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ORIGINAL ARTICLE

Variation among DNA banking consent forms: points for clinicians to bank on

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Abstract

Deoxyribonucleic acid (DNA) banking is an important laboratory service that preserves the option of future genetic testing. DNA bank consent forms are a critical tool to facilitate thorough and valid informed consent. The objectives of this study were to assess the level of consistency of current clinical DNA banking consent forms with the American Society of Human Genetics (ASHG) and the American College of Medical Genetics and Genomics (ACMG) guidance and to explore variation among the forms. The content analysis matrix included key points identified from the ASHG and ACMG documents (including benefits/risks, sample storage, access, disposition, and communication) and additional points beyond the ASHG and ACMG documents identified from the consent forms themselves during the analysis process. Forms were assessed for language addressing each point. Five consent forms were identified and analyzed for twelve key points and eight additional points. The average consistency for key points was 10.8/12 (range 8/12 to 12/12). The range for additional points was 1/8 to 5/8. There was variation across forms in the details provided related to key and additional points. Gaps in clinical DNA banking consent forms are barriers to achieving informed consent. Clinicians can consider the consent key and additional points discussed here to supplement and enrich their clinical DNA banking informed consent discussions, promote stewardship, and maximize downstream utility of banked DNA. The identification of multiple additional points beyond the ASHG and ACMG documents' key points indicates a need for this guidance to be updated.

Keywords DNA banking · Biobanking · Informed consent · Stewardship

Introduction

Deoxyribonucleic acid (DNA) banking refers to the secure storage of an individual's genetic material for future use. When offered as a clinical laboratory service, DNA banking can be an important tool for providing high-quality genetics care to individuals and their families over a continuum of time. Depositors (and/or their designated representatives) submit a biological specimen to banks and subsequently direct utilization. They have ownership of the stored specimen, which may be tested, withdrawn, transferred, or destroyed at their request. Clinical DNA banking is typically a service with an associated fee and is distinct from research biobanking (Coppola et al. 2019; Edwards et al. 2014).

Individuals and clinicians may consider banking DNA advantageous in multiple scenarios. For instance, banked DNA may be repeatedly interrogated during the course of a clinical evaluation. This is particularly useful when subsequent specimen collection is difficult or no longer possible. When current genetic testing is not informative or feasible, long-term DNA storage leaves open the possibility that future knowledge and clinical or research testing will enable a diagnosis (Overwater et al. 2014). DNA banking may be particularly impactful in the perimortem period (just prior to or soon after death) because it preserves the option for molecular autopsy and allows time to optimize a testing strategy (Middleton et al. 2013). This may be relevant to families in the setting of fetal demise, sudden infant death syndrome, sudden cardiac death, thoracic aortic dissection, and other unexplained deaths (Laracuente et al. 2019; Page and Silver 2020; Roman and De Backer 2022; Semsarian et al. 2015). Banking has also been framed as preserving a

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genetic legacy and may be pertinent and broached in end-of-life and palliative care situations (Cleophat et al. 2020; Quillin et al. 2010, 2018; Quillin et al. 2011a, b). This is in part because banked DNA is available for years after death to identify pathogenic variants that may be inherited and/or inform variant interpretation that can direct the future healthcare of family members (Daum et al. 2020; Quillin et al. 2011a, b). This impacts genetic counseling, testing strategies, medical surveillance, and interventions across a family.

In this genomics era, having the infrastructure to support clinical DNA storage and leverage its benefits is more impactful than ever. With the increasing understanding of molecular mechanisms of diseases, more accessible testing, and increased availability of therapies based on genetic variation, genetic medicine is influencing all medical specialties (Amendola et al. 2021; Boycott et al. 2019; Green et al. 2020; Phillips et al. 2018). While DNA banking is still most often coordinated by genetics professionals, it is likely that non-genetics providers will become more engaged in this process as genomics is increasingly incorporated across clinical medicine. Over a recent 5-year span at a large pediatric tertiary care hospital, DNA banking was increasingly ordered by clinicians in specialties apart from medical genetics (unpublished data). Thus, clinicians in multiple specialties require education in this area to support ordering DNA banking and interacting with patients and families with banked DNA.

