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ASHG REPORT
Statement on Informed Consent for Genetic Research

The American Society of Human Genetics

This is the final and official statement of the Board of Directors of the American Society of Human Genetics. The Board thanks the members of the Rapid Action Task Force on Informed Consent for Genetic Research for their work on this topic. The statement differs from the proposal submitted to the Board by the Task Force and does not necessarily reflect the views of its members.

The American Society of Human Genetics is committed to protecting the rights and welfare of those who participate in genetic research as subjects. Advances in genetic research now make it possible to perform genetic analyses on a wide array of biological materials. Because of these advances, there is a need to update considerations of informed consent. Several groups have recently developed statements concerning some aspects of these issues (Clayton et al. 1995; Grody 1995; ACMG Storage of Genetics Materials Committee 1995). In dealing with the issues specified below, researchers should try to keep the consent form as clear and brief as possible, given the number of issues that must be addressed.

General Considerations

The ethics of biomedical research evolve as relevant science progresses. Practices that are acceptable for the state of the research art at one time may need to be refined in new situations. In human genetics research, the speed with which basic investigations can yield clinically significant findings requires consideration of new ways to achieve the goals of expanding knowledge, and, at the same time, respecting the interests of those who volunteer themselves to be subjects. In this statement, the Society affirms traditional research practices in human genetics and recommends new ones that it believes can provide direction for ongoing developments.

Because of a variety of important and complex issues surrounding the use of previously collected biological samples, investigators are encouraged to develop procedures for obtaining informed consent when prospectively collecting specimens for genetic research purposes.

The implications of genetic information are complex for the individual, his or her family members, clinicians, and the researcher. Therefore, it is strongly recommended that research results only be transmitted to subjects by persons able to provide genetic counseling. Because of the sensitive nature of genetic information, even those institutions not covered by federal regulations should develop a process for human subjects review. The recommendations in this document apply to any specimen or sample that is used in genetic research.

Research Using Prospectively Collected Samples

In genetic studies that are designed to collect new biological samples from individuals, the investigators generally have the opportunity to communicate with potential subjects in advance and involve them in the research by obtaining their informed consent (fig. 1, table 1). This should be encouraged, except for the prospective studies in which samples are collected anonymously, or have been "anonymized."

Studies that maintain identified or identifiable specimens must maintain subjects' confidentiality. Information from these samples should not be provided to anyone other than the subjects and persons designated by the subjects in writing. To ensure maximum privacy, it is strongly recommended that investigators apply to the Department of Health and Human Services for a Certificate of Confidentiality (Early and Strong 1995). Investigators should indicate to the subject that they cannot guarantee absolute confidentiality.

Research results or samples should not be given to any of the subject's family members by the investigator

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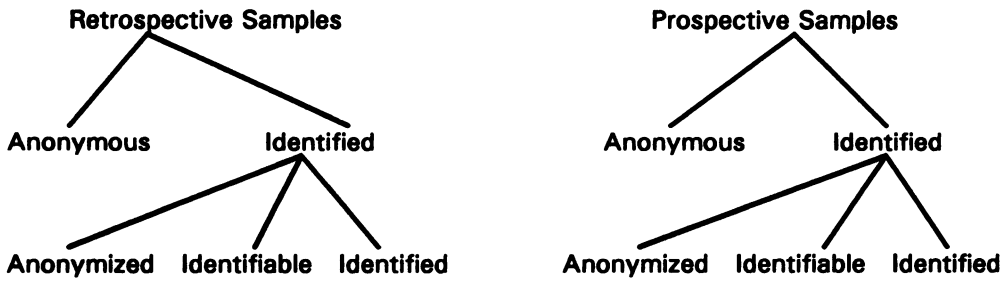

Figure 1 Flow diagram of types of biological samples used in genetic research, by type of study design and level of anonymity. Prospective research studies are those in which the collection of the new samples is part of the study design. Retrospective research studies utilize previously obtained samples collected for a purpose that is different from that of the project under study. Anonymous biological materials were originally collected without identifiers and are impossible to link to their sources. Anonymized biological materials were initially identified but have been irreversibly stripped of all identifiers and are impossible to link to their sources. This process does not preclude linkage with clinical, pathological, and demographic information before the subject identifiers are removed. Caution must be exercised so that the amount and type of linked information does not invalidate anonymity. Identifiable biological materials are unidentified for research purposes, but can be linked to their sources through the use of a code. Decoding can be done only by the investigator or another member of the research team. Identified biological materials are those to which identifiers, such as a name, patient number, or clear pedigree location, are attached and made available to researchers.

without the explicit, written permission of the subject, except under extraordinary circumstances (NAS/IOM 1994; President's Commission 1983). Within the limits of the law, the results must not be shared with employers, insurance companies, or other parties without the written permission of the subject.

