ANNOTATED CONSENT DOCUMENT FOR THE TEXAS CANCER RESEARCH BIOBANK

INTRODUCTION

The use of stored specimens in research is becoming increasingly more common as genomic research progresses. Consequently, there is a growing need for biobanks with collections of clinically annotated specimens for use in a variety of research endeavors. The banking of such specimens, though, presents unique challenges to the informed consent process. In particular, informed consent for biobanking is typically broad to allow for a wide range of potential downstream uses that are unspecified at the time consent is obtained.

Here we provide example consent language that we developed for our biobanking activities using language from publically available models, guides, best practices, and current literature,[1-7] and discuss the issues, challenges, and points to consider with regard to biobanking for each element of the consent form. We adopt a broad, forward-looking approach to maximize the utility of the specimens and associated data and minimize the need for reconsent in the future. Though we intend for this to be used as a template for those writing consent forms for their own biobanking projects, there are many ways in which biobanks can operate, making a one-size-fits-all approach impossible. As such, investigators should be sure to tailor their consent forms to their specific projects and institutional review board (IRB) requirements.

CONSENT FORM ELEMENTS

BACKGROUND

We use the background section of the consent form to introduce the project as a whole, including describing what a biobank is, how it works, and its general purpose. Since our biobank involves genetic research, we include a brief explanation of genetics and DNA sequencing. There is an inherent challenge in the need to discuss genetics and inform the participant that genetic analysis will be performed without being too specific about the types of technology that will be used, as they will likely change with advances in the field. There is currently controversy surrounding the question of whether or not whole genome sequencing should be addressed specifically in consent forms used for such research, as it is a distinct technology with associated risks. In this consent document we specifically mention whole genome sequencing, but that may not be deemed necessary by all IRBs.

> We are asking you to take part in a research project. Please read this information and ask any questions before you decide if you want to take part.
>
> For this project, we will collect, store, and use tissue samples and health information for research. Tissue samples are substances from the body, such as blood, or tumors that may be removed during surgery. If you agree, your samples and some of your health information will be put into a biobank.

A biobank is a collection of samples and health information. Samples from many people are stored so they can be used for research now and in the future. Researchers apply to the biobank to ask for samples for their studies. If a study is approved, the biobank will give the researcher samples and information from many people. The biobank will not give researchers any information that could directly identify you, like your name or address. The researchers will then use the samples and information to learn more about health and many different diseases.

Some researchers may use genetic analysis in some of the research they do on your samples. Researchers can learn a lot by studying genes. Genes are pieces of DNA that give instructions for building the proteins that make our bodies work. DNA stores these instructions in the form of a code. This is the code that you inherit from your parents and that you pass on to your children. One of the methods researchers might use to study your samples is called whole genome sequencing. This allows them to look at some or all of your genetic code. Researchers may also use other methods as they are developed. Studying genes along with health information will help us to better understand what causes certain diseases. It may also help us to understand how different patients respond to treatment. This knowledge could help us to develop treatments for everyone.

PURPOSE

Consent forms must state that the project is a research activity and explain the purpose of that research.[8] This requirement presents a challenge in developing consent forms for biobanking in that the full range of future research and the details of that research are generally unknown at the time of consent and banking. Delineating certain types of research in the consent form would likely result in either the restricted use of specimens and associated data or the need for re-consent later, which could cause additional costs and considerable delays in the research, as well as be potentially burdensome to the participant.[7] Therefore, following from best practice guidelines that propose that the nature of future research can be anticipated and described adequately enough to meet the Department of Health and Human Services' (DHHS) regulations,[3] we suggest that the consent be written in a way that gives the potential participant enough information to make an informed decision about the collection and storage of specimens and data, but takes a broad approach with regard to potential future use that does not significantly limit the types of research that could be conducted with the stored materials.

It seems that most IRBs are comfortable with this broad approach; nevertheless, investigators should be cognizant that some IRBs may require more specific information about future use. Additionally, even with consent language that covers broad, unspecified future research use of the specimens and associated data, it is possible that some proposed research may not be sufficiently covered under the original consent. Thus, we recommend that investigators also seek permission to recontact the participant (see "Recontact" below).

The purpose of this project is to collect tissue samples and some health information from many people. We will store these samples and information in a biobank so they can be used for research now and in the future. This research will help us understand more about health and many kinds of diseases.

