

## IRBMED Guidance for IRB Reviewers and Medical School Investigators Regarding Genetic/DNA Research Studies

The following is a list of issues that should be considered when reviewing protocols and informed consent documents involving storage and/or analysis of genomic DNA, especially when the explicit goal of the research is to identify inherited diseases or disease susceptibility states. To a large extent, these issues do not apply to studies involving tumor DNA, which may contain non-inheritable mutations. Be aware, however, that many researchers studying tumor DNA also obtain samples of genomic DNA (from blood or normal tissue) to use as a comparator. In such cases, many of the points outlined below may become relevant. Particularly those related to storage and sharing of DNA, since subsequent analysis of inheritable conditions may be possible.

### A. Confidentiality of Samples

1. Are the DNA samples that are collected stored in a manner that protects the privacy and confidentiality of the subjects, e.g., stored sample tubes are coded and do not have identifiable information on them. Is the code list to these samples stored in a secure way? Are these privacy and confidentiality issues stated in the consent?
2. Does the investigator plan to share the DNA sample or genetic information with other collaborators inside or outside of U of M? If so, how will the privacy and the confidentiality of the subject be protected when DNA or information is shared? Generally, it is expected that only coded information should be sent, where only the PI's team (and not the collaborating investigator) has the code. Please note that coded samples sent to other investigators remain identifiable, therefore OHRP regulations apply. (See [OHRP Repository Guidance](#) and [Research Involving Coded Private Information or Biological Specimens](#)). Please explain sharing provision and privacy protections in the informed consent document.
3. Has the research team obtained or are they in the process of obtaining a [federal "Certificate of Confidentiality"](#) to further protect against the release of private genetic information regarding subjects and family members? (This is not required, but should be strongly considered if information gathered or discovered in the research is very sensitive in nature.) Describe in the informed consent document.

### **B. Informed Consent Issues**

1. If a blood draw is included in a protocol for the purposes of extracting DNA or doing genetic research, is that stated in the consent document? Are the physical risks of the blood draw (e.g., pain, bleeding, bruising, lightheadedness/fainting) stated in the consent?
2. Are the social, psychological and legal risks of the research (parentage issues, knowledge of previously unknown condition, possible loss of insurability, etc.) disclosed in the informed consent document? Is the possible discovery of other unanticipated findings, such as the diagnosis or risk of conditions unrelated to the research study considered? For any of these possible findings is a plan for disclosure or purposeful non-disclosure explained to the subject in the consent?

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3. Does the investigator explain in the informed consent document if the DNA sample or genetic information will be shared with other collaborators inside or outside of U of M, and if so how the privacy and the confidentiality of the subject will be protected?
4. What consent provisions will pertain to current and future specimen use? The following is a list of the types of levels of consent that can be considered for the use of tissue/DNA. It is suggested that an investigator decide what level is necessary to achieve the goals of his research, and then specify that level accordingly in the consent document (with a place for the subject to check and initial that choice). More than one option for levels of access is allowed, but too many would be confusing to the subject.
  - No research use permitted
  - Only anonymous research use for initial project
  - Project specific use, secondary use anonymously only
  - Project specific use, no further contact
  - Project specific use, contact for future use
  - Project specific and related project use
  - Project specific and other study use (should this be allowable?)
  - Commercial use

**Please note:** New studies not covered under the original IRB protocol and consent will need to be submitted to the IRB for approval, even if the consent under which the tissue was originally collected allows for future use of the sample in one of the above ways. It is possible that the IRB may determine that the risk/benefit ratio is such that it will not allow the new “secondary use” research to use the samples previously collected without recontacting the subject for new project specific consent or de-identifying the samples in some way.

5. How long will the sample be stored? What will happen to the DNA sample and genetic information at the time the study ends or the PI leaves the institution? Most investigators will want to state that the study information and DNA will move with them (with approval from the University) if they relocate so their research in this area could continue and if the study ends they should dispose of the DNA samples or anonymize the DNA (destroying all links to the subject). Note: the University is the owner of any tissue, DNA or information collected in research done at the University. The University controls if an investigator can take specimens or data with them when leaving the institution. Are these pertinent points explained in the informed consent document?
6. Does the consent tell the subject when or how they can withdraw from the study? With DNA studies, there may be a point in time after which withdrawal is no longer possible, but disposal of the stored DNA sample is possible. If there is a point after which withdrawal of the data is no longer possible, that should be stated in the consent and a contact person should be provided for withdrawal notifications. Any time limits for withdrawal must be specified in the consent when this is applicable.
7. Are there any costs associated with participation in the research for the subject or family? This could include costs associated with genetic testing or analysis where results are

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disclosed at the subject's request, genetic counseling associated with result disclosure or costs to send blood samples to the lab for analysis. All possible costs to the subject should be explained in the consent document.

8. Are subjects enrolling in clinical research trials that include donation of tissue or DNA samples for research purposes given the option to withhold consent for tissue or DNA sample donation, but still allowed to participate in the clinical research trial? Is there a specific place for the subject to opt out of donation in the informed consent document?

