Chapter 23
Policy on Genetic Research

A subcommittee of HSS’ IRB was formed to create guidance for its IRB and investigators regarding the design, review, and conduct of genetic research. The Guidance produced by this subcommittee consists of: 1) guiding principles; 2) guidelines to aid investigators and IRB members in considering the ethical and other issues inherent in genetic research; and 3) guidelines for developing consent and HIPAA authorization forms.

I. Genetic Research Guidelines: (Supersedes: None). To provide guidance to the IRB and investigators in the review and conduct of genetic research. This guidance is not applicable to gene therapy.

Application of genetic technologies allows the potential for dramatic clinical advances and expansion of medical knowledge through genetic research. Genetic research has the potential positive outcomes of identifying the location of disease genes, the development of diagnostic tests, the discovery of novel therapies, and, ultimately, the development of preventive medicine strategies. Yet genetic research presents a range of risks to subjects and, potentially, to their family members – risks that may include psychological or emotional distress, psychosocial risks (e.g., unanticipated costs associated with counseling and long-term follow-up, changes to family dynamics), the possibility of misdiagnosis or misinterpretation of test results, and the risk of a breach of privacy or confidentiality that could result in stigmatization or discrimination in employment or insurance coverage.

The mandate of the IRB is to protect patient rights and privacy; the responsibility of an investigator is to conduct the research in accordance with applicable legal and regulatory requirements as well as all requirements specified by the IRB. To fulfill these obligations as they apply to genetic research, IRBs and investigators must resolve complex ethical issues and be aware of the various requirements of state and federal law. This guidance will acquaint IRB members and investigators with the ethical issues and legal requirements that they must consider when designing and reviewing protocols, consent documents, and HIPAA authorizations for the collection, storage, analysis, and banking of DNA samples for genetic research.

II. Guiding Principles
A. Protecting human research subjects is the IRB’s primary concern.
B. It is important first to determine who is a research subject (in genetics research, it may be family members or other third parties as well as the affected individual).
C. The IRB must be sensitive to the autonomy of individuals and their right to make decisions about their own lives and welfare.
D. Ensuring that subjects are truly informed of all significant known or anticipated risks, as well as benefits, is of paramount importance.
E. It is the IRB’s role (with the advice of HSS counsel, as necessary) to ensure that each HSS investigator conducts genetic research in compliance with federal, state (NYS law 79.1, see Appendix 1 at the end of this chapter), and local laws and regulations.

III. This Guidance will offer recommendations and guidelines for the evaluation of proposed genetic research. The Guidance reflects consideration of the following topics:
A. Federal Research Regulations and Guidance. At this time there are no federal regulations that impose specific or additional requirements upon genetic research (excluding gene therapy). There is, however, unofficial analysis and guidance in the form of reports and position statements on research and clinical testing issues produced by various federal advisory committees, including the DHHS Secretary’s Advisory Committee on Genetic Testing (2001) and the National Human Research Protections Advisory Committee (2002). See Appendix 2 at the end of this chapter.

B. Federal and State Medical Privacy Laws. The federal Privacy Rule, promulgated under the Health Insurance Portability and Accountability Act (“HIPAA”), does not contain provisions specific to genetic information, but does require all covered providers/entities to meet the requirements that apply to the use or disclosure of any individually-identifiable (as strictly defined by the Privacy Rule) health information (including genetic information) for research. State laws may impose similar or more extensive requirements upon the use or disclosure of medical information, and indeed, New York State law requires specific consent by an individual to the disclosure of his or her genetic testing information. See N.Y. Civ. Rights Law, Section 79.1 Appendix 1). The use or disclosure of medical and other health information for research must comply both with HIPAA and with the laws of the jurisdiction where the records are located, used and disclosed.

C. Federal and State Regulation of Clinical Laboratories. Under the federal Clinical Laboratories Improvement Amendments of 1988 (“CLIA”), as implemented by federal regulations at 42 CFR Part 493, laboratory tests, including genetic tests, are subject to federal oversight when performed for clinical or diagnostic purposes. All laboratory tests conducted for the purpose of providing information for use in diagnosis or health care must be performed by a CLIA-certified laboratory or a laboratory certified under state requirements that meet federal criteria. In New York, this means a laboratory that has been evaluated and granted a permit by the New York State Department of Health, via the Wadsworth Center’s Clinical Laboratory Evaluation Program (“CLEP”).

Although the research exemption under federal CLIA requirements might appear to permit researchers to report the results of genetic testing to subjects or subjects’ physicians if such reports are not intended for diagnostic or clinical purposes, representatives of the New York State Department of Health have advised that under state law and regulations, research testing will not be considered exempt from the laboratory permitting requirement if test results are reported to subjects or to subjects’ personal physicians for any purpose (with the possible exception of a treating physician who is also the researcher, but does not use the test report for any clinical/diagnostic purpose, does not record the test result in medical records, and does not disclose the test result to the patient).

Note: If genetic research involves the developing/testing/or use of a diagnostic test kit, FDA’s medical device regulations apply. Most genetic testing, however, involves in-house tests or “home brew” assays over which FDA has declined to exercise jurisdiction, with the exception of regulations that apply to the purchase and use of analyte-specific reagents (ASRs).

D. New York State Genetic Testing Law. Section 79.1 of the New York Civil Rights Law (See Appendix 1 at the end of this chapter) requires informed consent for genetic testing,
including testing for research, unless the proposed test is not a “genetic test” as defined by
the law (meaning that the test is not conducted to identify a genetic variation linked to a
predisposition to a genetic disease or disability in the test subject or his/her offspring). This
law also requires a specific form of consent for the storage of human tissue/samples for
future genetic testing, and prohibits use of samples for genetic tests other that those for
which specific consent has been obtained, unless (i) subjects have provided a general
consent for use of the samples in research, (ii) such consent is not further restricted; and (iii)
either all identifiers have been removed or an IRB-approved coding system has been
established. Consent of the next-of-kin is required for genetic testing of samples from
deceased persons.

1. The IRB is obligated to assure that all clinical investigators are aware of their
responsibilities in meeting the New York State law for genetic research testing and
for the proper handling of all samples collected at HSS, whether subsequent testing
occurs at HSS or at other centers. It is the investigator’s responsibility to review
the current literature and make the determination as to whether the proposed
genetic measurement is linked to a heritable predisposition for disease or disability,
or, if not, whether the proposed research seeks to link a genetic measurement to a
specific disease or disability. In the IRB application’s “Background” section, the
investigator should explain the method used to research any possible link and the
results of that search. If a link is found, or if the proposed methodology of the
research seeks to establish such a link, then the investigator must comply with the
requirements of the NYS Civil Rights Law, Section 79.1.

E. Issues of Research Design and Conduct. Guidelines provided in this document instruct
the IRB to evaluate the following:

1. How will subjects be identified and contacted?
2. Will the research involve family members or other third parties as human subjects?
3. Will the investigator obtain each subject’s consent and HIPAA authorization, or
will the IRB be asked to waive authorization and consent for the research?
4. To whom, and under what circumstances, will/may the investigator disclose
subject-specific results of genetic research?
5. What processes will be used to obtain informed consent (and assent, where
applicable?)
6. What procedures will be followed if a subject withdraws consent and/or
authorization for the research?
7. Do the investigator’s plans for banking samples and/or data, using samples/data for
future research, transferring samples/data to other investigators or institutions, and
disposing of samples/data, meet applicable legal, ethical, and regulatory
requirements?
8. Are issues of risk, storage, transfer, and future use addressed adequately in the
consent/authorization form(s)?
9. Will the investigator seek a federal Certificate of Confidentiality for the research?

