RESEARCH INVOLVING GENETIC TESTING

IRB Guidelines for Research Involving Genetic Testing

Research subjects require special protection when participating in studies which have a reasonable possibility of producing information about that subject's genetic make-up, especially when there is a possibility that such information, now or in the foreseeable future, could lead to diagnosis of a medical or behavioral condition, prediction of risks for these conditions, or identification of carriers. Investigators, therefore, must address specific issues relevant to protection of human subjects participating in this type of research. The IRB is cognizant of the fact that there is considerable variation in interpretation of the meaning of "genetic research", and investigators may therefore wish to seek advice from the IRB Office as necessary. Genetic testing means studies to identify or characterize human DNA, RNA, chromosomes, proteins or other gene products to detect genotypes, mutations, phenotypes, or karyotypes.

Combined Studies

If the study includes therapeutic or non-therapeutic interventions which are not considered genetic research, an application for Therapeutic or Non-Therapeutic Research must be completed, and separate consent and assent documents prepared for these interventions. In these situations, both consents (therapeutic or non-therapeutic research and genetic testing) must be signed if the subject is to participate in both aspects of the study.

In most cases, it is expected that subjects who object to participation in studies involving genetic testing will still be allowed to participate in the therapeutic or non-therapeutic study. However, investigators may require subjects in a non-therapeutic study to participate in an attached genetic testing protocol, especially if the genetic testing is an integral portion of the research. In this case, if a potential subject objects to participation, he/she must refuse participation in the entire research project.

Investigators may not require subjects in a therapeutic study to participate in a genetic testing protocol unless the genetic testing is directly relevant to the subject's disease and is an integral part of the protocol. Otherwise, if a potential subject objects to participation, he/she must still be allowed to participate in the therapeutic portion of the study.

Process of Consent

Due to the sensitive and uncertain nature of genetic testing, the process of consent to participate in genetic testing studies must include a thorough discussion of the risks and benefits associated with participation. In some cases, these discussions may be beyond the capabilities of the principal investigator of the study and it may be necessary to make
arrangements for another qualified party with experience in genetic counseling and testing to represent him/her to the potential subjects.

**Tracking of Subjects**

In some studies involving genetic testing it may be appropriate that subjects be advised when valid and valuable results are available. In such cases the investigator is obligated to make a reasonable effort to maintain information regarding the subjects' whereabouts. "Reasonable effort" will depend on the investigator's expectation of obtaining valid and valuable results relevant to the subject. This estimation must be made prior to beginning the research project, and must be disclosed to the IRB. Investigators are obligated to maintain this database for a minimum of *five years* following the enrollment of the last subject. In certain circumstances, the IRB may require a longer period of time.

**Disclosure of results**

Investigators should be prepared to inform subjects of the availability of research results in the event that these research results are, in the investigator's opinion, of material interest to the subject. This determination will be based on two criteria: (1) the validity of the results, based on analysis of data generated by the current study, as well as published literature which has become available since the protocol was approved by the IRB, and (2) utility and value of the information to the subject, as judged by a "reasonable person" standard.

The investigator must make a reasonable effort to contact the subject in writing and inform the subject that study results are available. "Reasonable effort" for contacting subjects depends on the utility and value to the subject of the information to be provided. Prior to disclosure, the investigator is required to submit to the IRB a full protocol for disclosure including a copy of the written notification form to be utilized.

The subject has the right to refuse to be informed of results of research. If the results of the research would be, in the opinion of the investigator, of significant health benefit to the subject, the investigator is obliged to ensure that a qualified person discusses fully with the subject the potential health effects of this non-disclosure.

The IRB believes that the process of disclosing either direct or incidental results to the subject must be conducted by a person qualified in discussing the significance, consequences and reliability of such results. In some cases, this qualified person should be a licensed genetic counselor. The investigator, or a trained genetic counselor, should remind the subject of the risks associated with genetic testing prior to disclosing those results.

**Cost of Counseling**

The IRB believes that it is the obligation the investigator to cover the costs associated with initial genetic counseling for the subject (or, in the case of minors, their parents). However, if repeated or longer term counseling is required, the financial obligation for such counseling belongs to the patients. The investigator is not obligated to cover costs associated with genetic counseling of family members of the subject, except as above.
Confidentiality

Disclosure to other persons, including other family members and physicians or care givers, may occur only with the consent of the subject. In the case that a subject refuses to allow disclosure of information of clinical utility to his or her physician or care givers, the investigator is required to ensure that a qualified person discusses fully with the subject the potential health effects of this non-disclosure.

Disclosure to other thirds parties, such as employers and insurers is prohibited unless such disclosure is specifically required by law, and consent is given by the subject. In situations where there is the reasonable expectation that disclosure will be required by law, this reasonable expectation must be revealed to the subject prior to enrollment, and this expectation must be specifically described in the consent document.

Enrollment of children and adolescents

The inclusion of children in genetic research studies may entail risks over and above those seen with adult subjects. The IRB generally supports the following principles regarding the use of children in genetic research. These principles are based, in part on the statement from the American Society of Human Genetics / American College of Medical Genetics (Am J Hum Genet 57:1233, 1995).

1. the potential for timely medical benefit to the child should be the primary justification for inclusion of children in studies involving genetic testing

2. potential for substantial psychosocial benefit to the competent adolescent may also be justification for inclusion of adolescents in studies involving genetic testing

3. if the potential medical or psychosocial benefits of genetic testing are not expected to accrue until adulthood, as in the case of carrier status or adult-onset diseases, children and adolescents should not be included in studies involving genetic testing.

