POLICY FORUM: ETHICS

Privacy in Genetics Research

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Rapid progress in the Human Genome Project has heightened public awareness of the positive impact of genetics research on human health. Along with these positive effects have come concerns about who will have access to personal genetic information and how it will be used. Here, we present policy recommendations (see the table) for protecting the privacy of genetic information in research (*1*).

A particular person's genetic information may be of interest to a wide variety of individuals and organizations. Insurers and employers may want to use it as a predictor of future illness, health-care costs, or the ability to perform a job. Family members, educational institutions, or the courts (in cases where custody is being challenged, for example) may also want access to genetic information. Indeed, genetic information has already been used to deny medical benefits to retirees with illnesses with a known genetic basis (*2*). Cases of insurance and employment discrimination based on genetic information have also been reported (*3*).

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Recommendations to restrict use of genetic information in health insurance and in the workplace have been developed by the National Action Plan on Breast Cancer (NAPBC) and the National Human Genome Research Institute (NHGRI) (*4*). State and federal laws restrict some uses of genetic information in health insurance and the workplace (*5, 6*). Nevertheless, comprehensive federal protections are not in place (*7*).

The privacy of medical information is protected principally by state law, although the level of protection varies widely from state to state. These laws generally restrict access to health-care records to those with signed authorizations or a court order, or in other limited circumstances.

The Federal Privacy Act of 1974 safeguards health, research, and other records held by federal agencies. Nevertheless, there are many instances in which disclosures without the consent of the individual are allowable. Other than federal statutes to protect research specific to crimes, health-care outcomes, or medical liability, there are no comprehensive federal laws to protect the privacy of research information (*8*).

Currently, the U.S. Congress is considering measures to protect the privacy and confidentiality of individually identifiable health information (*9*). Pending legislation addresses the responsibilities of individuals and organizations who maintain health information, describes who can have access to individual medical records, and outlines the process for obtaining access.

Of concern to the scientific community is the danger that experimental research records might be included inappropriately in the broad definitions of individually identifiable health information (*10*). Although it may seem paradoxical, inclusion of these records could allow unnecessary and inappropriate third-party access to this information (such as by law enforcement officials or courts). The social value of research, the altruistic nature of research participation, and the reliance of the research enterprise on volunteers necessitate stringent regulations to protect experimental research data from third-party access. (Recommendation 1.)

Unlike clinically validated medical information obtained for patient care, experimental research data often lack analytical and clinical validity. This means that research data may be clinically meaningless or misleading. Research studies to identify the genetic basis of a specific disease may generate very preliminary, inconclusive, or invalid experimental information linking a genetic alteration with risk of developing the disease. Unless a research protocol includes the clinical care of the research participant, experimental research data should be kept in the researcher's scientific files and not placed in the participant's medical record (*11*). (Recommendation 2.)

Individuals who participate in research are protected by the Common Rule (*12*), which requires that all research with human subjects that is supported, conducted, or regulated by federal agencies must be reviewed by an institutional review board (IRB). IRBs are responsible for ensuring that the participants' consent is informed and voluntary, that risks to the participants are minimized, and that the participants' rights and welfare are protected. IRBs also consider whether the proposed informed consent document includes "a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained" (*13*). The IRB guidebook recommends that data should not be released except as authorized by the research subject and that subsequent re-

RECOMMENDATIONS TO PROTECT PRIVACY IN GENETICS RESEARCH

1. Privacy protections for experimental research data in which health care is not delivered should exceed the protections established for medical records. Rules for third-party access to medical records should not be uniformly applied to experimental research data.
2. Researchers should not place individually identifiable experimental research data not utilized for health care in the medical record.
3. Informed consent for research participation should include information about all potential disclosures of research information and the nature and magnitude of the risks from such disclosures. Adequate measures to ensure compliance and punish violations should be in place.
4. Current practices to protect confidentiality of experimental research data should be studied and best practices should be developed.
5. Protections similar to Certificates of Confidentiality should be developed to protect research subjects from compelled disclosure of research results.
6. Research participants should have access to experimental research data except when:
   a. The information includes information obtained under a promise of confidentiality, is about another person, and patient inspection would cause harm to another individual;
   b. Access to the information may reasonably be expected to endanger the life or physical safety of the research participant or anyone else;
   c. Access would break the "masking" of the study or otherwise significantly interfere with the conduct or results of the study; or
   d. The research results are of unproven clinical validity, and the IRB has judged that there is no benefit to the research subjects. In such circumstances, the informed consent must explicitly state that individual research results will not be shared.