F. Ownership of Samples and Data. Any tissue, samples, DNA, or information obtained for
or used in research at HSS are governed by the applicable HSS policy on ownership of
research-derived materials. According to that policy, HSS, in consultation with the
investigators who collected the materials, will determine whether biological materials and/or information obtained for or used in research may be transferred to another institution on either a temporary or permanent basis (e.g., when the investigator who collected the materials/information becomes affiliated with a new institution). In all informed consent forms, subjects should be advised that, subject to the approval of HSS, the IRB, and the agency/entity funding the research, study information, DNA, and biological materials may be transferred to another institution if the investigator relocates to another institution, or if HSS, in consultation with the investigators, deems that there is a research or other scientific need for the transfer.

IV. Definitions:

A. Identifiable samples/information: Sometimes termed “coded,” or “linked” samples/information, this term applies to samples and/or data that contain either a personal identifier (e.g., name, address) or a code that can be linked to personal identifiers by at least one individual. Research that involves identifiable samples and/or identifiable private information is considered “human subjects research” under 45 CFR Part 46, unless the coding is performed by an individual who is not part of the research team (the sample/information custodian) and all investigators enter a written agreement with this custodian that prohibits disclosure of the identifiers or the code key to any investigator.

1. The agreement must include: (1) a statement that the investigator receiving the samples/information will not ask for identifiers or seek to re-identify the samples/information; (2) a statement from the custodian providing the samples/information that he or she will not release identifiers; and (3) a statement from the custodian certifying that the consent form that was used to collect the samples did not exclude use of the samples for future research. In order to satisfy HIPAA regulations for de-identification, the institution providing the samples also must assign codes that are not derived from any of the identifiers listed in 45 CFR 164.514(b).

   a. Note that under the HIPAA Privacy Rule, coded health information (or coded samples labeled with or linked to health information) remains “individually identifiable,” and thus, “protected,” unless each of a list of 18 specified identifiers (including dates, zip codes, and ages) are removed, rendering the data “de-identified.” The HIPAA Privacy Rule also specifies that linking codes in a “de-identified” data set must not be derived from other information about the subject (e.g., Social Security number, medical record number), and must not be disclosed or used by the HIPAA-covered entity for any other purpose.

   b. If coded samples/information will be disclosed for research under an agreement as described above, the institution providing the samples must be a legal entity separate from HSS, and cannot be an institution with which HSS has an established agreement containing a provision for combined/shared medical records (e.g., New York Presbyterian Hospital). The written agreement between investigators must be submitted to the IRB office. The IRB office will then verify that IRB review is not required.

   c. If the coded information to be disclosed is not fully “de-identified” under HIPAA, the IRB will determine whether the information meets the
requirements of a HIPAA “limited data set.” If so, the investigator and the custodial institution must enter a “data use agreement” that meets the requirements of HIPAA before any information (or samples labeled with health subject information) may be used or disclosed for the research.

B. Genetic research: Human genetic research involves the study of inherited human traits. Much of this research is aimed at identifying DNA mutations that can cause or contribute to specific health problems, developing methods of identifying those mutations in patients, and improving the interventions available to help patients address those problems.

C. Identifier: Any information that could reasonably allow for the identification of a human being, either alone or in combination with other available information. This includes but is not limited to name, address, social security number, telephone number, email address, date of birth, and medical history number. HIPAA regulations impose a stricter standard for de-identification in 45 CFR 164.514(b), and this standard must be met to avoid the application of HIPAA Privacy and Security Rule standards to genetic research data.

D. Unidentified samples: Sometimes termed “anonymous,” these samples lack any identifier or code (even if encrypted) that can link a particular sample to an identified specimen or a particular human being.

V. Guidelines. In addition to the standard review criteria IRB members currently use when reviewing and approving protocols, IRB members should consider the following additional issues when reviewing genetic research:

A. Initial contact: The initial contact of potential subjects for genetic studies may cause concern or alarm if the subject is not aware of a familial disease or other inherited condition, or if the subject has not anticipated that persons other than his or her provider will have access to the subject’s health information. IRBs should evaluate the proposed subject identification/recruitment plan carefully, to determine whether the plan minimizes potential invasions of privacy and complies with HIPAA requirements and all applicable institutional research recruitment policies.

1. Guidance:
   a. The approach that offers the greatest privacy protection is for the treating physician to contact the primary subject (proband) and to offer general information about the study and a contact number for the investigator. If the research extends to family members, the treating physician may request that the proband also recruit family members, and if family members are interested, they then may contact the investigator for details on study participation. (Note: If the investigator will review medical records of patients not treated by that physician in order to identify potential subjects, such review will require either written assurances or an IRB partial waiver of authorization. Consult the IRB for details on how to apply for such a waiver.)
   b. Alternatively, after a proband has been contacted by a treating physician or representative of the department and agrees to participate, the investigator could ask the proband for family member names, addresses and telephone
numbers. A letter could then be sent by the investigator to family members referencing the fact that names, but no medical information, were provided by the proband. In the letter, potential subjects could be informed about the study and that the investigator would be calling them by telephone shortly to discuss their interest in participation. The letter should include a post card or letter that could be returned if the subject does not want to be contacted. The telephone script should begin by asking the subject if they received the letter and offering to re-send it if the potential subject desires. (Note: This and all other subject recruitment methodologies that involve use of health information by persons other than direct treatment providers in order to contact potential subjects will require full or partial waiver of authorization under the IRB’s HIPAA policies and procedures.)

c. Other methods of subject recruitment may be proposed to the IRB, but should include detailed justification about how alternative recruitment methods offer adequate privacy protection and about why an explanation of why recruitment into a study is not practicable unless such alternatives are used.

B. Identification of subjects: A human subject is a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. Genetic research often involves the collection of identifiable data concerning family members. The investigator and the IRB therefore must assure that the investigator has identified all human subjects in the study.

1. Guidance: IRB members and investigators should use the following guidance (modified from National Human Research Protections Advisory Committee, Clarification of the Status of Third Parties When Referenced by Human Subjects in Research, Jan. 2002, see Appendix 2 at the end of this chapter), to determine whether family members of the primary subject or other third parties are persons about whom the investigator will obtain “identifiable private information,” rendering such third parties “human subjects” under 45 CFR Part 46.

   a. Are family members or other third parties to the research human subjects?

Although the IRB makes the final determination, both the investigator and the IRB should consider the following factors when determining whether information collected about third parties during the course of the research is both “private” and “identifiable”:

i. The quantity of information to be collected about third parties;

   ii. The nature of the information collected, including the sensitivity of the information and the possibility that its collection or disclosure might harm a third party (e.g., does the information concern health status, health history, behavior history, etc. ?);

   iii. The ability and intent of investigators to record information about third parties in a manner that protects the identities of those third parties; and
iv. The possibility that classification of a third party as a human subject may have an impact upon the rights or welfare of the originally-designated human subject. If such an impact is likely, the IRB must protect the interests of both the originally-designated human subject and the third party.