In the USA, there is longstanding guidance pertaining to clinical DNA banking from the American Society of Human Genetics (ASHG) from 1988 and the American College of Medical Genetics and Genomics (ACMG) from 1995 ("ACMG statement 1995; "DNA banking and DNA analysis: points to consider 1988). These documents recognize the utility of DNA banking in light of rapidly advancing genetic knowledge, highlight risks and operational considerations, and recommend written policies provided to prospective depositors in advance for informed consent. A contemporaneous exploration of consenting processes and internal policies at clinical DNA banks revealed that many banks established at that time did not have written depositor agreements or even any written internal policies (McEwen and Reilly 1995). The banks that did have written documentation variably included policies regarding specimen storage, access, disposition, and maintenance of contact between depositors and banks.

Now, more than 20 years later, we sought to characterize the current state of informed consent documentation for clinical DNA banks and to understand if these gaps persist. Informed consent is fundamental to protecting the individual and family, enabling depositors and/or their designated representatives to decide if the service is appropriate for their personal situation by formalizing the opportunity to ask questions and understand the service, its benefits, risks, and limitations. Gaps in consent forms for DNA banking would be a barrier to achieving informed consent. We evaluated DNA banking consent forms to assess the level of consistency with the ASHG and ACMG statements' key points, as well as relevant additional points. This analysis aims to inform and educate both genetics providers and the broad range of clinicians participating in clinical DNA banking consent and downstream use of banked specimens for the care of individuals and families. Awareness of possible gaps in consent forms, variations in the service among banks, and understanding the implications of DNA banking over time can enrich consent conversations, promote stewardship, and maximize downstream utility.

Materials and methods

Clinical DNA banking consent forms were identified by filtering the Genetic Testing Registry (GTR) (www.ncbi.nlm.nih.gov/gtr) by laboratory service for "DNA Banking." We limited the laboratory location to the USA, as we planned our analysis around recommendations from US-based professional societies. We identified publicly available consent forms on the laboratory websites and downloaded them for content analysis. We directly contacted the remainder of the laboratories listed to determine if they had a consent form. Each laboratory was contacted via their provided email addresses. If there was no response, a second request was sent. A number was assigned to each bank for the purposes of coding.

We performed directed content analysis (Hsieh & Shannon, 2005). We developed a content analysis matrix by reviewing the ASHG *DNA Banking and DNA Analysis: Points to Consider* and ACMG *Statement on Storage and Use of Genetics Materials.* These were parsed and distilled into "key points." In the process of analyzing the forms, topics not directly addressed in the ASHG and ACMG documents became apparent, prompting expansion of the content analysis matrix to include these "additional points." The points were further refined based upon relevant literature and author experience (Beskow et al. 2015; Cadigan et al. 2017; Edwards et al. 2014; McEwen & Reilly, 1995; Yates et al. 1989).

Each consent form was reviewed independently by two authors (SJH and DLS). A hard copy of the consent form was reviewed for direct and implicit language addressing each point of the content analysis matrix. The identified text was recorded and qualitatively assessed for consistency with the point. The text data was then coded as present or absent.

Finally, the forms, abstracted text and coding, were reviewed collaboratively to resolve differences.

Results

Filtering by laboratory service for "DNA banking" and limiting the laboratory location to the USA identified 14 entries on the Genetic Testing Registry. Six of the 14 entries led to a publicly available DNA banking consent form on the linked laboratory websites. We downloaded these publicly available consent forms in March of 2021. Two of those 6 entries led to the same consent form for the same DNA bank.

We directly contacted the remaining laboratories in May and June of 2022. We received 4 responses from the 8 remaining laboratories we reached out to directly. The first laboratory reported that they stored DNA on an ad hoc basis at clinician request but did not have a formal DNA bank and had no corresponding consent form for that process. The second laboratory did not perform DNA banking but disclosed on their genetic testing consent form that the laboratory retained excess specimen after testing. There is an option to contact this laboratory to have the specimen destroyed. The third laboratory responded that they did not perform DNA banking. The fourth laboratory indicated that they performed DNA storage only in support of research protocols and did not offer a clinical DNA banking service and therefore did not have a corresponding consent form. Ultimately, 5 unique consent forms were identified and analyzed.

