

Human Research Protection Program University of California, San Diego

ISSUES ON DNA AND INFORMED CONSENT

Regulatory changes will occur for investigators studying human DNA

The recent acceleration and widening applicability of human gene research raises new issues for the ethical conduct of research. These issues are being discussed at the national level with the intent to develop NIH mandated standards. Currently, these standards are being prepared by the NIH-DOE Joint Working Group on the Ethical, Legal, and Social Implications for Human Genome Research. Investigators need to be aware of these developments because they may affect the potential uses of specimens currently being collected and stored.

At this time, NIH, Office for Human Research Protection (OHRP) does not have any plans to add any new regulations. However, on April 17, 1996 OHRP issued a flow chart intended to clarify the applicability of four sections of the Department of Health and Human Services (DHHS) human subject regulations at Title 45 Code of Federal Regulations Part 46 (45 CFR Part 46) that are especially pertinent to research involving DNA materials. With this flow chart, OHRP is attempting to provide interpretation of the current regulations, as they apply to DNA/Genetics research. These interpretations will be applied to research at UCSD.

In order to facilitate understanding of the interpretations, the Human Research Protection Program is providing the investigators with this guide. The Committee is concerned that an investigator may initiate a study which is later deemed to be non-compliant with OHRP regulations, causing the study to end prematurely without hope of publication. **To assist you in designing or conducting a study, we offer the following as a guide for writing your Human Subjects protocols and consent documents.**

The types of studies that are affected by the new guidelines on DNA

DNA can be harvested directly from patient samples soon after their receipt. Alternatively, DNA can be prepared from stored tissues, blood, serum, cytological preparations, and pathology specimens. Also, because DNA is an informational molecule, the information or sequence of DNA stored in a computer is subject to the same considerations as DNA itself.

Many types of tissue and serum collections currently exist at UCSD; some involve samples from thousands of subjects collected over several decades. With the advent of PCR, all of these samples can now be used for DNA analyses (even serum contains some DNA). At the present time, the UCSD IRB is primarily concerned with ongoing or future studies that utilize DNA methods. Policies are still evolving on how to deal with DNA studies of archived samples from individuals who had no idea that the specimens given would later be used for genetic analyses. **We hope to avoid a situation where investigators would have to go back and obtain an additional DNA consent from subjects who donated their specimen years previously for a non-DNA study.**

The concerns that are driving these new regulations

On the whole, our subjects and the general public strongly support DNA research and see it as a source of hope. A recent example is the discovery of a breast cancer gene, which led to much interest in genetically screening women for breast cancer risk. On the negative side, the ability to use genetic information to predict future health raises the possibility of discrimination in employment, loss of insurance, use in criminal prosecution and matters of parentage and consanguinity.

DNA samples may be subpoenaed by prosecutors under certain circumstances, unless the investigator has obtained “Certificate of Confidentiality” (call the Human Research Protection Program Office at (858) 455-5050 for information about this).

Classification of DNA studies

At this point, the IRB will concentrate its efforts on prospective studies that involve the storage of DNA, DNA sequence data, or specimens from which these may be obtained. These studies fall into the following four general categories of subjects:

1. **Anonymous** donors, who are **untraceable** by any means. This would include anonymous HIV testing samples, or arbitrary sampling of leftover blood from clinical laboratories where only the sample and not any patient information was collected.
2. Donors whose identity is known or **traceable**, but where the investigator **will not track** the individual. An example would be a study where specimens were obtained, banked, and labeled with a key to the subject's name, yet no subject-related genetic testing is planned.
3. Donors who are the subjects of genetic studies. The identities of these subjects are **traceable** and the investigator intends to **inform the subject about the results of the genetic testing**. An example would be a study of a cancer susceptibility gene, where it would be possible for the subject to learn the test results if they wished. If the condition under study is very serious or emotionally charged, it may be important for the investigator to offer a counseling session(s) for individuals bearing a disease-related gene.
4. Donors who are the subjects of ongoing, prospective studies. The identities of these subjects are **traceable** and the investigator **intends to track the subjects** through continuing contacts for years into the future.

There will likely be almost no restrictions on the use of truly anonymous samples (Category 1). On the other hand, most investigators working with DNA will want to keep the subjects' name in their records, just in case they need to learn more about the subject later or discover something important to the subjects' health. Even investigators whose aim is to study normal genes and not a specific disease may wish to retain identifying information. Thus, most investigators will fall into Category 2. Category 3 has the potential for raising emotionally charged issues, and the subjects may make major changes in their life plans based on their test results (e.g., Huntington's Disease genes, etc.). In Category 4, where tracking will occur, the subjects have a much higher level of participation in the study (repeat visits, repeated testing, etc.). Because subjects in an ongoing study always retain their right to withdraw from the study, their decision to participate in a DNA study implies continuing consent as well as the one-time decision to sign the consent document.

The UCSD IRB expects that investigators will deal with the following issues in their DNA-related Human Subjects Protocols and consent forms. The questions that should be addressed from the subject's perspective are the following:

- 1) **Will your DNA or information about your genes be restricted to certain parties? How will your confidentiality and privacy be protected?**

The investigator must name all currently known collaborators and must also state in the consent if there might be future collaborators that are not known at this time. It is better to include broad language than be overly restrictive, since plans may change in the future. As an example,

"In addition to Dr. PI, your DNA may also be studied by Drs. X, Y, and Z. In the future, the All-Gene Corporation or another company performing pharmaceutical research may study your DNA in order to learn more about ..."