C. Consent and HIPAA authorization of subjects: All identified human subjects, including third-party human subjects, must be given the opportunity to consent to the proposed research, unless the IRB specifically waives informed consent under 45 CFR § 46.116. If the research involves any information deemed “protected health information” under the HIPAA Privacy Rule (even if samples are labeled with coded identifiers), a HIPAA-compliant form of authorization must be obtained from each subject for the research, unless the IRB waives authorization (or unless the information is used and disclosed for research only in the form of a limited data set, subject to a data use agreement).

1. Informed Consent:

IRB members and investigators should use the following guidance (as set forth in 45 CFR § 46.116(d), and as described in Botkin, J, Protecting the Privacy of Family Members in Survey and Pedigree Research, JAMA, Vol. 285, No. 2, 1/10/01) to determine whether informed consent may be waived for third parties determined to be human subjects of the research. **Waiver of informed consent must be applied for using the appropriate IRB form.**

   a. Does the research involve more than minimal risk?  
      The IRB will consider security of data, sensitivity of information, age of participants, etc. in answering this question.
   b. Does the waiver adversely affect the rights and welfare of the subjects?
   c. Can the research be practically carried out without the waiver?
   d. When appropriate, will subjects be provided pertinent information after completion of the research?  
      This criterion is a specific part of federal regulations (45 CFR § 46.116(d)(4)). The IRB must give careful consideration to this fourth criterion, because in some cases, the results of genetic research could be important to the personal health planning of third party subjects.

2. HIPAA Authorization:

IRB members and investigators should use the following guidance to determine whether HIPAA authorization may be waived for third parties determined to be human subjects of the research. **Waiver of HIPAA authorization must be applied for using the appropriate IRB form.**

   a. Does the research involve no more than minimal risk to the privacy of the third party subjects?  
      The IRB must consider whether the investigator has proposed an adequate plan to protect HIPAA
identifiers from improper use or disclosure and to destroy the identifiers at the earliest opportunity, consistent with the conduct of the research. In addition, the IRB must receive adequate written assurances that the protected health information will not be used or disclosed except as required by law or in compliance with the privacy rule.

b. Is it impracticable to seek authorization from the third party subjects?

c. Is it impracticable to conduct the research without access to and use of identifiable health information about the third party subjects?

D. Subject Selection/Disclosure of Results: The degree of risk of genetic research is often directly related to the possible disclosure of results to subjects and others. Whether disclosure of results to subjects is advisable or permissible depends upon the nature of the test, whether the research is primary research (versus research on stored samples) and how the risks and circumstances of disclosure are addressed in the consent form.

1. Guidance:
   a. Is Disclosure Permissible?
      i. If the genetic test is not performed by a NYS-permitted lab within one of the lab’s approved permit categories (or under provisions applicable to tests for which there are no approved permit categories), then the results may not be disclosed to research subjects or subjects’ physicians. If the investigator is in the dual role of researcher and personal physician to one or more of the subjects, then the results should only be disclosed to that investigator in his or her capacity as a researcher, and should not be entered into medical charts or disclosed to research subjects. It is the position of Wadsworth Laboratories of the New York State Department of Health that if the investigator uses a test result to make any decision about the diagnosis or health care of a study participant (e.g., eligibility or assignment to a study arm), then the research exception to state permitting laws is inapplicable. The results of tests sent to out-of-state labs must not be reported to patients or their treating physicians unless the out-of-state laboratory is CLIA-certified (or certified through a state laboratory licensure program deemed by CMS).

Note: If a test performed for clinical purposes is not offered by a NYS DOH-permitted laboratory, but is available from a non-permitted academic laboratory or an out-of-state laboratory that is not CLIA-certified for the test, it may be possible for such a laboratory to perform the test and report results to a treating provider in New York State under an “orphan disease exemption” (“ODE”), if approval for such exemption has been obtained from Wadsworth Laboratories. Such an exemption will only be granted on a patient-by-
patient basis when the testing is performed for clinical purposes. A separate exemption must be obtained for each patient for whom results will be released.

The ODE is inapplicable when an investigator wishes to obtain testing for all subjects in a protocol and the test in question has no established clinical validity. If the results of such testing will be reported to patients or treating physicians, or if the investigator will use the results to make any decision related to a study subject’s care or diagnosis, the testing laboratory (whether in-state or out-of-state) must apply for a NYSDOH permit. The laboratory will be asked to submit validity data, and state evaluators may, at their option, elect to limit their review to analytical validity. In such cases the State will issue the laboratory a permit to perform the test, but will require the test report to contain a caveat that the clinical validity of the test has not been established.

b. **No disclosure planned.** If there is no plan to disclose individual identified results to subjects, risks are usually minimized (i.e., less chance for psychosocial harm). However, since there is always the potential for intentional or unintentional disclosure of results to the subject or to unauthorized third parties, subjects should be told in the consent document that while New York state law offers protection against genetic discrimination in employment and health insurance, discrimination is still a possibility. Investigators should explain in the consent form what steps are being taken to minimize these risks.

   i. The consent document should inform subjects that the results of research genetic testing will not be disclosed, and explain the reason for non-disclosure (e.g., test has unknown analytical and/or clinical validity, or no known clinical utility).

c. **Is Disclosure Advisable?**

   i. If disclosure is permissible and there is a plan to disclose results, is there a compelling reason to do so? What plans are in place to minimize the impact on subjects? Have subjects been given the opportunity to refuse this? Has the investigator proposed the inclusion of genetic counseling prior to testing, and if applicable, prior to disclosing results? What sort of counseling would be offered if the results of the proposed genetic testing likely will not reveal any certain information about the subject’s health condition? Does the consent form adequately address who is responsible for these costs? Does the investigator outline a plan for keeping genetic information from outside parties (e.g., insurance companies, employers, etc.)? Does the investigator discuss how he/she will handle unanticipated/incidental findings (i.e., non-paternity, unexpected mutations, etc.)?

d. **If Disclosure is Planned**
i. Disclosure to adult primary subjects (probands) should be permissible where there is clear benefit (i.e., disease is preventable, treatable, or medically accepted standards indicate that early monitoring will reduce the genetic risk). The potential harm from failing to disclose should outweigh the potential harm from disclosure. In deciding whether to allow disclosure of results, the IRB will consider whether:
   - The test is performed by a CLIA certified (or NYS permitted) laboratory and is within the scope of the laboratory’s certification;
   - The findings are scientifically valid and confirmed;
   - The findings have significant implications for the subject’s health concerns, and
   - A course of action to ameliorate or treat these concerns is readily available.

ii. Discovery of pre-symptomatic conditions should not be disclosed without careful consideration and appropriate counseling and consent; however, any such conditions under which disclosure will not occur should be explained in the consent form.

iii. It should also be stressed to subjects in the consent form, during the informed consent process, and during pre-disclosure counseling that a large number of subjects may receive results of undetermined significance simply because of the nature of genetics. Applicable New York law, N.Y. Civ. Rights Law, Section 79-l.2(b)(3) requires a statement in the informed consent form that the individual may wish to obtain professional genetic counseling about the meaning of the test and its results. Therefore, an informed consent form for testing whose significance is not known or understood (e.g., testing in a research study designed to identify genetic markers) should contain a statement that genetic counseling is not available for the intended testing, due to the research nature of the testing and its lack of established diagnostic validity.

