Hospital of Philadelphia Cancer Center

Type of Organization: The Children's Hospital of Philadelphia Cancer Center

Type of Organization - Other: Academic Institution

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Cancer Genomics and Precision Cancer Care

1. **Utility and useability of this resource:**

This would be helpful to any study team drafting consent forms for their study, or looking to expand their protocol that allow for the sharing of their specimens and data. Additionally, it would be a good resource to existing study teams interested in collaborating with the NIH and looking for guidance on traditional consent language allowable for open sharing of data and specimens.

2. **Gaps or additional components that should be included:**

To keep with language at an 8th grade comprehension level, it would be helpful to ensure definitions or examples are provided for some of the terms used in the consent language. For example, providing a definition or examples by what is meant by “commercial entities”, “commercial value”, “your data”, “your biospecimens” would be helpful for readers.

3. **Specific language proposed in the informed consent sample language:**

Consider modify “your data and biospecimen” to “your (or your child’s) data and biospecimen”, or specify at the beginning that “you” includes “your child”.

4. **Hurdles or barriers to wider use of this resource by the community:**

As noted, there may be institutional or state guidelines that bar this resource from being used universally by study teams, especially for those planning to include vulnerable populations. Additionally, review and completion of “Voluntary Participation” language by subjects during the consent meeting introduces opportunities for error. It would be helpful to provide guidance to those using this resource on where this would be best implemented in the consent form.

5. **Other considerations relevant to this resource:**

Though not directly related to informed consent language, it may be helpful to provide guidance to study teams on receiving and subsequent sharing of biospecimens and data that have been transferred to the protocol under the following conditions: a) Identifiable data and specimens that were collected

under an IRB-approved protocol and the subject consented to permit storage and sharing of specimens and data for future use consistent with the objectives of this protocol b) Identifiable data and specimens to which the IRB has issued a waiver of informed consent and authorization for release and use of the specimens and data for a specific Collection Protocol; c) The specimens and data are de-identified (contain no PHI)

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/QshIAbIVHr.pdf

Attachment Description: Consent Form

Submission ID: 1711

I am responding to this RFI: On behalf of an organization

Name: Julian Arbuckle

Name of Organization: Industry Pharmacogenomics Working Group

Type of Organization: Industry Pharmacogenomics Working Group

Type of Organization - Other: Industry (Trade Association)

Role: Other

Role - Other: President

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Application of pharmacogenomics in drug development

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/jWYMCuoMNO.pdf

Submission ID: 1712

I am responding to this RFI: On behalf of an organization

Name: Piper Mullins

Name of Organization: International Society for Biological and Environmental Repositories

Type of Organization: International Society for Biological and Environmental Repositories

Type of Organization - Other: Professional Organization/Association

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Biorepository and biospecimen research

1. **Utility and useability of this resource:**

Please see attached pdf.

2. **Gaps or additional components that should be included:**

Please see attached pdf.

3. **Specific language proposed in the informed consent sample language:**

Please see attached pdf.

4. **Hurdles or barriers to wider use of this resource by the community:**

Please see attached pdf.

5. **Other considerations relevant to this resource:**

Please see attached pdf.

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/vErxEGYlOV.pdf

Attachment Description: General and specific comments from the International Society for Biological and Environmental Repositories

Submission ID: 1713

I am responding to this RFI: On behalf of myself

Name: Nat Jones

Name of Organization: USF Health Morsani COM

Type of Organization: Academic Institution

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Cancer epidemiology

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**

Would recommend defining what a biospecimen/biobank is at the beginning of the form, as this is jargon that may not be understood well by patients. For example, "A biospecimen is a tiny piece of tissue taken from your body. Biospecimens are stored in large collections, called biobanks, which are basically libraries of tissue that can be used for research."

4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1714

I am responding to this RFI: On behalf of an organization

Name: JOSEPH LESNY

Name of Organization: University of Colorado, Colorado Center for Personalized Medicine

Type of Organization: University of Colorado, Colorado Center for Personalized Medicine

Type of Organization - Other: Professional Organization/Association

Role: Institutional Research Oversight Committee Member

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Genetic research

1. **Utility and useability of this resource:**

The CCPM Biobank allows for over 80,000 samples, and data generated from those samples, to be shared for genetic research. We also offer the opportunity for Biobank participants to receive the the possible results of the genetic research that utilized their donated sample.

2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**

We are asking you to participate in the Colorado Center for Personalized Medicine (CCPM) Biobank research program, at the University of Colorado. The purpose of the Biobank is to collect and store biological samples, conduct research and clinical testing on those samples, collect and store medical information, and make the samples and data available for reporting clinical genetic test results and future research. Researchers and clinicians will use the data and samples to learn how differences among people, such as in their genetic information, affect health, and risk of disease. When studying your samples and information, the Biobank will also perform some clinical genetic tests that could result in information that may be directly relevant to your health. The primary benefit of participating in the Biobank is to help future research into the causes of health and disease. The primary risk of participation are concerns from finding out something medically relevant about yourself. Participation in the Biobank research program is completely up to you. If you decide not to participate, your decision will not affect your healthcare in any way. Your alternative is not to participate in the program. What is Genetic Research? Genetic research means we will study your DNA. We will get your DNA from your biological sample. DNA carries genetic information that is the "instruction book" for the cells in your body and determines what color skin, hair, and eyes you have, and influences health and disease. When we do genetic research, we may only look at small parts of your DNA, or we may look at all of your genetic information, known as your genome. What are Clinical Genetic Tests? Clinical Genetic tests are also known as DNA tests. These tests may: • Predict your risk of diseases such as some cancers, heart diseases, and muscle diseases. • Predict how you respond to medications. This may help a healthcare provider understand if you need a different medication or a different dose of a medication. • Identify you as being a ‘carrier’ for a disease. Carriers usually remain healthy and do not develop disease but there may be a higher risk of a genetic disease in their blood relatives including their children. Potential

Benefits We plan to study the information and samples in the Biobank for years to come. We hope our research will find better ways to predict, prevent, diagnose, or treat disease in the future. If we find information in your biological sample that is directly relevant to your health, we may return the result to your UCHealth electronic medical record. In some circumstances, we may contact you about your clinical genetic test results before placing them in your UCHealth electronic medical record. Will I be tested for all possible genetic conditions, risks, and responses to medications? No, the Biobank will only complete limited clinical testing on some selected genetic conditions, risks, and responses to medications. Over time, the number of Biobank tests may increase. The Biobank clinical genetic test results are NOT intended to be comprehensive or a substitute for a visit to a geneticist, genetic counselor, or healthcare provider. If you have symptoms or concerns about a genetic condition in you or your family, you should talk to a healthcare provider. When will I receive my clinical genetic test results? Testing your Biobank sample may not be finished quickly, and it could be months or even years before a clinical genetic test result is available. If you do NOT hear from the Biobank about test results, you may still be at risk of getting some diseases or having adverse responses to medications. You should continue to receive healthcare from your healthcare provider as you would normally do. How will I receive my clinical genetic test results? Clinical genetic test results about your responses to medications will be placed directly into your UCHealth electronic medical record. For test results about your risk for most other health problems, we will reach out to you to confirm that you want the result. If you agree, then the result will be placed in your UCHealth electronic medical record. We will help you to understand what the results mean for your health and what you may want to do about this information. Further information about the process for returning clinical genetic test results can be found on our website, cobiobank.org To generate your clinical genetic test results a test order must be placed by a physician. This physician is referred to as the “ordering provider.” The ordering of the test does not create a physician-patient relationship between you and the ordering provider. The ordering provider will not communicate the test results to you, or your healthcare provider(s), and you are solely responsible for reviewing your UCHealth My Health Connection account for Biobank clinical genetic test results. Any questions regarding your Biobank clinical genetic test results should be directed to your treating physician or healthcare providers. If you had a specific type of bone marrow transplant prior to donating a biological specimen to the Biobank, our clinical genetic test results may not reflect your own genetic makeup. The Biobank will not return clinical genetic test results to you if we find evidence in your medical record of an allogeneic bone marrow transplant. Will my clinical genetic test results affect my biological relatives? Your clinical genetic test results could contain information that may be important to your parents, your children, your siblings, and/or other relatives. You may need to discuss your results with a healthcare provider to decide if you should share your clinical genetic test results with family members. If we discover clinical genetic information after your death that might be important to the health of your family, we will try to reach one or more contacts listed in your UCHealth electronic medical record. If we are able to contact one of your family members, we will let that individual know that we have information that may be medically important to your family.

4. Hurdles or barriers to wider use of this resource by the community:

We have a limitation of only being able to collect samples from UCHealth patients as our main source of sample collection comes from a lab visit for a clinical blood draw.

5. Other considerations relevant to this resource:

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/ySgniBZuOM.pdf

Attachment Description: CCPM Biobank Consent Form

Submission ID: 1715

I am responding to this RFI: On behalf of an organization

Name: Lyndsey Buckner Baiamonte

Name of Organization: Ochsner Health

Type of Organization: Ochsner Health

Type of Organization - Other: Non-Profit Research Organization

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Biospecimen research, Clinical Trials, Oncology, Cardiology, Neurology, Multispecialty, Pediatrics, Women's Health, Infectious Disease

1. Utility and useability of this resource:

If this resource were widely marketed and provided to all researchers in a broad and informative way, it could ensure that patients are truly informed before consenting to a biospecimen collection study in a consistent and standardized manner.

2. Gaps or additional components that should be included:

Perhaps it should be considered that some communities may still have reading level that is below 8th grade. We write our forms to be approximately a 6th grade reading level.

3. Specific language proposed in the informed consent sample language:

Points of consider for the informed consent language for biospecimen collection may want to include the following information as well: 1) The different researchers that may utilize the specimens should be included, eg industry sponsors, academic researchers, etc. This should also include language that biospecimens may be shared with industry or sponsored researchers for compensation that covers the cost of collection. 2) The types of biospecimens being collected and brief descriptions. We have a list of potential specimens that can be initialed to indicate which are being collected for a particular patient. The patient has the ability to provide what they wish and initial appropriately. 3) The specimens may be utilized for research studies that evaluate genomics. Language pertaining to the GINA federal laws governing how genomic data won't affect health insurance or employment status, but may affect life insurance as things currently stand. 4) The specimen collection process will NOT interfere with standard clinical care for the patient. It is important to have language for patients to know that there is no hinderance of their medical care if they choose not to participate in a study. 5) Language should be included to indicate if specimens are surplus, collected along side standard-of-care procedures or whether they are research-only specimens collected with approval from appropriate medical physicians. For example, our tissue collection studies MUST have pre-approval or real-time approval from a pathologist to evaluate the release for research so as not to interfere with assessment for diagnosis or prognosis of a patient. 6) Language about stipends should be included and perhaps should be flexible in

the event that it is appropriate to compensate for a patient's extra time spent in providing specimens for research. This could be unexpected travel, etc.

4. Hurdles or barriers to wider use of this resource by the community:

I think the biggest hurdle will be informing the community that it exists for their use to design study documents appropriately.

5. Other considerations relevant to this resource:

I think one thing that should be considered as a whole, not just for this resource, but the capacity to provide different consent mechanisms. For instance, in-person, paper consents have been the gold standard. Many have moved on to electronic consents on devices, which is helpful for appropriate data collection directly uploading completed documents to an electronic medical record. In addition, it should be considered how consents could be performed verbally in-person as well as over the phone. In the era of COVID, these consent mechanisms have proven useful and efficient in addition to being safer for all parties involved. Having language for a verbal conversation for this purpose, may also be helpful as a resource.

Submission ID: 1716

I am responding to this RFI: On behalf of an organization

Name: Research Data Services & Research Service Coordinators Teams

Name of Organization: University of Minnesota Libraries Group

Type of Organization: University of Minnesota Libraries Group

Type of Organization - Other: Academic Institution

Role: Other

Role - Other: Librarians & Research Managers

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Academic institutional repository & research support group

1. Utility and useability of this resource:

Overall, we are very glad to see this guidance coming from NIH and we recognize that consent language for data sharing and biospecimens is a challenging area, for researchers, funders, and regulatory bodies.

2. Gaps or additional components that should be included:

This guidance seems out of sync with the data management and sharing guidance taking place in 2023. If NIH is mandating the sharing of data, they should take a stronger stance on encouraging researchers to INFORM their participants that their data or biospecimens will be shared. At the very least, this should be strongly encouraged. It should also be mentioned that several repositories that take in NIH data require non-restrictive consent language. For reference, the Final NIH Policy for Data Management and Sharing defines data sharing as "[t]he act of making scientific data available for use by others (e.g., the larger research community, institutions, the broader public), for example, via an established repository." There should also be a general notice that the language suggested here is designed for researchers who plan to share data in a limited access repository or in some other access-mediated way, not for those who plan to make their data publicly available. We would like to see language options for public or more open-access repositories as options in this document. Our perspective is that of an open access repository that ingests human participant data. The guidance recommended in this proposal does not support sharing in our repository.

3. Specific language proposed in the informed consent sample language:

IRBs need to be trained on data sharing and best practices. IRB responses to questions about data sharing in the absence of informed data sharing consent may not always align with the best ethical practices. Encourage giving specific examples of who explicitly should serve as "contacts" for questions of vulnerable populations and cultural/donor/sovereign groups. Unclear if this means community groups, IRB/national offices, or other institutional groups (data repositories, HIPCO offices, etc). Also clarify when these consultations should be occurring - before data collection? Only when storing/sharing? Both? Need to define what "limited" sharing might mean. Does this mean in terms of

restricted access to data by researchers? That researchers might approve of data sharing for only certain uses? Maintained for a certain amount of time? Referring to "approval" in terms of who has access to the data: much of the proposed language here refers to a managed, restricted access repository, rather than a public-access repository. Institutional repositories, used frequently by academia, are often completely open access. This will impact the language that is used and what participants need to be told. Need to expand on and be more specific about the "technology advances and de-identification" to include consideration of the fact technologies for re-identification are also improving, and that de-identification methods that "worked" at one time with one dataset may not be effective in the future and as more datasets are made available. Give suggestions or language on how researchers can make participants aware of the fact that things may not be perfectly "de-identified" Be specific about who has "permission" to access the "code key" to the data - research team and those who have been granted access to the data. Regarding "If the research protocol offers no prospect of direct benefit, then it may be reasonable for storage and sharing not to be optional," does not need to be all or nothing. Maybe this is a matter of wording: "If the research protocol offers a direct benefit, then data storage and sharing should be optional." Is this sentence even necessary? We encourage consent language that explicitly states data will be shared. Regarding "If the protocol is a repository protocol with the sole intent of collecting data and/or biospecimens for future use, no opt out mechanism is necessary," It's not 100% clear if "opt out" means opting out of the study or opting out of data sharing. If it means opting out of data sharing, repository protocol could be better defined - for example, an institutional repository often has the sole intent of collecting data for future use, but that doesn't mean participants shouldn't be able to opt out of sharing their data. In fact, it's perhaps even riskier given the open nature of most institutional repositories. Repository protocol is overall a vague term - we are unsure what, exactly, is meant. An operational definition of repository protocol, including reference to existing standards (such as ISO OAIS model, TDR, or Coretrustseal), should be provided in order to clarify.

4. Hurdles or barriers to wider use of this resource by the community:

See "Gaps or additional components" above.

Other considerations relevant to this resource:

It would also be helpful to provide guidance for researchers on how to choose the type of access (or repository, if applicable) appropriate for their data and how to determine the best language to inform participants of the way their data will be shared. We would also like to see explicit mention of when these decisions about data sharing should be made, and encourage researchers to make them BEFORE submitting IRB protocols. We suggest explicitly pointing to existing materials such as the Supplemental Information to the NIH Policy for Data Management and Sharing: Selecting a Repository for Data Resulting from NIH-Supported Research (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-016.html) Consider recommending to research teams that they educate research participants about data sharing beyond the consent form, highlighting benefits for science, openness, and transparency that come with researchers making the data from their studies available to others. UMN data sharing information template as an example (https://docs.google.com/document/d/19GuL5TJCDx3DiU59kWmiTh_E64O1pSZ40uCQvyBW0Ns/edit?usp=sharing) This may also have alignment with NIH's recently released strategic plan, which emphasizes the importance of data sharing, transparency, public engagement, and encouraging participation of

underrepresented groups in clinical trials. Public education and outreach to participants are mechanisms by which those goals can be operationalized within a single study.

Submission ID: 1717

I am responding to this RFI: On behalf of an organization

Name: Margaret Levenstein

Name of Organization: ICPSR

Type of Organization: ICPSR

Type of Organization - Other: Academic Institution

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/mkJlmJEyTR.pdf

Submission ID: 1718

I am responding to this RFI: On behalf of an organization

Name: Mina Ostovari

Name of Organization: ChristianaCare Health Services Inc.

Type of Organization: ChristianaCare Health Services Inc.

Type of Organization - Other: Other

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Health disparities

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

In this example of a consent form, there is no guidance on how participants may be contacted to provide new data or biospecimens. Providing sample language that describes how to reconnect with participants including an explanation about whether they should complete a new consent form or if the current form covers any future submissions of data or biospecimens will be useful. In addition, there is no specific language about contacting participants later to share the study findings or any published work. A bracketed section in the form for investigators to fill such information if it applies to their specific study should be added.