PROCEDURES

Informed consent documents must describe the procedures involved in the proposed research.[8] There are generally several basic steps involved in biobanking: collection of specimens, collection of clinical data (once or longitudinally), storage, and research access and use. To facilitate participant comprehension, we use section headings and describe these steps sequentially,[1,9] as well as use a question-and-answer format.

Collection of Specimens

Biobanking consent forms should include a description of the procedures by which the specimens will be collected. If the tissue will be solely residual tissue (i.e. tissue left over after all clinical care procedures, such as pathological analysis, have been completed), the consent form should state that this collection will occur but does not need to describe the clinical procedures and risks associated with those procedures.

If tissue will be collected solely for research purposes, the procedures and risks must be described in the consent form. For example, if there will be a blood draw that is not needed for the participant's clinical care, this must be clearly stated in the Procedures section and the physical risks of that blood draw described in the Risks and Discomforts section.

If the investigator intends to collect extra tissue for research during a clinical procedure (i.e. tissue beyond what is removed for clinical care), there is the added challenge of describing the risks of that collection if it is not known beforehand what kinds of additional tissue may be taken. Likewise, IRBs may be hesitant to approve protocols and consents that state that additional tissue may be taken when the level of risk is unspecified. Thus, we have included in our consent form the statement that additional tissue will be taken only if doing so will not significantly increase the risk to the participant. We also address this issue under Risks and Discomforts.

Investigators should be sure that this section covers all other types of specimens that may be collected for banking. For example, in our consent form, we cover the collection of urine, buccal, fluids, and sputum specimens. We also cover the creation of cell lines and xenografts in this section.

> Where do samples come from?
>
> Some tissue may be removed from your body during a procedure that is needed for your clinical care, such as a blood draw, surgery, or a biopsy. Your doctor will use this tissue first to help diagnose your medical condition and/or to decide how to treat you. Your care is the first priority.
>
> After the surgery or biopsy, or after a fluid tap, and all the tests are done, there may be some tissue and body fluids left over. The tissue and body fluids could be discarded or destroyed because they are not necessary for your care; or, you may choose to let them be used for research.
>
> In some cases, we may take extra tissue for research. This will be done during your surgery or biopsy. We will only take this extra tissue if doing so will not significantly increase the risk to you.

> We may also ask to collect and store up to 75 ml (about 5 tablespoons) of your blood for research. We can use this blood to learn more about DNA and how it is related to health and disease. For example, with diseases like cancer, we can compare the DNA from someone's blood to the DNA from his or her cancer tissue. We can do this to learn more about many diseases.
>
> Additionally, we may ask you to give us a urine sample. We may also ask for samples like saliva or mucus by having you spit or cough into a cup, or by swabbing the inside of your cheek.
>
> We may use your sample to create a cell line or a xenograft. This means that we would treat the cells from your sample in a way that allows us to grow them in a laboratory. We do this so that we can have an unlimited supply of cells for research for a long time, maybe forever. These cells would also be stored and used for research.

If your consent form also includes a statement on where research will be conducted, as many IRBs require, we suggest also explaining that although the specimens and information will be collected at those locations, researchers from many different places may be able to access and use the biobank specimens and data for their research.

> The research will be conducted at the following location(s): [Locations].
>
> We will be collecting samples and information from people at the locations listed above. However, researchers from many different places may apply to study the samples and information stored in the biobank.

Collection of Health-Related Data

The procedures section should also include a clear description of any personal or clinical information collected. Best practice guidelines suggest that longitudinal data be collected and stored, potentially through ongoing access to medical records.[2] Therefore, even if the investigator does not currently anticipate collecting longitudinal data, we recommend including this in the consent form. This will allow the investigator to go back to the medical records for additional and/or longitudinal data in the event the research changes or additional funding is secured.

> What information will you collect?
>
> Basic Information: We will ask you for some basic information. This will include things like name, age, sex, and race or ethnic group. We will also ask about your family's health history.

> Clinical Information: We will collect information from your medical records that is related to your health and/or disease history. Some examples include results of tests, medical procedures, images (such as X-rays), and medicines you take. Researchers will use this information to better understand how genes affect health and response to treatment. We will look at your medical record from time to time to update this information. This will take place for as long as your sample is stored in the biobank, which may be many years, unless you tell us to stop.