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quests for information should be subject to the agreements in the informed consent (*14*). However, current practices are diverse, and there are no specific mandates or requirements for even the most basic levels of privacy and confidentiality protections. (Recommendation 3.)

The public focus has been on privacy of information acquired in the clinical setting (*15*); privacy of experimental research data has received comparably little attention. There has been no systematic analysis of methodologies used to protect privacy of research records or of breaches of confidentiality. An assessment of current practices and development of best practices to protect research data from third-party access is needed. (Recommendation 4.)

As early as 1977, the Federal Privacy Protection Study Commission strongly favored "statutory immunity which protects the rights and interests of the individual" research participant (*16*). The Public Health Service Act provides for Certificates of Confidentiality (*17*) that protect personally identifiable research information. These certificates can be obtained by privately funded as well as federally funded research projects of a sensitive nature, including projects involving information that "could reasonably lead to social stigmatization or discrimination" (*18*). They provide a legal defense for researchers against compelled disclosure of identifiable research information as a result of a subpoena or court order (*19*) and can be a critical device for the protection of genetic research data (*20*). However, they do not provide legal protection for research participants from compelled disclosure. (Recommendation 5.)

"Experimental research data should be kept in the researcher's scientific files and not placed in the participant's medical record."

It is universally accepted that individuals should have access to their own medical information. At first examination, it seems straightforward to conclude that this should apply to experimental research data. There are several key characteristics, however, that differentiate medical information from experimental research data. Unlike medical records, research records contain experimental data and analyses necessary to test hypotheses. The clinical significance of the results of a particular experiment may only be established after many years of additional research, if ever. This means that research data may be clinically meaningless or misleading, thus lacking the clinical and analytical validity of medical records (*21*).

In a specific case, 5209 people were recruited to participate in a longitudinal study of factors that contribute to cardiovascular disease (*22*). Subsequently, the study enrolled another 5124 adult children and spouses of the original group. The subjects gave permission for genetic studies, the collection of medical histories, and physical examinations. Tests were performed in a research laboratory that can tolerate a 1 to 2% error rate that would not be tolerated in a clinical laboratory because the study was evaluating the significance of genetic variants among thousands of persons, not the relevance to one individual.

Concern about sample integrity as well as analytical and clinical validity of medical tests provides the basis for a federal law (CLIA) that requires laboratories providing data back to patients to meet a number of quality standards (*23*). Many research laboratories are not CLIA approved. Consequently, there is concern that transmitting the outcome of these studies to the research participants would result in the transmission of false-positive or false-negative results.

Providing such data to subjects may entail significant risks and cause erroneous conclusions to be made that could result in physical, psychosocial, or economic harms. If genetic research results are to be given to the subjects, the protocol must provide for counseling before and after the test (*24*). For a study with about 10,000 participants, the cost of counseling is estimated to be more than $500,000 per year. Although this cost is warranted in studies that generate data useful to individual participants, in the case described above the expenditure may be unwarranted. If a policy mandating return of clinically meaningless data were implemented, associated costs and personnel might provide an obstacle to doing the study. Thus, in the absence of clinical validity there should not be an absolute requirement for data to be returned to subjects. For research in which data are not provided to subjects, the researcher should demonstrate absence of clinical validity, an IRB should be required to review and approve the exception, and the informed consent document should state explicitly that the data will not be returned to the research subject. (Recommendation 6.)

Implementation of our recommendations is imperative to maintain the trust placed in the research process and to realize the potential of genetics research to benefit human health.