Consent Disclosures

Subjects providing consent to prospective studies should be told about the types of information that could result from genetic research. Subjects must be given sufficient information to understand the implications and the limitations of research. Individuals should be told the purpose, limitations, possible outcomes, and means of communicating results and maintaining confidentiality. They should be informed of what information may reasonably be expected to result from the genetic study. Importantly, subjects should also understand that unexpected findings, including identification of medical risk, carrier status, or risk to offspring affected by genetic disease, may arise.

During the course of molecular genetic diagnosis, the results may indicate that the child is not the offspring of one or both the presumed parents. The investigator therefore should consider including in the consent form a statement that misidentified parentage will not be disclosed. Another example of unforeseen outcome is genetic heterogeneity in which disorders which were initially thought to be due to defects in a single allele or locus are associated with new ones.

Additional risks that should be disclosed to subjects of certain genetic research studies include the possibility of adverse psychological sequelae, disruption of family dynamics, and social stigmatization and discrimination. All genetic research studies involving identified or identifiable samples in which disclosure of results is planned should have medical geneticists and/or genetic counselors involved to ensure that the results are communicated to the subjects accurately and appropriately. The consent form should not promise significant breakthroughs in diagnosis, treatment or outcome to entice participation. Also, careful attention by all parties involved in genetic research

Table 1

Suggested Guidelines on the Need to Obtain Informed Consent in Genetic Research, By Type of Study Design and Level of Anonymity

	Study Design	
Level of Anonymity	Retrospective	Prospective
Anonymous	Not applicable	No
Anonymized	No	No
Identifiable	Usually yes (except if a waiver is granted)	Yes
Identified	Yes	Yes

should be given to avoiding actions that could be coercive to potential subjects.

Disposition of Samples and Results

Depending on the study, subjects may be given the opportunity to determine if they want to be informed of the results of their testing. Subjects should be informed if the sample will be stored for later study, but they also need to be told that there is always the possibility of storage failure. Decisions related to disposition of results or samples after the subject's death should be specified by the subject.

In some studies researchers may wish to disclose results to subjects. If so, it is the obligation of the subjects to keep the investigator informed of how they may be contacted. Investigators should indicate to study subjects that certain results may not allow definite answers until an analysis of the entire study has been completed (and, sometimes, not even then). Under such circumstances, results cannot be communicated expeditiously.

Subjects involved in studies where the samples are identified or identifiable should indicate if their sample should be used exclusively in the study under consideration. If the sample is to be used more generally, subjects should be given options regarding the scope of the subsequent investigations, such as whether the sample can be used only for a specific disease under investigation, or for other unrelated conditions. It is inappropriate to ask a subject to grant blanket consent for all future unspecified genetic research projects on any disease or in any area if the samples are identifiable in those subsequent studies.

Subjects involved in studies in which the samples are identified or identifiable should indicate if unused portions of the samples may be shared with other researchers. If the subject is willing to have the sample shared with other researchers, it is the responsibility of the principal investigator to distribute the sample, so as to ensure that the agreement embodied in the informed consent is upheld. Finally, subjects should decide if subsequent researchers may receive their samples as anonymous or identifiable specimens

Retrospective Studies of Existing Samples

We endorse the use of anonymous samples for genetic research. Importantly, in retrospective research proposing to use samples collected anonymously or anonymized, there is no possibility, or need, to obtain consent.

For many studies, there may be benefits to making identifiable samples anonymous, because this effectively protects subjects from some of the risks of genetic research. Importantly, making samples anonymous will eliminate the need for recontact to obtain informed consent. This will also reduce the chance of introducing bias due to inability to recontact some, or the possible refusal of others to participate. On the other hand, investigators should consider the appropriateness of anonymizing samples, especially when there is available medical intervention for the disorder being tested.

For research involving identifiable samples, the investigator should be required to recontact the subjects to obtain consent for new studies. However, an investigator may seek a waiver based on the following criteria of 45CFR46.116:

(1) The research involves no more than minimal risk to the subjects;
(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;
(3) The research could not practicably be carried out without the waiver or alteration; and
(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

For research involving samples that retain identifiers, consent should be obtained. Waivers may be granted, although the waivers will be difficult to justify by the above criteria if identifiers are retained.

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