Criteria for, and procedures regarding, disclosure of study results to children or adolescents must be formulated by the investigator. This analysis should consider the long term consequences of information supplied to a subject, and this analysis must consider the age and developmental characteristics of the non-adult subject. It is the opinion of the IRB that if there is adequate justification to enroll adolescents in the research then, in most cases, it is inappropriate to refuse to reveal the results of the research to these adolescent subjects.
Application Addendum

If subject identifiers are maintained, answers to the following questions must be incorporated into the appropriate sections of the IRB Applications for Therapeutic Research or the IRB Application for Non-Therapeutic Research.

Methods and Procedures

1. Criteria for Disclosure of Study Results to Subjects. What criteria will be used to determine when study results will be made available to subjects, or, in the case of minors or incompetent subjects, to their parents or guardians. What criteria will be used to determine when incidental findings obtained in the course of the study will be made available to subjects? If there are no plans to disclose result to subjects, this must be justified. Note: Investigators should be prepared to inform subjects of the availability of research results in the event that these research results are, in the investigators opinion, of material interest to the subject. This determination will be based on two criteria: (1) the validity of the results, based on analysis of data generated by the current study, as well as published literature which has become available since the protocol was approved by the IRB, and (2) utility and value of the information to the subject, as judged by a “reasonable person” standard.

2. Process of Disclosure. If there are plans to disclose results to subjects, then briefly describe the plan for tracking subjects after participation in research, for contacting subjects if results or incidental findings become available, and plans for disclosure of these results. Note: The investigator must make a reasonable effort to contact the subject in writing and inform the subject that study results are available. The definition of “reasonable effort” will depend on the utility and value to the subject of the information to be provided. Prior to disclosure, the investigator is required to submit to the IRB a full protocol for disclosure (see IRB guidelines) including a copy of the written notification form to be used.

3. Disclosure of Study Results to Other Parties. If there are plans to disclose results to subjects, then Will results of the study be disclosed to any party other than the subject? Will results of the study be disclosed to the subject’s physician or other care giver? If any such disclosure is anticipated, discuss the method used to obtain consent from the subject for this disclosure, and the process of disclosure, with special reference to plans for preservation of confidentiality. Note: Disclosure to other persons, including other family members, may occur only with the consent of the subject. In the case that a subject refuses to allow disclosure of information of clinical utility to his or her physician or care givers, the investigator is required to ensure that a qualified person discusses fully with the subject the potential health effects of this non-disclosure.
4. Disclosure of Results to Minors. If there are plans to disclose results to subjects, then Will results of the study, or of incidental findings obtained in the course of the study be disclosed to non-adult subjects? If so, briefly describe the process. Will parental consent be required prior to disclosure of study results to children or adolescents? Note: Investigators must make a thoughtful analysis of the risks and potential benefits of disclosure of study results to children or adolescents. This analysis should consider the long term consequences of information supplied to a subject, and this analysis must consider the age and developmental characteristics of the non-adult subject. If there is adequate justification to enroll adolescents in the research then, in most cases, it is inappropriate to refuse to reveal the results of the research to these adolescent subjects.

Potential Risks:

5. What are the risks associated with data obtained in the course of the genetic testing (either as a direct result of the test, or as a result of incidental finding)? Note: Potential harm may come to the subject as a consequence of data obtained from the research. These risks include, but may not be limited to, psychologic or emotional burden at being informed of a potentially serious genetic defect or predisposition, impact on family relationships, psychosocial impacts on other family members, discrimination in employment and insurability, risks associated with disclosure of false negative or false positive results (i.e., forgoing potentially preventive or therapeutic interventions, or undergoing potentially harmful preventive or therapeutic interventions). These risks may be more significant in magnitude if children or adolescents are to be included as subjects. The information included in this section is critical to the determination of a risk benefit relationship of the research. The IRB requires the investigator to make a thoughtful and comprehensive assessment of these risks.

Protection Against Risks:

6. Protection Against Risks Associated With Results of Genetic Testing. What procedure(s) will be used to prevent/minimize any potential risks associated with data obtained in the course of the genetic testing (either as a direct result of the test, or as a result of incidental finding)? Note: The information included in this section is critical to the determination of a risk benefit relationship of the research. The IRB requires the investigator to make a thoughtful and comprehensive assessment of these risks, and how possible harms can be prevented or minimized. In addition to any specific comments, the investigators must address the following points.

a. Confidentiality. What methods will be employed to assure confidentiality of results obtained? Will other investigators at UNMC or at other locations have access to biological material or data generated or obtained in the course of this study? If so, what methods will be employed to assure subject confidentiality?

b. Counseling. What provisions have been made for the counseling of subjects prior to involvement in this study, and at the time that study results are to be disclosed to subjects? Note: The IRB believes that, due to the sensitive and uncertain nature of genetic testing,
the process of consent to participate in such studies must include a thorough and knowledgeable discussion of the risks and benefits associated with participation. In some cases, these discussions may be beyond the capabilities of the principal investigator of the study. The investigator must give evidence of this capability to the IRB, or make arrangements for another qualified party with experience in genetic testing and counseling to represent him/her to the potential subjects. Similarly, the IRB believes that the process of disclosing either direct or incidental results to the subject must be conducted by a person qualified in discussing the significance, consequences and reliability of such results.