3. **Specific language proposed in the informed consent sample language:**

Overall, the language used in this sample is adequate with a few exceptions that can be improved upon. In the sample language section, component one: it would be useful to have a brief definition or sample language defining what data and biospecimens mean, preferably with examples. Researchers are familiar with these terms; however, participants should not be expected to know definitions of such terms. As these elements could vary between studies, maybe add a bracketed section where the investigators can plug in some language about the specific data and biospecimens they plan to collect. Another example of the language that might be unclear for the participants is this phrase: “commercial entities”. Maybe add a bracket so investigators would write the definition with specific examples of what it could be for their study. In component 2, option 1, there is this explanation: “It is your choice whether or not to let researchers share your data and biospecimens for research in the future. If you say “yes,” you can change your mind later, but your data and biospecimens might still be used if they have already been shared”. The way the participants choice is explained is unclear. It implies that if the participant changes their mind that would not have any impact at all and their data and biospecimens could still be used. Some more explanation would be useful here for justification. It would make more sense if component 3 on the discontinuation precedes components 2, as it provides additional information that the participant should have before they say yes or no to allowing their data to be used in other studies. Here is a suggestion for sample language to help clarify the explanation about the data collection and future use: “This study is collecting data and biospecimens from you. Although the data is

being collected specifically for our study, in order to advance health sciences, we will be adding your data, not your identity, to a data set such that other researchers and institutions can advance healthcare and understanding of diseases". To reduce the wordiness of the discontinuation or withdrawal section maybe consider making some changes for example: "You have the right to withdraw from the study at any time simply by informing a study team member. If you choose to withdraw your data and biospecimens will be removed from the study going forward. In the case where your de-identified data is already being used, it will continue to be used."

4. **Hurdles or barriers to wider use of this resource by the community:**

5. **Other considerations relevant to this resource:**

Submission ID: 1719

I am responding to this RFI: On behalf of an organization

Name: Nathalia Henry Whitely

Name of Organization: Northwestern University

Type of Organization: Northwestern University

Type of Organization - Other: Academic Institution

Role: Other

Role - Other: IRB/HRPP Leadership

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**

Overall guidance is of utility and usability for the target IRB audience and for institutions/IRBs of all sizes and variable research focus areas. Such guidance serves to inform on both the educational as well as operational fronts. In addition, a resource such as this serves to inform agencies, foundations and commercial sponsors.

2. **Gaps or additional components that should be included:**

Consider including language to address what should be disclosed to a participant if a departure of the PI occurs. Another often unaddressed issue is disclosure of the custodian of research data and biospecimens after a study is closed at IRB, but the storage of research data and biospecimens continues. Sharing of genetic data implications (risks, data sharing with NIH, etc.), if data includes identifiable biospecimens, whether future research may include whole genome sequencing.

3. **Specific language proposed in the informed consent sample language:**

Informed Consent sample language is proposed in the attached document as track change suggested edits to consider.

4. **Hurdles or barriers to wider use of this resource by the community:**

Hurdles or barriers to wider use of this resource by the community might include certified translations of the document in the major languages used in the U.S.

5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/sBTIlkMgWm.pdf

Attachment Description: Consent language suggested edits with tracked changes

Submission ID: 1720

I am responding to this RFI: On behalf of an organization

Name: Dominique Pichard

Name of Organization: International Rett Syndrome Foundatoin

Type of Organization: International Rett Syndrome Foundatoin

Type of Organization - Other: Research Participant/Patient Advocacy Organization

Role: Other

Role - Other: Chief Science Officer

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Neurodevelopmental disorders, rare disease, genetics and genomics research

1. Utility and useability of this resource:

Responding on behalf of a Foundation for a rare genetic neurodevelopmental disorder, we strongly support this effort by NIH to develop sample language for informed consent for data and biospecimen storage and sharing. This effort is especially critical to support the storage and sharing of data and biospecimens in the realm of rare disorders. By definition, data and specimens pertaining to individuals with rare disorders are rare and thus, extremely valuable and critical to advance knowledge and support research to enhance diagnosis and treatment. Having sample language available for informed consent documents that incorporates relevant principles of ethical research conduct using sample language at the appropriate reading level should broaden participation from research sites with limited prior experience in rare diseases. This effort will facilitate an expansion of the data collection network in rare disorders.

2. Gaps or additional components that should be included:

It would be helpful to have sample language for assent of an able minor. Re-contacting of individual/family is mentioned in Component 1 in the context of additional data gathering. It would be helpful to also include guidance or sample language regarding the option of re-contacting an individual/family if future research identifies a significant health risk or significant secondary finding based on banked specimens. Should this be an opt in or opt out option?

3. Specific language proposed in the informed consent sample language:

In Component 1: in the first paragraph, it specifies that studies may be done by researchers at other institutions. To cover research projects performed at the enrolling site, it may be helpful to reword: “These studies may be done by researchers at this institution or other institutions including commercial entities.” In Component 4: In the sample language for benefits, consider changing the word “will” to “may”: [Benefits] You may not receive any direct benefit from sharing your data and biospecimens. However, sharing your data and biospecimens may contribute to research that helps others in the future.

4. Hurdles or barriers to wider use of this resource by the community:

We anticipate the only barrier to wider use of this resource will be awareness of its availability. Hopefully, this resource will be well promoted by NIH so that many of the barriers will be overcome. This resource will need to be shared widely and actively promoted. IRBs or researchers at institutions with established informed consent language may be less likely to utilize this resource.

5. Other considerations relevant to this resource:

Submission ID: 1721

I am responding to this RFI: On behalf of an organization

Name: Christine Suver

Name of Organization: Sage Bionetworks

Type of Organization: Sage Bionetworks

Type of Organization - Other: Non-Profit Research Organization

Role: Other

Role - Other: Research Governance & Ethics

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

All of them!

1. Utility and useability of this resource:

We would like to commend the NIH for undertaking this important initiative. This resource will help harmonize consent best practices across the biomedical research ecosystem if done thoughtfully and carefully. In particular, using consistent language to describe core concepts about future use of data and biospecimens (so long as they are accurate, comprehensive, and relevant) will be a step forward for participants, helping to improve the comprehensibility of the terms of research informed consents generally. Just as the Federal Demonstration Partnership has provided well-vetted language that institutions are comfortable using to streamline data-sharing agreements, this resource has the potential to provide a streamlined and well-accepted standard that will be widely used across the research community. However, it must be vetted by IRBs, participant communities, and researchers for this to be adopted broadly. To this end, further information about how the language for this resource has been tested with participant audiences would be helpful for those using the resource to feel confident in its value. For the resource to have maximal impact, there will need to be a better delineation between language that is best left unaltered, and language that could (or should) be supplemented with more contextual information. Consider making core, unalterable concepts that can not be edited. On the other end of the spectrum, for sections where it is known that there will likely be study-specific alterations needed, the instruction of “Adjust language as needed” might not provide enough guidance. A selection of language options that accommodate different scenarios may improve the utility of the resource. Additionally, we recommend considering alternative communication methods (iconography, privacy labels, videos, etc.) in addition to text explanations. Moving beyond text-heavy, informed consent will broaden the accessibility and comprehensibility of the content, consistent with our ethical obligations for truly informing our participants.

2. Gaps or additional components that should be included:

Component 4: Risk of reidentification must be more transparently and specifically addressed, including the consequences of this risk (regardless of its likelihood) Topics that should be considered as new sections or inclusions in current sections: - Alternatives to participation - Return of information and the

right not to know - Data licensing - Certificates of Confidentiality - Mandated reporting of research data (e.g., public health, abuse, etc.) - Familial consent (given the nature of genomic data from the use of biospecimens)

3. Specific language proposed in the informed consent sample language:

See below for several proposed language modifications: Component 1, Option 1: the phrase "The code key will be kept in a locked location separate from your information," should be redacted or modified to reflect the current state of best practices. This is an inaccurate statement in the era of cloud computing. Something like: "The key linking your identity from the rest of your data will be kept in a separate secure location." Component 1, Option 2: we express concern that this sentence is misleading, "Investigators cannot link your identifying information to the data and biospecimens." While investigators can not link the identifying information held by the study team to the data and biospecimens, participants can still be reidentified using other means; this point should not be obfuscated. Component 2, Option 1: There are more choices than just yes/no. For example, one alternative option could be "contact me." The options presented might depend on the nature of the data, the nature of the community from which the data are collected, etc. More nuance is needed here. Component 2: we appreciate that the examples given are opt-in, and we strongly recommend eliminating the "opt-out" option throughout informed consent documents. Participant choice should be explicit rather than implied. Explicit consent should be the standard for all research, consistent with the ethical principles that underlie voluntary participation. Component 3: this language will be very hard to operationalize and should be reconsidered, "We will do our best to retrieve all your data and biospecimens that have already been shared, but it may not be possible. For example, suppose some research with your data and biospecimens has already started. In that case, the information from that research may still be used." What do we mean when we say "do our best"? What is the standard for "doing our best" in this regard? What do participants think "doing our best" means? Component 5: should be opt-in. [see the note above] Component 5: must also be more clear and simplified for easier readability. Replace "The use of your data and biospecimens may lead to new tests, drugs, devices, or other products or services with commercial value." with "Your data or biospecimens may be used to make products or services." Replace "These products or services could be patented and licensed." with "You will not own these products or services." Replace "There are no plans to provide any payment to you should this occur." with "You will not receive any payments." or "You will not receive any money from this."

4. Hurdles or barriers to wider use of this resource by the community:

Based on our experience with the All of Us Research Program's informed consent development process (documented here: https://pubmed.ncbi.nlm.nih.gov/30963079/), we have a few learnings that may be relevant to this resource. In particular, one key challenge we found was that institutions and IRBs had specific language that they wanted to include in the informed consent process that was not based on state or federal law and was not necessarily informing to participants. This guideline should directly address the need to step away from arguably spurious institution-specific language that is perceived to lessen the legal liability of the institution. Other potential barriers to broader use include the need to comply with emerging digital privacy laws (at the state level) as well as demonstrated acceptance from IRBs, participant communities, and researchers, as outlined in the first section of this response.

5. Other considerations relevant to this resource:

Consider including a glossary of terms. - In addition to reading level/grade level, additional readability metrics should be addressed to maximize comprehensibility, for example, Reading Ease, percent of passive sentences, and sentence, paragraph, and document length. - Consider reviewing the following resources: The Global Alliance for Genomics and Health's recent informed consent clause catalog is archived here: https://www.ga4gh.org/genomic-data-toolkit/regulatory-ethics-toolkit/ . See especially: Consent Policy, Consent Clauses for Genomic Research, Familial Consent Clauses, Machine Readable Consent Guidance, Model consent clauses for rare disease research, Sage Bionetworks' best practices in informed consent: https://sagebionetworks.org/tools_resources/elements-of-informed-consent/

Submission ID: 1722

I am responding to this RFI: On behalf of myself

Name: Allyson Rosen

Name of Organization: Palo Alto VA

Type of Organization: Government Agency

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

cognitive neuroscience of aging and dementia

1. **Utility and useability of this resource:**

Thank you so much for crafting language for consent! Having this language will make me more comfortable incorporating biomarkers and genetics in my protocol.

2. **Gaps or additional components that should be included:**

IF feasible you might want to allow researchers to indicate if people will be informed if new treatments or diagnostic tests become available. This would be a real incentive for donating. Also, I think that legally you can not patent biological materials so it might be wise to mention this under the profit issue. What you can patent what is derived from these materials. I wonder if this might be reassuring. It is also worth confirming this.

3. **Specific language proposed in the informed consent sample language:**

Language is great

4. **Hurdles or barriers to wider use of this resource by the community:**

I don't see any other than it might be good if investigators could be given options of where to store their data that NIH provides.

5. **Other considerations relevant to this resource:**

Having this approach to crafting template language and such widespread vetting throughout the country is SO powerful!!! Thank you for taking this on!!!

Submission ID: 1723

I am responding to this RFI: On behalf of an organization

Name: Barbara E. Bierer, MD

Name of Organization: Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard

Type of Organization: Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard

Type of Organization - Other: Academic Institution

Role: Other

Role - Other: Faculty Director and Professor of Medicine

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

The integrity, safety, and rigor of global clinical trials

1. **Utility and useability of this resource:**

please see attached

2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/ILmrXQjYTn.pdf

Attachment Description: Responses to questions posed.

Submission ID: 1724

I am responding to this RFI: On behalf of an organization

Name: Shana Dodge

Name of Organization: The Association for Frontotemporal Degeneration

Type of Organization: The Association for Frontotemporal Degeneration

Type of Organization - Other: Research Participant/Patient Advocacy Organization

Role: Other

Role - Other: Director of Research Engagement

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Frontotemporal Degeneration

1. Utility and useability of this resource:

The Association for Frontotemporal Degeneration (AFTD) supports the initiative to standardize and disseminate template consent language for future use of biospecimens and data. Data sharing presents opportunities to maximize data efficiency and impact which ultimately reduces redundancy and delays in developing effective interventions. In the approximately 7,000 rare diseases (which collectively impact 25-30 million Americans), there is data paucity and often a lack of FDA approved therapies. Therefore, data sharing is essential to address the unmet medical needs and research questions, big and small, of millions. Data sharing and access is one of the primary concerns of researchers. This is particularly true in rare diseases where data and biospecimens are relatively hard to obtain. Concurrently, Alzheimer's Disease research participants and their loved ones were shocked and angered to learn their data was not being shared beyond the initial study in which they were consented [(Hake, A. M., Dacks, P. A., Arnerić, S. P., & CAMD ICF working group. (2017). Concise informed consent to increase data and biospecimen access may accelerate innovative Alzheimer's disease treatments. Alzheimer's & Dementia: Translational Research & Clinical Interventions, 3(4), 536-541)]. While persons diagnosed with frontotemporal degeneration (FTD) and their loved ones have not been polled, it stands to reason that other populations of adult-onset, progressive, fatal neurodegenerative disorders would also want to ensure their samples are being fully used. In diseases like FTD that are rare, hard to diagnose, and lack FDA approved treatments, people diagnosed and family members may be even more concerned about samples being maximally utilized. Both of these key stakeholders groups – researchers and research participants – are seemingly aligned in wanting increased data sharing beyond the life of a single research study. Patient advocacy organizations, such as AFTD, would greatly benefit from sample language that could be shared with our academic and industry research partners. Sample informed consent language around data sharing coming from the NIH would also reassure Institutional Review Boards and help guarantee these oversight bodies and the informed consent process do not stand as barriers to sharing.

2. Gaps or additional components that should be included:

Additional components AFTD suggests addressing: Explicit consent language surrounding whether data/biospecimens can be sold. The specific groups biospecimens might be shared with (health authorities, IRBs, etc.). While there are safeguards in place, anonymity cannot be absolutely guaranteed. Clarification that individuals will not be notified when samples are shared and/or destroyed.

3. Specific language proposed in the informed consent sample language:

Per the Flesch-Kincaid formula, the proposed language is estimated to be at about an 11th grade reading level. We suggest using simpler language and/or defining words that are not commonly used (e.g., "biospecimens, "commercial entities"). Hake and colleagues published proposed sample informed consent addendum language to ensure future data and sampling that may be used as a reference (Hake et al., 2017). We suggest aligning language with General Data Protection Regulation (GDPR) language to facilitate international data sharing. Regarding the proposed language "These products or services could be patented and licensed. There are no plans to provide any payment to you should this occur." We suggest including additional verbiage on the fact that the participant will not be entitled to payment and the reasons why (e.g., the process is lengthy, there is a high degree of risk for the developers).

4. Hurdles or barriers to wider use of this resource by the community:

It is important to involve the specific community being targeted by the research study and to not make assumptions about what people want or need to hear. Researchers should anticipate cultural differences across disorders, geographic areas, demographic factors, and other variables. Shah and colleagues, for example, found a significant association between country of origin and perspectives on data sharing [Shah, N., Coathup, V., Teare, H., Forgie, I., Giordano, G. N., Hansen, T. H., ... & Kaye, J. (2019). Motivations for data sharing—views of research participants from four European countries: a DIRECT study. European Journal of Human Genetics, 27(5), 721-729.]. While template language is needed and encouraged, we advocate for researchers, whenever possible, to survey their specific targeted population to better understand their concerns and values with respect to biospecimen data sharing. For adult-onset neurodegenerative disease, such as FTD, researchers will also need to address assessing capacity for consent and include language that is broad enough to endure beyond a loss of ability to consent [Thorogood, A., Mäki-Petäjä-Leinonen, A., Brodaty, H., Dalpé, G., Gastmans, C., Gauthier, S., ... & Team, D. T. (2018). Consent recommendations for research and international data sharing involving persons with dementia. Alzheimer's & Dementia, 14(10), 1334-1343.].

5. Other considerations relevant to this resource:

Submission ID: 1725

I am responding to this RFI: On behalf of an organization

Name: Kelsey Dillehay McKillip

Name of Organization: American Society for Investigative Pathology

Type of Organization: American Society for Investigative Pathology

Type of Organization - Other: Professional Organization/Association

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Pathology

6. **Utility and useability of this resource:**

We commend the Office of the Director for developing sample informed consent language for the future research use and sharing of data and biospecimens. The instructions for use are clear and concise. There is appropriate acknowledgement of the additional considerations required for vulnerable populations and culturally diverse populations. This resource will serve as a useful guide for both the research community and IRBs. This resource will also encourage clear and efficient communication with potential research participants facilitating both individual autonomy and promoting trust in the biomedical research enterprise.

7. **Gaps or additional components that should be included:**
8. **Specific language proposed in the informed consent sample language:**
9. **Hurdles or barriers to wider use of this resource by the community:**
10. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/RFtisogqwp.pdf

Submission ID: 1726

I am responding to this RFI: On behalf of an organization

Name: Victoria Yorke-Edwards

Name of Organization: MRC Clinical Trials Unit at University College London

Type of Organization: MRC Clinical Trials Unit at University College London

Type of Organization - Other: Academic Institution

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Clinical Trials and their underpinning methodology

1. **Utility and useability of this resource:**

We are pleased to see the interest of the NIH in providing guidance and sample language for use in informed consent for data and biospecimen sharing. This is an area that is fraught with difficulty, and the provision of resources in this area could really help the community to ensure that research participants are appropriately asked for consent, and that that consent is adequate.