Storage

The consent form should include a description of how tissues and information will be stored, including whether identifiable or coded information will be stored with the specimens. In order to protect privacy and minimize the potential for breach of confidentiality, best practice guidelines recommend that biobanks store specimens in a coded fashion,[2,3] meaning that traditionally identifying information is removed and replaced with a unique code. Access to the key to this code should be limited to only those within the project for whom access is necessary (i.e. clinical staff who will input the information). To this end, our consent form addresses the storage and coding of specimens and information. Additionally, we specify that tissues will be kept in locked freezers in locked buildings and that information will be kept on secure computers.

> Who will have access to my samples and information?
>
> We will store your samples and information in the biobank. We will remove your name and any other information that could directly identify you from your materials. We will replace this information with barcodes. We will keep a master list that links those barcodes to your materials. Only certain project staff can access this master list. We will keep the samples in locked freezers in locked buildings. We will keep health information and research data on secure computers. These computers have many levels of protection.

Researcher Access and Use

Our consent form explains that the coded specimens and information may be shared with researchers, research projects (for example, The Cancer Genome Atlas project)[10], and other biobanks. We outline the procedures by which researchers can access the materials, but keep our description of the governance structure fairly broad in order to accommodate potential changes. Still, we make it clear that researchers must apply and their projects must be approved in order to access the materials, and that they will not receive any traditionally identifying information with the materials.

The governance of the biobank is an important issue to consider. Best practice guidelines recommend that biobanks develop procedures for researcher access to specimens and data.[3] Guidelines also suggest that such procedures include an oversight mechanism, such as a tissue utilization committee, by which requests for materials are reviewed in order to prioritize and ensure fair distribution.[2] The focus of the tissue utilization

committee is often the scientific merit of the proposed research, but some committees also include ethical review in their oversight. Some biobanks utilize the IRB for such review, requiring that the applicants first submit their protocol to an IRB for approval, exemption, or a 'not human subjects' determination. Ethical review of the requests could be used to protect participants in various ways, such as, for example, ensuring that the proposed use of the materials is consistent with the original consent. Furthermore, even if the specimens were collected using a broad consent form, there may be some cases in which the proposed use of the materials presents risks that were not conveyed in the original consent and/or is inconsistent with the wishes of the participants. Ensuring that the biobank materials are used in an ethical manner is an important factor in fostering public trust, which is necessary for continued participation.

Additionally, as consent forms must include a statement regarding the expected duration of the subjects' participation in the research,[8] as well as information on how long health information will be kept,[11] we follow best practice guidelines[3] and state that the specimens and information may be stored and used for research indefinitely. We recommend that investigators take a similar approach regardless of whether they anticipate keeping the materials indefinitely. This may help to reduce the chance of having to re-consent participants later in the event the circumstances of the investigator's research change.

[Continued under the heading "Who will have access to my samples and information?"]

Researchers can ask to study the materials stored in the biobank. This includes researchers from [Institution], as well as from other universities, the government, and drug or health companies. Some researchers will be from the U.S.; some may be from other countries around the world. An oversight committee will review each request. This kind of review is to make sure that any risks are minimized and that your rights and welfare are protected. If a study is approved, we might give a part of your sample and information to the researchers. We would give them your materials along with samples and information from many other people.

We may also share your materials with other biobanks and research projects.

All of the samples and information will be labeled with barcodes. We will not share information that could directly identify you (like your name, social security number, and address) without your permission.

There is no limit on the length of time we will store your samples and information. We may keep using them for research indefinitely unless you decide to withdraw from the project.

OTHER PROCEDURAL ELEMENTS

The following section describes other elements that we recommend including within the procedures section of the consent form.

Large-Scale Data Sharing

Genomic information is now frequently submitted to genetic databases, both controlled and open access, through which such information is shared with many different researchers. Current National Institutes of Health (NIH) policy strongly recommends that anyone using federal funds for genome-wide association studies (GWAS) deposit all data into their database of Genotypes and Phenotypes (dbGaP).[12,13] Researchers who access and use the materials from the biobank may use federal funds for their research, requiring them to adhere to this policy. Furthermore, these recommendations may soon be expanded beyond GWAS projects to cover all sequence data.[14] In order to submit data to dbGaP, the NIH requires that investigators have appropriate consents. Therefore, even if the investigator does not currently plan to submit data to genetic databases such as dbGaP, we strongly recommend that biobank consent forms cover large-scale data sharing in order to be compliant with these policies and to avoid setbacks later.

