A Consumer Perspective on Forensic DNA Banking

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The currently evolving debate over ethical and legal approaches to DNA data banks reflects, in part, shifting societal perceptions of dividing lines between humanity and commodity, definitions of genetic inheritance between individuals and families, and the rights of the individual versus the rights of the community.[1] Tensions arise whether the data bank has been created for medical or for forensic purposes. The authors, through their work as community activists described more fully below, have come to realize that the key to resolving these tensions and developing ethically acceptable DNA data bank practices is meaningful community engagement. Not unlike medical DNA data banks, personally identifiable DNA samples are routinely retained by states long after a convict's or arrestee's DNA profile has been derived from it and entered into the state database. The question arises, then, as to what, if any, non-forensic uses can these samples – ethically – be put. Medical DNA data banks and the evolution of legal and ethical approaches to their creation and use may serve as a guide when considering this question. This article describes the experience and viewpoint of the authors as consumer advocates who have developed a model designed to permit appropriate consumer influence on the development, design and use of DNA data banks. For the purposes of this discussion, "consumers" refer to individuals or their representatives who have DNA samples retained in a DNA data bank.

To date, consumers have participated in the ethical debate in an attempt to further their interests in the DNA data bank. They have done so individually and in organized efforts, and have spoken in many voices. For example, in well-publicized cases consumers have demanded ownership of samples[2] and benefits derived from donation of biological samples.[3] However, with an estimated hundreds of millions of DNA samples in the world's laboratories, most individuals and groups have donated samples freely with no demands for ownership or benefits.

This article supports neither the legal theories advanced in the cases mentioned above, nor the free no-strings-attached donations by the vast majority of

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individuals whose samples are retained for research purposes. These approaches fall short of best practices in consumer decision-making about biological samples collection, archiving and future use. Rather, this article espouses a model designed to focus on the narrower group of consumer stakeholders. This model values input of consumer stakeholders in key decisions, including contracts detailing relationships between donors and the bank, and researchers and the bank. In this model, benefit sharing is not the motivation for donating samples, but a by-product of keeping research focused on health outcomes. The following sections provide background information on consumer stakeholders in DNA research, describe and discuss the community engagement model, and provide two examples of the community engagement model: PXE International, and Genetic Alliance BioBank. The article concludes with a consideration of community engagement and forensic DNA data banks.

Background

The community model discussed herein is focused on community "stakeholders." Stakeholders often describe themselves as having crossed the line dividing health and disease, which gives them a unique perspective of the world and their situation. The mother of a child with a life-threatening illness is willing to donate the child's and her own blood and tissue with the hope that a treatment that could prolong her child's life will be found. In that case, the risks and consequences associated with DNA banking are minimal compared to the devastating effects of the disease. Likewise, a woman diagnosed with breast cancer may donate tumor tissue at the time of surgery, in an attempt to help other cancer patients in the future. For stakeholders, the rights of the individual are more easily subjugated to a greater good – to the benefit of the disease community, where a greater bond is felt by virtue of sharing a genetic condition. Thus, those who stand to gain more from DNA research are willing to give much more, despite the risks.

A nuanced consumer perspective is an important element in determining what is ethical in DNA banking, especially as such banks are expanding in number and size. In our experience, ethicists, lawyers, and policymakers too often fail to see the heterogeneity of "consumers," thereby failing to acknowledge the differences among subsets of consumers, particularly in their willingness to assume risk. Insofar as the consumers are themselves affected by the information gained in biomedical experiments, they are stakeholders. Therefore, while it is theoretically true that we are all consumers, the subset of consumer-stakeholders experience these risks and benefits differently from the larger subset of healthy consumers. The very act of defining consumers as a single interest group dilutes the voice of the stakeholder. In fact, though some ethicists may consider it best to remove all research risks through stringent regulation or protections, this is neither best nor desirable in the view of consumer-stakeholders (hereinafter referred to as stakeholders). From a stakeholder perspective, this strategy impedes important research, and is not an optimal solution. For those with a vested interest in discovering a treatment for a disease, a high risk may be acceptable if there is a promise of high benefit. That is, high risk may be mitigated by high need. In short, stakeholders measure risk in different ways depending on their experience with disease.