2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**

We had a number of concerns about the readability of the informed consent sample language, which did not always seemed to be written with patients/ participants in mind. Where language is unfamiliar or complex it detracts from the ability of participants to give informed consent, as they may not feel they adequately understand what they are signing. Below we have pulled out some specific examples: - The word 'biospecimens' is unlikely to be familiar to participants. It is complex and not in common use, so would need at minimum an explanation/ definition, and preferably should be replaced with a simpler word/s, such as 'samples' - The word 'entities' is also unlikely to be familiar and is not plain language. We would suggest 'organisations' would be a more widely used alternative. - The word 'investigators' may be confusing and can sound like a reference to the police. We suggest that 'researchers' might be more appropriate. - Again, to simplify the language we would suggest replacing 'participate' with 'take part in' and 'participating' with 'taking part in'. Although the General Points to Consider section does state that the sample language was developed with a goal of 8th grade reading level or below we would suggest that not all of these words are familiar (a substantial number of people have a reading age lower than this), or that they can have differing meanings to different communities (see our comment on investigators above).

4. **Hurdles or barriers to wider use of this resource by the community:**

5. **Other considerations relevant to this resource:**

Submission ID: 1727

I am responding to this RFI: On behalf of an organization

Name: Brock Sullivan

Name of Organization: Arkansas HIV Reform Initiative

Type of Organization: Arkansas HIV Reform Initiative

Type of Organization - Other: Foundation

Role: Member of the Public

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Patients and other participants in biomedical or public health research might think twice about whether their safety, privacy, and bodily autonomy are protected if information used for research is not obtained with their full informed consent. People living with HIV (PLHIV) have been confronted as vectors for disease for decades, and are at risk of being subject to criminal and immigration proceedings largely because of their health status. However, the issue isn't a hostile criminal justice system alone, since federal, state and local governments have proceeded with a molecular HIV surveillance (MHS) program despite an abundance of community concern. I believe it is clear that MHS is public health research and that informed consent requirements should extend to HIV-testing related data collected in the administration of direct care but then used for future research and analysis. PLHIV have the right to know when and how their private medical data is used, to consent to such usage, and to opt out of future usage at any time. NIH can and should work together with government agencies, community organizations, PLHIV, and advocates to enshrine better protections for collected data used in public health research. NIH must also implement the tools necessary to require informed consent for all future use of collected data, and respect the rights of PLHIV to opt-out of future use of their data for research.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/QhJnQddFZO.pdf

Submission ID: 1728

I am responding to this RFI: On behalf of myself

Name: Sallie T

Type of Organization: Not Applicable

Role: Research Participant/Patient/Advocate

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Patients and other participants in biomedical or public health research might think twice about whether their safety, privacy, and bodily autonomy are protected if information used for research is not obtained with their full informed consent. People living with HIV (PLHIV) have been confronted as vectors for disease for decades, and are at risk of being subject to criminal and immigration proceedings largely because of their health status. However, the issue isn't a hostile criminal justice system alone, since federal, state and local governments have proceeded with a molecular HIV surveillance (MHS) program despite an abundance of community concern. I believe it is clear that MHS is public health research and that informed consent requirements should extend to HIV-testing related data collected in the administration of direct care but then used for future research and analysis. PLHIV have the right to know when and how their private medical data is used, to consent to such usage, and to opt out of future usage at any time. NIH can and should work together with government agencies, community organizations, PLHIV, and advocates to enshrine better protections for collected data used in public health research. NIH must also implement the tools necessary to require informed consent for all future use of collected data, and respect the rights of PLHIV to opt-out of future use of their data for research.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1729

I am responding to this RFI: On behalf of myself

Name: Hannah Covert

Name of Organization: University of Pittsburgh

Type of Organization: Academic Institution

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology): environmental epidemiology

1. Utility and useability of this resource:

It is very helpful to have a guide and some common language around informed consent for future use of data and biospecimens.

2. Gaps or additional components that should be included:

a) The consent allows for listing where biospecimens and data will be stored. If data and biospecimens are shared and used in unrelated studies, however, they will be transferred and stored in multiple locations. Even if there is no data sharing, a PI might leave an institution and take the data and biospecimens to the new institution. Thus, I question the utility and ultimately the veracity of stating that they will be stored in one specific location. b) The consent states that biospecimens and data may be shared with investigators around the world. Why is it important to signal that data may be shared internationally? It seems the central issue is that they will be shared and used for studies that may have nothing to do with the original study.

3. Specific language proposed in the informed consent sample language:

While the General Points to Consider states that the language level is aimed at 8th grade or below, it could be further refined and the language level lowered: a) the consent language repeatedly uses the terms 'data' and 'biospecimens', but does not define them; b) 'researcher' and 'investigator' are used interchangeably - just one of these words should be used consistently with researcher probably being the easier word to understand; and c) some other examples of language level being too high are: commercial entity, identifying information, commercial value. I suggest a thorough review of the language level.

4. Hurdles or barriers to wider use of this resource by the community:

A barrier, related to what I mentioned in #3, is the language level. It is still too high for many members of the general public in the US, as well as study participants for international cohorts in low- and middle-income countries.

5. Other considerations relevant to this resource:

It would be helpful to know if NIH expects this common consent language to apply to international as well as US-based cohorts.

Submission ID: 1730

I am responding to this RFI: On behalf of an organization

Name: Morgan Farrington

Name of Organization: GoodWorks: North Alabama Harm Reduction

Type of Organization: GoodWorks: North Alabama Harm Reduction

Type of Organization - Other: Other

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Patients and other participants in biomedical or public health research might think twice about whether their safety, privacy, and bodily autonomy are protected if information used for research is not obtained with their full informed consent. People living with HIV (PLHIV) have been confronted as vectors for disease for decades, and are at risk of being subject to criminal and immigration proceedings largely because of their health status. However, the issue isn't a hostile criminal justice system alone, since federal, state and local governments have proceeded with a molecular HIV surveillance (MHS) program despite an abundance of community concern. I believe it is clear that MHS is public health research and that informed consent requirements should extend to HIV-testing related data collected in the administration of direct care but then used for future research and analysis. PLHIV have the right to know when and how their private medical data is used, to consent to such usage, and to opt out of future usage at any time. NIH can and should work together with government agencies, community organizations, PLHIV, and advocates to enshrine better protections for collected data used in public health research. NIH must also implement the tools necessary to require informed consent for all future use of collected data, and respect the rights of PLHIV to opt-out of future use of their data for research.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/teozHoeZuz.pdf

Submission ID: 1731

I am responding to this RFI: On behalf of an organization

Name: Catherine Hanssens

Name of Organization: Center for HIV Law & Policy

Type of Organization: Center for HIV Law & Policy

Type of Organization - Other: Non-Profit Research Organization

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Legal, policy, and human rights issues that affect people living with HIV and other stigmatized disabilities

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

The following represents our suggested revisions of the introduction and points to consider provided by NIH. A version with tracked changes is attached to this submission, along with further comment on how the subsequent use of data obtained for molecular HIV surveillance should be subject to informed consent requirements prior to participation. Consent for Data and Biospecimen Sharing for Future Use: Points to Consider and Sample Language I. Introduction: As a steward of the nation's biomedical research enterprise, NIH is dedicated to ensuring that when data and biospecimens are shared, that it is done ethically and securely, and with respect for the privacy, autonomy, and well-being of research participants and the communities to which they belong. As part of this commitment, NIH is working with stakeholders to identify best practices for developing and implementing effective consent practices to inform prospective research participants about potential risks and benefits of data and biospecimen sharing for future research. The following resource outlines suggested points to consider when addressing data and biospecimen storage and sharing in consent language and provides supplemental sample language that could be modified as needed when constructing informed consent forms. Of note, the sample language provided below is intended to serve as a helpful resource and is not a substitute for addressing federal, state, local, or tribal requirements that may apply to informed consent. Use of the information provided in this resource, including sample language, is completely voluntary. II. Instructions for Use: This document presents points to consider, instructions for use, and optional sample language that is meant to supplement informed consent forms for research studies that include the storage and sharing of data and biospecimens. This resource is neither a linear nor comprehensive consent template. Additionally, the sample language does not address all possible scenarios for which informed consent may be needed for data and biospecimen storage and sharing. The sample language will need to be tailored to institutional and study specific requirements. It is the responsibility of investigators and institutional review boards (IRBs) to determine the appropriate use of the sample language including which components, if any, are relevant to a specific study's informed consent and the most appropriate section to incorporate the sample language within when doing so (e.g., the risks of storage and sharing may be included in the study's informed consent "risk" section or in another appropriate section). Not all of the components will be appropriate for every informed consent form.

Investigators should carefully select language appropriate for the study, and IRBs should ensure that the proposed language meets all applicable regulatory and policy requirements, including federal, state, local, and tribal requirements. Documented informed consent is necessary for research involving the use of identifiable health data. However, uUse of this sample language is completely voluntary. This language is being provided as a resource for the research community and there are no requirements that any portion of the language be used in an informed consent form for an NIH-supported or -conducted study as long as the essential elements of informed consent are met. This resource consistently refers to “data and biospecimens” as a means to capture all identifiable information and biospecimens that research participants may contribute as part of a research study. “Data and biospecimens” includes information collected from, or about a research participant during the course of a primary study or health care service (e.g., surveys, medical images, electronic health records, wearable device information) as well as human material (e.g., blood, tissue, urine, extracted DNA). Some sample language includes embedded instructions to fill in specific information pertaining to the research study. These embedded instructions are identified in [bold, bracketed text] and will need to be replaced after study-specific language is inserted or removed entirely based on the instructions provided. III. General Points to Consider: ● Data and biospecimens may involve distinct storage and/or sharing procedures. Some protocols may require separate consent language to inform how data versus biospecimens are stored and shared. ● Those responsible for study conduct and oversight are encouraged to consider the reading level of the entire informed consent form, with the goal of creating understandable language that conveys the necessary information. The sample language in this resource was crafted to ensure an appropriate reading level (with a goal of %8th grade reading level or below). Additional resources on evaluating readability can be found from the National Cancer Institute (NCI). ● Studies that involve a category of participants who are considered vulnerable to coercion, or undue influence or criminal legal processes, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, or persons from over-policed communities, or research with pregnant women, fetuses or neonates may require additional considerations regarding the storage and sharing of data and biospecimens. Those responsible for study conduct and oversight are encouraged to revise the sample language to reflect these considerations. We strongly encourage consultation with the appropriate contacts to determine and take into consideration the applicable regulations, policies, and laws relevant to studies involving these populations, including assent for participants under 18, prior to storage and sharing of data and biospecimens. ● Some cultural/donor/sovereign groups may have preferences or requirements regarding how data and biospecimens are handled, including the disposition of biospecimens. For example, sovereign Tribal Nations may have laws/regulations/policies governing research that may impact the storage and sharing of data and biospecimens. We strongly encourage consultation with the appropriate contacts to determine applicable regulations, policies, and cultural preferences or tribal laws that will need to be taken into consideration prior to storage and sharing of data and biospecimens. ● Additional considerations may be applicable for research studies that include the storage and sharing of genomic data. We recommend that those responsible for study conduct and oversight review community standards, such as NIH resources provided by the National Human Genome Research Institute (NHGRI) on informed consent and the NIH Genomic Data Sharing Policy. ● If the future use of data and biospecimens will be limited, this information should be specified in the consent language. ● As technology advances for coding and de-identifying data and biospecimens, consider the implications for privacy and confidentiality and adjust language as appropriate.

3. Specific language proposed in the informed consent sample language:

The following represents our suggested revisions of the sample language components provided by NIH. A version with tracked changes is attached to this submission, along with further comment on how the subsequent use of data obtained for molecular HIV surveillance should be subject to informed consent requirements prior to participation. IV. Sample Language Components: Component 1: Introduction - Description Considerations for those responsible for study conduct and oversight: The Introduction-Description component is meant to provide prospective research participants with an introduction to, and description of the storage and sharing of data and biospecimens in the study. ● If participants may be re-contacted to collect new or replacement data or biospecimens, include language to address re-contacting. ● Those responsible for study conduct and oversight will need to consider the appropriate timeframe for data and biospecimen storage based on their study and anticipated uses. For some, the appropriate timeframe may be indefinite, while others may have a clear, limited timeframe. Instructions for those responsible for study conduct and oversight: See sample language below for the Introduction-Description component. If using this sample language, include the first three paragraphs then choose either Option #1 or Option #2. Replace embedded instructions identified in [bold, bracketed text] with specific information pertaining to the study and remove [Option #1 and #2 text]. Sample Language: We are This study is collecting data and biospecimens from you that can be used for a research study. We also would like to make your data and biospecimens available for other research studies that may be done in the future. The research may be about similar diseases or conditions to this study. However, research could also be about unrelated diseases, conditions, or other aspects of health. These studies may be done by researchers at other institutions, including commercial entities. Our goal is to make more research possible to learn about health and disease. However, you have the right to opt out of the use of your data for additional studies. If you consent to additional use of your personal data and biospecimens, you have the right to be informed of each additional research use in advance, and to opt out off further sharing of your data. Your data and biospecimens will be stored [indicate the name of the institution where they will be stored, including any biobanks to be utilized]. We plan to keep your data and biospecimens for [indicate time frame or “indefinitely,” or until “used completely,” etc.]. Your data and biospecimens may be shared with investigators around the world. However, access to the data and biospecimens is controlled by [indicate which entity has control]. To use your data and biospecimens, researchers must get approval and they must agree not to try to identify you. [Option #1: If the data/biospecimens are coded and can be linked back to the participant] We will protect the confidentiality of your information to the extent possible. Your name and other identifying information will not be on any data and biospecimens you provide. The data and biospecimens will have a code that links to your identifying information. The code key will be kept in a locked location separate from your information. The code key can only be accessed by people who have permission. You have a right to know who will have access to your personal information, and the purposes for which it will be used. [Option #2: If the data and biospecimens are completely delinked from identifiers and cannot be linked back to the participant] Your name and identifying information will not be on any data and biospecimens you provide. Investigators cannot link your identifying information to the data and biospecimens. Component 2: Voluntary Participation Considerations: The Voluntary Participation component informs prospective research participants about the voluntary nature of data and biospecimen storage and sharing. ● In general, participants should be given the option to agree to, or opt out of, having their data and biospecimens stored and shared for current or future research. Providing options for participants to agree to, or opt out of, having their data and biospecimens stored

and shared is particularly important in studies that offer the prospect of direct benefit to the participant. Mandating agreement to storage and sharing may be considered coercive if the participant does not want to agree to sharing of data and biospecimens or is a member of a community or group that is at higher risk of coercion or social risk but feels compelled to agree anyway in order to join a possibly beneficial clinical trial. Even ifIf the research protocol offers no prospect of direct benefit, then it is still may be reasonable for storage and sharing not to be optional if unanticipated sharing of identifiable data poses any risk of adverse consequences to the participant. ● If the protocol is a repository protocol with the sole intent of collecting data and/or biospecimens for future use, no opt out mechanism is necessary. Instructions: Choose either Option #1 or Option #2. Remove [Option#1 and #2 text]. Sample Language: [Option #1: When sharing of data and biospecimens will be optional (e.g., for studies that have potential benefit)] It is your choice whether or not to let researchers share use your personal data or to share your data and biospecimens for research in the future. If you say "yes," you can change your mind later, but your data and biospecimens might still be used if they have already been shared. If you say "no," you can still fully participate in this study. Please initial next to your choice: _____YES, use my data and biospecimens in this and other research studies _____NO, do NOT use my data and biospecimens in other research studies _____NO, do NOT use my data and biospecimens in any research studies [Option #2: When sharing of data and biospecimens will not be optional (e.g., for studies where sharing is integral to the purpose of the study)] Participating in this study means you agree to share your data and biospecimens. You can change your mind later, but researchers may still use your data and biospecimens that have already been shared. If you do not want your data and biospecimens used for other projects without your knowledge, you should not participate in this study. Component 3: Discontinuation/Withdrawal Considerations: The Discontinuation/Withdrawal component describes what will happen if the participant changes their mind about storage and sharing. Instructions: Adjust language as necessary. Sample Language: You can change your mind about sharing your data and biospecimens at any time. If you change your mind, please contact the study team to let us know. We will not share your data and biospecimens going forward. We will do our best to retrieve all your data and biospecimens that have already been shared, but it may not be possible. For example, if some research with your data and biospecimens has already been done, the information from that research may still be used. We will not know which data and biospecimens are yours if the identifying information was removed. Also, if the data and biospecimens have been shared already with other researchers, it might not be possible to get them back. Component 4: Risks & Benefits General Considerations: The Risks & Benefits component describes the reasonably foreseeable risks/discomforts related to storage and sharing of data and biospecimens, and any benefits related to storage and sharing of data and biospecimens that prospective participants may receive. Considerations - Risks: If identifying information (e.g., key to the code) will remain with the data and biospecimens during storage and sharing, include language that addresses the additional measures designed to safeguard participants' privacy (e.g., access controls). ● Ensure that the safeguards listed are consistent with language addressing the storage and sharing of data and biospecimens in the introduction. ● Adjust language if there is a specific risk associated with loss of privacy due to storage and sharing, such as stigma or the ability to obtain certain types of insurance. Instructions: Adjust language as needed. Remove [Risks] and [Benefits] unless needed as a section heading. Sample Language: [Risks] When we share your data and biospecimens, there is a small risk that people or government agencies may get access to it who are not supposed to. We will protect your data and biospecimens as much as possible during storage and when they are shared. However, there is a small chance your identity could be

discovered. This includes government and law enforcement agencies that demand access to identifiable health data in the possession of public health providers and researchers. [Benefits] You will not receive any direct benefit from sharing your data and biospecimens. However, sharing your data and biospecimens may contribute to research that helps others in the future. Component 5: Commercial Application Considerations: The Commercial Application component informs prospective participants about whether their data and biospecimens may contribute to products with commercial value. If research participants will receive any payments related to commercial or product development, adjust language in the last sentence to reflect this. Instructions: Adjust language as needed. Sample Language: The use of your data and biospecimens may lead to new tests, drugs, devices, or other products or services with commercial value. These products or services could be patented and licensed. There are no plans to provide any payment to you should this occur.

4. Hurdles or barriers to wider use of this resource by the community:

5. Other considerations relevant to this resource:

Please see attached comments concerning the closely-related issue of how research is defined, and more specifically, that molecular HIV surveillance (MHS) is the subsequent use of personal health data for a purpose unrelated to the individual's health care or even basic surveillance, and therefore is research subject to the requirements of informed consent to prior to participation.