Table 1 The 12 key points derived from the ASHG and ACMG documents used in the content analysis, along with a brief description of each point. A shaded cell indicates the presence of language addressing that point on the corresponding DNA banking consent form. A blank cell indicates the absence of such language

Deoxyribonucleic acid (DNA) Banking Key Points			DNA Bank Number				
Category (source)		Description	1	2	3	4	5
1	DNA banking description (ASHG, ACMG)	Briefly describe DNA banking	■	■	■	■	■
2	Benefits (ASHG, ACMG)	Identify potential benefits of downstream use	■	■	■	■	■
3	Risks (ASHG, ACMG)	Identify potential risks associated with DNA banking	■	■	■		■
4	Storage duration (ASHG, ACMG)	Specify duration of storage	■	■	■	■	■
5	Storage conditions (ASHG, ACMG)	Describe how banked specimen will be stored	■	■	■	■	■
6	Permission to access specimen (ACMG)	Define who can access banked specimen (including process of identifying and changing designated representatives, if applicable)	■	■	■	■	■
7	Specimen retrieval protocol (ASHG, ACMG)	Describe protocol for depositors and/or designated representatives to retrieve specimen for use	■	■	■	■	■
8	Ability to transfer specimen (ACMG)	State the ability of depositors and/or designated representatives to transfer banked specimen	■	■	■		■
9	Ability to destroy specimen (ACMG)	State the ability of depositors and/or designated representatives to destroy banked specimen	■	■	■		
10	Depositor and/or designated representative responsibilities to contact bank (ASHG)	Describe circumstances that should prompt contact with bank	■	■	■	■	■
11	Bank responsibilities to contact depositor and/or designated representative (ASHG, ACMG)	Describe circumstances that should prompt contact with depositor and/or designated representative	■		■		■
12	Bank research activities disclosure (ASHG, ACMG)	State whether specimen may be used for research other than as directed by the depositor and/or designated representative	■	■	■	■	■
Total			12/12	11/12	12/12	8/12	11/12

Twelve key points were identified from the ASHG and ACMG documents, and we found variation in the inclusion of these 12 key points across the five consent forms (Table 1). The average number of key points included was 10.8/12 (range 8/12 to 12/12), with 2 of the consent forms addressing all 12 points. Four key points that were absent in some of the forms included the risks of DNA banking (1/5), ability to transfer specimen (1/5), ability to destroy specimen (2/5), and responsibilities to maintain contact between banks and depositors (and/or designated representatives) (2/5).

Table 2 lists the eight points identified in this analysis that were not included in the ASHG and ACMG documents, along with a brief description, and indicates the consent forms that addressed each point. These additional points were kept separate to distinguish them from the key points of the ASHG and ACMG documents. There was more variation among consent forms for these additional points compared to the above key points. None of the consent forms addressed all eight additional points, with the range being 1/8 to 5/8. The storage fee was the additional point most frequently addressed, on 4/5 consent forms. The remaining points were each addressed in varying combinations on 2/5 to 3/5 of the consent forms.

Discussion

Clinical DNA banking is an important laboratory service that preserves the option of future genetic testing and can inform the healthcare of depositors and their families. Consent forms play a critical role in disclosing DNA banking processes, benefits, risks, limitations, and future expectations to prospective depositors, designated representatives and families. Gaps in consent form content are barriers to achieving informed consent. Understanding the variation across consent forms as well as the strengths and gaps of a particular form can enrich clinician and family consent conversations, promote stewardship, and maximize downstream utility. In this study, we observed variation across DNA banking consent forms that encompassed not just the presence or absence of each point, but also the details provided. These details may shape the considerations of clinicians, depositors, designated representatives, and families on a case-by-case basis.