Due to concerns over the potential identifiability of publicly accessible DNA data,[15] most data are now shared in controlled access databases like dbGaP. Therefore, we recommend that the consent form cover—at a minimum—sharing in controlled-access databases. It should be noted, though, that these policies are changing quickly and some data continue to be shared in public databases, such as the database of Single Nucleotide Polymorphisms (dbSNP)[16]. In order to prepare for a potential shift back to more open access release and to allow for public release of even limited datasets, as well as in recognition that the biobank is set up as a community resource, we adopted the approach of covering data release to both controlled and open access databases.

We describe in our consent both open and controlled access databases, including their purpose and the types of information that may be submitted. We also make mention here of the privacy risks involved in large-scale data sharing, but cover these issues further under the Risks and Discomforts section, as well.

> Who else will have access to my genetic information?
>
> Researchers can do more powerful studies when they share with each other the information they get from studying human samples. They share this information with each other by putting it into scientific databases. These databases store information from many studies conducted in many different places. Researchers can then study the combined information to learn even more about health and many different diseases.

There are different kinds of databases; some are publicly accessible and some are restricted. Anyone on the Internet can access publicly accessible databases. Only researchers who apply and are approved can access restricted databases. There are many restricted databases; some are maintained by [Institution], some are maintained by the federal government, and some are maintained by private companies. Some of your genetic and health information could be placed into one or more of these publicly accessible or restricted databases.

Your name and other information that could directly identify you (such as address or social security number) will not be placed into any scientific database. 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. Researchers will always have a duty to protect your privacy and to keep your information confidential.

Another important aspect to consider with regard to large-scale data sharing is the sharing of pediatric data, as the issue is currently controversial. Some suggest that pediatric data should not be shared in order to preserve the autonomy of minors,[17] while others feel that restricting the sharing of such data will be detrimental to research on children's health.[18-20] The data-sharing policies of the NIH do not exclude pediatric data, but researchers may request exceptions. However, it is possible that the ability of the researcher to share the resulting data may influence NIH funding decisions.[21,22]

Therefore, in order to balance the utility of the specimens with concerns about sharing pediatric data, we make large-scale data sharing an option in the pediatric version of the biobank consent form. Investigators should be aware that if they choose to make large-scale data sharing an option, they will need a reliable mechanism for tracking these responses so as to ensure that data from those who opt out of data sharing are not released.

I agree that my child's genetic and health information may be released to scientific databases as described above.

Yes_____ No_____ Initials_____

Return of Results

Consent documents should state whether or not research results—individual or aggregate— will be returned to the participant.[3] Return of individual results, though, is also a contentious issue. While some argue that there is a moral imperative to return at least some individual research results,[23-26] others disagree, recommending that results be returned rarely or never.[27-29] Although there is currently no consensus in the U.S., available guidelines generally suggest that results that are valid, clinically significant, and relate to a treatable or preventable condition may be returned.[30-32] Any discussion of returning individual research results needs to be worded very carefully to avoid unanticipated liability.

One possibility for the biobank consent form is to offer the participant the option of receiving certain individual research results. Though this option would preserve the participant's right not to know, it is difficult to anticipate the kinds of results that may be produced from biobank research in the future, thereby making it difficult, if not impossible, for the participant to make a true, informed decision in advance.

Therefore, we take the approach of informing participants that they should not expect to receive any individual results, but also leave the option open to potentially return results in the future. Furthermore, our consent explains that in the event of a returnable result, the participant will be contacted to find out if he/she wants to learn more, preserving the participant's right not to know. However, it is not always possible to locate individuals. So to avoid potential liability we are careful to state that though we may contact the participant if something important is found, we cannot guarantee that he/she will be contacted.

> Will I find out the results of the research?
>
> You should not expect to get personal results from research done through the biobank. Researchers will study samples and information from many people; it will take many years before they know if the results have any meaning. However, in the future it may be possible for researchers to give you your genetic research results. There is also a small chance that researchers could find something that might be important to your health. If this happens, we may contact you to find out if you would like to learn more. However, even if we find something important to your health, we cannot guarantee that you will be contacted.