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/ZYMDRbyLyG.pdf

Attachment Description: Additional comment from The Center for HIV Law & Policy, Positive Women's Network-USA, and the US People Living with HIV Caucus (with tracked changes to provided sample language)

Submission ID: 1732

I am responding to this RFI: On behalf of myself

Name: Judith

Name of Organization: Montenegro

Type of Organization: Non-Profit Research Organization

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Community Based Participatory Research

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Patients and other participants in biomedical or public health research might think twice about whether their safety, privacy, and bodily autonomy are protected if information used for research is not obtained with their full informed consent. People living with HIV (PLHIV) have been confronted as vectors for disease for decades, and are at risk of being subject to criminal and immigration proceedings largely because of their health status. However, the issue isn't a hostile criminal justice system alone, since federal, state and local governments have proceeded with a molecular HIV surveillance (MHS) program despite an abundance of community concern. I believe it is clear that MHS is public health research and that informed consent requirements should extend to HIV-testing related data collected in the administration of direct care but then used for future research and analysis. PLHIV have the right to know when and how their private medical data is used, to consent to such usage, and to opt out of future usage at any time. NIH can and should work together with government agencies, community organizations, PLHIV, and advocates to enshrine better protections for collected data used in public health research. NIH must also implement the tools necessary to require informed consent for all future use of collected data, and respect the rights of PLHIV to opt-out of future use of their data for research.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/yHfAiizKNQ.pdf

Attachment Description: Coalition statement

Submission ID: 1733

I am responding to this RFI: On behalf of myself

Name: Brian Minalga

Role: Research Participant/Patient/Advocate

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

HIV and other infectious diseases

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Patients and participants in biomedical or public health research may question their safety, privacy, and bodily autonomy in situations where their information used for research is obtained without their full informed consent. This is the case with molecular HIV surveillance (MHS). Federal, state, and local governments have proceeded with MHS despite an abundance of community concern. MHS is in fact public health research. Patient data are collected in the administration of direct care, but these data are later used for future research and analysis--including NIH-funded research--without the consent of patients from whom the data were collected as part of their clinical care--not research. Informed consent requirements should extend to MHS. PLHIV have the right to know when and how their private medical data is used, to consent to such usage, and to opt out of future usage at any time. The NIH can and should work together with government agencies, community organizations, PLHIV, and advocates to enshrine better protections for data used in public health research. NIH must also implement the tools necessary to require informed consent for all future use of collected data and respect the rights of PLHIV to opt-out of future use of their data for research.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/kXMYYaeTHe.pdf

Attachment Description: NIH RFI Comment from CHLP, PWN, US PLHIV Caucus

Submission ID: 1734

I am responding to this RFI: On behalf of an organization

Name: Deborah Motton

Name of Organization: University of California, Office of the President

Type of Organization: University of California, Office of the President

Type of Organization - Other: Academic Institution

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. Utility and useability of this resource:

On a regular basis and by their regulatory authority, Institutional Review Boards (IRBs) successfully provide input on consent language, which can vary depending on the nature of the study, the data or biospecimens collected, the research participant population, and any local requirements. Their experience and expertise allows them to account for differences in consent language to best protect human subjects and continue important research. To encourage flexibility and the appropriate exercise of IRB discretion, UC recommends that the NIH retract the sample language provided in this RFI and issue guidance instead. The NIH could flesh out the General Points to Consider section by providing evidence-based guidance on what IRBs should contemplate when considering consent language for future data and biospecimen sharing. The NIH could also include guidance on the NIH's interpretation of broad consent requirements, as described further below.

2. Gaps or additional components that should be included:

UC is unclear whether this RFI is meant to address the requirement in 45 CFR 46.116(b)(9) regarding the future use of deidentified data or biospecimens or if it is meant to move the community towards using broad consent for future use of identifiable data or biospecimens. Section II, Instructions for Use describes identifiable data and biospecimens obtained for primary research implying that 45 CFR 46.116(b)(9) is at play, but the RFI subsequently discusses sharing data and biospecimens for future research without noting whether the information should be deidentified, such as in Section IV, Component 1, Sample Language. This creates confusion as to whether the RFI's intended goal is to address broad consent requirements in 45 CFR 46.116(d). If the NIH wants to address broad consent in the RFI, then it should be clear about this objective so that the sample language could be reviewed in that light. UC suggests that if achieving broad consent is NIH's objective, then it would be helpful to have guidance on NIH's expected requirements and subsequent application of using broad consent (such as, what are the implications if research participants say "no" to a study or "no" to the opt-in option for future research with the data or biospecimens from the current study; can they be asked to participate in other studies; what actions need to be taken if participants opt out later and how far back should an institution look to apply a participant's "no"?).

3. Specific language proposed in the informed consent sample language:

Section IV, Component 2: Voluntary Consideration IRBs are well trained in ensuring that consent language is not coercive or unduly influential, however the first and second bullets collectively in the Considerations section seems to imply that having an opt-out option for any future data or biospecimen sharing is the best way to prevent coercion. UC recommends that the NIH provide a more balanced explanation of why certain studies may not be able to offer an opt-out option. Further, UC recommends that the NIH avoid including an opt-out option for future data or biospecimen sharing. Instead a well-developed consent process should explain the risks and benefits of data/biospecimens sharing and participants should be able to decide whether the study is right for them. Otherwise, the language included within the opt-out option should be explicit regarding the inability to "un-share" previously shared information. Lastly, the opt-out option does not align with the values of the NIH's data sharing policy, which emphasizes the importance in using already collected information and biospecimens.

4. Hurdles or barriers to wider use of this resource by the community:

Applicable laws and regulations, including the Health Insurance Portability and Accountability Act (HIPAA) and an abundance of state privacy laws, impact language in the consent form. Also, FDA-regulated clinical investigations are subject to specific FDA regulations and guidance regarding informed consent. UC strongly endorses the comment provided by the Council on Governmental Relations (COGR) to include the following text as part of the General Points to Consider: A variety of national, state, and/or local laws, regulations, and policies (collectively "Laws") may apply to the research, and these Laws may impact the nature and content of the informed consent process and documentation. Before using any of the sample language, persons responsible for the study should consult appropriate legal counsel and IRB contacts to determine which Laws apply to the research, whether the sample language conforms to those Laws, and how those Laws otherwise affect the consent process and documentation. [Additional text to be added if FDA clinical investigations fall within the scope of the RFI: Importantly, clinical investigations of FDA-regulated articles have their own informed consent requirements that must be considered.]

5. Other considerations relevant to this resource:

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/ZzSSClzFDZ.pdf

Submission ID: 1735

I am responding to this RFI: On behalf of myself

Name: Clayton Allen Siem

Role: Member of the Public

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Patients and other participants in biomedical or public health research might think twice about whether their safety, privacy, and bodily autonomy are protected if information used for research is not obtained with their full informed consent. People living with HIV (PLHIV) have been confronted as vectors for disease for decades, and are at risk of being subject to criminal and immigration proceedings largely because of their health status. However, the issue isn't a hostile criminal justice system alone, since federal, state and local governments have proceeded with a molecular HIV surveillance (MHS) program despite an abundance of community concern. I believe it is clear that MHS is public health research and that informed consent requirements should extend to HIV-testing related data collected in the administration of direct care but then used for future research and analysis. PLHIV have the right to know when and how their private medical data is used, to consent to such usage, and to opt out of future usage at any time. NIH can and should work together with government agencies, community organizations, PLHIV, and advocates to enshrine better protections for collected data used in public health research. NIH must also implement the tools necessary to require informed consent for all future use of collected data, and respect the rights of PLHIV to opt-out of future use of their data for research.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/ESgpQJZICD.pdf

Submission ID: 1736

I am responding to this RFI: On behalf of an organization

Name: JD Davids

Name of Organization: High Impact Strategies

Type of Organization: High Impact Strategies

Type of Organization - Other: Research Participant/Patient Advocacy Organization

Role: Research Participant/Patient/Advocate

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Public Health, Complex Chronic Conditions, Health Equity, Infectious Diseases

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Patients and other participants in biomedical or public health research might think twice about whether their safety, privacy, and bodily autonomy are protected if information used for research is not obtained with their full informed consent. People living with HIV (PLHIV) have been confronted as vectors for disease for decades, and are at risk of being subject to criminal and immigration proceedings largely because of their health status. However, the issue isn't a hostile criminal justice system alone, since federal, state and local governments have proceeded with a molecular HIV surveillance (MHS) program despite an abundance of community concern. I believe it is clear that MHS is public health research and that informed consent requirements should extend to HIV-testing related data collected in the administration of direct care but then used for future research and analysis. PLHIV have the right to know when and how their private medical data is used, to consent to such usage, and to opt out of future usage at any time. NIH can and should work together with government agencies, community organizations, PLHIV, and advocates to enshrine better protections for collected data used in public health research. NIH must also implement the tools necessary to require informed consent for all future use of collected data, and respect the rights of PLHIV to opt-out of future use of their data for research

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/aXYZWrTPup.pdf
Attachment Description: CHLP, PWN, US PLHIV CAUCUS - NIH RFI COMMENT_ Consent for Data and Biospecimen Sharing for Future Use_ Points to Consider and Sample Language.pdf

Submission ID: 1737

I am responding to this RFI: On behalf of an organization

Name: Marc Fliedner

Name of Organization: Disability Rights New York, PAIR Rpgram

Type of Organization: Disability Rights New York, PAIR Rpgram

Type of Organization - Other: Other

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

For your careful consideration: Patients and other participants in biomedical or public health research might think twice about whether their safety, privacy, and bodily autonomy are protected if information used for research is not obtained with their full informed consent. People living with HIV (PLHIV), whom the DRNY PAIR PRogram serves, have been confronted as vectors for disease for decades, and are at risk of being subject to criminal and immigration proceedings largely because of their health status. State and local governments have proceeded with a molecular HIV surveillance (MHS) program despite an abundance of community concern. As MHS is public health research agency, informed consent requirements should extend to HIV-testing related data collected in the administration of direct care but then used for future research and analysis. PLHIV have the right to know when and how their private medical data is used, to consent to such usage, and to opt out of future usage at any time. NIH can and should work together with government agencies, community organizations, PLHIV, and advocates to enshrine better protections for collected data used in public health research. NIH must also implement the tools necessary to require informed consent for all future use of collected data, and respect the rights of PLHIV to opt-out of future use of their data for research.

Submission ID: 1738

I am responding to this RFI: On behalf of an organization

Name: MARTHA F. JONES

Name of Organization: Mass General Brigham

Type of Organization: Mass General Brigham

Type of Organization - Other: Other

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Biomedical research

1. Utility and useability of this resource:

We commend the NIH's efforts to develop and disseminate effective consent practices to inform prospective research participants about intended future use and sharing of data and biospecimens for research. We wholeheartedly agree with the need to include clear and precise language in consent forms informing subjects about intended future use and sharing of data and biospecimens for research, including risks, benefits, intentions, and parameters around this use. As a general practice, we have already implemented this expectation across our research studies and welcome harmonization with NIH-recommended language, which we believe has excellent utility to improve this aspect of consent language across institutions. From our perspective, the primary challenge to usability lies in consent form lengths and consent form language. Any lengthening of already too long consent forms risks decreasing utility, subject attention, or subject comprehension. As such, any additions must be clear and concise. Regarding language, we appreciate the NIH's efforts to develop language with a goal of 8th grade reading level or below. This effort is particularly challenging for the topic at hand, wherein the word biospecimens itself has five syllables and pushes the reading level and the concepts of identifiability, de-identification, and potential for re-identification are similarly quite challenging to explain in easily understandable language.

2. Gaps or additional components that should be included:

The "General Points to Consider" section underscores important complexities and implementation concerns regarding the sample consent language. In particular, the need for assent for participants under 18 is highlighted. We suggest also including plans for re-consent upon subjects turning 18 as part of implementation. Another highlighted point to consider by NIH centers on inclusion of genomic data. We suggest specifically calling out potential for whole genome sequencing, either by way of sharing existing sequencing data or potential future analyses, in an effort to harmonize with Common Rule requirements. A third point to consider by the NIH notes: "As technology advances for coding and deidentifying data and biospecimens, consider the implications for privacy and confidentiality and adjust language as appropriate." We completely agree with this and would suggest that the advancing science of re-identification (rather than de-identification) has even more significant potential implications for subjects and future use of their data and biospecimens to be considered moving forward. For example,

the Component 1 sample language for data and biospecimens delinked from identifiers could potentially need to be revisited in the future due the advancing science of re-identification.

3. Specific language proposed in the informed consent sample language:

In Component 1 (Introduction), the Sample Consent language intends to delineate between use of data/biospecimens that are coded compared to those that are completely delinked from identifiers and cannot be linked back to the participant. We appreciate and agree with this effort, though in our experience, find the added complexity that many studies also consent for retaining and using identifiable data/biospecimens for future research purposes makes these distinctions incredibly challenging for subjects to truly comprehend. Although we recognize the NIH's work here is focused primarily on de-identified future use of data/biospecimens, we believe institutions adding this sample consent language to existing consent form templates that already contain language about potential identifiable data/biospecimens sharing risks causing significant confusion, and we suggest that the NIH consider including Sample Language in Component 1 that comprehensively includes and delineates between identifiable, de-identified/coded, and delinked sharing/use in as simple a manner as possible for subjects to understand. When not relevant for specific studies, the not applicable option could then be omitted. Building on response 1 above, we additionally recommend Component 1 (Introduction) clearly defines biospecimens in lay language for subjects. In Component 2 (Voluntary Participation), the NIH recommends inclusion of opt out language for storage, future use, and sharing of de-identified data/biospecimens, with a suggestion to potentially parse out this option based on potential direct benefit of the study. While we enthusiastically support the desire to respect participant autonomy with this addition, we do note this is a departure from common current practice and the Common Rule requirements, which require only notification – and not opt out – regarding future use (e.g., 45CFR46.116(b)(9)(i): "A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility.)" In the current environment, we believe tracking opted out samples to be a substantial hurdle to authentically offering this option to subjects and suggest ongoing public discourse on how to implement these types of protections most effectively.

4. Hurdles or barriers to wider use of this resource by the community:

See response 1: From our perspective, the primary challenge to usability lies in consent form lengths and consent form language. Any lengthening of already too long consent forms risks decreasing utility, subject attention, or subject comprehension. As such, any additions must be clear and concise. Regarding language, we appreciate the NIH's efforts to develop language with a goal of 8th grade reading level or below. This effort is particularly challenging for the topic at hand, wherein the word biospecimens itself has five syllables and pushes the reading level and the concepts of identifiability, de-identification, and potential for re-identification are similarly quite challenging to explain in easily understandable language.

5. Other considerations relevant to this resource:

We appreciate the opportunity to provide input and would welcome future opportunity to continue to work on this important effort.

Submission ID: 1739

I am responding to this RFI: On behalf of myself

Name: Jonda Clemings

Type of Organization: Other

Type of Organization - Other: Non-profit health

Role: Member of the Public

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

CHLP Molecular Surveillance

1. **Utility and useability of this resource:**

I believe that there should be limits imposed on utilizing someone's HIV testing blood work for other types of research without first obtaining client informed consent. This can be seen as unethical behavior and pose a negative reaction to clients when they find out. This would provide researchers (local, state, and federal) to use information when pressing charges on a person living with HIV/AIDS (PLWHA). I have concerns about not having a confidential or private way of preserving the type of information that is being sought. Medical mistrust is high especially with Black, Indigenous, and People of Color (BIPOC) and could grow even higher when people realize that their blood work (data) is being utilized in various research projects. There is already a stigma around being a PLWHA and throughout the 30+ years of the disease, advocates have worked long and hard to reduce stigma. By having your HIV/AIDS blood work in hand, researchers currently can do as they please with whatever other information is gleaned from this research. Policies and procedures need to be set to so that researchers do not utilize lab work and other body fluids, biopsied material, etc. without informed consent by the client.

2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1740

I am responding to this RFI: On behalf of an organization

Name: Theresa Alban

Name of Organization: Cystic Fibrosis Foundation

Type of Organization: Cystic Fibrosis Foundation

Type of Organization - Other: Research Participant/Patient Advocacy Organization

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/YPQuaDBqkw.pdf

Attachment Description: Cystic Fibrosis Foundation Comments on Data and Biospecimen Sharing RFI

Submission ID: 1741

I am responding to this RFI: On behalf of an organization

Name: Jennifer Darragh

Name of Organization: Research Data Access and Preservation Association (RDAP)

Type of Organization: Research Data Access and Preservation Association (RDAP)

Type of Organization - Other: Professional Organization/Association

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

FAIR data from all disciplines

1. **Utility and useability of this resource:**

Overall this is a very helpful resource, however some additional clarification on repository options, access to physical specimens, and less focus on controlled access would be beneficial.

2. **Gaps or additional components that should be included:**

Address the responsibility of the researcher to the binding language of the consent form. Open science options for physical specimens. Consent language that addresses biobanks because not all information is accessible via the internet. Would be useful to distinguish access points for digital data and physical data.

3. **Specific language proposed in the informed consent sample language:**

Advise researchers to be more specific about repository and biobank options whenever possible. Perhaps providing separate sample language for both individually and when collected together.

4. **Hurdles or barriers to wider use of this resource by the community:**

De-identified digital data that poses little to no risk of harm to participants should not be behind controlled access. Thus the language that says 'there is a small risk that people may get access to it who are not supposed to' prohibits open access to digital data.

5. **Other considerations relevant to this resource:**

NIH should advocate for a strategy to integrate PIDs (persistent identifiers) for physical specimens (such as a DOI) to allow them to be more easily linked to other studies.