Our content analysis matrix included key points from the ASHG *DNA Banking and DNA Analysis: Points to Consider* and ACMG *Statement on Storage and Use of Genetics Materials*, as well as additional points identified in the analysis process. The 12 key points were addressed by the majority of the 5 clinical DNA bank consent forms

Table 2 The 8 additional points identified and used in the content analysis, along with a brief description of each point. These points were derived from the content of the consent forms beyond the ASHG and ACMG documents. A shaded cell indicates the presence of language addressing that point on the corresponding DNA banking consent form. A blank cell indicates the absence of such language

Deoxyribonucleic acid (DNA) Banking Additional Points			DNA Bank Number				
Category		Description	1	2	3	4	5
1	Legal chain of custody	State that clinical DNA banking does not typically meet legal chain of custody	■	■			
2	Storage fee	State fee to bank DNA	■		■	■	■
3	Achieving age of majority	For DNA banked from minors, state that control of specimen will transfer upon achieving age of majority, when applicable	■		■		
4	Bank closure	State possibility of bank closure and describe plan for specimen disposition	■				■
5	Outside facility testing disclosure	State that DNA bank is not responsible for testing or results generated by outside laboratories		■	■		■
6	Limitations of future testing	State that banked specimen may not be usable or suitable for all future testing or downstream uses		■			■
7	Specimen type	Specify specimen type from which DNA will be extracted		■	■		
8	Possible conflicts	State that banking and downstream uses of banked specimen may involve conflict among stakeholders	■	■			
Total			5/8	5/8	4/8	1/8	4/8

analyzed. Nevertheless, there were gaps, with each of the following key points not being addressed on one or two consent forms: risks, ability to transfer or destroy a specimen, and communication from banks to depositors and/or designated representatives. There was more variation across the 8 additional points, which may impact downstream stewardship and utility of a banked specimen.

The identification of multiple additional points beyond the content of the ASHG and ACMG guidance suggests a need for the guidance to be updated and expanded. It is notable that the statements from the ASHG and ACMG were published in 1988 and 1995, respectively. Over the intervening decades, the increasing capabilities of genomic science and its pervasive impact upon in clinical medicine have added layers of nuance to the seemingly simple act of storing DNA. The varying additional points across the reviewed DNA bank consent forms are indicative of individual banks' efforts to address anticipated legal, financial, technical, and ethical issues. These issues loom for all banks. Updated guidance from the professional societies on the elements to include in clinical DNA bank consenting could serve as a framework to bring the banks across the country into closer alignment. More comprehensive consent forms could also reduce the burden on clinicians to identify and supplement different gaps across different forms and improve clarity for depositors. While one, uniform DNA banking consenting document may be convenient for clinicians, there are challenges to achieving this including the disparate commercial and academic entities involved and local regulations and statutes, as well as factors specific to each clinical DNA bank and population. Guidance from our professional societies should continually be re-evaluated and updated as the field evolves.

In the following sections, we discuss the importance and practical considerations of each key point and additional point related to DNA banking identified in this study.

DNA banking, benefits, and risks

Describing the service along with its benefits and risks are key elements of informed consent. Understanding the purpose of DNA banking, its myriad downstream possibilities, and corresponding implications is the foundation for clinician and patient discussion during the consent process. All of the consent forms describe DNA banking (Key Point 1) as long-term storage and include potential benefits (Key Point 2) such as informing future medical care and life planning of depositors and family members by preserving the specimen for testing and research. While the process of DNA banking may appear straightforward and relatively benign, the risks (Key Point 3) should also be presented. The four forms with language addressing risks all alluded to inadvertent specimen loss. Notably, specimen loss is specifically called out in both the ASHG and ACMG documents. Two forms also addressed physical risks from obtaining DNA, such as from a blood draw or amniocentesis. One of these forms additionally highlighted risks of genetic testing. Depending on the individual's circumstances, different benefits and risks may be appropriate to emphasize, so conversations should be tailored accordingly to supplement the content of the consent form.

Storage parameters

All 5 consent forms addressed storage duration (Key Point 4) and storage conditions (Key Point 5). These storage parameters are intrinsic to DNA banking as long-term storage and should be clearly indicated. Storage durations varied across the DNA banks. While some banks provided a targeted storage duration, ranging from 10 and 50 years, others stated an intent to store specimen for as long as possible. At some of the banks with a targeted storage duration, the form indicated that storage could be extended for an additional fee. It is important to understand that specimens are exhaustible with testing, so it is possible that a specimen may be depleted prior to the target duration. While all 5 consent forms addressed storage conditions, there were differences in the details provided. While some forms simply indicated that steps would be taken to store the specimen safely, securely, and to maintain medical utility, 2 forms additionally elaborated that the specimen would be stored in freezers in separate locations. This redundancy is consistent with the axiom that banked specimen may be extremely valuable to depositors and families. Two consent forms also specified that the storage parameters of the banks do not satisfy a legal chain of custody (Additional Point 1).