Community Engagement

Individuals affected by the outcomes of genetic research are stakeholders that must have a voice in determining use of DNA samples. As noted above, this model does not seek ownership or benefits derived from donations of biological samples, nor does it embrace the free donation of samples. Rather, the community engagement model is focused on taking responsibility for use of the samples in a way that fosters appropriate balancing of risks, while accelerating translational research. Community engagement, resulting in both formal and informal contractual relationships, is a critical step in understanding risk, mitigating it through the shared experience of the community, and accelerating translational research as a result. The development of contractual relationships is, of course, made possible by the commodification of genetic information, a community-centered commodification that is the principle bargaining tool of community engagement. As implied in the "community-centered" commodity, the stakeholder's focus is typically broader than their own self-interest. This finding is supported in the frequency that DNA donors cite "for the benefit of others" as a primary reason for donation. The consumer's perception of DNA as a commodity includes obligation and honor, generosity, and stewardship – more akin to a Native American construct than European-American one of responsibility, power, affluence, and ownership.[4] Thus community engagement enhances, rather than

limits, effective DNA bank policy-making. It decries the concept of human dignity as a barrier to research, and an increase in regulatory restrictions is of serious concern.[5]

The following sections describe the two community groups that the authors have found indispensable to the success of their own community engagement initiatives: PXE International, a rare disease advocacy group, and Genetic Alliance, a coalition of over 600 disease-specific advocacy organizations. In addition to the influence of the advisory board in DNA sample collection, archiving, and appropriate uses, contract law also plays a key role. Contracts detail the relationships between the donor and bank and researchers and bank, as well as approaches to benefit sharing.

Elements of Community Engagement: Flexible Governance and Voice

Once the stakeholder community is defined, a system for representing their rights in the operation of the bank must be developed. Flexibility and an ability to address unique or near-unique situations is critical to that representation. Standard codes of conduct or strict rules and regulations will not suffice. Rather, a flexible mechanism such as a DNA bank advisory board is a more appropriate mechanism for protecting the stakeholder's interests. This concept is modeled on the community advisory boards that have experienced success in setting health care policy that benefits the community.[6] Provided the stakeholders who donate DNA have representation in the decision-making, similar success can be experienced by DNA banks. These stakeholders, given the appropriate process of engagement with the broader community (e.g., researchers, academic institutions, funders, etc.) can bring an important and even indispensable perspective to setting policies for firewalls and boundaries to protect DNA banks, as well as for appropriate uses of DNA banks. These stakeholders *must* have a voice in policy making.

Contract Law and Community Engagement

In both basic and translational research, there are many of the same biological issues with only the nuance of different challenges and complexities which include law, ethics, economics, and contract law. In determining how best to collect, archive, and use donor samples, contract law and parlance are the tools that stakeholders have found most useful, since they clearly define mutual responsibility in a situationally defined context. Like DNA bank governance, it is impossible to achieve this with blanket standard codes of conduct. In the following examples we look at how we have used community engagement and contracts to define mutual responsibilities for the stakeholder and researcher.

PXE International[7]

In 1994, our two children, Elizabeth and Ian Terry, were diagnosed with Pseudoxanthoma Elasticum, or PXE. This disease causes central vision loss, blindness by the third or fourth decade, gastrointestinal disease, cardiovascular disease, and various other manifestations. As parents of a seven- and a five-year-old, we came to some very quick conclusions: little was known about this disease, we needed treatment, and we needed to figure out how to get there. We also quickly realized that no one was "in charge" of making sure that well coordinated research would be conducted.

We began by surveying the literature and interviewing researchers who had written peer-reviewed journal articles on PXE. We also investigated issues with the consumer community through the Genetic Alliance, a coalition of disease advocacy organizations. The challenges that we faced included conflicting medical advice, a limited pool of willing participants, inadequate funding, and a competitive, fragmented, and unfocused research environment. We soon realized that this was common for all rare conditions.[8]

These challenges create redundant small collections of DNA, poor confidentiality protections, a variable informed consent process, inaccurate disease characterization, and limited reporting to participants. We began to recognize that our agenda was one among many, and the moral force of our mission alone would not suffice to reach our goal. Therefore, we brought our agenda to the table with a willingness to respect and work with agendas of other stakeholders. Our experience was critical to help find a way to accelerate research by forging collaborations across these cultures.