Submission ID: 1742

I am responding to this RFI: On behalf of an organization

Name: Nora Darling

Name of Organization: AIDS United

Type of Organization: AIDS United

Type of Organization - Other: Non-Profit Research Organization

Role: Other

Role - Other: research/advocacy associate

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology): prevention & treatment to end the HIV epidemic

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Patients and other participants in biomedical or public health research might think twice about whether their safety, privacy, and bodily autonomy are protected if information used for research is not obtained with their full informed consent. People living with HIV (PLHIV) have been confronted as vectors for disease for decades, and are at risk of being subject to criminal and immigration proceedings largely because of their health status. However, the issue isn't a hostile criminal justice system alone. The widespread implementation by federal, state and local governments of molecular HIV surveillance (MHS) technologies, and a lack of community consultation about potential risks and costs prior to use of this strategy, has fueled concern and a vigorous conversation among advocates about whether these new technologies offer benefits that are worth the potential incursions on patient privacy, the collateral legal consequences arising from HIV stigma and criminalization, and the investment of resources that might be used more efficiently to accomplish the same goals. MHS clearly falls under the scope of public health research; as such, informed consent requirements should extend to HIV-testing related data collected in the administration of direct care but then used for future MHS research and analysis. PLHIV have the right to know when and how their private medical data is used, to consent to such usage, and to opt out of future usage at any time. NIH can and should work together with people living with HIV, government agencies, community organizations, and advocates to enshrine better protections for collected data used in public health research. NIH must also implement the tools necessary to require informed consent for all future use of collected data, and respect the rights of PLHIV to opt-out of future use of their data for research.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/qixKkrpDTi.pdf

Attachment Description: AIDS United Molecular Surveillance Statement_06.16.20

Submission ID: 1743

I am responding to this RFI: On behalf of myself

Name: Sara R Jordan

Name of Organization: Future of Privacy Forum

Type of Organization: Non-Profit Research Organization

Role: Other

Role - Other: Senior Researcher AI & Ethics

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Privacy and data protection in data sharing for research purposes

1. Utility and useability of this resource:

Thank you for the opportunity to comment on the "Developing Consent Language for Future Use of Data and Biospecimens". I agree with the NIH that the four components of sample informed consent language for secondary use of biospecimens and data will help Institutional Review Boards to streamline explanations of secondary uses of data and biospecimens. Clarity and similarity of language used by IRBs around the US and the globe will undoubtedly help participants and patients navigate complex consent forms as used for collection of biospecimens. However, I remain concerned that the draft language does not clarify well enough the risks associated with secondary use of data that does not include or pertain to biospecimens. I encourage the NIH to work with organizations, like the Future of Privacy Forum, who have on-going initiatives concerned with secondary data use, including efforts to draft informed consent language specifically for secondary use of data derived from studies that are not bio-medical in nature. I recommend modifications to each of the four components to differentiate a standard informed consent form for secondary uses of data and for secondary uses of biospecimen data. These are reflected in the appropriate section of this comment form.

2. Gaps or additional components that should be included:

I applaud the NIH for this effort but encourage you to work with the National Science Foundation and the Department of Education to develop model informed consent language for secondary use of research data from studies that do not involve biospecimens. As presented in this RFI, research involving secondary uses of "data" and research involving secondary use of previously collected "biospecimens" present the same privacy risks and potential public benefits. I respectfully disagree with this characterization and propose that this exercise be limited to considerations of informed consent for secondary use of biospecimens and a subsequent, separate, exercise be undertaken for secondary use of social, behavioral, and educational data. I welcome the opportunity to work with NIH to correct this characterization and draft model informed consent language.

3. Specific language proposed in the informed consent sample language:

With respect to component 1, "Introduction-- Description", I recommend that revisiting the language ascribing individual, sovereign, ownership of data, and considering modifications for secondary use of

non-biospecimen data. Specifically, I recommend changing the phrases, “we would like to make your data and biospecimens” to “we would like to make the data we collected about you”. Further in this section, you have not specified cloud storage and third-party cloud storage vendors (e.g., Amazon AWS or Google) as potential locations for storage and platforms for sharing. Cloud vendors may or may not have access to the data and may or may not use it for their purposes. I encourage NIH to work with NIST and appropriate vendors to clarify this. I am concerned that the language addressing cross-border sharing of research data does not indicate to participants that the legal and regulatory frameworks governing the uses of that shared data will vary. I recommend that the NIH revisit the recommendations of the GDPR Article 40 working group on sharing research data to ensure alignment with, at least, our European partners. With respect to component 2, “Voluntary Participation”, I recommend revisiting the Option #1 language concerning agreement to share and withdrawal of that agreement. While you have indicated that an option for withdrawal exists, even where an actionable deletion of data or right to be forgotten is not available, the language used does not provide sufficient clarity for reuse of non-biospecimen data. For example, you indicate that: “if you say “yes”, you can change your mind later, but your data and biospecimens might still be used if they have already been shared”. If data that was shared is already used to train machine learning systems, there is no effective way to untrain those systems from use of that data. Adding that there is an option to change one’s mind muddies the ability of participants to make a truly informed decision that data, once shared and used, becomes part of the systems that used that data. Similar concerns persist for Component 3-- “Discontinuation and Withdrawal”-- there is no effective way to unlearn from data used and the sample language included here perpetuates a myth that there is truly a “right to be forgotten” that has actionable consequences for alteration of shared and stored research data. With respect to Component 4-- “Risks and Benefits” the sample language elides the risks associated with breach and re-identification when data is stored and when it is shared. The risks of re-identification from breach of stored data is not equivalent to the risks of re-identification from honest but curious or even malicious adversarial inquiry of shared data resources. To elide the two situations will create confusion regarding the risks of data storage and sharing. Per the use of “your data” and personal data sovereignty language in sample language for component 1, the specification of benefits from “your data” would be more accurate if it were stipulated as “data about you”. The language change would read “However, sharing data about you may contribute to research projects that helps others like you in the future”. With respect to Component 5 “Commercial application”, this is clear regarding the use of data for development of commercial applications but it is not clear with respect to use of data for advertising purposes. This language should be modified to clarify whether the dta shared could be used for targeted advertising purposes by either third parties or the organizations responsible for storing or using the data.

4. Hurdles or barriers to wider use of this resource by the community:

This resource is presently useful for biomedical research and research involving biospecimens. An entirely separate exercise should be conducted to develop sample informed consent language for secondary use of data that does not involve medical research, treatment, or use of biospecimens. I would be pleased to work with NIH to develop model consent language for secondary use of non-biomedical research data.

5. Other considerations relevant to this resource:

Submission ID: 1744

I am responding to this RFI: On behalf of myself

Name: Lydia Babcock

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

epidemiology, Ethnography, Meaningful involvement of PLHIV

1. **Utility and useability of this resource:**

Consent should be obtained for literally everything. It is not ethical to do any given 'public health' intervention or project without consent. If consent is not obtained, how is this different than Tuskegee, for example? Providers didn't bother asking for consent there, either.

2. **Gaps or additional components that should be included:**

Patients and other participants in biomedical or public health research might think twice about whether their safety, privacy, and bodily autonomy are protected if information used for research is not obtained with their full informed consent. People living with HIV (PLHIV) have been confronted as vectors for disease for decades, and are at risk of being subject to criminal and immigration proceedings largely because of their health status. However, the issue isn't a hostile criminal justice system alone, since federal, state and local governments have proceeded with a molecular HIV surveillance (MHS) program despite an abundance of community concern. I believe it is clear that MHS is public health research and that informed consent requirements should extend to HIV-testing related data collected in the administration of direct care but then used for future research and analysis. PLHIV have the right to know when and how their private medical data is used, to consent to such usage, and to opt out of future usage at any time. NIH can and should work together with government agencies, community organizations, PLHIV, and advocates to enshrine better protections for collected data used in public health research. NIH must also implement the tools necessary to require informed consent for all future use of collected data, and respect the rights of PLHIV to opt-out of future use of their data for research.

3. **Specific language proposed in the informed consent sample language:**

You have the right to refuse the use of any biospecimen or data collected from you for research or public health purposes without punishment or denial of care. You can still access care and treatment without consenting.

4. **Hurdles or barriers to wider use of this resource by the community:**

People who object to this have the interest of targeting PLHIV instead of HIV and should therefore critically reflect inwards and ask themselves what their real agenda is.

5. **Other considerations relevant to this resource:**

MHS displaces the problem epidemiologists and public health professionals are trying to address (HIV) onto people (PLHIV) and treating PLHIV as something outside of people deserving rights such as

confidentiality and privacy. It is harmful, it is misinformed, and it is contradictory to the very goals of public health as it further fuels patient's reluctance to get into care due to the type of treatment they receive (ie not being treated as a person deserving rights). Is this tool truly useful if it ends up discouraging PLHIV from treatment and care by increasing mistrust? Is identifying clusters more important than helping people get quality, non-judgemental, and supportive care?It is simply unethical to get information from PATIENTS who are PEOPLE without their consent. It is a direct violation of rights and shows that public health professionals do not think of people living with HIV as people deserving rights. How can anyone trust their doctor or provider if they don't respect their right to privacy? Is that an equal or fair relationship where someone can access care without fear of their information being used without their consent?

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/GORrxywCDG.pdf

Submission ID: 1745

I am responding to this RFI: On behalf of an organization

Name: Christine Swanson-Fischer

Name of Organization: NINDS

Type of Organization: NINDS

Type of Organization - Other: Government Agency

Role: Government Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Neurological Disorders

1. **Utility and useability of this resource:**

Extremely valuable to researchers with the NIH extramural community but also for those in industry and in the NGO space as well

2. **Gaps or additional components that should be included:**

See uploaded word document with suggested edits to incorporate as appropriate. Incorporate language as needed for GDPR compliance

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**

May need to better delineate the data types that studies will collect (as appropriate). Stating that sharing of biospecimens will not be optional certainly has ethical considerations.

5. **Other considerations relevant to this resource:**

May also evaluate ethical considerations (risk and benefits) for sharing of data and biospecimens for ultra rare diseases and risk of re-identification. May be worth reaching out to these communities for further input.

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/qMdTaPhefn.pdf

Attachment Description: NINDS response to NOT-OD-21-131

Submission ID: 1746

I am responding to this RFI: On behalf of an organization

Name: Armonte Butler

Name of Organization: Advocates for Youth

Type of Organization: Advocates for Youth

Type of Organization - Other: Other

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Patients and other participants in biomedical or public health research might think twice about whether their safety, privacy, and bodily autonomy are protected if the information used for research is not obtained with their full informed consent. People living with HIV (PLHIV) have been confronted as vectors for disease for decades, and are at risk of being subject to criminal and immigration proceedings largely because of their health status. However, the issue isn't a hostile criminal justice system alone, since federal, state, and local governments have proceeded with a molecular HIV surveillance (MHS) program despite an abundance of community concern. I believe it is clear that MHS is public health research and that informed consent requirements should extend to HIV-testing related data collected in the administration of direct care but then used for future research and analysis. PLHIV have the right to know when and how their private medical data is used, to consent to such usage, and to opt-out of future usage at any time. NIH can and should work together with government agencies, community organizations, PLHIV, and advocates to enshrine better protections for collected data used in public health research. NIH must also implement the tools necessary to require informed consent for all future use of collected data and respect the rights of PLHIV to opt-out of future use of their data for research.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/IGTaSFQYSy.pdf

Submission ID: 1747

I am responding to this RFI: On behalf of myself

Name: Nahid Turan

Name of Organization: CORIELL INSTITUTE FOR MEDICAL RESEARCH, INC.

Type of Organization: Non-Profit Research Organization

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

CORIELL INSTITUTE FOR MEDICAL RESEARCH, INC.

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

If renewable biospecimens will be created such as immortalized cell lines, this information should be specified clearly in the consent language. If induced pluripotent stem cells will be created with the potential to differentiate into a variety of downstream cell types (such as neurons or organoids), this information should be specified clearly in the consent language. If biospecimens and/or data may be shared for research purposes that are more general than the described research study (i.e., general research use), this information should be specified clearly in the consent language.

Submission ID: 1748

I am responding to this RFI: On behalf of an organization

Name: Collaborative group representing the semantics of biobanking (OBIB) and consent (ICO)

Name of Organization: Collaborative group representing the semantics of biobanking (OBIB) and consent (ICO)

Type of Organization: Collaborative group representing the semantics of biobanking (OBIB) and consent (ICO)

Type of Organization - Other: Other

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology): Semantics of biobanking and informed consent forms

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Informed consent is an ethical and legal requirement for biomedical research. Federal policy for the protection of human subjects under the Common Rule addresses several basic elements required for the informed consent process. However, in the era of genomic research, biobanking and data sharing, several challenges arise in pinning down exact obligations included on consent forms, giving rise to ambiguity and the potential for misinterpretation of what has been consented to. These ambiguities are particularly challenging in tiered consent forms that include biobanking components and have been the subject of discussion by our collaborative group representing the semantics of biobanking (OBIB) and consent (ICO) (Url: http://obofoundry.org/ontology/obib.html.) Work is needed to expand existing data standards or ontologies (e.g., the Informed Consent Ontology and the Ontology for BIoBanking) to enable the capture of detailed permission related data that serves as the basis of specimen and data sharing on biospecimens collected under a variety of research protocols including, but not limited to "broad consent" for biobanks. Examples of consents for specimen collection under different conditions include: Withdrawal of specimens: e.g., samples stored for a limited time, or unlimited time or no time period specified. Included identifiers: e.g., can identified samples be used by future researchers. Participant recontact: e.g., defaults to recontact for future research is allowed; possible recontact (opt in or opt out at the patient level); de-identified samples only (no possible contact); time limit placed on possible recontact. Allow access to medical records: e.g., linking of specimens and result data to medical records, identified or de-identified access. Genetic research: opt in/opt out for both genetic and non-genetic research (could be tiered at the patient level). The objective is to allow information sharing across different protocols and different research sites and use of re-use of collected specimens under these different conditions.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1749

I am responding to this RFI: On behalf of an organization

Name: Rina Saperstein

Name of Organization: Caracole, Inc.

Type of Organization: Caracole, Inc.

Type of Organization - Other: Other

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Molecular Surveillance-HIV

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Caracole supports the Center for HIV Law & Policy, Positive Women's Network-USA, and the US People Living with HIV Caucus position on Molecular HIV Surveillance (MHS). Molecular HIV surveillance programs should be specifically defined as public health research; informed consent requirements should extend to HIV-testing related data collected in the administration of direct care but then used for future research and analysis. People living with HIV (PHIV) have the right to know when and how their private medical data is used, to consent to such usage, and to opt out of future usage. NIH should require better protections for collected data used in public health research; implement the tools necessary to require informed consent for all future use of collected data, and respect the rights of PLHIV to opt-out of future use of their data for research.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1750

I am responding to this RFI: On behalf of an organization

Name: Lisa Voltolina, MS, CCRP, CIP

Name of Organization: New York Stem Cell Foundation

Type of Organization: Non-Profit Research Organization

Role: Other

Role – Other: Associate Director, Clinical Research and Regulatory Compliance

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

New York Stem Cell Foundation

1. Utility and useability of this resource:

Section II of the proposed resource states that references to data and specimens throughout the document captures all identifiable information and biospecimens (e.g., "This resource consistently refers to "data and biospecimens" as a means to capture all identifiable information and biospecimens that research participants may contribute[...]." However, the sample language at times reads as if it applied to deidentified material as well. For example, Component 1 appears relevant only to deidentified data and biospecimens as defined by the Common Rule (e.g., all options apply to data and biospecimens for which the identity of the subject cannot be readily ascertained). Elsewhere, as in Component 4, the proposed template language refers to coded data and biospecimens where the key to the code remains with the data and/or biospecimens (which is not an option under Component 1). If the intent is for NIH's resource to apply to all research regulated by the Common Rule, this should be made clear.

2. Gaps or additional components that should be included:

1. The proposed language does not cover all the required components of broad consent (45 CFR 46.116(d)). The broad consent model is an important opportunity to give potential participants better control over use of their identifiable data and biospecimens – compared to waivers of consent – and support secondary research conduct. Implementation challenges of broad consent notwithstanding, the proposed language should meet requirements for stand-alone broad consent and merged specific and broad consent. If NIH's resource will not apply to broad consent, this should be made clear. 2. Consent language (and the informed consent discussion) related to security and confidentiality of identifiable data and biospecimens has become increasingly challenging as research involving genomic data becomes more prevalent. Concepts related to genomics are difficult to convey. Further, the pace of advances in genome sequencing and attitudes/understanding of genomic privacy places limits on the utility of static template language. Including links to the National Human Genome Research Institute's informed consent resources in Section III is helpful, but the most useful resources (e.g. Educational Tools and Resources for Participants) require a deeper dive into the site. Direct linkage to those resources in Section III would increase visibility and regular use of these important resources, which would further support a valid informed consent discussion.