Clinical DNA banking is a laboratory service that commonly has an associated fee, which may play a role in decisions to bank or not. While a storage fee (Additional Point 2) is not specifically mentioned in either the ASHG or ACMG documents, 4 of the 5 consent forms indicated a storage fee, ranging from $85 to $450. The additional fee to extend storage duration was not indicated on the consent forms of banks with targeted storage durations. The DNA banking fee may not be covered by medical insurance, and the cost may drive disparities in healthcare access and downstream benefit (Prudent et al. 2021).

Points to bank on: benefits, risks, and storage considerations Including benefits and risks in consent discussion allows for individuals and families to broadly consider how the specimen might be used.

The storage duration sets stewardship expectations, pertinent to maintaining communication and documentation. Discussing costs up front can reduce unexpected financial burden.

Specimen access and disposition

Using a specimen for testing is the payoff of DNA banking. The resulting genetic information may impact medical care and management, be sensitive, and have implications across generations of a family. Therefore, clarity about who can access the specimen (Key Point 6) and the procedures to retrieve a specimen for testing (Key Point 7) is paramount. A consequence of the long-term nature of DNA banking is that stewardship of a specimen may change over time, across families and through generations. All of the consent forms outline protocols for sharing and/or transferring access. Of interest, only 2 consent forms specifically highlight that ownership of a banked specimen derived from a minor will automatically transfer to that individual upon achieving the age of majority (Additional Point 3). This aligns with the ethical principle of respect for autonomy and is an important discussion point when DNA is banked for minors. All of the consent forms indicated that written authorization from the depositor and/or designated representative is required to retrieve a specimen. Subsequent clinical testing requires coordination with an ordering provider and the laboratory performing the testing. Research testing requires coordination with the research laboratory. It may also be possible for depositors and/or designated representatives to retrieve a specimen for direct-to-consumer testing.

The majority of consent forms indicated that depositors and/or designated representatives could transfer a specimen out of the bank or have the bank destroy the specimen (Key Points 8 and 9, respectively). One of the consent forms did not mention transferring a specimen, and two of the consent forms did not mention destroying a specimen. These are specifically noted in the ACMG statement and are the mechanisms by which depositors and/or their designated representatives may terminate a contract with a DNA bank.

Communication

The consent forms should facilitate setting expectations for communication between the depositors and/or designated representatives and banks (Key Points 10 and 11). Contact information should be clear. All of the consent forms mentioned specific circumstances for depositors and/or designated representatives to contact the banks, including changing contact information, determining disposition at the end of the storage period, and requesting specimen access, transfer, or destruction. Banks should clarify if they will contact depositors and/or designated representatives about changes affecting the storage of the specimen, including at the end of a targeted storage duration. Two of the consent forms note the possibility of bank closure (Additional Point 4) and state that the banks will attempt to contact depositors and/or designated representatives to determine specimen disposition. A third consent form indicated that the bank could contact the depositor and/or designated representative about possible research. Overall, clear expectations of when and whom to contact promote specimen stewardship through such transitions.

Points to bank on: access, disposition, and communication The nature of long-term DNA storage necessitates anticipation regarding access and disposition. Who can consent to withdraw a specimen over time? Minors become adults, designated representatives and individuals may pass away, and people may be difficult to contact over years if they move locations and change contact information. Clear expectations and communication support ongoing specimen stewardship.

Research

The ASHG document specifically states that depositors should be informed regarding "the conditions under which DNA can be used for purposes not requested by the depositor, e.g., research" ("DNA banking and DNA analysis: points to consider 1988). The ACMG also recommends clarifying permissions for research use ("ACMG statement 1995). Two of the forms specifically indicated that the specimen may be used by the banks for research activities (Key Point 12), potentially *without* additional consent. The other forms generally stated that no testing would be performed without the consent of the depositor and/or designated representative. Banked DNA is a finite resource that can be depleted with testing over time. Therefore, it is important to know if there are other ways that the specimen may be used once in the bank. Of course, depositors (and/or their designated representatives) may choose to transfer part of their specimen to a research study or biobank.