   - **Secondary Subjects.** New York State law prohibits contacting family members for any purpose (including disclosure of results from testing of the original subject) **unless the specific family members and the purpose of the contact were identified in the consent form signed by the original subject (proband).** State law also provides that genetic test information from the consenting subject may not be incorporated into the records of non-consenting family members, “nor shall any inferences be drawn, used, or communicated regarding the possible genetic status of the non-consenting [family members].”

   - **Children.** Generally, asymptomatic children should not have results disclosed for adult onset conditions for
which no benefit through therapeutic options or preventive measures is available during childhood. The principal reasons against disclosing results to children and their parents are that disclosure removes a child’s personal choice to seek or decline this information once the child becomes an adult, raises the possibility of stigmatization within the family and in other social settings, and could have serious educational and career implications.

- Disclosure may be justified where the disease is preventable or treatable, when therapeutic interventions are available in adulthood, or when medically accepted standards indicate that early monitoring will reduce the genetic risk. As with the adult population, the harm from failing to disclose should outweigh the harm from disclosure, and, as required by state law, subjects (or the parents of minor subjects) must be permitted to decline disclosure.

- **Stored Samples.** Under NY State law, when samples are used for research other than that for which specific consent was obtained (i.e., secondary studies), subjects may not be contacted for disclosure of results or any other purpose, unless the original consent form signed by the subjects granted consent for future contact for disclosure of results or for other purposes, AND the consent form explained the benefits and risks to the subject of consenting to contact for such purposes. If the IRB determines that individuals who had originally consented to be contacted should now be contacted to be offered the results of secondary studies, consideration should be given to working through the original investigator(s) to make contact with the subjects. This should be done in order to prevent undue alarm to the subjects, who would likely be unfamiliar with the research team working on the secondary study.

c. **Unanticipated Results.**

  i. With proper thought and planning, the need for an investigator and IRB to determine whether unanticipated findings should be disclosed to subjects should be minimal. The IRB does, however, recognize that not every situation can be anticipated and there may be some instances in which disclosing results to a subject may be in the subject’s best interest, even when they were initially told they would not receive results.

  ii. If an investigator happens upon a result that is serious or life-threatening, the investigator must disclose this information to the IRB before taking any other action. The IRB will consult with experts to
determine the validity of the research result as well as the clinical utility of disclosing the result to the subject. The IRB will then make a determination as to whether these results may and should be released to the subject.

**Note:** Remember, however, that under New York law, no subject may be contacted for disclosure of the results of a genetic test unless that subject has given specific consent for the contact. When the protocol involves secondary research, the IRB may not permit disclosure of genetic testing results to subjects unless the original consent under which the samples were collected specifically permits such contact.

f. **Process for Disclosure.**
   
i. As a matter of research ethics and New York State law, it is imperative that subjects of genetic testing be given the opportunity to consent to, or to refuse to consent to, the disclosure of test results. In studies where a specific disease is being studied, it would be necessary to include an area in the consent form for subjects to indicate their preference for learning individual results (provided that disclosure of results is permissible). For studies where multiple diseases are being studied or there is uncertainty as to what may be found, a newsletter may be the most appropriate tool to inform participants of general results. Investigators may offer, through a newsletter, the opportunity for individuals to learn results at a general or group level. In either case, the need for or appropriateness of pre- and post-disclosure genetic counseling, including who will cover the cost, should be considered and discussed in the consent form or newsletter. Subjects should be informed of the plan for such a newsletter in the consent document and given the opportunity to consent to, or to refuse consent to, receipt of the newsletter. Remember also that any use of subjects’ health information to send mailings to or contact subjects must be authorized by the subject in writing, unless the IRB has waived such HIPAA authorization.
   
ii. If a clinical, non-genetic test is available for the disease being studied, subjects who have consented to receive test results should be referred for clinical consultation. In situations in which a clinical test is not available, it may still be appropriate to disclose results to primary or proband subjects of the research, following the principles described above. Remember that if the research involves stored samples, genetic test results may not be released to subjects unless such disclosure was specifically provided for in the original consent form under which the samples were collected.
iii. Disclosure of the results of genetic research must be approved by the IRB and may require consultation with the Office of Legal Affairs. Care should be taken to release research results only after appropriate counseling of subjects as to the implications of such results. Where applicable, the consent form and consent process used prior to release of specific genetic test results must stress that the information being conveyed is a result of research and is not an established clinical test. Because of the NYSDOH Wadsworth Laboratory position that no research testing results produced by non-CLIA-certified laboratories should be disclosed, any decision to inform subjects of such testing results should be carefully reviewed and approved in advance by the IRB and the HSS Office of Legal Affairs.

E. Informed consent process: Genetic research does not always involve face-to-face contact with all subjects. This can present special problems in obtaining informed consent. Has the investigator proposed a consent process that truly allows for informed consent? If contact by letter or telephone is proposed, has a letter/script been provided to the IRB for review and approval?

1. Guidance:
   a. Obtaining consent in a face-to-face manner allows for the greatest interaction and therefore generally is seen by the IRB as the most favorable approach. If consent in this manner is not feasible, the specifics of other methods proposed should be noted in detail in the IRB application, and a copy of any proposed written correspondence and/or telephone script must be submitted to the IRB for review.

F. Assent: Since genetic research usually involves families, minors may be asked to participate. If the investigator is proposing to enroll subjects who are under 18 years of age, is a process for obtaining the minor’s assent outlined (as discussed in item 4 of this document)? If the researcher (or HSS) plans to retain samples on a long-term basis, how does the investigator propose obtaining the consent of minors once they reach the age of majority?

1. Guidance:
   a. The IRB generally requires that assent be obtained from subjects age 7 or above. In addition, if the research is long-term and the intention is to retain samples beyond the point at which subjects reach the age of majority (18 years), consideration must be given to consenting (and obtaining the HIPAA authorization of) participants who previously provided assent. The process, or any justification for not including such a process, should be detailed in the IRB application.

G. Withdrawal from a study: Does the investigator outline a plan for destruction of samples and data if a subject decides to withdraw from the study? Does the consent form discuss any limitations on a subject’s ability to withdraw completely from the project (e.g., after a cell
line or commercial product has been developed, or if the sample has been placed into a research databank/tissue repository but in a de-identified and anonymized format, so that retrieval is impossible)?

1. **Guidance:** Participants must be allowed to withdraw from the study and/or to revoke authorization for the use or disclosure of PHI in research. If a subject asks to be withdrawn from a study, the investigator should engage in a conversation with the subject to determine from what specific aspects of the study the subject wishes to withdraw. At a minimum, the subject should be given the option to:
   a. withdraw from future interaction and data collection through any means (e.g., review of medical records, interaction with family members), but allow the researcher to use previously collected samples and data; or
   b. withdraw from future interaction and data collection, and also have their sample and related data destroyed, except to the extent already used to support an accepted or published manuscript, cell line, or commercial product. Future use of this data is prohibited. In the case of an accepted or published manuscript, withdrawal should include destruction of samples/data that do not support the publication.

If samples and data are unidentified, destruction of a specific sample and related data will not be possible, and subjects should be informed of this in the consent form.