3. Specific language proposed in the informed consent sample language:

Flesch Reading Ease, Flesch-Kincaid, and SMOG place primary emphasis on average number of syllables per word and average number of words per sentence. However, recent research suggests that word familiarity may be a stronger indicator of a document's readability. Small changes can have a meaningful impact; for example, "biospecimens" could be replaced with the more familiar "samples." Suggestions to improve readability are described below: Component 1, Introduction-Description: Sentence length and syllable density are appropriate; however, more familiar words could be used to replace or define research jargon (e.g., "commercial entity," "biospecimens," and "identifying information"). Component 1, Option 1: The coding process described in Option 1 does not read fluently and does not make clear that the code is not shared along with data or biospecimens. Current Language: "We will protect the confidentiality of your information to the extent possible. Your name and other identifying information will not be on any data and biospecimens you provide. The data and biospecimens will have a code that links to your identifying information. The code key will be kept in a locked location separate from your information. The code key can only be accessed by people who have permission." Suggested Revised Language:: "Your name and other information that could be used to identify you will not be on any data or samples you provide. Instead, we will label your data and samples with a code that links to your identifying information. The key to the code will be kept separate from your data and samples and can only be accessed by a limited number of people with permission to see your identifying information. The key to the code will not be shared along with your data or samples." Component 1, Option 2: The language oversimplifies the deidentification process, especially as applicable to biospecimens. The result is that researchers could overpromise on their ability to deidentify data and biospecimens. The text should be revised to describe more realistically that all reasonable steps will be taken to remove identifiers, but complete de-identification can never be guaranteed. Current Language: "Your name and identifying information will not be on any data and biospecimens you provide. Investigators cannot link your identifying information to the data and biospecimens." Suggested Revised Language: "We will take steps to keep your name and identifying information confidential, but we cannot guarantee total privacy. [Describe precautions in place to protect confidentiality, such as collecting data anonymously or coding samples immediately.]" Component 2: The template text sacrifices fluency for less meaningful attributes of readability such as syllable and word-per-sentence count. Current Language: "It is your choice whether or not to let researchers share your data and biospecimens for research in the future. If you say "yes," you can change your mind later, but your data and biospecimens might still be used if they have already been shared. If you say "no," you can still fully participate in this study. Please initial next to your choice:" and "Participating in this study means you agree to share your data and biospecimens. You can change your mind later, but researchers may still use your data and biospecimens that have already been shared. If you do not want your data and biospecimens used for other projects, you should not participate in this study." Suggested Revised Language: "It is your choice whether to let us share your data and samples for use in future research. If you decide to let us share your data and samples now, you can change your mind later. We will make our best effort to retrieve any data and samples that have been shared, but there is a chance this may not be possible and that your materials will continue to be used. You can still fully participate in the study even if you do not choose to share your data and samples for use in future research. Please initial next to your choice." and "Participating in this study means you agree to share your data and samples for use in future research. If you choose to participate now, you can change your mind later. We will make our best effort to retrieve any data and samples that have been shared, but there is a chance this may not be possible and that

your materials may continue to be used. You should not participate in this study if you do not want your data and samples used for other research projects." Component 3: This language overpromises on the data and biospecimen retrieval process and may encourage unrealistic expectations if a participant withdraws or discontinues from a study (e.g., "We will do our best to retrieve ALL your data and biospecimens that have already been shared" [emphasis ours].) It would be most appropriate to provide alternatives for stakeholders to choose from as applicable to a specific study. For example, potential participants could be informed that data and biospecimen sharing will stop upon receipt of a request to discontinue or withdraw, but any previously shared material will continue to be used. At a minimum, the last sentence in the proposed text should be removed as it simply reiterates sentence 4. Current Language: "You can change your mind about sharing your data and biospecimens at any time. If you change your mind, please contact the study team to let us know. We will not share your data and biospecimens going forward. We will do our best to retrieve all your data and biospecimens that have already been shared, but it may not be possible. For example, if some research with your data and biospecimens has already been done, the information from that research may still be used. We will not know which data and biospecimens are yours if the identifying information was removed. Also, if the data and biospecimens have been shared already with other researchers, it might not be possible to get them back." Suggested Revised Language: "You can change your mind about sharing your data and samples at any time. If you change your mind, please contact the study team to let us know. We will not share your [identifiable/deidentified] data or samples going forward. We will make our best effort to retrieve any data and samples that have been shared with other researchers, but there is a chance this may not be possible and that your materials may continue to be used." Component 5: The fluency of this section could be improved by replacing jargon with higher frequency terms and shortening the last sentence to make the point directly. Current Language: "The use of your data and biospecimens may lead to new tests, drugs, devices, or other products or services with commercial value. These products or services could be patented and licensed. There are no plans to provide any payment to you should this occur." Suggested Revised Language: "The use of your data and samples may lead to new tests, drugs, devices, or other products that could be patented, licensed, or sold for financial profit. There are no plans to pay you if this happens."

4. Hurdles or barriers to wider use of this resource by the community:

Quality improvement is often not prioritized within IRB or other regulatory offices due to insufficient resources—specifically time constraints due to outsized workloads. Organizations will need to build consensus and implement creative forms of incentivization to drive change at the local level. Common metrics, including submission-to-approval turnaround time, may serve as a motivator. For example, IRBs are likely to find that reviews are completed more accurately and expeditiously if study teams are provided with template language that minimizes complexity and can be adjusted easily to meet individualized study needs. However, closer examination of local motivators and attitudes will likely be necessary to achieve optimal outcomes.

5. Other considerations relevant to this resource:

The proposed language appropriately states that participants will not directly benefit from sharing data and biospecimens. However, the second sentence could be expanded to describe how sharing this material may help others in the future. If the placement of such language is seen as potentially coercive, language elsewhere in the consent should describe the scientific and societal value of data and

biospecimens sharing so potential participants can better understand why the request is being made; this information could serve as an intrinsic motivator for research participation, without necessarily being coercive.

Submission ID: 1751

I am responding to this RFI: On behalf of an organization

Name: Glenn Martin MD DLFAPA CIP

Name of Organization: Icahn School of Medicine at Mount Sinai

Type of Organization: Icahn School of Medicine at Mount Sinai

Type of Organization - Other: Academic Institution

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. Utility and useability of this resource:

While we have specific suggestions, as a whole the document is well organized, addresses important points and will be help to the feild.

2. Gaps or additional components that should be included:

There are several overarching concerns that we believe should be addressed. 1-The combining of samples and data is potentially problematic. The risks associated with the potential for re-identification of samples through genetic analysis is quite real and is not the same for much research data. That risk may be mitigated but it is real and only likely to increase. Similarly, the risks of sequence data are different than other forms of data, e.g., a time series of lab values and self-rating scales. 2-The use of the pronoun “We” in the consent may refer to the PI, the research team or the institution. This becomes particularly important in situations where samples/data will be held “indefinitely” and the need to contact those responsible for the samples may occur years after participating. 3-Use of absolutes should be avoided. For example, “Investigators cannot link your identifying information to the data and biospecimens” is very likely not to be accurate, given time and effort 4-There is a strong push from federal sponsors for data and samples to be used for “general research purposes” which is wider than “… research could also be about unrelated diseases, conditions, or other aspects of health.” We suggest that IRB’s be advised to consider this issue and that possible language be suggested for use where needed, that includes non-medical research, e.g., human origins, migrations, etc.

3. Specific language proposed in the informed consent sample language:

Component 1: It should be made clearer that data and samples may end up stored in various locations AND that while the investigators may control samples in their possession, once they are shared, they are likely out of their direct control and further restrictions cannot be guaranteed. This could/should be in the risk section, but in this section the different banks that may be used to store the samples/data and the different levels of control should be made clear. There should also be sample language provided for those cases of repositories with free access where “researchers must get approval and they must agree not to try to identify you” is not true. This is becoming more frequent in our experience. Something along the lines of the text below is suggested: • Your data may be deposited in a free access databank

where anyone with internet access can use the data in any way they see fit. In those situations where the samples/data will be used without specific subject notification, involvement or permission we suggest incorporating the suggested wording from guidance around broad consent, that is… • That means that a research project might be done that you would not consent to if provided with the details of that research project. Component 2: In our experience we find offering other options can increase participation. For example, allowing participants to limit future uses to related projects vs. general or medical research uses could be offered. We suggest: • Do you give the researchers permission to keep the information and/or specimens indefinitely and use them for future studies that are not related to the purpose of the current study (for example, a different area of research)? • From time-to-time researchers outside of medicine and related sciences would like to use this information. This might be in the field of anthropology, human origins, mapping human migration patterns etc. Do you give permission to use your information and/or specimens outside the fields of medicine and biological sciences? Component 3: Nothing to add Component 4: We would suggest that the risks described in previous documents from NIH, and which have to be considered by IRBs to allow for sharing in various NIH repositories, be cited here to allow for easy incorporation. The current version we use, with some minor tweaks and additions follows: Group Risks - Although we will not give researchers your name, we will give them basic information such as your race, ethnic group, and sex. This information helps researchers learn whether the factors that lead to health problems are the same in different groups of people. It is possible that such findings could one day help people of the same race, ethnic group, or sex as you. However, they could also be misused to support harmful stereotypes or even promote discrimination. Privacy Risks - Your name and other information that could directly identify you (such as address, date of birth or social security number) will never be placed into a scientific database [if true]. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small, but may grow in the future. Since the database includes genetic information, a break in security may also pose a potential risk to blood relatives as well as yourself. For example, it could be used to make it harder for you (or a relative) to get or keep a job or insurance. If your private information was misused it is possible you would also experience other harms, such as stress, anxiety, stigmatization, or embarrassment from revealing information about your family relationships, ethnic heritage, or health conditions. Insurance Risks – There is a Federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most employers of over 15 people to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Component 5: Nothing to add

4. **Hurdles or barriers to wider use of this resource by the community:**

5. **Other considerations relevant to this resource:**

We thank you for not using the term de-identified in the document. We thank you for the opportunity to submit comments.

Submission ID: 1752

I am responding to this RFI: On behalf of an organization

Name: Mathias Brochhausen

Name of Organization: University of Arkansas for Medical Sciences - TRI

Type of Organization: University of Arkansas for Medical Sciences - TRI

Type of Organization - Other: Academic Institution

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

translational research

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

The current resource provides helpful informed consent sample language.. However, we suggest that the sample language should take into consideration not only current practices but also future ones. Without this consideration, the sample language may quickly become outdated, forcing researchers to retrofit their informed consent documents The sample language currently is not paired with a machine-understandable counterpart. Having a representation of the content of the sample language in a formal language that is machine-interpretable is useful to international informed consent protocols and data. In addition, such a resource will enable automatic assessment or verification of consistent use of the sample language and ensure comparability and reproducibility of outcomes. For example, the sample language contains the following statement: “use my data and biospecimens in other research studies.” This leaves it open what e.g. a biospecimen or a research study is. Thus, there can be semantically grounded disagreement on what constitutes a biospecimen or a research study. In our practice in data integration, we see these problems typically becoming obvious once (meta)-data is shared or integrated with other data. We propose that this gap be filled by creating a machine-interpretable representation of the content of the sample language using existing standards, e.g. the W3C standards Resource Description Framework (RDF) and Web Ontology Language (OWL).

3. **Specific language proposed in the informed consent sample language:**

The UAMS Center for Health Literacy has provided feedback, edits, and suggestions. General points to consider 2a: In addition to encouraging readability (reading level of the entire consent form) we would suggest promoting other elements of plain language writing. To this bullet, you might add: “In addition to readability, we encourage the use of other writing techniques that facilitate understanding and action. Some examples of plain language tips that could be incorporated include: Use active voice to make it clear who will do what Avoid using jargon or defining words that may not be familiar Use bullets for lists (or numbers for sequential steps) Address the reader directly (use “you”) To learn more, visit https://www.plainlanguage.gov/guidelines/. “ General points to consider 2b: Regarding the additional resources on “evaluating readability” resource: The link includes appropriate guidance for cleaning a document and describes some common readability formulas. A concern is that it forwards the reader to

an online readability calculator. Each online readability calculator website has its own privacy protocols, and uploading content from an ICF may result in ICF content being stored or shared in unanticipated ways, potentially threatening any proprietary or otherwise confidential details contained therein. It is suggested that this guidance include this disclaimer. Also, we have noted errors in online calculators' formulas, so we would encourage comparison with hand calculation before choosing an online solution. General points to consider: Suggest merging bullets 1 and 6 to read: "Data and biospecimens may involve distinct storage and/or sharing procedures. Some protocols may require separate consent language to inform how data versus biospecimens are stored and shared.If the future use of data and biospecimens will be limited, this information should be specified in the consent language."

4. **Hurdles or barriers to wider use of this resource by the community:**

5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/wolBWSyTNL.pdf

Attachment Description: Cover Letter & plain language suggestions

Submission ID: 1753

I am responding to this RFI: On behalf of myself

Name: Alfredo Trejo

Role: Research Participant/Patient/Advocate

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Patients and other participants in biomedical or public health research might think twice about whether their safety, privacy, and bodily autonomy are protected if information used for research is not obtained with their full informed consent. People living with HIV (PLHIV) have been confronted as vectors for disease for decades, and are at risk of being subject to criminal and immigration proceedings largely because of their health status. However, the issue isn't a hostile criminal justice system alone, since federal, state and local governments have proceeded with a molecular HIV surveillance (MHS) program despite an abundance of community concern. I believe it is clear that MHS is public health research and that informed consent requirements should extend to HIV-testing related data collected in the administration of direct care but then used for future research and analysis. PLHIV have the right to know when and how their private medical data is used, to consent to such usage, and to opt out of future usage at any time. NIH can and should work together with government agencies, community organizations, PLHIV, and advocates to enshrine better protections for collected data used in public health research. NIH must also implement the tools necessary to require informed consent for all future use of collected data, and respect the rights of PLHIV to opt-out of future use of their data for research.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/mfvFCIFgNv.pdf

Submission ID: 1754

I am responding to this RFI: On behalf of an organization

Name: Tom Hume

Name of Organization: RARE-X

Type of Organization: RARE-X

Type of Organization - Other: Research Participant/Patient Advocacy Organization

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

All Rare Diseases

1. Utility and useability of this resource:

Patients and patient advocacy groups help to drive much of the rare disease research through their data contributions. They are driving data collection efforts by leveraging platforms that can support the interoperability and interconnection of multiple data sources relevant to that patient. Other data sources patients want to be connected to their data sets include genetic reports, biological samples, other health, other study data, and future data. This approach also requires creating governance and a patient-centric consent process supported by technology designed for the future life of data. Rare disease patients are proving they are willing to share their de-identified data widely with researchers. Of the patients consenting on the RARE-X platform our studies show: ● 66% of Patients Selected Maximum Data Sharing (Researchers, Biopharma, Citizen Scientists), with another 31% willing to share their data with health, medical, and biomedical researchers. ● 40% already have provided biospecimens they have submitted for research that they would like to connect with their patient data ● 80% would share medical health records and 68% would be interested in connecting data from other past research ● Over 51% of enrolled patients have a genetic report they would upload to RARE-X for sharing with researchers Patients want to own their data. They also want the platforms they use for data collection to store their data, share their data with selected and appropriate researchers, and patients to access copies of their data whenever requested. For example, by capitalizing on technology, RARE-X has taken an approach to governance and consent that is forward-looking and provides needed flexibility to ensure data lives beyond its initial and expected use, maximizing potential usage of this data to understand disease and develop therapies. These efforts also aim to avoid requiring participants to enter the same data repeatedly over time.

2. Gaps or additional components that should be included:

Increasingly, researchers in rare disease have come to recognize that the breakthrough to treatments for one disorder may lie in the insights provided in a different disorder. To enable these types of insights, data needs to be structured to ensure that it can be connected and interoperable. Unfortunately, too often rare disease researchers have their hands tied with their own protocols and well-intentioned protections of participants ensuring they would not share the data they collect. Rare and ultra-rare diseases can be heterogeneous and that it’s critical to get data from a large enough

sample of participants to provide meaningful insights. Too often, research studies based on small patient samples are not representative of the true broad population with a given condition. As the patient population grows, the insights are not updated quickly enough to provide the newest insights. By lowering barriers to participation for rare disease patients while protecting their privacy and allowing them to retain ownership of their own data, researchers will discover patients where they are (location, education level, engagement abilities), rather than relying on an academic center of excellence to identify them. This will help researchers access a larger pool of patients with a given disorder, accelerate the enrollment of clinical trials, and help entice biopharmaceutical companies to pursue treatment for disorders by helping them better understand the size of a patient population and the nature of a condition. With an estimated 13,000+ rare diseases, looking at them one at a time will not be the best approach to yielding the answers patients seek. Looking across rare disease can make it possible for researchers to understand correlations between diseases and may reveal common biologic pathways, shared features, or common mechanisms underlying different conditions. A data-collection program with a technical platform and governance that enables a new generation of research that moves beyond an isolated researcher looking at a single disease to a collaborative and cross-disciplinary approach where biomedical researchers, bioinformaticians, computer scientists, data scientists, mathematicians, and others can contribute their unique talents to solving challenges of diagnosing, treating, and curing rare diseases.

3. Specific language proposed in the informed consent sample language:

Consent documents can be long, difficult to understand, and overwhelming for research participants to work through. Often consent agreements do not contemplate or allow for the future use of data beyond the immediate intended use. To minimize the burden on participants while ensuring understanding of the consent document, data collection owners need to break down the consent process into short, readable pieces. By using straightforward language that can be understood by people of any education level, the consent process can be completed without requiring a significant investment of time or sacrificing participants' understanding of what they are agreeing to do. Different participants may have different interests and needs with regards to what may be considered effective data to collect. As such, the consent process needs to support all types of participants and participant relationships for the consent process. Organizations need to do this with an eye toward enabling multi-stakeholder data sets to support cross-disease research. A modular approach to surveys is required and surveys need to be designed to be short and easy to complete. Based on the participants' responses, participants should be invited to answer other short surveys, and they should not be asked to complete surveys that do not apply to them. The data collection owners need to apply this same approach to its consent agreement. Consent forms should include a Q and A format to provide a more granular understanding. Consent agreements are legal, binding documents that do not change over time. They remain in force until they are revoked or replaced with a new consent agreement. RARE-X has turned the traditional consent process on its head. By restricting the consent document to the agreement of data collection and using a separate data sharing preference survey, it allows the participant to easily change their data sharing preference without altering their initial consent agreement. This separate survey allows participants to choose with whom they are willing to share their data and how it may be used. It allows them to choose to do such things as participate in biospecimen collections, share their data with rare disease drug developers, or share it with patient communities. Their responses to the data preference survey create a data-sharing ontology that codes their data. RARE-X then uses that ontology to automatically manage

who can access the data based on the data-sharing selections tied to it. All of this needs to be enabled by technology that can easily track and allow sharing according to a participant's stated preferences. As an example of the power of this flexible approach, a participant may not want to share their data with industry today, but if a company reaches out to RARE-X in the future because of a new clinical study for which a participant would qualify, RARE-X is able to reach out to notify the participant of the opportunity. There is no need to go through a new consent process. All the participant needs to do is update his or her data-sharing preferences, if desired.