Confidentiality is critical for Category 3 DNA research, especially if information from DNA sequences may affect future health, employment, or insurability. The consent must state how the investigator will deal with this issue. If DNA information obtained as part of a research study is included in the patient's medical record, this might compromise the confidentiality of very sensitive data. When dealing with sensitive data, the IRB often suggests that an investigator obtain a "Certificate of Confidentiality" which protects the data from Court subpoenas and makes it a crime to disclose the information. If one has been obtained for the project, this should be stated in the consent.

If the study involves genetic testing, the following should be included in the consent:

"Federal and State laws generally make it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways: a) Health insurance companies and group health plans may not request your genetic information that we get from this research. b) Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums. c) Employers with 5 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment."

2) What are my rights to my DNA sample? Who will have control of it and who will own it?

SUBJECTS MAY NOT BE ASKED TO GIVE UP THEIR RIGHTS TO THE DNA. BOTH OHRP AND FDA MAKE IT CLEAR THAT THE CONSENT DOCUMENT MAY NOT CONTAIN EXCULPATORY LANGUAGE. UNDER 45 CFR 46.116, "NO INFORMED CONSENT, WHETHER ORAL OR WRITTEN, MAY INCLUDE ANY EXCULPATORY LANGUAGE THROUGH WHICH THE SUBJECT OR THE REPRESENTATIVE IS MADE TO WAIVE OR APPEAR TO WAIVE ANY OF THE SUBJECT'S LEGAL RIGHTS...."

In order to assure that this occurs, the investigator must put a "Moore Clause" in the consent:

"Biospecimens (such as blood, tissue, or saliva) collected from you for this study and/or information obtained from your biospecimens may be used in this research or other research, and shared with other organizations. You will not share in any commercial value or profit derived from the use of your biospecimens and/or information obtained from them."

3) Can I withdraw my DNA sample from a study at any time?

Once a subject's DNA or DNA-containing specimen becomes a part of the study, the investigator has the discretion to retain it for legitimate scientific purposes. If an investigator adopts this position, it must be clearly stated in the consent. As an example,

"If you decide later that you do not want the specimens collected from you to be used for future research, you may tell this to Dr. PI, who will use his/her best efforts to stop any additional studies. However, in some cases, such as if your cells are grown up and are found to be generally useful, it may be impossible to locate and stop such future research once the materials have been widely shared with other researchers."

4) How long do you plan to keep my DNA sample?

The investigator should tell the subject in the consent how long (minimally and maximally) he/she plans to keep the DNA sample and/or data. This is **at the discretion of the investigator** and the maximum time may be **indefinitely**. As an example,

"Dr. PI, his associates, or his successors in these studies will keep your DNA specimen and/or the information derived from it for up to 50 years."

5) What are my rights to know about any DNA results?

There are three possible positions that the investigator may elect to take. However, the investigator should be clear from the beginning which of these three positions he/she is taking and state so in the consent. The three possibilities are:

1. Tell the subject anything he/she wants to know.
2. Will provide only information identified in the informed consent.
3. Will provide the subject no information.

If the investigator plans **not** to disclose DNA information, this should be stated in the benefits section of the protocol and consent document. The wording could be as follows:

"There will be no direct benefit to you from this study since you will not be provided with any results or information regarding your DNA test. The investigator, however, may learn more about..."

Alternatively, if the investigator plans on disclosing DNA information the following language could be used:

"If as a result of participation in this study we obtain information that could significantly affect your health or well being, we will attempt to inform you of the existence of this information. You may then decide if you wish to know what we have learned."

6) Will other people have access to my DNA sample in the future?

Clearly state in the consent if there is a possibility that others will have access to the specimens or the genetic information derived from them in the future. For an example, see point 1 above.

7) Will scientists use my DNA for other purposes?

If this is the case, clearly state it in the consent. Suggested language would be as follows:

"Your DNA or the information from it may be used by other scientists for additional research in the future." Again, use the Moore clause if you foresee the possibility of generating anything of commercial value.

8. What is the general genetic risk information that should be contained in the informed consent?

There is a chance that participation in this study could cause psychological distress, economic and social

harm, i.e., *“Some people involved in genetic studies have felt anxious about the possibility of carrying an altered gene that they could possibly pass on to their children.” “Even though we will do our best to keep your information confidential, there is a possibility that your genetic risk for certain diseases is accidentally divulged to the wrong source, if that happens you might be discriminated against in obtaining life or health insurance, employment or ability to adopt children.”*

OR

“You should also be aware that we may detect instances of non-paternity. For example, if a person you believe is one of your parents is not actually your biological parent, the testing may inadvertently detect this. Ordinarily, you will not be informed of this, if it occurs.”

If a study is likely to reveal sensitive information the investigator should provide access to experienced genetic counselors at the study's expense.

Another risk that the researcher should warn the subject about is the possibility of a breach in confidentiality and the information of the genetic test was accessed by a third party. This information could affect the subject's ability to obtain health insurance as well as discrimination in employment. It would probably be a good idea if the researcher using DNA specimens as research only, and will not furnish the results of the analysis to anyone, including the subject and his/her physician. You could use the following language in the consent:

“Instances are known in which a subject in research has been required to furnish genetic information as a precondition for in applying for health insurance and/or a job. Participation in this study does not mean that you have had genetic testing. Genetic testing means having a test performed and the results provided to you and your doctor. If you are interested in having genetic testing performed you should consult your doctor, as some commercial tests are available. Your doctor can provide you with the necessary information to determine if such a test would be appropriate for you.”

You must also warn patients that there is no absolute legal protection against discrimination on the basis of genetic information.

DNA: *The genetic material inside your cells.*

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