Future testing possibilities and limitations

The long-term nature of DNA banking opens the exciting prospect that unsolved cases of today may be elucidated in the future by new medical knowledge and testing technologies. Thoughtful stewardship of specimens over time maximizes the possibility of benefiting from future advancements. However, there is no guarantee that testing on banked DNA will provide diagnostic answers. Three consent forms stipulated that the corresponding banks are not responsible for testing performed or results generated by outside laboratories (Additional Point 5). Test failures are possible, and results may be uncertain. Additionally, two consent forms addressed that banked specimen may not be usable or suitable for all genetic testing methods or downstream uses (Additional Point 6). This particular technical limitation is important to highlight for the clinician, individual,

and family to establish clear expectations and to avoid storing a specimen for a specific test that requires a different specimen. In our institutional experience, this has caused confusion for both patients and clinicians, specifically with regard to ordering cytogenetic testing on banked DNA. Most cytogenetic tests, such as karyotypes, require cells and cannot be performed on the extracted DNA that is typically banked. Another example of this limitation occurs in cases of mosaicism, where only some of the cells in the body harbor the genetic variant of interest (Thorpe et al. 2020). If the banked DNA was not derived from the affected tissue, then the genetic variant simply cannot be detected by testing that DNA. Specific documentation of the specimen type (Additional Point 7) can help clarify suitability for analysis in this scenario. Finally, the suitability of banked DNA for genetic testing technology developed in the future is unknown.

Points to bank on: future testing While banked DNA specimens are appropriate for many genetic tests, it is important to clarify that it may not be usable or suitable for all genetic testing methods or downstream uses. If one specific test is anticipated, the decision to bank a specimen should involve discussion of whether the specimen is acceptable for that test and method.

Conflict

Because genetic information is inherited and may be sensitive and prognostic, the continuum of decision-making, from whether to pursue genetic testing to disseminating results, may precipitate conflict. In general, when depositors have decision-making capacity, they direct the use of their banked specimen to learn genetic information about themselves. However, when the locus of decision-making shifts away from the depositor, additional complexities may drive conflict, exacerbated by the particular context of DNA banking (Additional Point 8). One consent form alluded to possible conflict, mentioning impact on family relationships as a potential risk of genetic testing. For example, there may be multiple designated representatives, potentially with differing interests and goals, who may become gatekeepers to genetic information that may impact the entire family. One other consent form highlighted the specific circumstance where parents/legal guardians of a minor may have conflicting instructions for the bank and outlined how the bank would respond. Finally, because specimens are exhaustible, only a finite number of tests may be performed. Testing for one indication may preclude testing for another. Testing now, which may have an immediate impact, may preclude potentially more informative testing in the future.

Points to bank on: conflict It is incumbent upon depositors, designated representatives, and families to acknowledge the possibility of conflict regarding specimen utilization at the time of consent. Given the long-term nature of DNA banking, ongoing dialogue is imperative as new sources of conflict may arise. Managing conflict over time is entwined with stewardship and is essential to appropriate specimen utilization to benefit the depositor and their family.

Considerations for clinicians

Clinicians participating in consenting for DNA banking should aim to enrich consent by identifying and addressing the key and additional points and potentials gaps, as well as tailoring conversations to the particular circumstances. If clinicians are centering their consent discussion based upon points in one particular form, then important information might not be relayed to depositors, representatives, and families. Depending on knowledge and experience, the clinician may be unaware that this has occurred. Even with an appropriate informed consent discussion, banking often occurs at stressful times, when an individual is being evaluated for a suspected genetic condition, is critically ill, at the end of life, and in post-mortem settings. As such, the details of the banking process may not be a priority at those times and may be forgotten. The consent forms can serve as an important long-term reference but may be incomplete. For clinicians involved downstream in the care of individuals and families with banked DNA, it may be prudent to gauge the knowledge and expectations of depositors, representatives, and families. In response, clinicians may need to address points that have been initially missed, forgotten, or become applicable over time.