Our solution was to create a community centered on a commodity. We established the PXE International Blood and Tissue Bank, and designed it to be a strong catalyst for coordinating ethical research. In general, affected DNA donors feel mined for their DNA and isolated in their disease. We wanted these individuals to know they would have a voice in the process, and be adequately and fairly represented.

The Bank defines a community that recruits individuals in an atmosphere of trust and support with ongoing education, engages in a culturally sensitive, comprehensive, informed decision-making process, and encodes identifiers in a centralized database maintained by the advocacy foundation. Of particular significance is its informed decision-making process. This does not presume consent for use of DNA samples, as do informed consent documents. The associated database contains not only genotypes, but also a robust

phenotype registry of well-annotated samples of all types, including over 900 fields of data on each individual.

The PXE International provides a firewall between the research enterprise and the participants who engage in the research. This helps to bridge the differences between the two cultures, allowing each community to feel appreciated, heard and represented. Participants are re-contacted for additional samples or information, and receive general (not personal) updates and reports. All identifiers are blinded and researchers have a much easier time securing institutional review board approval. PXE International manages all issues with regard to ethics, allowing research to go forward as quickly as possible.

In the same way PXE International engaged the community of individuals with PXE, it also engaged the research community. Interested researchers apply directly to PXE International. More than fifty scientists have agreed to collaborate with PXE International, and with other scientists. They provide regular scientific and lay reporting. Researchers give assurance that they have IRB approval for research, and that samples will not be shared with other labs, to maintain the integrity of the Bank's high standards. Researchers do not contact donors or report results to donors.

While some might hope that community engagement and the altruism of science and medicine are enough, we contend that the relationship and its products are healthier, clearer and more focused because they are the result of shared agreements. Researchers share benefits arising from the use of samples with PXE International because expectations are clarified contractually prior to research being undertaken. Material transfer agreements and memorandums of understanding govern all of PXE International's agreements. Thus, we have seen that contractual arrangement increases awareness and clarity of mutual expectations, thereby raising the ethical bar of these transactions.

Contrary to published accounts,[9] including some reports on the Internet as well as in printed peer review journals, PXE International did not negotiate for inventorship or property rights. US Patent Law does not allow negotiating for a patent; the group instead met the test of US and international harmonization standards of inventorship by participating materially in the research. Further, although many ethicists have made a fuss over their perception that patents create barriers to research, it is actually licenses that could create these barriers, since they determine access to the object of invention. We have engaged in both exclusive and non-exclusive licensing, aware that an exclusive license is sometimes the only motivation someone has for working on pseudoxanthoma elasticum (PXE). At other times, co-licensing is more appropriate, as several entities work together toward a common goal. Also contrary to these accounts, PXE International did not sign any profit-sharing agreements with researchers. It is PXE International's belief that contributing samples does not entitle anyone to inventorship and/or profits from downstream products. It is also speculated that PXE's work is in response to the Canavan case, when in fact, it preceded the Canavan case.[10] This case involves a lawsuit brought by parents and not-for-profit organizations, alleging that Miami Children's Hospital secretly obtained a patent for the gene associated with the disease called Canavan, without consenting the donors or sharing benefits from the licensing agreement. All of PXE International's agreements were crafted in 1997, before any media coverage of the Canavan case's issues surfaced publicly.

Since we are part of a community, and have consulted with and engaged this community, holding the patent to the gene associated with pseudoxanthoma elasticum (PXE) is a considered and weighty responsibility. We are bound in a stewardship relationship with the altered disease gene, and with all of the people to whom this gene matters a great deal. In this way, not only are our children in our care, but also the thousands of individuals registered with us and all those thousands with whom we have not yet interacted.

While this process does permit donors to retain some control over the samples and their use, mere control of the process is not a central consideration of our efforts. Rather, our primary concern is to accelerate the research – to create a community through the commodity of blood and tissue and clinical information. This commodity has inspired individuals affected by the condition to join together, and motivates researchers to collaborate with one another in a way that they would not have otherwise.

The benefits of PXE research include a large increase in lab collaboration, and significant research advances. At present, PXE International is working with the Food and Drug Administration (FDA) to approve a genetic test for PXE. This will be the first rare disease genetic test sponsored by an advocacy group to apply for FDA's diagnostic review and device clearance. All other devices approved by the FDA have been sponsored by for-profit companies.