Conversely, the return of aggregate results, as opposed to individual results, is recommended.[2,33] Research shows that the return of generalized information about the findings of research using biobank materials is considered by participants to be important in terms of reciprocity, as well as for staying updated on the progress and types of research being done through the biobank.[34,35] Additionally, keeping participants updated in this way helps to make tangible the participants' right to withdraw from the project,[7] as they can opt to withdraw in the event they find the research being done objectionable or undesirable. Although this is not yet a common practice for most biobanks, we chose to follow best practice recommendations[2] and create a public website through which to communicate with participants and provide information about the biobank. The website could also serve as a mechanism for providing participants with updates on current research endeavors, as well as aggregate research results. Information about the biobank website is included in our consent form.

> You can get more information about the biobank by visiting our website: [URL].

Recontact

Best practice guidelines recommend that participants be given an option in the consent form to select whether or not they would be willing to be contacted in the future.[3] Obtaining permission for recontact is important because it is likely impossible to write the biobank consent form broad enough to cover any and all future use of the

materials. Some more specific reasons why investigators may want to contact the participant in the future are: to ask the participant for another specimen, to update information in the biobank, to request further health information, or to offer the option of participating in other research.

Therefore, in our consent, we list some of the potential reasons for recontact, describe the process by which the participant could be contacted, and then give the option of consenting to future contact.

> Will I be contacted in the future about this or other research?
>
> We may want to contact you in the future. You can decide now whether or not you want to be contacted. You can also change your mind later.
>
> If you agree, we may contact you for several reasons. For example, over time, stored samples may be used up or decrease in quality, so we may contact you to ask for more samples. We may also contact you to update basic information or request information about your health.
>
> Additionally, we may want to contact you to see if you want to participate in other research. We will not notify you every time your samples and information are used. However, some researchers might apply to do a study for which they would need to contact you. For example, they might want to ask you to give another sample or to fill out a survey. Or they might ask you to do a phone interview or come in to be seen by a researcher or doctor. If a study like this is approved, someone from this project will contact you. They will tell you about the study so you can decide if you want to receive more information. There will be a new consent process just for that study. You can decide then to take part or not take part. If at any time you decide you no longer want to be contacted about future studies, you can call [Investigator] at [phone number].
>
> I agree that my doctor or someone from this project may contact me in the future.
>
> Yes_____ No_____ Initials_____

POTENTIAL RISKS AND DISCOMFORTS

Informed consent documents must include a description of any foreseeable risks to the participant.[8] In our consent form, we describe both the physical and privacy risks involved in participating in the biobank.

Physical Risks

We describe the potential for physical risks by stating that since the tissue collected is residual, then there are no additional risks to the participant if he/she takes part in the project. We also use this section to reiterate that any additional tissue taken solely for banking during the clinical procedures would not significantly increase the risk to the participant (see Collection of Specimens). Additionally, we describe the physical risks of a blood draw, as, for our purposes, blood may be drawn outside of clinical procedures specifically for banking purposes.

Investigators should be sure that the physical risks described in this section accurately reflect reasonably foreseeable risks of any planned specimen collections for research purposes.

> Potential Risks and Discomforts
>
> What are the potential physical risks and discomforts?
>
> When the tissue we collect is left over from a procedure that is part of your clinical care, there are no additional physical risks to you if you take part in this project. Any additional tissue we take during your procedure will not significantly increase the risk to you.
>
> If we collect a blood sample, you may feel brief pain or have some bruising from the needle. There is also a small risk of infection, light-headedness, and fainting.

Privacy Risks

Risks to participants in biobanking are generally not physical, but rather related to privacy and the potential for misuse of information, particularly genetic information. Best practice guidelines recommend that the risks related to genetic research be explained in the consent document.[3] Although these privacy risks may seem small, due to the pace of scientific progress, there is inherent uncertainty in predicting such risks. Therefore, we must assume some level of uncertainty with regard to privacy and ask the potential participant to do the same. To this end, we make clear that in addition to those risks we describe, there may be further, unforeseeable privacy risks. We also underscore this by stating that though we will make every effort to protect the participant's privacy, we cannot guarantee it.[7]

> [Continued under the heading "Potential Risks and Discomforts"]
>
> What are the potential privacy risks?
>
> We will take many steps to protect your privacy, but because your DNA is unique to you, it is possible that someone could trace it back to you. There is also a risk that someone could get access to the data we have stored about you. If those data suggested something serious about your health, it could be misused. For example, it could be used to make it harder for you to get or keep a job or insurance. There are laws against this kind of misuse, but they may not give full protection. There may also be other unforeseen privacy risks.
>
> We believe the chance these things will happen is very small, but we cannot make guarantees. Your privacy and the confidentiality of your data are very important to us; we will make every effort to protect them. These efforts are described below under the section "How will my privacy be protected?"