4. Hurdles or barriers to wider use of this resource by the community:

Over the years, traditional consent forms have become constructed to include more legal jargon to serve the legal and ethical review requirements of the institutions collecting the data rather than focusing on the participant's understanding of the study procedures. As such, traditional consent agreements focus on the immediate purpose for which the data is being collected. They are not concerned with addressing potential future uses for the data that may arise or realizing the broadest potential benefits from the data being collected. There are many barriers to data-sharing. The best way to remove obstacles to sharing data is to enable patients to control who can access their data and use it. Academic researchers may not want to share data ahead of publishing. Drug companies may not want to share data because of competitive reasons. Rare disease organizations working within the same disease area may refuse to share data with other organizations they view as competitors. Even well-intentioned data owners who wish to share data may be prohibited from doing so because of narrowly written consent agreements. The goal should be to ensure that patients have control and can share their data with whomever they like. Governance and consent forms need to be built for this purpose. It allows patients to decide who they share their data with, and it allows them to change their minds over time.

5. Other considerations relevant to this resource:

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/nWXMstLwIc.pdf

Attachment Description: White Paper on Patient-Centric Consent for Data Collection

Submission ID: 1755

I am responding to this RFI: On behalf of an organization

Name: Rajni Samavedam

Name of Organization: Booz Allen Hamilton

Type of Organization: Booz Allen Hamilton

Type of Organization - Other: Other

Role: Other

Role - Other: Principal/Director

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Multi-sector including Life Sciences

1. Utility and useability of this resource:

The sample language developed by NIH for use in informed consent documents for data and biospecimen sharing responds to the needs and requests of the research community. NIH's efforts to develop such sample language is timely, appreciated, and critically needed by the scientific community for four reasons, in Booz Allen's view: a) To adhere to the 2018 Common Rule (45 CFR 46) and implement robust informed consent practices; (b) To encourage participants to share data and biospecimens for research by ensuring their data privacy, autonomy, and well-being; (c) To ensure informed consent documents are more aligned with technological advances in data science, data transformation, and data storage; and (d) to improve the utility and usability of informed consent forms to support the use of data and biospecimens beyond the scope of the research addressed in the consent form for a given study, including for other relevant research, unrelated research, and commercial applications. It is strongly advisable to have language that covers the use of data and biospecimens for research purposes that are already known as well as unknown future research, and the sample language does encourage and ensure consent for a wide range of research purposes. Component 1 clearly informs study participants that the data and biospecimens collected may be used for other future research purposes, including research about diseases, conditions, and health aspects unrelated to the initial study, and by other researchers and institutions. With the increasing quest for biomedical data worldwide, increasingly complicated data sharing policies, and constantly advancing tools and technologies for data transformation, it is challenging to define the extent and boundary to which data and biospecimens may be used in the future. The sample consent language effectively addresses these technical challenges and ensures transparency. As part of our Life Sciences Practice, Booz Allen is involved in many biomedical data sharing activities as well as biospecimen management efforts for NIH – these efforts have highlighted that privacy is of increasing concern for study participants, and the literature clearly shows that a remarkably small amount of data can be used to re-identify study participants. The sample language in Component 4: Risks & Benefits tells the participant that there is a "small risk"/"small chance" that there identity could be discovered but it does not quantify the likelihood of reidentification – however, the risk is not really that small [1]. Linking extant data with a

primary dataset further increases challenges with protections and use. Governance of data, therefore, would need to be enhanced considering the re-identification challenge. NIH is exploring via the Office of Data Science Strategy (ODSS) techniques to enhance privacy in linked data beyond data encryption, such as Privacy-Preserving Record Linkages. Perhaps more sample language could be added to note that "Government-accepted and required methods and technologies available will be used to protect your data"; however, this would require NIH to mandate data protection methods. Also, if known at the time of consent, informing participants where the data and results of the study will be shared would be courteous and perhaps enhance participation. Sample language also aids in addressing constraints and limitations to recruiting clinical trial participants. Recruitment and retention of clinical trial participants is one of the key challenges for clinical investigators and institutions. It is estimated that the recruitment and subsequent enrollment of clinical trial participants consumes nearly 40% of a clinical trial's budget. [2] With growing challenges in both recruitment and retention of study participants, FDA has encouraged better usage of technology and data available to investigators for precision medicine research, to make the most use out of the data collected [3]. The proposed sample language is also well aligned with the scope and vision of FDA to maximize the use of data and biospecimens for multiple future research purposes where possible. [1] Sweeney L, Yoo JS, Perovich L, Boronow KE, Brown P, Brody JG. 2017. Re-identification Risks in HIPAA Safe Harbor Data: A study of data from one environmental health study. Technol Sci. 2017082801. [2] Carroll J. 2018. RWE continues to shape the future clinical research landscape. PharmaVoice. https://www.pharmavoice.com/article/2018-06-rwe/ [3] Statement by FDA Commissioner Scott Gottlieb, MD, on new strategies to modernize clinical trials to advance precision medicine, patient protections and more efficient product development. 2019. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm633500.htm

2. Gaps or additional components that should be included:

Definition of data and biospecimens: The proposed consent language in the RFI defines "Data and biospecimens" to include information collected from, or about, a research participant during the course of a primary study (e.g., surveys, medical images, electronic health records, wearable device information) as well as human material (e.g., blood, tissue, urine, extracted DNA). With advancements in data science and bioinformatics, participant data can be converted easily from one type to the other. For example, omics data from a biospecimen may be retrieved and stored. Genome sequences may be annotated, protein sequences may be converted to structural forms and stored in protein structure databases, and multi-omics data may be converted to predictive models. This could be addressed in the informed consent language to indicate the possibility that data may be transformed to other forms for different applications. Biospecimens Consideration: Unlike biospecimens, data can be used indefinitely without any limitations. With advancements in omics technology, biospecimens can be converted to data forms such as genomic, proteomic, or metabolomic data. It is vital to explicitly include the risks and benefits for data versus biospecimens and specify the possibility of converting biospecimens to different data forms (that may not be specified in the original proposed research) in the consent language. For example, biospecimens received for histochemistry analysis may be used for omics analysis. Due to growing challenges in recruiting participants, increasing use of data science technologies, and high demand for clinical data, this strategy/language would allow the use of clinical resources for a wide range of applications. Addressing vulnerable populations: Clear communications are key to ensuring that participants have all the information necessary to make an informed decision about participating in the study and agreeing to the collection and sharing of data and biospecimens. It is particularly challenging,

however, for the informed consent to clearly describe the technical aspects of complex research as well as the uncertainties around the ways the data and biospecimens may be used in the future. Research involving specific populations (e.g., children, prisoners, individuals with impaired decision-making capacity) raise special challenges. It may be helpful to integrate instructional design principles as well as layout (e.g., formatting and graphics) to help convey high-level details, risks, and benefits of the research specific to the unique subgroup(s) of participants. Meeting the data and biospecimen processing requirements of different cultural groups: Challenges exist in ensuring that consent language will adhere to the requirements of different cultural, tribal, donor, or sovereign groups with detailed information on how data and biospecimens are handled and adhering to specific protocols including the disposition of biospecimens. It may be beneficial to include specific language that address their concerns from a cultural standpoint and engender trust. Vetting with tribal leaders and other cultural group leaders who are influencers in the specific community might be helpful. Being transparent about how data and biospecimens will be handled (including disposition of biospecimens) and the policies related to data sharing can also help address this challenge.

3. Specific language proposed in the informed consent sample language:

Introduction: The primary theme of the suggested edits/considerations that we have included below is to ensure clarity of the informed consent sample language. This includes making the consent language clear and understandable by all participants, regardless of reading level, and taking note of special considerations for vulnerable populations. In addition, we also suggest the use of visual presentation and formatting (such as the use of bolding, underlining, capitalizing, bullets, etc.) to make the consent language easier to read and understand. Component 1—Introduction-Description: As stated in the RFI, the purpose of this component is to provide participants with an introduction to the study, and a description of the storage and sharing of data and biospecimens. Below are suggested edits/considerations specific to the Introduction-Description sample language: As mentioned earlier, specify the possibilities of data transformed to other forms for different applications, e.g., define “data” in the beginning of the sample informed consent to include “transformed data” that is explained in plain language Move language about why “we would like to make your data and biospecimens available for other research studies that may be done in the future” to earlier in the introduction-description section, so that is immediately clear why the request is being made Add that additional studies may be done by researchers at the current institution or by researchers at other institutions (just like the language informing participants that research may be done about similar diseases or unrelated diseases) Replace “plan to keep your data” with “will keep your data”, as the participant will be explicitly agreeing to their data and biospecimens being stored for the time frame listed. If flexibility is important, language can be included to highlight how any changes in the time frame will be communicated to participants Clarify the phrase “shared with investigators around the world”, e.g., replace with “shared with researchers both inside and outside of the U.S.”, or include some constraints such as “shared with investigators around the world with appropriate privacy and security protections in place.” Clarify language about researchers getting approval to use data and biospecimens, and who has permission to access the code key Specify the time frame that all researchers would be allowed to use data and biospecimens—not just current researchers but future researchers as well Clarify if data and biospecimens will be collected with identifying information and then deidentified versus collected without identifying information, as it gives the participants a clearer picture of the data collection and linking process and assists IRBs and/or Privacy Boards in determining HIPAA privacy related requirements Component 2—Voluntary

Participation: As stated in the RFI, the purpose of this component is to inform participants about the voluntary nature of data and biospecimen storage and sharing. Below are suggested edits/considerations specific to the Voluntary Participation sample language: Consider providing more detailed information about when the sharing of data and biospecimens will be required versus optional, e.g., how it will be decided if sharing is required or optional for the current study, what it means for participation in the current study. This way, researchers can quickly update the informed consent language, and participants can make a more informed decision about whether to participate in the current study Double-barreled statements set forth below are confusing. Revise to list each agreement that the participant needs to make when signing the consent to provide clarity and full transparency: Asking for agreement to participate in the study and agreement to share data and biospecimens Asking for agreement to share data and biospecimens with current researchers and sharing with other researchers in the future Provide instructions for how exactly a participant can "change their mind later" if they initially agree to share their data and biospecimens for future research but later wish to revoke their agreement. For example, provide the name and contact information of the principal investigator (PI) or the Study Coordinator and the method for revoking the participant's prior informed consent Component 3—Discontinuation/Withdrawal: As stated in the RFI, the purpose of the Discontinuation/Withdrawal language in informed consent documents is to describe what will happen if the participant changes their mind about storage and sharing of their data and biospecimens. Below are suggested edits/considerations specific to the Discontinuation/Withdrawal sample language: Specify how a participant can "contact the study team", e.g., provide a single and durable contact information for the PI, Study Coordinator, or other researcher As mentioned in the introduction, it can be challenging to define the extent and boundary to which data and biospecimens may be used in the future. Thus, transparency in the informed consent language is key. For example, if it is impossible to identify and retrieve the participant's data and biospecimens because the data were collected anonymously, and thus researchers will be able to continue to use the data and biospecimens, then this needs to be explicitly stated Component 4—Risks & Benefits: As stated in the RFI, the purpose of the Risks and Benefits language in informed consent documents is to describe the risks/discomforts related to storage and sharing of data and biospecimens, and benefits from the use of data and biospecimens that participants may receive. Below are suggested edits/considerations specific to the Risks and Benefits sample language: List benefits before risks to start with positive outcomes [1,2] Revise the benefit language to state: "may contribute to research and medical progress that helps others in the future." Consider the implications of using the term "risk" (as opposed to "possible negative consequence" or a similar term), given that different people make different judgments and estimates about the characteristics and severity of a "risk" Clarify that there may be possible negative consequences (risks) associated with collecting/storing and with sharing data and biospecimens—the risks of unauthorized people getting access and identities being discovered apply to both Distinguish between the possible negative consequences (risks) and benefits for data versus biospecimens Replace "when we share your data and biospecimens" with "if you agree to let us share your data and biospecimens", so that participants do not feel like sharing is a foregone conclusion [1] Slovic P, Peters E. 2017. Risk Perception and Affect. Current Directions in Psychological Science. 15(6) 322-325. [2] Slovic P. 1987. Perception of risk. Science. 17; 236(4799): 280-285. doi: 10.1126/science.3563507. PMID: 3563507.

4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

NIH may want to consider adding a notation in its proposed consent template stating that the proposed consent language was specifically developed to help guide adherence to the consent requirements within the Common Rule. For typical data sharing, the institution holding the PHI data is the one who has the participant sign the consent. However, for large research studies where PHI will be gathered and used/disclosed likely from multiple covered entities, it is highly recommended to get the HIPAA authorization and consent signed at the same time, or even better, have the documents combined. HIPAA authorization details may be included to the consent language or the authorization can be developed at the same time. This will help avoid each covered entity from having to get the release/HIPAA authorization.

Submission ID: 1756

I am responding to this RFI: On behalf of an organization

Name: Helen M. Moore

Name of Organization: National Cancer Institute

Type of Organization: National Cancer Institute

Type of Organization - Other: Government Agency

Role: Government Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Biobanking

1. Utility and useability of this resource:

Thank you for the opportunity to comment on this important document. I am responding on behalf of the National Cancer Institute (NCI) Biorepositories and Biospecimen Research Branch. Our Branch develops best practices for biobanking, sponsors research on biospecimen science, and leads the collection of biospecimens to serve critical research needs for NCI and NIH programs. Appropriate informed consent documents and procedures are critical to our work and to the extramural research we sponsor. Our experience has been that there can be considerable confusion and misunderstanding about appropriate informed consent documents and procedures. This can lead to extended periods of review, discussion and revision of informed consent documents and procedures, which in turn can delay the launch of important research initiatives. The resource presented here could be a valuable tool in reducing confusion and accelerating research. The document provides vetted, standardized language on common consent topics, using plain language principles, to facilitate and promote more effective communication to potential participants about considerations associated with biospecimen and data sharing. Our high-level comments are as follows: • Separation of biospecimen use and use of associated data: a major point of confusion in informed consent policy and procedures is the somewhat artificial separation of the use of biospecimens and the use of associated data. Biospecimens collected for research are collected for the primary purpose of analysis and data generation; thus, data generation and data sharing are necessarily part of any biospecimen collection endeavor and should be part of any biospecimen informed consent. Demographic and medical record data is also generally collected in any biospecimen collection program. It would be helpful for the potential users of this resource to outline the importance of addressing in the informed consent the anticipated use of both the biospecimens and the associated data (analytical and medical data), as they are inextricably woven together in research. Research participants can understand this if we explain it clearly. • Scope of document: an introductory statement could be added to explain whether the resource is intended for any use of biospecimens and associated data for research, or only for future unspecified research. • Relationship of this resource to the Common Rule/45 C.F.R. 46 and other policies: an introductory statement could be added to clarify that this document does not supersede existing policies such as 45 C.F.R. 46, subpart A (the Common Rule) and the NIH Genomic Data Sharing policy; rather, it outlines considerations and approaches for informed consent that are consistent with these policies. • Return of results: the return of results of

research to participants has not been addressed. A consent form and process that covers the question of whether results will be returned could be considered mandatory in today's world. From a regulatory perspective, results may be returned when the data has been generated in a clinical laboratory (CLIA-accredited laboratory). Biospecimens may be considered part of the analysis system that produced the results, and for this reason a biorepository that is receiving and processing biospecimens may also be required to hold CLIA accreditation. Incidental findings must also be addressed in the consent form. • Informed consent template: it is clear that this document is not intended to provide a template for informed consent. However, we suggest that an online, dynamic, user-driven informed consent template could be developed by NIH for use by funded investigators. Such a tool could provide a critical and practical partner to the resource proposed here.

2. Gaps or additional components that should be included:

• Section III: General Points to Consider o The points mentioned may be misconstrued as an entire set of considerations, when it is an incomplete list. The reasoning behind the scope of this section is unclear; some critical information may be missing. General points to consider could also include, for example, information to increase the transparency of the research, such as: Why are we doing this study? Why do we want you to participate? What will happen with the biospecimens and data? Will results be shared back with participants? o The points in this quoted section of the Common Rule should be made and/or referenced (italics added): 46.116.5 (i) "Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension." o "Data and biospecimens may involve distinct storage and/or sharing procedures. Some protocols may require separate consent language to inform how data versus biospecimens are stored and shared." Most if not all protocols require language about storage and sharing of both data and biospecimens. o "If the future use of data and biospecimens will be limited, this information should be specified in the consent language." Add: "…and a rationale provided." o "As technology advances for coding and deidentifying data and biospecimens, consider the implications for privacy and confidentiality and adjust language as appropriate." It is important to explain to participants what we do and why to protect privacy and confidentiality. Specific examples of coding and deidentifying can be provided in the informed consent form. Studies have shown that it is still possible to identify an individual using data collected from biospecimens by triangulation of information with data scraped online or by other methods, even if the individual's identifying information has been de-linked. For transparency, we suggest adding text to explain that it is not possible to completely safeguard against identification. o Physical custody and accessibility of biospecimens: Suggest adding text to explain that individuals may not be able to retrieve their biospecimens, should they or a representative wish to request access. Impermanence of individual and institutional custodians: suggest explaining that, over time, biospecimens and/or associated data may be moved to a new location, and/or subsumed by another study, or come under the custodianship of another entity. o Plain language: Consideration of reading level is well described. An additional sentence could be added for investigators to consider principles of plain language communication. For example, for better comprehension, write in conversational style, including using contractions; define words that may be unfamiliar to participants; use shorter sentences with one topic each; be consistent with terms, for example, use either "investigator" or "researcher."

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**

Hurdles and barriers may include the following: • Lack of awareness of the resource. • Lack of understanding of the benefits of the form language to patients and research studies. • Misunderstanding of the instructions. • Mismatch with existing informed consent language or style. • IRBs or other regulatory bodies not wanting to adopt new language/new form/new approach. • Lack of understanding by investigators and/or IRBs about how this document relates to other resources and policies including the Common Rule and the NIH Genomic Data Sharing Policy. • Ongoing challenges for inclusion of information in informed consent, comprehension of informed consent, and facilitating informed consent: o Increasing complexity and perceived complexity of biomedical research, leading to custom approaches to consent per study. o Low rates of health literacy. o Balancing the need for thorough explanation with the movement to shorter but more clear consent forms. o Limited time for investigators to engage in the process of revamping approaches and revising informed consent forms. o Limited medical staff time for the consenting process.