**H. Storage, retention and disposition of samples and data:** Genetics research often involves the long-term storage and shared use of samples and data. Has the investigator addressed where and for how long samples and related data will be stored, how samples and data will be secured (e.g., anonymized, coded, kept in a locked freezer, etc.), who will have access to the samples, and whether this access will include access to identifiable data? Subjects should be informed that, subject to the approval of HSS, the IRB, and the funder/sponsor of the research, samples and genetic information may be transferred if the investigator moves to another institution.

1. If applicable, can a study subject participate in the main portion of the study without participating in the sample collection/storage portion, or without having samples and genetic information banked for future research? If not, does the investigator adequately justify why subjects cannot be given this opportunity? Overall, do procedures for storage, retention and disposition of samples adequately protect the privacy and confidentiality of subjects?

**Note:** The storage or banking of samples and/or health information for future research requires a separate, IRB-approved protocol for creation and maintenance of the database/repository unless the stored samples will be rendered fully anonymous (i.e., stripped of all identifiers, including linking codes.). Consent for the banking of stored tissue for future genetic research is also a requirement of New York State law. Any protocol seeking a secondary use of stored identifiable (including coded) samples and/or health information for research not approved in the original protocol and specifically described in the original consent form must receive a new IRB approval and a waiver of HIPAA authorization.
The HIPAA Privacy Rule does not permit an authorization for use or disclosure of health information in the primary study to include an authorization for the banking of health information (including samples labeled with health information), unless in that same authorization, the subject is clearly given the option of participating only in the primary study and at the same time declining to permit his/her identifiable health information to be stored or banked for future use.

In some studies sponsored by commercial companies (e.g., medical device manufacturers) and in some studies funded by federal or other grant sources, there may be requirements in the clinical trial or grant agreement that the HSS investigators provide to those companies or funding agencies either identified data or tissues for databanking or tissue banking purposes. Once data and tissues have left HSS, the HSS IRB, HSS administration and HSS investigators have no control over the use and disposition of such data and samples. Indeed, outside of research institutions and academic medical centers, the use and disclosure of such data and tissues may not be governed by 45 CFR 46 or by other federal or state research regulations. In the case of genetic testing and disclosure of genetic information, however, laws of many states, including New York State, may apply to the post-study database and tissue banking activities (e.g., secondary research) of commercial research sponsors or other entities. In order to protect the rights and privacy of HSS study subjects, investigators and others who understand or become aware of the intent of research sponsors or funders to obtain HSS subjects’ identified data and/or tissues for secondary research purposes should promptly inform the IRB and the HSS Office of Legal Affairs, so that these issues might be clarified, both in any applicable clinical trials or grant agreement, as well as, if necessary, in the informed consent and HIPAA authorization forms. At the very least, subjects have a right to know if their identified data and tissues will be handed over to other entities and then used for secondary research purposes outside of the control of HSS and its investigators.

2. Guidance:

   a. Risks are minimized when storage procedures ensure the highest degree of confidentiality and when samples and identifiable data are destroyed as soon as possible after the research is finalized. Samples should contain a code rather than a direct identifier. The legend to the code should be able to be accessed by a very limited group of researchers or research staff. Whenever possible, the legend and the samples should be maintained in a locked or otherwise secured area.

   b. A scientific reason for maintaining identifiable samples and/or health information beyond the duration of the study should be specified. Long-term banking and future use of any samples and/or health information retained beyond the original study period or purpose must have IRB approval. A banking protocol should include the following elements: (1) description of the samples and information to be banked; (2) measures taken to assure confidentiality of samples and data; (3) conditions under which data and specimens will be accepted and shared (i.e., from whom will samples be accepted, who has access to the banked material, and what types of samples and data are provided); (4) conditions under which results from future studies will be released to subjects; (5) person or group responsible for reviewing and approving release of samples and data to researchers; and (6) IRB responsible for providing oversight of the sample bank.
Note: As described above, any subsequent use of identifiable (including coded) banked samples for research will require a separate, IRB-approved protocol and waiver of HIPAA authorization. If a secondary study is expected to generate any information that could be useful or important for subjects, the investigator and IRB should consider whether and how subjects could be identified (through linking codes for coded specimens) and contacted. In New York State, as set forth above, no subject may be contacted with results of genetic tests unless the subject had consented to such contact in the informed consent used in the study in which the subject’s specimen was originally collected. Note, however, that for non-genetic tests that may be conducted in secondary studies, New York State law has no such requirement of pre-consent for contact. In such cases, therefore, IRBs and investigators must consider carefully whether contact is warranted, and how it might be accomplished.

When the genetic analysis is only a portion of a larger clinical study, participants must be offered the opportunity to consent to the clinical study apart from the genetic analysis, unless a scientific reason is provided for requiring consent to both.

The risks of undefined future research are unclear. The IRB believes, however, that there may be greater psychological risks associated with research that is not restricted to the condition for which the subject first provided consent. For this reason, the IRB encourages researchers to limit future research on stored samples to the same condition for which they were originally collected. Any such research will not be permitted unless the investigator has complied with HIPAA, state law, and IRB policies when creating and maintaining the sample/data bank.

I. Consent form: If applicable, have all genetic risks been adequately addressed in the consent form? Please refer to the genetic consent form template for suggested language for genetic research.

1. Guidance:
   a. Risks in genetic research are unique. These include psychosocial (e.g., changes in self-perception, unrealized costs associated with counseling and long-term follow-up, changes to family dynamics), and privacy/confidentiality risks (e.g., discrimination in employment and insurability, loss of individual privacy based on a family member’s decision to participate.

J. Certificate of Confidentiality: If the IRB approves the protocol, will the research apply for a federal Certificate of Confidentiality from the NIH? Certificates are available to qualified projects, regardless of the source of project funding, and protect the identities of research subjects from compulsory disclosure during the course of a specific study. For further information, see http://grants.nih.gov/grants/policy/coc/index.htm.

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REFERENCES

The following documents were consulted during development of these guidelines:


6. Marshfield Clinic Research Foundation, IRB Meeting Minutes, Presentation: Genetic Privacy Law and Other Genetic Issues, 1/30/01.


8. Reference Manual for the Use of Human Subjects in Research, University of Pittsburgh, Appendix E: Special Considerations for the Collection and Use of Tissue Samples and Biological Specimens for Genetic Studies and Other Research Projects, on-line version, 3/16/01.


APPENDIX 1

New York State Civil Rights Law, Section 79.1, provides as follows:

79.1 Confidentiality of records of genetic tests

1. As used in this section, the following terms have the following meanings:

(a) “genetic test” shall mean any laboratory test of human DNA, chromosomes, genes, or gene products to diagnose the presence of a genetic variation linked to a predisposition to a genetic disease or disability in the individual or the individual’s offspring; such term shall also include DNA profile analysis. “Genetic test” shall not be deemed to include any test of blood or other medically prescribed test in routine use that has been or may be hereafter found to be associated with a genetic variation, unless conducted purposely to identify such genetic variation.

(b) “genetic predisposition” shall mean the presence of a variation in the composition of the genes of an individual or an individual’s family member which is scientifically or medically identifiable and which is determined to be associated with an increased statistical risk of being expressed as either a physical or mental disease or disability in the individual or having offspring with a genetically influenced disease, but which has not resulted in any symptoms of such disease or disorder.