Privacy Protections

Consent forms must also describe how confidentiality will be maintained[8] and who will have access to protected health information.[11] Though we explain how traditional identifiers are removed and replaced with barcodes under the Storage section, we reiterate here that researchers who receive specimens and information from the biobank do not receive any traditional identifiers. We also explain that no information from this project, nor resulting research will be put into participants' medical records, and that researchers who use the biobank materials must sign an agreement stating that they will not attempt to determine the participants' identities.

Furthermore, because literature shows that the public has concerns about genetic privacy with regard to genetic research projects,[36,37] we describe the privacy protections afforded by federal laws. The Genetic Information Non-Discrimination Act (GINA) prohibits health insurers and employers from discriminating against individuals based on genetic information. However, there are limitations to what GINA covers, as it does not provide protection for life, disability, or long-term care insurance.[38] We make these protections and limitations clear in the consent form.

> [Continued under the heading "Potential Risks and Discomforts"]
>
> How will my privacy be protected?
>
> We will not give information that identifies you to anyone without your permission, except as required by law. This project takes many steps to protect the privacy of people who take part.
>
> Research records are separate from medical records. We will not place any information from this project in your medical records.
>
> Researchers who study your sample and information will not know who you are. We will give them only barcode numbers; we will not give them any information that directly identifies you. The researchers must sign an agreement that they will not try to find out who you are.
>
> There are laws that protect against unauthorized access to your information. There is also 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 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.

In addition to describing project-specific privacy protections, language related to the Health Insurance Portability and Accountability Act (HIPAA) may also need to be included.[11] The HIPAA Privacy Rule essentially builds upon the confidentiality protections afforded by the Common Rule[8] by determining the circumstances within which a participant's protected health information (PHI) may be used or disclosed for research purposes. Generally, IRBs provide template HIPAA language for research consent forms. We have reproduced Baylor College of Medicine's template language on PHI below.

Your Health Information

We may be collecting health information that could be linked to you (protected health information). This protected health information might have your name, address, social security number or something else that identifies you attached to it. Federal law wants us to get your permission to use your protected health information for this study. Your signature on this form means that you give us permission to use your protected health information for this research study.

If you decide to take part in the study, your protected health information will not be given out except as allowed by law or as described in this form. Everyone working with your protected health information will work to keep this information private. The results of the data from the study may be published. However, you will not be identified by name.

People who give medical care and ensure quality from the institutions where the research is being done, the sponsor(s) listed in the sections above, representatives of the sponsor, and regulatory agencies such as the U.S. Department of Health and Human Services will be allowed to look at sections of your medical and research records related to this study. Because of the need for the investigator and study staff to release information to these parties, complete privacy cannot be guaranteed.

The people listed above will be able to access your information for as long as they need to, even after the study is completed.

If you decide to stop taking part in the study or if you are removed from the study, you may decide that you no longer allow protected health information that identifies you to be used in this research study. Contact the study staff to tell them of this decision, and they will give you an address so that you can inform the investigator in writing. The investigator will honor your decision unless not being able to use your identifiable health information would affect the safety or quality of the research study.

BENEFITS

It is unlikely that participants will receive any direct health benefits from participating in the biobank project. Thus, we state that personal benefit is unlikely, but that participation may lead to a better understanding of health and disease in the future. We continue to use broad language here rather than name any particular disease in order to be consistent with the rest of the consent, which states that specimens and information may be used for many different types of research.

Investigators should note that if they intend to make payments to subjects for their participation, this should be described as reimbursement for time and any other expenses incurred, rather than as a benefit of participation. Any description of such payments should be included in the consent form under a separate section titled Subject Costs and Payments (see Costs, Payment, and Commercialization below), rather than in the Benefits section.

> You will receive no direct benefit from your participation in this project. However, your participation may help the investigators better understand how to prevent, detect, and treat health problems in the future.

ALTERNATIVES

Potential participants should be informed of any alternatives to the proposed research. As the only such alternative to participating in the biobank project is to not participate, we state so. However, not all IRBs require a statement to this effect; the option to not participate is fully addressed in sections of the form emphasizing that participation is voluntary.