References and Notes

1. The NAPBC is a public-private partnership designed to stimulate progress in eradicating breast cancer by advancing knowledge, research, policy, and services.
2. Department of Defense Directive 1332.
3. L. N. Geller *et al.*, *Science Eng. Ethics* **2**, 71 (1996).
4. See K. L. Hudson, K. H. Rothenberg, L. B. Andrews, M. J. Ellis Kahn, F. S. Collins, *et al.*, *Science* **270**, 391 (1995); K. Rothenberg *et al.*, *ibid.* **275**, 1755 (1997); D. Shalala, "Report of the Secretary to the President: Health insurance in the age of genetics" (July 1997); Department of Labor *et al.*, "Genetic Information and the Workplace" (20 January 1998).
5. For a listing of relevant state legislation, see http://www.sciencemag.org
6. Health Insurance Portability and Accountability Act, 104 Public Law No. 104-191, 701, 110 Stat 1936 (1996); 42 U.S. Code Annotated (U.S.C.A.) § 12101, *et seq.*; Equal Employment Opportunity Commission, Compliance Manual, Section 902, 15 March 1995.
7. See H.R. 293, 106th Cong., 1st Sess. (1999); H.R. 2457, 106th Cong., 1st Sess. (1999); H.R. 2555, 106th Cong., 1st Sess. (1999); S. 543, 106th Cong., 1st Sess. (1999); S. 1322, 106th Cong., 1st Sess. (1999); S. 1344 (Title II), 106th Cong., 1st Sess. (1999).
8. 42 U.S.C.A. § 3789g(a); 42 U.S.C.A. § 299.
9. See H.R. 1057, 106th Cong., 1st Sess. (1999); H.R. 1941, 106th Cong., 1st Sess. (2999); H.R. 2404, 106th Cong. 1st Sess. (1999) H.R. 2470, 106th Cong. 1st Sess (1999); S. 573, 106th Cong, 1st Sess. (1999); S. 578, 106th Cong., 1st Sess. (1999); and S. 881, 106th Cong., 1st Sess. (1999).
10. See S. 578, 106th Cong., 1st Sess. (1999) for a formal definition of protected health information.
11. See Mayo Clinic, "Institutional Review Board policy regarding genetic research", 5 May 1998.
12. 56 Federal Register, 18 June 1999; 45 Code of Federal Regulations (CFR) 46.
13. 45 CFR 46.116 (a)(*5*).
14. Office for Protection from Research Risks, Protecting Human Research Subjects: Institutional Review Board Guidebook, pp. 3–27 (1993).
15. R. O'Harrow Jr., *Washington Post*, 27 September 1998, p. A1. See also United States General Accounting Office, "Medical records privacy: Access needed for health research but oversight of privacy protections is limited" (February 1999).
16. Privacy Protection Study Commission, *Personal Privacy in an Information Society*, p. 579 (1977).
17. Public Health Service Act § 301(d).
18. Health and Human Services, "Interim Policy Statement: Protection of Identity—Research Subjects (5-22-89)".
19. L. O. Gostin, *Cornell L. Rev.* **80**, 451 (1995).
20. C. L. Earley and L. C. Strong, *Am. J. Hum. Genet.* **57**, 727 (1995).
21. The National Institutes of Health (NIH)/Department of Energy Task Force on Genetic Testing, Promoting Safe and Effective Genetic Testing in the United States (1997).
22. National Heart, Lung, and Blood Institute, Framingham home page, http://www.nhlbi.nih.gov/about/framingham/index.html (1998).
23. The Clinical Laboratory Improvement Amendments of 1988, Public Law 100-578 (1988).
24. L. B. Andrews *et al.*, Eds. *Assessing Genetic Risks: Implications for Health and Social Policy* (Institute of Medicine, National Academy Press, Washington, DC, 1994).
25. The views expressed are those of the Privacy Workshop Planning Subcommittee of the NAPBC. No official endorsement by the NIH or the Department of Health and Human Services is intended or should be inferred.