Point/Counterpoint

Biospecimen ''Ownership'': Counterpoint

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With more than 300 million human specimens currently in storage in the United States, human biological samples have become an integral component of the research infrastructure (1, 2). It is, however, a fragile component. Human ''biobanking'' depends heavily on the public's trust in the research enterprise and the willingness of individuals to contribute specimens. That cooperative spirit, in turn, will be significantly affected by the policies and practices we use in collecting, processing, maintaining, and distributing these specimens.

The recent legal battle over ''ownership'' of banked biological specimens in a Washington University prostate cancer repository shows how easily flawed policies can put the public trust, and thus biobanking, at risk. In *Washington University* v. *Catalona*, Washington University filed an action ''seeking to establish ownership, and thereby, the destiny of certain research biological materials currently stored at the University'' (3). It is not difficult to understand the desire of Washington University to protect its interests in a biorepository it maintained, administered, funded, and staffed and for which it assumed the legal, regulatory, and compliance risks. Nor it is surprising, given the facts of the case and legal precedence about ''human specimens as property'' (2), that the Court would decide that Washington University is ''the true and rightful owner and possessor of all biological materials including but not limited to blood, tissue and DNA samples. . .'' (3). It is disheartening, however, that the Court chose to frame the issues involved as a narrow problem of ownership at the expense of appreciating the importance of maintaining a respectful and trusting relationship with current and potential research participants.

From the participants' point of view, ownership is rarely the issue. Volunteers entrust their samples to researchers and institutions under the assumption that they will be used in the best interests of the research participant and the public at large, who ultimately stand to benefit from the research (and often indirectly funds much of the research). A false trichotomy of ownership, which pits the Institution (Washington University) against the Researcher (Catalona) and the Research Participant(s) (~30,000 prostate cancer patients), ignores the principles that participants expect to be definitive in research decision making: respect for their considered choices as participants and loyalty to their interests. These foundational principles are echoed in every research ethics discussion, including the seminal works, which guide ethical research conduct internationally (Nuremberg Code, Helsinki Document) as well as nationally (Belmont Report, 45CFR46, including the Common Rule).

One illustrative example of the shortcomings of a purely legal analysis of the biorepository issues is its implications for the ethical imperative to allow research subjects to withdraw from studies at will. On this issue, Catalona confuses two different but related concepts: providing the research participant an option to terminate participation in a research study (or biobank) at any time and providing an option to withdraw samples from the biobank and transfer them elsewhere. Federal regulations, which mandate that a research subject be given the option to terminate participation in a research study, were written at a time when biobanking and repositories were not a part of the research plan. Consequently, the regulations do not address situations when a research participant decides to terminate participation in a biorepository. In Catalona, the following interpretation was made:

> ''The Court finds that the right to discontinue participation in a research project means nothing more than the RP [research participant] has chosen not to provide any more biological materials pursuant to one or more research protocols; i.e., not to make any more *inter vivos* gifts of donated biological materials to WU. Nothing more can or should be read into this right possessed by the RPs at all times (3).''

Viewing the issues in the case as a tug-of-war over who ''owns'' the stored biological materials as tangible property leads the Court to declare that a research participant with samples in a biorepository has made an irrevocable gift and has relinquished all further interest in those samples. As Ness points out in the companion commentary, the Court was concerned that, if research participants began routinely treating their samples as ''chattel,'' they might begin withdrawing or transferring samples from one repository to another, resulting in chaos for the research infrastructure (4). But this concern seems to be primarily an artifact created by the focus of the Court on property rights. As director of national and institutional tissue banks, housing thousands of specimens, it has not been my experience that research subjects expect to be able to withdraw, deposit, or transfer specimens at a moment's notice from one repository to another as they would do in a financial bank. They do expect, however, that repository decision making will turn on their interests rather than the property interests of institutions. They expect those interests to be determined by their own preferences, outlined in the informed consent document, or, when informed consents lack this specificity, by a ''best interest'' standard similar to that taken on by stewards or trustees (5).

For example, under the ''stewardship or trustee model'' (5-7), common among many cancer specimen banks (2, 8), when a research participant requests that their participation in a biobank be terminated, the specimens remaining in the bank are either destroyed (for DNA or fluids) or returned to the treating institution that originally submitted the tissues (for surgical pathology paraffin-embedded tissue). In this way, the specimen(s) is no longer used in future research, a decision that respects the research participant's request for termination of participation. Does this mean that the specimen(s) that has already been distributed to researchers must be returned

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and associated research results destroyed? No. This would be unrealistic and not be in the best interests of the researchers or the funding agencies or the public. The decision point would be determined by what remains in the repository at the time of the request for termination. For prospective specimen collections, these decisions, interpretations, and intent must be clearly described in the consent process and articulated in the informed consent document.

By contrast, the legal blinders of the Catalona court take it in just the opposite direction when an individual elects to discontinue participation in the biobank:

''If a RP chooses to discontinue participation, federal and state regulations govern the options WU has regarding the tissue/blood/DNA sample. The undisputed testimony was that 1) WU may destroy samples it no longer needs for research; 2) store the samples indefinitely; and/or 3) choose to ''anonymize'' the samples and continue to use them in certain areas of research. To ''anonymize'' a sample, all links to the RP's personal identifying data is removed and the sample is no longer ''linked'' to a particular RP... (3).''

Aside from the issue of whether the specimens were indeed contributed by the research participants with the intent of making a gift of material property to Washington University, these statements and interpretations run counter to conventional research practice and, more importantly, do not honor the ethical principle of ''respect for persons.'' If we uphold the interpretation that to discontinue participation in a biorepository means that samples can continue to be used, we violate an individual's right to self-determination, voluntariness, and autonomy. Furthermore, the decision to discontinue participation is in relation to continued use of the stored specimen, not the future use of a yet-to-be-collected specimen. Regardless of whether the sample(s) is coded or even anonymized to protect a research participant's privacy, use of an individual's sample in research following a specific request to terminate participation in a biobank (and thus not have their samples used in any future research) would be a direct violation of the research ethics tradition that supports our current regulatory system. This action would also be contrary to the research participant's expectations and would be antithetical to maintaining the public's trust in the research enterprise.

I agree with and support the sound principles of the American College of Epidemiology articulated by Ness in the accompanying comment (4). They help to ensure that the interests of researchers and the progress of science are protected. However, except for a provision to protect the privacy of research subjects, the voice of the research participant is largely absent. This is also true of the Catalona ruling. One way to ensure that all stakeholder voices are heard is to change the conversation from one that is fixated on ownership of property to one that broadly balances all of the interests at stake—those of the researcher, the institution housing the specimens, the research participant, and the public. This can be accomplished through a stewardship model in which research decision makers are acting as a steward, not an owner, and their responsibility includes respect for the research participants. This approach is needed especially when there are no variables or preferences indicated in the informed consent document to otherwise guide decision making. A university using the stewardship model would respect the research participant's request to terminate participating in a DNA biorepository by destroying DNA remaining in the repository, not by continuing to use the specimen. The stewardship model would also require that the implications of a request for termination be transparent so that the expectations of the research participant as well as the researcher and institution are met.

In summary, decisions about control of human specimens should turn on the ethical principle of respect for persons, which is embraced by a stewardship, not an ownership model. If we are to realize the promises of this most exciting time in biomedical and epidemiologic research, these decisions must have their foundations within an ethical, not legal framework, motivating all stakeholders in the scientific process.

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