(c) “biologic sample” shall mean any material part of the human body or of discharge therefrom known to contain DNA, including but not limited to tissue specimen, blood, or urine.

(d) “institutional review board” shall mean a human research review committee established and approved under the provisions of article twenty-four-A of the public health law, or an institutional review board established and approved under the provision of 45 CFR part 46 or 42 USC 30 V-1, for the purpose of reviewing and monitoring research involving human subjects.

2. (a) No person shall perform a genetic test on a biological sample taken from an individual without the prior written informed consent of such individuals provided in paragraph (b) of this subdivision, except as otherwise provided in paragraph (c) of subdivision two and by subdivision nine of this section.

(b) Written informed consent to a genetic test shall consist of written authorization that is dated and signed and includes at least the following:

(1) a general description of the test;

(2) a statement of the purpose of the test.; a statement indicating that the individual may wish to obtain professional genetic counseling prior to signing the informed consent.

(3) a statement that a positive test result is an indication that the individual may be predisposed to or have the specific disease or condition tested for and may wish to consider further independent testing, consult their physician or pursue genetic counseling;

(4) a general description of each specific disease or condition tested for;

(5) the level of certainty that a positive test result for that disease or condition serves as a predictor of such disease. If no level of certainty has been established, this subparagraph may be disregarded;

(6) the name of the person or categories of persons or organizations to whom the test results may be disclosed;
(7) a statement that no tests other than those authorized shall be performed on the biological sample and that the sample shall be destroyed at the end of the testing process or not more than sixty days after the sample was taken, unless a longer period of retention is expressly authorized in the consent; and

(8) the signature of the individual subject of the test, or if that individual lacks the capacity to consent, the signature of the person authorized to consent for such individual.

c) A general waiver, wherein consent in secured for genetic testing without compliance with paragraph (b) of this subdivision, shall not constitute informed consent. Notwithstanding the provisions of this section, for purposes of research conducted in accordance with the provision of subdivision nine of this section, a general waiver for the use of samples for research may be granted which would authorize the use of samples for these research purposes.

d) Any further disclosure of genetic test results to persons or organizations not named on the informed consent shall require the further informed consent of the subject of the test.

e) Written consent by an individual for tests to be conducted on a biological sample and to the lawful possession and ownership of such sample by a laboratory shall not be deemed written informed consent for the performance of any genetic test on that sample, except as further provided in subdivision four of this section.

(f) For medical research purposes, with the approval of an institutional review board and the written informed consent of the subject, samples may be kept for longer than sixty days and utilized for scientific research. The requirements of subparagraphs three, four and five of paragraph (b) of this subdivision may be modified by the institutional review board in case the research protocol does not permit such degree of specificity.

3. (a) All records, findings and results of any genetic test performed on any person shall be deemed confidential and shall not be disclosed without the written informed consent of the person to whom such genetic test relates. This information shall not be released to any person or organization not specifically authorized by the individual subject of the test. Unauthorized solicitation or possession of such information shall be unlawful, except for the unintentional possession of such information as part of a health record created prior to the effective date of this section and provided no action adverse to the interest of the subject are taken as a result of such possession. Nothing in this section shall preclude the release of such information, with the subject’s consent, to a health insurer or health maintenance organization of any information reasonably required for purposes of claims administration, provided, however, that further distribution within the insurer or to other recipients shall require the subjects informed consent in each case.

(b) No person who lawfully possesses information derived from a genetic test on a biological sample from an individual shall incorporate such information into the records of a non-consenting individual who may be genetically related to the tested individual; nor shall any inferences be drawn, used, or communicated regarding the possible genetic status of the non-consenting individual.

4. (a) Notwithstanding the provisions of subdivision two of this section, genetic tests may be performed on anonymous samples for research or statistical purposes, pursuant to a research protocol approved by an institutional review board which assures the anonymity of the sources of the samples.

(b) Notwithstanding the provisions of subdivision two of this section, genetic tests may be performed without the consent of the person who is the subject of the tests pursuant to an
order of a court of competent jurisdiction or as provided pursuant to article forty-nine-B of the executive law or as provided by section twenty-five hundred-a of the public health law.

(c) Notwithstanding the provision of paragraph (a) of subdivision three of this section, the results of a genetic test may be disclosed to specified individuals without the consent of the subject of the test as provided in an order of a court of competent jurisdiction or as provided pursuant to article forty-nine-B of the executive law or as provided by section twenty-five hundred-a of the public health law.

(d) In authorizing a genetic test or the disclosure of genetic test results to specified individuals, the court shall consider the privacy interests of the individual subject of the genetic test and of close relatives of such individual, the public interest, and, in the case of medical or anthropological research, the ethical appropriateness of the research. Disclosure shall be permitted only to individuals or agencies expressly named in court orders.

5. Penalties.
   (a) Any person who violates the provision of subdivision two or three of this section shall be guilty of a violation punishable by a civil fine of not more than one thousand dollars.
   (b) Any person who willfully violates the provision of subdivision two or three of this section shall be guilty of a misdemeanor punishable by a fine of not more than five thousand dollars or by imprisonment for not more than ninety days or by both such fine and imprisonment.

6. Nothing in this section shall be applicable to an authorized insurer, as defined in paragraph ten of subsection (a) of section one hundred seven of the insurance law, or a person acting on behalf of an authorized insurer who is in compliance with section twenty-six hundred twelve of the insurance law nor shall anything in this section be deemed to prohibit or limit an authorized insurer from obtaining information pursuant to section twenty-six hundred twelve of the insurance law.

7. Notwithstanding the provisions of subdivision two of this section, genetic testing of newborn infants may be performed as provided pursuant to article twenty-five and section forty-one hundred thirty-five-b of the public health law.

8. Notwithstanding the provision of subparagraph seven of paragraph (b) of subdivision two of this section, additional genetic testing may be performed on a given sample without additional consent of the person tested provided such testing is necessary and required to demonstrate the integrity of the sample tested or to resolve the analysis of a test with a previously indeterminate result.

9. (a) Notwithstanding the provisions of subdivisions two and ten of this section, samples may be used for tests other than those for which specific consent has been obtained, for purposes of research conducted in accordance with applicable law and regulation and pursuant to a research protocol approved by an institutional review board, provided that the individuals who provided the samples have given prior written informed consent for the use of their sample for general research purposes and did not specify time limits or other factors that would restrict use of the sample for the test, and (1) the samples have been permanently stripped of identifying information; or (2) a coding system has been established to protect the identity of the individuals who provided the samples, and an institutional review board has reviewed and approved the procedures for the coding system.

   (b) If consent to storage of the tissue sample is withdrawn at any time, the entity storing the sample shall promptly destroy the sample or portions thereof that have not already been used for research purposes.
(c) In no event shall family members of an individual who provided a stored tissue sample be contacted for clinical, research, or other purposes without consent from the individual who provided the tissue sample with respect to the specific family members who will be contacted and the specific purpose of the contact.

(d) In no event shall any information about an individual derived from genetic tests performed on stored human tissue or information linking an individual with specific results of genetic tests be released to any organization or person without the explicit written consent of the individual who donated the stored tissue to release of the information for the purposes set forth in the written consent document.

