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Culture clash on consent

All research on human subjects requires their informed consent. Obtaining valid consent from isolated minorities can be particularly challenging, but scientists need to avoid the temptingly easy way out, so as to prevent further exclusion of these vulnerable populations from biomedical research.

This April, two lawsuits pitting the Havasupai Native American tribe against scientists from Arizona State University (ASU) were finally settled after 6 years of litigation. The Havasupai, a small group of about 650 people, began to collaborate with ASU scientists in the early 1990s in an effort to identify genetic causes for the tribe's unusually high incidence of diabetes. More than 100 Havasupai donated blood samples after signing a broadly phrased consent form allowing "study [of] the causes of behavioral/medical disorders." The scientists, in addition to testing for diabetes-linked alleles, also used the samples for research into schizophrenia genetics and Native American ancestry and migrations. When they learned of this, the Havasupai sued ASU for unauthorized use of blood samples, claiming up to $60 million in damages for having suffered "severe harm, extreme distress, and emotional trauma." Under the settlement, the samples were returned to the tribe and ceremonially buried, tribal members will share $700,000 cash, and the university will help provide badly needed medical and educational services. Although this may be good news for the Havasupai, biomedical scientists may be further discouraged from working with disadvantaged minority groups because of the litigation and anti-science publicity associated with this case. Chasing off science cannot be in underserved groups' best interest.

A fundamental misunderstanding about consent lay at the root of this sad breakdown of an initially promising collaboration. The scientists did not speak the Havasupai language and therefore relied on anthropologist colleagues and tribal mediators to recruit study participants. They tried to keep consent forms as simple as possible, but also, because of the open-endedness of scientific research, as broad as possible. The Havasupai, on the other hand, were motivated by the desire to understand and combat the diabetes that was ravaging their community. They were not familiar with genetic research, its process and methodologies. They could not foresee that research on "the causes of behavioral/medical disorders" might move into directions they would not want to support. Neither, apparently, were the geneticists able to imagine the Havasupai's culturally based reservations, even though they worked closely with an anthropologist colleague who knew the tribe well. From the tribe's point of view, it amounted to sheer betrayal to use their blood samples for anything but the study of diabetes. Although the geneticists and the university believed that the signed informed-consent forms allowed the pursuit of essentially any biomedical question, the Havasupai claimed that they had never explicitly permitted anything except diabetes research.

Since work with the Havasupai began 20 years ago, the understanding and practice of informed consent for genetic studies have been substantially extended and refined (http://www.genome.gov/27026589). Obtaining consent is now understood as a process rather than just a signature on a form. It requires research participants to understand not only what a study is about and what possible physical risks they may encounter, but also to evaluate the privacy safeguard problems that may arise from potentially indefinite storage of genetic data in publicly accessible databases. University of California Los Angeles's Nelson Freimer, who studies Tourette's and bipolar disease in genetically isolated communities in Costa Rica, notes that a grasp of these mostly hypothetical, but possibly serious, issues is difficult for anyone, not just isolated tribal people. For studies involving Native tribes and other identifiable groups where privacy may be even more difficult to maintain than in the general population, the US National Institutes of Health now recommends that geneticists consult with the community as a whole, in addition to obtaining informed consent from individual participants (http://bioethics.od.nih.gov/named_populations.html).

With advancing scientific and data-mining technologies, the possible risks associated with genetic research are becoming ever more complex, but consent forms still need to be comprehensible to participants from any educational background. One suggestion (http://blogs.law.stanford.edu/lawandbiosciences/2010/04/23/the-havasupai-case-and-how-to-make-consent-forms-better/) is to make the forms more interactive. Research participants can be given options to choose from, agreeing to have their DNA used for a specific project and time frame only or agreeing to possible extensions, all the way up to agreeing (or declining) to have their anonymized genetic data kept on file for as-yet-unplanned future research. Such choices, apart from their face value, serve to actively engage participants in the consent process and thereby help to make their signatures a more reliable token of consent.

The difficulties of obtaining valid consent are exacerbated for scientists who work with isolated minorities, having to convey the complex risks associated with genetic research to participants whose language and experience may entirely lack the necessary vocabulary. Given that not all of these studies pay scientific dividends—no genetic clues to either diabetes or schizophrenia were identified in the Havasupai samples—such hurdles may be enough to put many scientists off studying such populations altogether. But this would be a mistake. Research on distinct ethnicities has for decades greatly advanced our understanding of genetic causes of disease and has indeed helped the minority groups themselves; one may recall the numerous genetic conditions first identified in Ashkenazi Jews or the distinct risk factors for diabetes found in the Gila River Pima tribe. The combined progress in genetics, genomics and bioethics makes informed consent more complicated, but this must not lead to researchers dropping the study of such valuable and vulnerable populations. ■