5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/LBzYQOVBbp.pdf

Attachment Description: Word document of entered response.

Submission ID: 1757

I am responding to this RFI: On behalf of an organization

Name: Rick White

Name of Organization: National Organization for Rare Disorders

Type of Organization: National Organization for Rare Disorders

Type of Organization - Other: Research Participant/Patient Advocacy Organization

Role: Research Participant/Patient/Advocate

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology): National Organization for Rare Disorders

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/VDPIGvebSq.pdf

Submission ID: 1758

I am responding to this RFI: On behalf of an organization

Name: Mary Majumder

Name of Organization: CSER Consortium ELSI & Diversity Working Group, Consent RFI response task force

Type of Organization: CSER Consortium ELSI & Diversity Working Group, Consent RFI response task force

Type of Organization - Other: Other

Role: Bioethicist

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology): Clinical Genomic Research

1. Utility and useability of this resource:

We appreciate this opportunity to review and provide information relevant to "Consent for Data and Biospecimen Sharing for Future Use: Points to Consider and Sample Language." Our response represents viewpoints from the Clinical Sequencing Evidence-Generating Research (CSER) Consortium ELSI and Diversity Working Group. It has not been endorsed by the full Working Group, and it may not represent the viewpoints of all Working Group members. The CSER Consortium projects have needed to be thoughtful about informed consent, especially because of the goal of enrolling diverse participants, including those with low literacy (1). The CSER Consortium published recommendations for informed consent for clinical sequencing in 2018 (2). Those recommendations were guided by an appreciation that there can be an inverse relationship between the quantity of information disclosed to prospective study participants and the quality of their comprehension of the information. With this in mind, we commend the current effort to reduce the amount of extraneous information conveyed in order to improve understanding of key information at the time of enrollment. Based on our collective experiences, input from CSER patient stakeholders, as well as current literature, we offer reflections to support improvements in this document. Overall, the language choices in the consent process should help participants make decisions consistent with their values about whether to participate in research. The implication of this goal is that information about potential benefits and risks needs to be presented, but that consent language should not presuppose the relative importance of these risks and benefits. We noted a general tendency in the document toward somewhat negative framing of research data sharing, and away from clearly stating the positive implications of use of already-collected data and/or specimens in future research. The sample language overall has a discouraging tone. Suggestions for adding to or modifying the sample language included for specific components follow in the text below.

1. Amendola LM, Berg JS, Horowitz CR, Angelo F, Bensen JT, Biesecker BB, Biesecker LG, Cooper GM, East K, Filipski K, Fullerton SM, Gelb BD, Goddard KAB, Hailu B, Hart R, Hassmiller-Lich K, Joseph G, Kenny EE, Koenig BA, Knight S, Kwok PY, Lewis KL, McGuire AL, Norton ME, Ou J, Parsons DW, Powell BC, Risch N, Robinson M, Rini C, Scollon S, Slavotinek AM, Veenstra DL, Wasserstein MP, Wilfond BS, Hindorff LA; CSER consortium, Plon SE, Jarvik GP. The Clinical Sequencing Evidence-Generating Research Consortium: Integrating genomic sequencing in diverse and medically underserved populations. Am J

Hum Genet. 2018 Sep 6;103(3):319-327. 2. Yu JH, Appelbaum PS, Brothers KB, Joffe S, Kauffman TL, Koenig BA, Prince AE, Scollon S, Wolf SM, Bernhardt BA, Wilfond BS; Clinical Sequencing Exploratory Research (CSER) Consortium Informed Consent and Governance Working Group. Consent for clinical genome sequencing: considerations from the Clinical Sequencing Exploratory Research Consortium. Per Med. 2019 Jul;16(4):325-333.

2. Gaps or additional components that should be included:

3. Specific language proposed in the informed consent sample language:

Component 1 - Introduction/Description Overall the sample language for this component is clear, other than the term “commercial entities,” which is vague. However, either this section or Component 5 should be more explicit about development of new commercial products being an intended goal of data sharing (where commercial data use is permitted) and state the potential benefits of commercialization. The NIH is well aware that NIH-funded research often benefits the public only through the development of commercial products. It is important to communicate this to research participants. For example: “When data are shared, other researchers, including those who work in companies that create health-related products, may be able to use the data to make better products that help future patients.” In addition, regarding “controlled by…,” controlled access may be the default data sharing mechanism. However, if some datasets will not be controlled, e.g., open or public access, it may be useful to provide an example of alternate language. Finally, encouraging specificity (naming an entity, for example, a particular repository) could create challenges for a study encountering data sharing changes down the road (for example, with the CSER Consortium, the transition from dbGaP to AnVIL). A more general description, such as “an NIH-designated repository or trusted partner,” would be an appropriate alternative where such change is anticipated or possible. Component 2 - Voluntary Participation While we agree that researchers should be permitted to make data sharing a choice for participants in some contexts, especially when community input supports making data sharing optional, this document suggests it should be encouraged in general. It is not clear why this recommendation is being made. The commitment that guides Component 1, which is to promote data sharing as a social good, supports more nuance in the points to consider. Further, the suggestion that it is more important to make data sharing optional when there is a potential for direct benefit does not stand up to scrutiny. First, it reflects a vague use of the concept of coercion (3). A more careful and contextualized approach would recognize that there are ethical considerations that weigh both in favor of and against bundling consent for participation in research with consent for sharing. When the associated risks are small, favorable results of bundling might include maximizing the value of the social investment in research and simplifying the informed consent and data management processes. Risks of adopting such an approach might include discouraging some eligible patients from participating in clinical trials, which is a particular problem if those who object to data sharing come from groups that are underrepresented in research, even if conditioning the offer of enrollment on data sharing is not coercive. In interviews conducted with CSER/UCSF research participants, it was noted that data security was a primary concern among persons who did not wish for data to be broadly shared. In part this stemmed from concerns about data security in general rather than specifically data sharing in respect to the NIH and/or biomedical research. However, there were concerns expressed by some with respect to the sharing of genetic data in combination with medical records. The latter concern might well need to be addressed explicitly in consent in respect to ongoing discussions of learning healthcare systems as informed by genetic research. Second, many empirical studies, as well as input from our patient stakeholders, suggest clinical

trial participants are motivated to help others and favor greater cooperation among scientists (4). We would support a recommendation that engagement with patient/community stakeholders guide the choice to make data sharing optional or non-optional considering the particular research context. Also, consistency in the use of either “may” or “might” could improve otherwise acceptable language. “May” has connotations of both chance and allowance, whereas “might” simply implies chance. Component 3 - Discontinuation/Withdrawal While the full and unqualified ethical right to withdraw from research involving interventions or interactions is essential, it is not clear that there is an analogous right of withdrawal of already-collected data shared for future research (5). Ability to withdraw from ongoing active participation is critical because participants’ circumstances can change over time, and so withdrawal is fundamental to the respectful treatment of participants. However, withdrawal of data is different because the participants' direct involvement is over (although treatment of their data may change over time). Potential participants who do not want their data shared, for whatever reason, should be discouraged from consenting to research wherein data sharing is integral to the objectives of the studies being undertaken (see Component 2). Further, as noted in the sample language, withdrawal of data is often not feasible. Even when possible, it can be very resource intensive. Similarly, it may be poor stewardship of resources and unfair to force researchers to start over when analysis is already underway. Existing examples of alternative language capturing these nuances include: Cartagene: “However, data and samples that have already been used by researchers cannot be withdrawn from current or completed studies.” Global Alliance for Genomics and Health (GA4GH) consent clauses: “If you let us know, we can stop your information from being shared in the future. However, data that has already been sent to other researchers or research databases cannot be removed.” “Data sent to other researchers around the world cannot be withdrawn if already used or published.” Component 4 - Risks & Benefits Here there seems to be an emphasis on risks over benefits. This section reads as if it is intended to discourage participation. We recommend stating benefits first, and stating them positively. This suggestion is based on published data from several PCORI studies, as well as feedback from CSER patient stakeholders. For example, the sample language might be revised to read “sharing your data and biospecimens can contribute to research that would help others in the future. However, you will not…” This should not be considered coercion as it accurately reflects the purpose of the research being undertaken, rather than hides this as a secondary factor behind potential risks. Component 5 - Commercial Application Some of the comments to Component 1 could be addressed here, as part of the considerations. Specifically, sample language could describe the social value of commercialization, and more importantly, that commercialization is often foundational to creating and distributing products to help patients. At the same time, it could acknowledge that commercialization raises concerns (for example, related to patenting/licensing and conflicts of interest). It is also important to avoid any implication that commercialization always results in societal benefit. In general, we have found consultation with research participants and community stakeholders to be of great value in navigating challenges related to informed consent generally. We believe that this is an area in which a consultation process undertaken by or at the behest of the Office of Science Policy would be helpful in developing additional model language. Balanced and accessible explanatory language would assist investigators and institutions in responding to the call for greater transparency about commercialization (6). 3. Alan Wertheimer, for example, argues that the concept of coercion should be reserved for situations in which A’s proposal creates a choice situation for B such that B has no reasonable alternative but to do X AND it is wrong for A to make such a proposal. Further, the dominant philosophical view is that threats are coercive but offers are not. A makes a threat when, if B does not accept A’s proposal, B will be worse off

relative to B's baseline position. See Wertheimer A. Coercion (Princeton University Press, 1987). 4. See, for example, Mello MM, Lieou V, Goodman SN. Clinical trial participants' views of the risks and benefits of data sharing. N Engl J Med. 2018 Jun 7;378(23):2202-2211. 5. Melham K, Moraia LB, Mitchell C, Morrison M, Teare H, Kaye J. The evolution of withdrawal: negotiating research relationships in biobanking. Life Sci Soc Policy. 2014;10:16. 6. Spector-Bagdady K, De Vries RG, Gornick MG, Shuman AG, Kardia S, Platt J. Encouraging participation and transparency in biobank research. Health Aff (Millwood). 2018 Aug;37(8):1313-1320.

4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Submission ID: 1759

I am responding to this RFI: On behalf of an organization

Name: Cara M. Weismann, PhD

Name of Organization: Orphan Orphan Disease Center and Gene Therapy Program, Perelman School of Medicine, University of Pennsylvania Disease Center and Gene Therapy Program,

Type of Organization: Orphan Orphan Disease Center and Gene Therapy Program, Perelman School of Medicine, University of Pennsylvania Disease Center and Gene Therapy Program,

Type of Organization - Other: Other

Role: Other

Role - Other: Multiple roles: research, medicine, data science, community engagement

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Rare disease research

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/NFhhkxCsrx.pdf
Attachment Description: 210929 - RFI NOT-OD-21-131, Orphan Disease Center and Gene Therapy Program, UPenn

Submission ID: 1760

I am responding to this RFI: On behalf of myself

Name: Lloyd M. Mueller

Name of Organization: Connecticut Tumor Registry

Type of Organization: Government Agency

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Cancer

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**

The genomic data sharing (GDS) policy requires that NIH-funded researchers obtain informed consent for bio-specimen tissue obtained after 2015. In my opinion, this requirement presents an undue burden for some studies. Specifically, for research studies that make use of previously collected, de-identified tissue and patient data, and which would qualify as being exempt from the standard IRB requirements for human subjects research, the GDS patient consent requirement seems out of place. The process of gaining patient consent for previously collected bio-specimens can be time-consuming and costly. I understand that due to the difficulty imposed by this GDS requirement, some cancer researchers specifically seek out private funding to avoid this difficulty. A policy that encourages researchers to avoid public funding and seek out private sources may have the unintended consequence of biasing the types of bio-specimens esearch that are conducted. These increased costs are also likely to force researchers to reduce the size and diversity of their study samples. Requiring informed consent tailored to the specific study at hand will also reduce the opportunity for researchers to contact patients with highly fatal cancers while they are still alive. Of course, those cancer sites are precisely where more research is most needed. On balance, I did not believe removing the GDS informed consent requirement for studies based on the de-identified data would increase risk much at all, but it certainly should increase the beneficial volume and diversity of these types of research studies. These comments are informed by my experience working in the Connecticut Tumor Registry. I am a Senior Epidemiologist and the Principal Investigator for the Connecticut's NCI SEER registry. As a population-based cancer registry, we work to facilitate cancer researcher's access to the registry data for a wide variety of studies.

5. **Other considerations relevant to this resource:**

Submission ID: 1761

I am responding to this RFI: On behalf of an organization

Name: Krista Martel

Name of Organization: The Well Project

Type of Organization: The Well Project

Type of Organization - Other: Research Participant/Patient Advocacy Organization

Role: Organizational Official

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Cis and trans women in HIV prevention, treatment, and cure research

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**

Patients and other participants in biomedical or public health research might think twice about whether their safety, privacy, and bodily autonomy are protected if information used for research is not obtained with their full informed consent. People living with HIV (PLHIV) have been confronted as vectors for disease for decades, and are at risk of being subject to criminal and immigration proceedings largely because of their health status. However, the issue isn't a hostile criminal justice system alone, since federal, state and local governments have proceeded with a molecular HIV surveillance (MHS) program despite an abundance of community concern. I believe it is clear that MHS is public health research and that informed consent requirements should extend to HIV-testing related data collected in the administration of direct care but then used for future research and analysis. PLHIV have the right to know when and how their private medical data is used, to consent to such usage, and to opt out of future usage at any time. NIH can and should work together with government agencies, community organizations, PLHIV, and advocates to enshrine better protections for collected data used in public health research. NIH must also implement the tools necessary to require informed consent for all future use of collected data, and respect the rights of PLHIV to opt-out of future use of their data for research.

3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/lzIVgUvZGB.pdf

Submission ID: 1762

I am responding to this RFI: On behalf of an organization

Name: Shawn M. Sweeney

Name of Organization: AACR Project GENIE

Type of Organization: AACR Project GENIE

Type of Organization - Other: Professional Organization/Association

Role: Investigator/Researcher

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

Oncology, real-world data

1. Utility and useability of this resource:

The NIH suggested patient consent language would be helpful to any collaborative project team developing consent forms for their study or looking to expand their protocol to allow for the sharing of their specimens and data. Additionally, it would be a good resource to existing project or study teams interested in collaborating with the NIH and looking for guidance on traditional consent language that facilitates open sharing of consented patient data and/or biospecimens.

2. Gaps or additional components that should be included:

To keep with language that patients and families at every level could comprehend, it would be helpful to ensure definitions or examples are provided for some of the terms used in the consent language. For example, providing a definition or example by what is meant by “commercial entities”, “commercial value”, “your data”, “your biospecimens” would be helpful for readers, patients, and their families.

3. Specific language proposed in the informed consent sample language:

a. In addition, many of our GENIE centers see and treat pediatric patients. To be inclusive, the NIH should consider modifying the suggested language to include “your data and biospecimen” to “your (or your child’s) data and biospecimen” or specify at the beginning that “you” includes “your child”. b. Regarding Component 2, “Voluntary Participation”, the suggested language developed by NIH is reasonable to ensure that patients can benefit from clinical trials without compulsory biospecimen sharing. This is an important point and one is referenced in a manuscript published by one our AACR Project GENIE Steering Committee Members, Dr. Shannon McCall: Precision Pathology as Part of Precision Medicine: Are We Optimizing Patients’ Interests in Prioritizing Use of Limited Tissue Samples? | JCO Precision Oncology (ascopubs.org) In the manuscript, it is mentioned that often clinical patient informed consents for clinical trials do not mention that the associated archival biospecimen collection could deplete the patient’s only remaining clinical sample and result in new invasive procedures if they need additional tissue for biomarker testing or sequencing down the road. We suggest that this issue should be specifically addressed in NIH’s informed patient consent language as indicated in the paper. That is to say, clinical trial patient consent forms must distinguish clearly between biospecimens that are required to stratify patients for enrollment and biospecimens which are being collected either for

optional correlative science or even being collected for potential future use as part of a biorepository. Patients enrolling onto clinical trials are vulnerable; our policies should ensure truly informed consent.

4. Hurdles or barriers to wider use of this resource by the community:

a. The NIH should be aware that there may be institutional, local, or state guidelines that limit or bar this language from being used universally by project study teams and health care systems. This limitation may apply to study teams or healthcare systems who see or treat vulnerable populations. b. Additionally, review and completion of "Voluntary Participation" language by patients and families by healthcare providers or navigators during the patient consent meeting often introduces opportunities for error. It would be extremely helpful to provide guidance to those using this resource (providers and patient navigators) on where this language would be best implemented in the consent form.

5. Other considerations relevant to this resource:

Although not directly related to the NIH's suggested informed consent language, it may be helpful to provide guidance to project study teams the receipt and subsequent sharing of biospecimens and patient data that have been transferred under the following conditions: a. Identifiable data and specimens that were collected under an IRB-approved protocol and the subject consented to permit storage and sharing of specimens and data for future use consistent with the objectives of this protocol b) Identifiable data and specimens to which the IRB has issued a waiver of informed consent and authorization for release and use of the specimens and data for a specific Collection Protocol; c) The specimens and data are de-identified (contain no PHI

Attachment: https://osp.od.nih.gov/wp-content/uploads/rfiapr2021/uploads/ItTfVsBurD.pdf

Attachment Description: Letter summarizing comments

Submission ID: 1763

I am responding to this RFI: On behalf of an organization

Name: Danielle M Pendrick

Name of Organization: Columbia University Irving Medical Center

Type of Organization: Columbia University Irving Medical Center

Type of Organization - Other: Academic Institution

Role: Other

Role - Other: Director- Columbia University Biobank

Domain of research most important to you or your organization (e.g. cognitive neuroscience, infectious epidemiology):

All

1. **Utility and useability of this resource:**
2. **Gaps or additional components that should be included:**
3. **Specific language proposed in the informed consent sample language:**
4. **Hurdles or barriers to wider use of this resource by the community:**
5. **Other considerations relevant to this resource:**

Attachment: https://osp.od.nih.gov/wp-content/uploads/NIH-notice-NOT-OD-21-131-CUIMC-Response.pdf