### C. Notification of Results of Genetic Testing

1. Does the PI clearly state in the informed consent document that the findings are considered research and are not the same as "genetic testing" results performed in clinical diagnostic laboratories? Does the PI plan to share the genetic research findings with the subjects if the subjects so choose? If so, does the PI provide this choice in the consent with appropriate check boxes and a place to initial this choice? Does the researcher state at what stage in the research that sharing of results is possible? The IRBMED reviewer should consider whether sharing research findings is appropriate, with the exception of labs that have CLIA certification for the test in question. Labs that are providing research findings for medical use (e.g., affected patients will be recommended for surgery, drug therapy or the research result will be used to guide other aspects of medical management) should be encouraged to obtain CLIA certification for the test. When available, subjects should be advised that they can be retested by a commercial CLIA certified lab.
2. If research results are going to be shared with the subject, the IRBMED recommends that appropriate genetic counseling be provided to give and explain this information. In this situation, does the consent specify that genetic counseling will be provided? If so, does it say if the cost of the genetic counseling will be the responsibility of the subject or provided by the research team?
3. If the research team is providing research information to the subject, does the researcher state the potential psychological or emotional ramifications to the subject of knowing this information? Are other risks such as impact on insurability or employability and other potential forms of discrimination stated if appropriate to the disease being studied? These issues could also come into play when research information is unintentionally released, e.g., a consent form in a medical record that is seen by an insurance company. The research should state what precautions will be put in place to protect the subject from these possibilities. Researchers can and should request an exemption from placing the consent in the medical record if harm could be done to the subject from its inclusion there. It is allowable under federal regulations to waive written documentation of consent completely if the documentation is the only record linking the subject and the research and the principal risk would be potential harm from a breach of confidentiality. Each subject should be asked whether they want documentation linking them with the research and their wishes will govern. Although the documentation of consent may be waived by the IRB, it is still necessary for the researcher to explain all the required informed consent elements in the informed consent educational process.

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4. If the research team is not planning to provide research findings, have they laid out a plan to deal with the discovery of unanticipated information that could be medically compelling to the subject? Does the research team state in the consent that in situations where unanticipated information that could be of important medical significance to the subject is found, whether the subject will be contacted? Does the research team give the subject the opportunity in the consent to accept or deny being contacted in this situation? Does the research team state who will decide when something is of this importance? Is genetic or other counseling provided in the event unanticipated information is to be released? Is there a cost to the subject for this counseling?

### D. Family History and Testing Issues

1. Will family history information be collected? If so, will information be collected on family members that have not consented to participate in the study? If so, are protections in place to not collect identifying information (full names, addresses, social security or hospital registration numbers, etc.) on non-consented individuals? Information may not be collected on non-consented individuals (such as relatives) unless the IRB has found and documented that waiver of informed consent is allowable under the federal regulations. When identifying confidential medical information is collected for research purposes through a second party, the PI must get direct informed consent for the individual whom the information is about, unless appropriately waived by the IRB. See JAMA articles by Dr. Jeffrey Botkin for more information on this topic: (free/open access) [\*Privacy and Confidentiality in the Publication of Pedigrees: A Survey of Investigators and Biomedical Journal\*](#) and (requires UM password and authentication) [\*Protecting the Privacy of Family Members in Survey and Pedigree Research\*](#).
2. The investigator must state in the informed consent document what precautions will be put in place to protect the privacy and confidentiality of subjects and families when information is published or publicly presented. Be mindful of the fact that for rare disorders or families with unique structures, publication or presentation of the pedigree may easily identify the family.
3. Does the PI state in the informed consent document how family members will be contacted? Allowing subjects to give the PI names and contact information of relatives, without their relative's consent or knowledge, is not appropriate. The PI should ask the subjects already in contact to serve as the go-between to send/give information about the study to other relatives. Those other relatives can then contact the PI if interested in participating or return a permission to be contacted card to the PI. Family members acting as go-betweens should be educated not to force or coerce relatives into participating. Likewise, physicians referring families of interest to the research team should serve as the contact mechanism to the family or subjects and not give the research team contact information for subjects that have not consented to be contacted.
4. In general, does any proposed recruiting strategy for family members protect those relatives from coercion or undue influence? Remember that while one individual may be very keen to know their genetic status (and may need samples from relatives to obtain

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definitive information), others may specifically not want to know, may not want to be tested or may not want to be involved in the research study at all. Researchers should be discouraged from attending family reunions or other family gatherings to collect blood samples on family members. This is considered coercive in that it forces the family members to make decisions in front of the group and does not protect their privacy.

5. Has the PI protected against the release of information about family members to each other? For example, a pedigree is seen during the course of an interview, or comments are made about the disease status of family members in an attempt to confirm information that is being gathered or to solicit new information.

### **E. Issues Relevant to Vulnerable Subjects**

Has careful attention been paid to vulnerable populations involved in this type of research, such as the mentally incompetent and children? The involvement of children in genetic studies, particularly where the disease or condition is of adult onset or incomplete penetrance, should be very carefully evaluated. In most cases, children should not be included in testing or research where predictive genetic information may be obtained that they might have decided they didn't want discovered if making the decision as an adult. The potential harm to the emotional health and well being of a child and the parents' interactions with that child if identified to have a disease later in life could be significant.

### **F. Risk Assignment**

Research utilizing DNA or genetic information will not be viewed as “expeditable” by the IRBMED. Also the reviewer should consider if the non-physical risks of the research should warrant a risk classification higher than that of “minimal risk.”

**University of Michigan Medical School IRB**

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**NOTE: These guidelines were developed for use by the University of Michigan IRB. They are based on the application of the principles that govern IRBs and the current thinking on the regulation of DNA studies.**

**OHRP guidance for IRBs and investigators with regard to genetic/DNA studies can be found in the 1993 IRB Guidebook Chapter 5 at**

**[http://www.hhs.gov/ohrp/irb/irb\\_chapter5.htm](http://www.hhs.gov/ohrp/irb/irb_chapter5.htm)**

**OHRP guidance on repositories can be found at <http://www.hhs.gov/ohrp/policy/index.html>**