RESEARCH ETHICS

Policy on DNA Research Troubles Tissue Bankers

About a decade ago, a group of biologists at the Centers for Disease Control and Prevention (CDC) in Atlanta decided to collect blood from thousands of people of different ethnic backgrounds to create a repository for research on genetic diseases. Although no one knew precisely how the samples would be used, the archive kept growing and now stands at 17,000 DNA samples. But don't expect to see published results from this priceless collection anytime soon: It hasn't been used for research yet because the CDC is concerned that its original procedures for obtaining consent fall short of today's standards.

CDC's struggle to satisfy its ethical responsibilities has alarmed bystanders. Some researchers—particularly pathologists—fear efforts to define the rules for genetic research on archived blood and tissue will set an impossibly high standard for other institutions around the country.

Last week leaders of several professional groups met to discuss such concerns at a meeting in suburban Maryland hosted by the National Institutes of Health's Center for Human Genome Research (NCHGR). The center is funding the development of ethical principles in this area, and its staffers have helped draft a set of guidelines for work on archived specimens. In addition, language from a model "genetic privacy act" developed with NCHGR support in 1994 has been incorporated into a few state plans, and there is a bill in Congress that would ban genetic discrimination (*Science*, 22 December 1995, p. 1911).

The rush to regulate genetic data, according to one prominent pathologist, could "totally cripple" research on archived specimens. Some draft ethics proposals would define "genetic test" so broadly, said another pathologist, that the rules would cover almost any material containing DNA. "How can you do cell biology if you can't use human cells?" she asked in exasperation. Pathologists are also worried that ethical principles may block the use of a potential gold mine for genetic studies—human tissue in paraffin blocks, with its DNA intact, that is kept in all major hospitals. For example, an NCHGR-backed panel recently concluded that patients should be informed if their specimens are to be used in genetic studies but that the wording of the typical hospital consent form can only "rarely" be construed as "providing an adequate basis for inferring consent."

CDC's dilemma—and the pathologists' problem—stems from the fact that most consent forms are not explicit about the possibility of using blood or tissue as a source of DNA for research. As genetic research technology has become more sophisticated in recent years, so have the standards for obtaining patients' consent. Although the consent form used by CDC seemed fine in the 1980s, says Karen Steinberg, chief of the molecular biology branch at CDC's National Center for Environmental Health, "I didn't think it was all right" for DNA research in the 1990s. Steinberg sought help from a bioethics group funded by NCHGR. It took a year and a half for a working group funded by NCHGR to hammer out the details, and the result was published in the 13 December 1995 issue of the *Journal of the American Medical Association* (JAMA).

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On hold. Stored specimens at the Armed Forces Institute of Pathology. Ethical concerns could hinder genetic research on archives like these.

The proposal would establish different standards for pre-existing archives like CDC's and for collections being started from scratch. Researchers would also have other options within each category. However, each of the proposed choices would impose burdensome requirements on researchers. The NCHGR working group said that those using pre-existing archives could obtain more precise agreements from the original donors, or they could try to strip personal data out of the records to prevent identification.

The first option would be extremely time-consuming and expensive. Steinberg herself worries that it might bias the sample by driving out individuals who suspect their families are prone to some genetic risk. On the other hand, federal law permits research without consent on truly anonymous data. But complete anonymity is hard to achieve. Ethicists say that if a sample is "linkable" to a donor by any means—even if doing so requires serious detective work—it isn't truly anonymous. And many clinicians argue that anonymity isn't desirable: They feel duty-bound to contact patients who test positive on genetic tests and to offer treatment or other help.

For researchers who want to build a new tissue collection for genetic research, the procedural challenge would be at least as great as for those using older archives. According to the formula in JAMA, they would have to get donors to sign a multilayered consent form. (One pathologist joked that patients would need to give informed consent even to get a haircut, as hair contains DNA.) Donors would be asked whether they want their samples used only for anonymous research, or for studies that identify individual risks. Patients would be allowed to rule out certain tests, or withdraw samples at a later time, should they have a change of heart.

Researchers would also need to tell DNA donors that if they do not insist on anonymity they might experience depression or other psychological distress if they test positive for a disease gene. And they would have to be warned about the risk of economic discrimination if their DNA data were disclosed by accident. This approach—with "more options and permutations than an airline frequent-flier program," wrote pathologist Wayne Grody of the University of California, Los Angeles—would greatly complicate research if adopted as standard practice.

Responding to such concerns, NCHGR chief Francis Collins met on 19 January at NIH to discuss the working group's recommendations with managers of tissue collections, pathologists, government officials, leaders of genetics and pathology associations, and representatives of at least one major patient activist group, the National Breast Cancer Coalition. The meeting was organized by David Korn, a prominent Stanford pathologist on sabbatical at the American Association of Medical Colleges. Collins ejected a reporter for *Science*, however, saying that the subject was "sensitive" and the session wasn't open to the public because NCHGR was not receiving advice.

Although the meeting didn't produce a specific agreement, according to a government participant in attendance, it made clear that changes sweeping through the world of genetics research—including new ethics rules—have "caught many people by surprise." In response, Collins and his staff are planning a series of sessions to help researchers adjust to the new ethical standards, including a public meeting later this year. As for the pathologists, the government official said, they have a lot of catching up to do. And CDC is still waiting for approval from its own human subjects review board of a genetic study of spina bifida.

–Eliot Marshall