(e) **Written informed consent for use of stored human tissue for general research purposes shall consist of written authorization that includes at least the following:**

1. a statement that the sample will be used for future genetic tests;
2. the time period during which the tissue will be stored, or if no time limit is specified, a statement that the tissue will be stored for as long as deemed useful for research purposes;
3. a description of the policies and procedures to protect patient confidentiality;
4. a statement of the right to withdraw consent to use of the tissue for future use at any time and the name of the organization that should be contacted to withdraw consent;
5. a statement allowing individuals to consent to future contact for any or all purposes, including the following: (i) research purposes; (ii) provision of general information about research findings; and (iii) information about the test on their sample that may benefit them or their family members in relation to their choices regarding preventive or clinical care; and
6. a statement explaining the benefits and risks of consenting to future contact for the purposes set forth in subparagraph five of this paragraph. In no event shall information about specific test results on stored human tissue donated for general research purposes be disclosed to an individual without obtaining informed consent for the disclosure as required by paragraph (b) of subdivision two of this section.

10. Notwithstanding the provisions of subdivision two of this section, DNA samples may be stored for up to ten years in the absence of genetic testing, if authorized in writing by the subject. Prior to the performance of any genetic test upon stored samples, informed consent must be obtained as provided in subdivision two of this section. Retention of a DNA sample past a period of ten years requires explicit consent for a longer or indefinite period of retention.

11. Genetic testing may be performed on specimens from deceased persons if informed consent is provided by the next-of-kin as specified in subdivision two of this section.
APPENDIX 2

The content of this document does not represent the official views or policies of the Office for Human Research Protections (OHRP) nor of the Department of Health and Human Services (HHS). The content represents solely the advice and views of the National Human Research Protections Advisory Committee that were provided to the Secretary of HHS, the Assistant Secretary for Health, and OHRP for their consideration.

The National Human Research Protections Advisory Committee (NHRPAC) approved the following recommendations on Confidentiality and Research Data Protections at the July 30-31, 2002 Committee meeting.

Recommendations on Confidentiality and Research Data Protections

National Human Research Protections Advisory Committee

These recommendations are intended to advise the Secretary and Assistant Secretary for Health, Department of Health and Human Services, as well as the Director of the Office of Human Research Protections. They may be used in the preparation of guidance for local Institutional Review Boards or in issuing advice to research investigators.

Researchers in the biomedical as well as social and behavioral sciences are expected to be proactive in designing and performing research to ensure that the dignity, welfare, and privacy of individual research subjects are protected and that information about an individual remains confidential. This expectation is expressed in the ethical codes of conduct of professional societies. Protecting the confidentiality of information collected about individuals is also vital to fulfilling the ethical responsibilities described in the Belmont Report.

Research in the biomedical and social sciences encompasses a broad array of topical areas, designs, and degree of risk. Many studies pose minimal risk to research subjects. Some studies, however, are inaccurately perceived as conveying minimal risk. In such studies, disclosure of identifiable data may present a significant risk to the subject as a result of the sensitive nature of the topic, the variety of social interactions, or possible financial or legal implications of the activity being studied. In such research, especially in the social and behavioral sciences, protecting the confidentiality of data collected from or about private individuals is often the key element in minimizing risk.

In addition to protecting research subjects from harm that might result from their participation in research, applying appropriate confidentiality protections provides other important benefits. Confidentiality protections minimize subjects’ concerns over the use (or misuse) of the data. Subjects consequently provide more accurate information to investigators, thereby improving the data used in the analysis and thus the overall quality of the research. Confidentiality protections allow researchers to continue to conduct difficult research on important societal problems (e.g., drug abuse, the spread of HIV, genetic predispositions, high risk sexual behaviors, violence). Such research provides a scientifically-informed basis for making important public policy decisions and fosters advances in medicine and in all fields of science. The benefits of these results accrue not only to the research subjects, but to society at large.
Confidentiality issues need to be recognized and considered at every stage of the research process. These stages include the initial study design; identification, recruitment, and consent processes for the study population; security, analysis, and final disposition of data; and publication or dissemination of data and results.

Intentional or inadvertent breaches of confidentiality by investigators or their staff may occur. In addition, there may be attempts (usually in a legal context) to force or compel disclosure of confidential information for non-research purposes. The likelihood of such an attempt cannot be anticipated by virtue of the subject matter or setting of the research. [An informative overview of this issue can be found in Joe S. Cecil and Gerald T. Wetherington, Special Editors, Court-Ordered Disclosure of Academic Research: A Clash of Values of Science and Law 59 LAW AND CONTEMPORARY PROBLEMS. Number 3, Summer 1996."

The purpose of this paper is not to address all dimensions of this issue, but to focus on those aspects that are especially important in protecting against breaches of confidentiality.

Reducing Risk Through Confidentiality Protections

Confidentiality issues do not inhere in all human subjects research. For example, observation of behavior in public places where there is no interaction between the observer and the observed and where data are recorded in anonymous form involves no issue of confidentiality for subjects, investigators or IRBs. In some studies, the consent agreement establishes that research subjects neither seek nor want confidentiality (e.g., a political science study of legislative changes where directors of interest groups agree to participate knowing that what they report will be presented as part of the analysis of factors leading to change). In circumstances where a promise of confidentiality is not a part of an informed consent agreement, the protocol makes clear to IRBs the nature of the consent agreement and why biographical anonymity and confidentiality are not sought.

Issues of data confidentiality typically come into play when biomedical, social or behavioral science research involves data collection on identifiable individuals. Confidentiality protections should be developed consistent with the study design and the potential risk of harm from breaches of confidentiality. As the risk of harm incurred by disclosure increases, so should the level of protection from such harm. In some cases, the collected data may not require as high a level of security as in other cases (e.g., laboratory studies on the level of boredom associated with repetitive tasks does not involve the same risk of data disclosure as surveys of personal sexual orientation and experience; clinical laboratory data generally do not involve the same risk of disclosure as data from genetic testing or screening). In all cases where a promise of confidentiality is included in the consent agreement, it must be granted and secured—regardless of the level of risk.

Much of the risk in social and behavioral science research is related to inadvertent or unintended disclosure. An adequate data protection plan can and should reduce the risk of such occurrences. The OHRP has clarified that the Common Rule allows institutions and IRBs the flexibility to review and approve appropriately designed confidentiality protections.

Protocols should be designed to minimize the need to collect identifiable data by determining whether there is a legitimate reason to collect or maintain identifiers. Data can often be collected anonymously, or the identifiers can be removed and destroyed after various data have been merged. When it is necessary to
collect and maintain identifiable data, a data protection plan should describe the appropriate level of confidentiality protections based on the potential magnitude of the risk of harm from disclosure. All members of the research team and staff should receive appropriate training about securing and maintaining confidentiality and safeguarding data. Data should be physically secure, and all identifiable, confidential data not intended for secure archiving should be destroyed.

**Recommendation**

(1) OHRP should issue guidance to IRBs and the research community indicating that the degree of confidentiality protection required in research protocols be commensurate with the degree of risk of harm associated with the type of data collected. This guidance should emphasize that a good data protection plan can reduce or ameliorate the degree of risk of harm. (Such guidance will help IRBs in their work and will emphasize to individual investigators and their research teams the relationship between risk of harm and data protection.)
Confidentiality Protections

Efforts can and should be made to buffer or insulate research data from encroachment. When a determination is reached that the sensitive nature of the data and the potential risk of harm to individual subjects occasion legally supported confidentiality protections, the investigator (with the support of the institution) should pursue appropriate protections.

