

The American Society of Human Genetics

Policy Statement

March 2000

ASHG Family Medical History and Privacy Advisory Statement

Should family members about whom you collect only medical history information for your research be considered "human subjects"?

ASHG members who work in clinical human genetics and genetic epidemiology, e.g., characterizing diseases or doing genetic linkage and association studies, need to ask themselves this question. In a widely publicized case, all research projects involving human subjects were suspended at the Virginia Commonwealth University in response to an investigation that was prompted by complaints about privacy issues by the father of a subject who was being recruited for a twin study. The federal Office for Protection from Research Risks (OPRR) has ruled that the local Institutional Review Board (IRB) should have considered this potential risk to family members in the study design (see the 1/12/00 Washington Post article by Jay Mathews entitled "Father's Complaints Shut Down Research, US Agencies Act on Privacy Concerns").

There are clear lessons to be learned for the human genetics research community, and, therefore, the ASHG Board of Directors wishes to alert the membership to the potential threat to human genetic research if existing federal regulations are ignored. It will be important to be proactive in following these developments to assure that informed decisions are made that will not impede research. Geneticists, both researchers and clinicians, need to work with their IRBs to help them understand the issues involved and the importance of family history to genetic research.

The regulations concerning human subjects in research are specified in the Department of Health and Human Services, Human Subjects Regulations, Title 45 Code of Federal Regulations Part 46 (45 CFR 46). These regulations are published at:
<http://grants.nih.gov/grants/oprr/humansubjects/45cfr46.htm>.

The OPRR has developed a graphic aid that assists investigators and IRBs in decision-making about who should be considered a "human subject" in research. This chart can be found at:
<http://grants.nih.gov/grants/oprr/humansubjects/guidance/decisioncharts.htm>.

If, in large family studies, each family member must be enrolled as a "human subject", with informed consent procedures, before any medical information about them can be collected, obtaining family histories will be enormously cumbersome and prohibitive, and will seriously impede medical research. Unless a "waiver" is granted, the project may no longer be feasible. Section 46.116(d) specifies under what conditions the research protocol may be eligible for IRB waiver of informed consent. All four conditions have to be met:

- 1) The research involves no more than minimal risks to the subjects (in this case, the family members);
- 2) The waiver will not adversely affect the rights and welfare of the subjects;

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- 3) The research could not practicably be carried out without the waiver; and
- 4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

The critical issues are points 1 and 2. First, the IRB needs to consider and determine that the research involves no more than minimal risk, as would be the case in collecting family history data on individuals related to a research subject who is formally enrolled in a study. Second, the IRB has to consider and determine that the rights and welfare of these family members would not be adversely affected. In the Virginia case, the father claimed that his privacy had been violated and, therefore, that his rights and welfare had been adversely affected. The OPRR agreed with that claim.

The other crucial point in determining who should be considered a "human subject" concerns whether "identifiable private data/information is obtained for this research in a form associable with the individual". The criterion of "associable" applies if "the identity of the subject is or may readily be ascertained or associated with information." This can be interpreted to mean that someone whose name, birth date, address and social security number are not part of the information collected can still be "identifiable" if he is identified as the father of a subject formally enrolled in the study.

This is not a new issue. The Code of Federal Regulations Title 45 Part 46 was published in 1991. The OPRR's interpretive chart was created in 1998. This issue, however, has not previously been formally addressed by the ASHG. There are two potentially pertinent ASHG reports on record:

[1] The "Statement on Informed Consent for Genetic Research" concerns itself with issues of sample collections, identifiable or not. It does not address the issues of collection of medical family history information. However, the four conditions for granting a waiver for research involving identifiable samples are also stated in this report (Am. J. Hum. Genet. 59:471,1996).

[2] A paper entitled "Professional Disclosure of Familial Genetic Information" was prepared by the ASHG Social Issues Subcommittee on Familial Disclosure (Knoppers et al., Am. J. Hum. Genet. 62:474, 1998). This report addresses the conflicts that arise between the duty of confidentiality and the duty to warn. The "Points to Consider" include the general rule of confidentiality, exceptional circumstances permitting physician disclosure if harm from failing to disclose should outweigh the harm from disclosure, and the ethical duty to inform the patient of familial implications. The report concludes that genetic information, being both individual and familial in nature, should be considered as medical information. This report does not address the issues raised by the recent events and OPRR and FDA rulings.

As investigators and IRB members, human geneticists need to be concerned about protecting volunteer subjects in research from any potential harm. On the other hand, the danger that undue regulatory burdens will impede progress in genetic and epidemiological research also has to be seriously considered.

At this time, there is no overarching rule stating that informed consent must be obtained from

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family members on whom medical history information is collected through someone else in their family who is a full participant in a research study. The determination about whether collecting this information represents more than minimal risk and affects the subjects' rights and welfare will have to be made in each case, as research protocols are reviewed at the local level. IRBs will need to address the question whether collecting family history data indeed represents a "violation of privacy" of the living relatives about whom information is collected. One could argue that this information is not strictly private, as it has obviously been shared with other family members. Furthermore, family history data falls into the category of "hear-say", unless it is confirmed by objective medical records. To obtain such records would, of course, require consent of the individual involved.

It is up to the individual IRB to decide whether the conditions specified in HHS Regulations at 45CFR46.115(d) are met and the requirement to obtain informed consent can be waived. OPRR rules will be satisfied if the minutes of the IRB meeting state that the potential social, psychological, and legal risks presented by research that involved the collection of detailed social and medical history information about relatives were considered, and that the decision to waive the requirement for informed consent was made after discussion.

The ASHG envisions that meetings and further discussions will have to take place between representatives of regulatory agencies, professional societies, patient advocacy organizations and researchers to fully explore the issues from all vantage points. The planning for such a meeting is in progress. The ASHG hopes that such discussions will lead to a better set of regulations that will adequately protect participants in research without impeding the progress leading to discoveries that will benefit all of humanity.