The process utilized by PXE International certainly does have its criticisms. Such criticism often grows out of concern that consumer stakeholders will slow the research and translation process.[11] In addition, concerns have also been expressed that PXE International's efforts inappropriately champion patenting, slow down the discovery of the ultimate solution, degrade science, alter the face of life science intellectual property law,

and have sparked a major change in the status quo encouraging donors to demand royalties that may create exorbitant costs for biotech companies. However, it is the group's belief that sample ownership is essential to taming PXE through industrialized translational research. Owning and managing a sample Bank allows PXE International to scale, focus, and initiate unique collaboration.

Genetic Alliance BioBank

Pressed by a number of disease advocacy organizations, we expanded beyond PXE International, and founded a larger, umbrella bank, the Genetic Alliance BioBank. Incorporated October 14, 2003, The Genetic Alliance BioBank and its associated IRB serve a number of advocacy organizations, allowing them to participate in the research enterprise in a meaningful way. The bank follows the PXE International model and houses biological samples as well as data, including DNA, RNA, cell lines, tissue, organs, self-reported data, medical images and medical records. Members of the BioBank include Angioma Alliance, CFC International, Inflammatory Breast Cancer Research Foundation, Joubert Syndrome Foundation, National Psoriasis Foundation, NBIA Disorders Association, Noonan Syndrome Support Group, and PXE International.

The Genetic Alliance BioBank recruits participants, not subjects. This is a critical distinction and a result of the concept of community engagement. Recruitment is done in an atmosphere of trust with the highest privacy and confidentiality protections. It also empowers these participants by providing ongoing education for them. These individuals engage in informed decision making, in a refined version of the PXE International process. They're educated and informed. Consenting is only one part of this process and is not necessarily an outcome, thus the term "informed consent" as an indicator of the process is a misnomer in this context. BioBank informatics encode identifiers in a centralized database maintained by the advocacy organization. The BioBank has a research focus – disease and treatment research in concert with academic collaborators and partnerships with industry.

BioBank functions include centralized and standardized bar-coded collections and archiving; maintaining the integrity of advocacy organizations collections and data; ensuring proper use of samples and data; enabling ethical recontact and follow-up for genotype-phenotype correlations, natural history and longitudinal studies; regular communications to key constituents; and advocacy organization control and benefit sharing. We are often asked if benefit sharing means holding the patent, receiving royalties and making sure profits are shared. The system we have developed for BioBank is broader than a purely monetary system. To stakeholders, benefit sharing often means sharing information, assuring forward progress and ultimately sharing a treatment or technology, or simply a mutual understanding for the need of quality, affordability, and access. It rarely has anything to do with intellectual property rights, royalties, or financial conditions.

The data banking portion of the BioBank is undergoing an upgrade. Specifically, the data bank upgrade plan includes strong privacy and confidentiality protections. This means a highly secure industry grade validated IT structure with comprehensive access control in capability. The data bank will encompass an effective dynamic data aggregation portal with scalable web-based architecture. It will also have integrated clinical research management tools: applications that integrate consent, clinical and genomic data, and sample banking. It has capabilities to reuse and share donor's resources. It will include dynamic consenting and patient recontact mechanisms, and data representation standards that include support for data exchange and data mining.

In addition, the BioBank provides a home to the community of donors, on a bank-wide level as well as a disease-specific level. We envision cross-disease research one day, again a result of the donors' explicit recognition that they are part of a community. We already share properly consented samples as control samples across a wide range of diseases.

Genetic Alliance BioBank member organizations pay an annual membership fee. They enter into a contractual arrangement with the Genetic Alliance BioBank. As a result, they receive template protocols, technical assistance and personnel training. They access the infrastructure for banking that includes DNA, tissue, cell lines, tumor cells, and the clinical data system. They receive IRB approved, heavily vetted, documents for informed decision-making, researchers' applications for samples, and donor recruitment. In addition, organizational members share resources such as gene discovery, mutation characterization, genetic testing, and subsequent research.