One such mechanism involves securing a certificate of confidentiality from the Department of Health and Human Services for applicable categories of research (biomedical, behavioral, clinical, mental health, drug or alcohol abuse).\(^1\) Another involves investigator and institutional compliance with mandatory confidentiality protections such as those provided through statutes covering the DOJ and DOEd.\(^2\) It is important to note that each of these confidentiality provisions has important limitations. It may apply only to certain categories of research or to research sponsored by a specific agency. It may protect the identity of the research subject, but not the data. Or, it may provide protection against compelled disclosure of data, but not voluntary disclosure (see examples in Table 1). OHRP should lead efforts to strengthen the current system of confidentiality protections.

Given the limits of these statutory protections, both investigators (and their research teams and staff) and their institutions are morally obligated to resist attempts to breach confidentiality through compelled or forced disclosures (e.g., subpoenas). This not only fulfills ethical obligations to the research subject, but also serves to prevent important breaches of confidentiality. It is important to note that courts may subpoena either data or investigators who have had conversations with participants.

Recommendations

(2) OHRP should clarify current research confidentiality protections, specifically (a) what certifications are available to protect data and how each certification works; (b) which agencies are authorized to grant which certifications; (c) when certifications may be sought; (d) exactly what each certification protects (e.g., only the identifiers or all of the data); and (e) what confidentiality gaps exist in certification (e.g., for some research, certificates of confidentiality that prohibit voluntary disclosure are needed). OHRP should lead an effort to ensure the adequacy of certificates of confidentiality issued by federal agencies.

(3) OHRP should lead a federal review of existing legal authorities, including statutes and regulations, that provide research confidentiality protections. This review should identify what the various laws protect, how the protections are obtained, who administers them, and where potential gaps in the protections exist. Where outstanding issues or gaps in research confidentiality are identified, a proposal to address these gaps in research confidentiality should be developed through a consensus process involving the scientific, research participant, and legal communities.

(4) OHRP should consider establishing an electronic clearinghouse linking information on all federal and state research confidentiality protections.

Limits in Confidentiality Protections

\(^1\) As provided under the Public Health Service Act [USC § 241(d)]
\(^2\) Department of Justice [USC and implementing regulations 28 CFR 22] or US Department of Education National Center for Education Statistics [USC 122 le-1]
In some instances, statutes and regulations limit when confidentiality can be maintained (e.g., mandatory reporting of child abuse), and IRBs and investigators need to consider such limits when evaluating confidentiality protections. Conflicts between the promise of any confidentiality safeguard and reporting statutes must be understood and resolved before the research begins. In such situations, it is important that all consent processes and documents and research protocols be designed and administered to describe clearly the limits on confidentiality so that subjects fully comprehend these limits when considering their participation. All potential conflicts between protecting confidentiality and requirements to release information (such as institutional policies or professional ethical requirements) should be explicitly communicated.

**Recommendation**

(5) OHRP should develop guidance for accurately and effectively describing confidentiality protections and limitations during the consent process. Special care should be given to describing how information will be maintained, when and under what circumstances confidentiality will or will not be maintained, and any reasonably anticipated risk associated with the disclosure of the information.

**Institutional Support**

The role of the research institution crosses the spectrum of research activities from the beginning stages of the study to final disposition of research data. Thus, the institution plays a critical role in ensuring the confidentiality safeguards stipulated by their investigators and their institutional IRBs. Specifically, investigators and IRBs are responsible for ensuring, implementing and evaluating the efficacy of data protection plans, and institutions are responsible for supporting those plans and their mechanisms for evaluation consistent with existing legal protections.

**Recommendation**

(6) Host research institutions should recognize and fulfill their obligations to actively support the investigator in protecting all confidential information from compelled disclosure or as otherwise agreed to in the data protection plan. To this end, OHRP should require this institutional responsibility as a term and condition of the assurance, and any future accrediting bodies should establish requirements in this area.

**Sharing Non-public Use Data**

As part of the research enterprise, scientists are encouraged by federal agencies and scientific societies to make their research data available to other scientists. This is often done in the form of public use files (discussed by NHRPAC in separate recommendations). The primary investigator is responsible for ensuring that shared data are protected. Occasionally identifiable research records are transferred to another investigator for additional analyses (in accordance with IRB approval of such restricted use). In such circumstances, secondary users must agree to protect the confidentiality of data even when it is shared or transferred. Specific consideration should be given to (1) communicating explicitly the data protection plan that needs to be in place by secondary users; (2) determining whether the original consent agreement limited the use of the data in future studies; and, (3) obtaining a written and binding agreement from the recipient that the data are bound by all of the conditions governing its original collection.

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3 NHRPAC adopted recommendations on Public Use Data Files at the January 28-29, 2002 Committee meeting. These recommendations address both the review of protocols to create public use data files and the use of such files. See NHRPAC website at http://ohrp.osophs.dhhs.gov/nhrpac/documents/dataltr.pdf
**Recommendation**

(7) OHRP should develop guidance for use by Investigators and IRBs clarifying that when identifiable data are shared by investigators, the same conditions for protecting and using the data that were present when the data were initially collected obtain for secondary users of those data.
TABLE 1.

Examples of Limitations and Differences in Federal Research Confidentiality Protections

I. Confidentiality Protections Limited to Specific Research Categories
   - Protections provided via BBS certificates of confidentiality (sexual attitudes, preferences, or practices; use of alcohol, drugs or other addictive products; illegal conduct; information damaging to financial standing, employability, or reputation; medical records which could lead to stigmatization or discrimination; psychological well being or mental health; genetic information). 42 U.S.C. §241(d)
   - Research on drug abuse or other controlled substances. 21 U.S.C. §872(c).

II. Confidentiality Protections that Apply to Research Conducted or Supported by a Specific Federal Agency
   - U.S. DOJ/Office of Justice Programs all research sponsored under the Omnibus Crime Control Act. 42 U.S.C. §3789(g) and 28 CFR part 22.
   - U.S. Department of Education, National Center for Education Statistics
   - National Center for Health Statistics. 42 U.S.C. §242m(d)
   - Agency for Healthcare Research and Quality. 42 U.S.C. §299c-3(c)
   - Federal Statistical Confidentiality Order

III. Confidentiality Protections that Protect Against Compelled Disclosure but not Voluntary Disclosure
   - Protections provided via HHS certificates of confidentiality
   Note: Most other federal statutes or regulations provide for release of identifiable data for other than research or statistical purposes if consent is obtained from the individual at the time the data are collected.

IV. Confidentiality Protections that Provide Conditions for Transfer of Identifiable Data
   - U.S. DOJ/Office of Justice Programs. 28 CFR part 22.
   - U.S. Department of Education, National Center for Education Statistics

V. Confidentiality Protections that Apply to Identifiable Information about Individuals and Organizations
   - U.S. DOJ/Office of Justice Programs. 28 CFR part 22
   - Agency for Healthcare Research and Quality. 42 U.S.C. §299c-3(c)