Over time, clinicians may continue to be involved in a variety of ways that promote banked DNA stewardship and maximize downstream utility. Clinicians may facilitate conversations with new designated representatives and depositors upon achieving the age of majority. They may help craft an overall testing strategy and manage possible sources of future conflict by facilitating discussions with the various stakeholders to arrive at shared expectations. These are complex discussions that are highly individualized and require clinical judgment (Bester et al. 2016). Details of conversations that clarify a family's particular wishes and desires should be documented. As banked DNA can have myriad possible downstream clinical and research uses, the opportunities to use it and the purpose and implications of that use may evolve during the lifecycle of the specimen, warranting ongoing dialogue.

Research warrants a particular spotlight. For those individuals with undiagnosed or rare disease, clinicians consenting for clinical DNA banking should consider exploring relevant research opportunities and research biobanking as well. As with clinical testing, research participation should be revisited over time as relevant research opportunities arise, such as to identify new genes associated with disease or to develop therapies. Because it may be burdensome to clinicians to stay

current with ongoing research across multiple phenotypes in their patient population, clinical DNA banks could explore integration with existing frameworks such as the Matchmaker Exchange as an avenue for researchers to identify and reach out to relevant individuals instead (Philippakis et al. 2015). Clinical DNA banking preserves the ability for the depositor or their designated representative to participate in multiple research studies without the need for new specimen collection. Even if the depositor is deceased, the designated representative is still empowered to collaborate with researchers to use a specimen to benefit the family, other affected individuals, and the overall research endeavor.

Practically, clinicians should document DNA banking in their clinical notes to maintain a record of this storage for posterity. This should include the date, original specimen type, storage duration, designated representatives, DNA bank name, and the bank's contact information. If updates occur, such as changes to name, contact information, or designated representative, it should prompt re-contact of the DNA bank to update the information and then also be documented in the medical record. Depending on the electronic medical record system, this information could also be saved and tracked in a way that could generate alerts based upon dates and laboratory orders (Grebe et al. 2020). Of course, depositors and representatives should keep their own records as well. This is critical information that informs future genetic testing using the banked specimen, perhaps initiated by other providers. Because banking may be performed as part of a specialty consultation with a limited therapeutic relationship, the clinical notes are an accessible place for primary or other long-term care providers to find this information, to incorporate into their own documentation, and track any future changes.

Limitations

This study had a limited scope. It only included clinical DNA banking consent forms that were available from laboratories based in the USA. Additionally, our search was limited to the GTR. Registration in this database is voluntary; thus, the sampling of consent forms reflected those laboratories that chose to submit information to this database. Nevertheless, the laboratories performing DNA banking that the authors were familiar with were represented in the GTR. It is unknown exactly how many laboratories conduct clinical DNA banking activities.

Conclusions

The act of clinical DNA banking belies much underlying nuance, and variation in DNA bank consent forms was identified even among just 5 banks. DNA bank consent forms are a critical tool to facilitate thorough and valid informed consent for depositors and representatives. When a consent form has gaps, of which clinicians and patients may be unaware, it is a barrier to achieving informed consent. Clinicians can consider the range of key points and additional points discussed here to supplement and enrich their clinical DNA banking informed consent discussions. The identification of multiple additional points also suggests a need to update the ASHG and ACMG guidance. The long-range nature and implications of DNA banking also warrant ongoing communication among the depositor, clinicians, and DNA bank beyond a one-time, initial consent conversation in order to facilitate specimen stewardship and utility. Thorough documentation can serve as a safety net, a backup for banking details, a guide for planned testing, and a record of stakeholder wishes and desires. Clinicians caring for individuals with banked DNA should be familiar with the uses, limitations, and complexities of the service.

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Data availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval This study did not involve human participants, individual-level data collected from humans, or bio-samples collected from humans.

Conflict of interest Darci L. Sternen is employed by Seattle Children's Hospital Laboratory, which offered a DNA bank service until 2020. Laura M. Amendola is an employee of Illumina, Inc. Samuel J. Huang declares no potential conflict of interest.

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