Researchers interested in any of the Genetic Alliance BioBank material are directed to the advocacy organization that manages those samples. The advocacy organization is encouraged to ask the researcher for: 1) institutional review board approval, 2) agreement to provide regular scientific and labor force reports, 3) assurances that the samples will not be shared with other labs and that there will be no end run around the advocacy organization, 4) no contact with donors to report individual results, 5) benefit sharing in a manner that is beneficial to both the researcher and the

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organization, and 6) that the advocacy organization is recognized as a prime collaborative.

This method of management assures compliance with all oversight and regulatory guidelines, including emerging guidelines. A robust informed decision-making process takes place and, just as with the precursor PXE International, there's a firewall between identifiers and samples. It also provides access to comprehensive archive of samples including information such as genotypes and phenotypes to all interested researchers. It creates and/or maintains the integrity of various world and local community collections and research projects resulting in increased trust in collaboration, and empowers affected individuals and the advocacy organization. It keeps the research focused and coordinated on affected individuals and their families, particularly on issues researchers might not initiate. And it allows safe ethical contact and follow-up for genotype-phenotype correlations, central history and longitudinal studies. Benefits of advocacy committee organizations include focused biomedical research, genotype-phenotype correlations, a rigorous but not onerous participant of protections, and cross-disease research. The results of this new paradigm are individuals and organizations as full partners with researchers to ensure benefits are worth the risks and accelerate the translation of research treatments.

Implications for Forensic Banks

The examples above indicate that, given a process of community engagement and contractual agreement, stakeholders are able to agree to a contractual arrangement to define data access, both the information systems and the data management, in a transparent manner. The question of whether such data banks should ever be used for non-forensic purposes is beyond the scope of this paper. Unlike the models discussed herein, forensic samples are not donated for research purposes, and, in the case of criminal DNA data banks, samples are collected by the force of law. However, should forensic samples be used for research purposes, the best scenario is one that includes engagement of the community of stakeholders. These communities will vary widely. For example, in the case of the World Trade Center bombing, the community includes survivors and the relatives of individuals who died in the bombing. In the case of prisoners, the community will include prisoners, their relatives and those who are responsible for them. As the scope of criminal DNA data banks expands, the relevant community will be broader, of course. In all cases, an advisory committee or other representative body must be given real responsibility of being stewards of the collection. In addition, the community must decide the best process to lead to the communally determined ultimate goal. While the ability to enter into contracts may not be present in the forensic scenario, a process sensitive to the community voice will be necessary. While creating this process would not be easy, it would necessitate a nuanced examination of the issues inherent in the multiple cultures represented in the community.

Conclusion

It is critical that stakeholders – those whose lives are touched by science, banking, and by forensics – have a voice. If ethicists, lawyers, and policy-makers are concerned that the populace is incapable of making informed decisions, then it may be their moral obligation to educate the community, rather than paternalistically making decisions about their biological samples, and risking onerous regulation that impedes research.

Ethicists, lawyers, and policy-makers see the issues inherent in biological sample donation-privacy, confidentiality, risk-as issues affecting the entire population. These professionals believe that they are representing donors as stakeholders because they mistakenly assume that actual donors, individuals touched by genetic disease, share the same goals as the healthy population. In our experience, the stakes, and therefore the ethical analysis, change once an individual crosses the line from good health to disease. Becoming a stakeholder changes perspective. That perspective now includes a willingness to accept more and different kinds of risks, a willingness to sacrifice more to attain benefits, and understanding our shared inheritance in a profound way.

Individual consumers, communities and their advocacy organizations need to be involved in the reshaping and reframing of the enterprise, including decisions about forensic banking and access to those banks. The engagement of communities, through representation in advisory boards or proxy groups, allows the formulation of the most relevant and ethical decisions. Community engagement has come of age, even to the point of being a topic for a new journal, *Progress in Community Health Partnerships: Research, Education, and Action,* published by Johns Hopkins University Press. The cry of underserved and underrepresented communities captures the spirit of our notion of community

engagement: "nothing about us without us." We are hopeful that even as large population studies are being planned, stakeholder communities will be involved in the planning from the start. It is time to engage communities to accelerate science past its fears, fabricated mythology of potential harms, and the undue influence of the litigious age. It is time to move forward with tempered urgency, exchanging a hundred years of basic science discoveries for tangible health benefits.

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