> You may choose to not participate in this study.

WITHDRAWAL

Consent documents must state that research participants may discontinue participation at any time.[8] This particular requirement poses a pertinent question with regard to biobanking, namely, what does it mean to discontinue participation in a biobank? While it may be possible to remove or destroy stored specimens and information, the issue becomes more complex when the materials have already been distributed for specific research studies. As retrieving specimens and information after distribution would be difficult, best practice guidelines suggest that only remaining materials still stored in the biobank be destroyed upon request.[2,3] We explain that the participant may withdraw at any time for any reason and describe how he or she can do so, but also describe the limitations of withdrawal, specifically that participants cannot withdraw materials or data that have already been distributed and that it may not be possible to remove information from databases once it has been distributed.

We explain to participants that, if they decide to discontinue their participation, they will be given several options as to what is done with the remaining materials. The options given to a withdrawing participant are: no more contact, no further access to medical records, destruction of the link between the code and traditionally identifying information (anonymization), and/or destruction of any remaining specimen.

Lastly, the consent document must include information on the participant's right to withdraw consent for the use of his or her protected health information. This is covered in our consent form by our institution's template language on privacy (see Privacy Protections above).

> Can I change my mind after I agree to let my samples be used?
>
> You have the right to stop participating in this project at any time. If you want to leave the project, call [Investigator] at [phone number] to let us know. You will be given some options and can choose what you want us to do with your unused samples. You can also tell us to stop using your medical records. However, you cannot withdraw your samples and information from studies that have already begun. We cannot get samples and information back once they are shared with other researchers. Also, it may not be possible to remove your genetic information from scientific databases once it has been distributed.

COSTS, PAYMENTS, AND COMMERCIALIZATION

The consent form should cover information regarding any costs or payments involved in participating in the proposed research. If investigators intend to make payments to participants, this should be described as reimbursement for expenses incurred in participation, rather than a benefit. As participants in our biobank project will not pay any costs, nor receive any payments, we use our institution's template language for this section (reproduced below).

Participants should also be informed whether their materials could be used by private and/or for-profit companies. In some circumstances, it may not be possible to limit access to downstream users; for example, data shared in dbGaP are accessible by for-profit companies. Thus, researchers should be cautious about promising that the specimens and associated data will not be used by for-profit companies. The consent form should also state whether or not participants will receive any payments stemming from the development of any commercial products from their materials.

For this consent form, we cover the use of specimens and data by private companies under the section describing access to materials (see Research Access and Use). We use our institution's template language (below) to cover the issue of payments resulting from commercialization, which our group does not intend to make.

> Subject Costs and Payments
>
> You will not be asked to pay any costs related to this research.
>
> You will not be paid for taking part in this study.
>
> This institution does not plan to pay royalties to you if a commercial product is developed from blood or tissue obtained from you during this study.

VOLUNTARINESS

Consent forms must include a statement that participation in the research is voluntary and that the potential participant may refuse or withdraw without losing any benefits, services, or rights to which he or she is

otherwise entitled.[8] Most institutional IRBs will make this language available for investigators to use in their consent forms (ours is reproduced below).

> Subject's Rights
>
> Your signature on this consent form means that you have received the information about this study and that you agree to volunteer for this research study.
>
> You will be given a copy of this signed form to keep. You are not giving up any of your rights by signing this form. Even after you have signed this form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.
>
> If you choose not to take part in the research or if you decide to stop taking part later, your benefits and services will stay the same as before this study was discussed with you. You will not lose these benefits, services, or rights.

CONTACT INFORMATION

Information, including telephone numbers, about whom to contact for the following reasons should be included in the consent form: questions about the research, questions regarding subjects' rights, and research-related injury. Contact information for several groups may be necessary, including the primary investigator, the research group, the institution's IRB, and/or legal counsel. Investigators should check with their IRBs to ensure they include the correct information. Our institution's template language follows.

> The investigator, [Name], and/or someone he/she appoints in his/her place will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury related to the research, you may speak with a member of the study staff: [Name] at [phone number] during the day and after hours.
>
> Members of the Institutional Review Board for [Institution] (IRB) can also answer your questions and concerns about your rights as a research subject. The IRB office number is [number]. Call the IRB office if you would like to speak to a person independent of the investigator and research staff for complaints about the research, if you cannot reach the research staff, or if you wish to talk to someone other than the research staff.

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