Genomics Guidance – Ethical Considerations

Overview
“Breakthroughs in genomics research and technology hold the potential for significant and wide-reaching clinical, scientific, and societal benefit. Such advances have disrupted traditional notions of identifiability and have introduced new considerations for IRBs, researchers and research subjects regarding the attendant risks and benefits presented by genomics research.” (PRIM&R Webinar: Forward-Looking Strategies for IRBs in the Genomic Age: Preparing for Shifting Concepts of Identifiability, 2018).

Genomic research has tremendous benefit to individual research participants and society at large. Genomics research usually generates identifiable information about an individual and those biologically related to them and/or within the same group in a region. Genomics research may uncover information about the participant that has a direct bearing on their/their family's future. This information may be unsuspected and it has potentially wonderful and potentially harmful consequences to the individual or their relatives.

This document serves as a guide to understanding the ethical considerations on completing genomic research.

Genetic information is information about…
- An individual's genetic tests (including genetic tests done as part of a research study)
- Genetic tests of an individual's family members
  - Family is defined as dependents and up to and including 4th degree relatives
- Genetic tests of any fetus of an individual or family member who is a pregnant woman, and genetic tests of any embryo legally held by an individual or family member utilizing assisted reproductive technology
- The manifestation of a disease or disorder in an individual's family members (family history)
- Any request for, or receipt of, genetic services or participation in clinical research that includes genetic services (genetic testing, counseling, or education) by an individual or an individual's family members

Definitions and General Information
For more definitions, please see Appendix A

Genome: A genome is an organism's complete set of DNA, including all of its genes. Each genome contains all of the information needed to build and maintain that organism. In humans, a copy of the entire genome—more than 3 billion DNA base pairs—is contained in all cells that have a nucleus (https://ghr.nlm.nih.gov/primer/hgp/genome).

Genotype: An individual's collection of genes. The genotype is expressed when the information encoded in the genes' DNA is used to make protein and RNA molecules. The expression of the genotype contributes to the individual's observable traits, called the phenotype.

Genomic(s): “Genomic” testing looks for variations within large segments of genetic material, regardless of whether its function is known or not.
Genomic Studies Usually Fall into One of these General Categories:
Anonymous donors, who are untraceable by any means. This would include samples that have been collected or will be collected solely for non-research purposes, such as pathology samples, where only the samples and not any identifying information linking the samples to individuals will be provided to the researcher.

Donors whose identity is known or traceable, but the investigator does not plan to track the individual.
- An example would be a study where specimens are obtained, banked, and coded by the investigator, or the investigator obtains samples and associated data from a public, private or commercial repository (and there is a key linking these to the subject’s name/identifying information), but no subject-related genomic analysis is planned at this time. (However, the investigator retains identifying information or ability to identify individual subjects should plans change in future.)

Donors whose identity is known or traceable, where the investigator plans to link genomic analyses to other study data from the specific individual, but will not inform subjects of the results of the analyses.
- An example would be a study about whether impulse control is hereditary, where the investigator would compare individual DNA data to behavioral assessment data, but would not inform the subject of these results.

Donors who are the subjects of genomic studies. The identities of these subjects are traceable and the investigator intends to inform the subject about the results of the analysis.
- An example would be a study of a cancer susceptibility gene, where it would be possible for the subject to learn the test results if they wished.
- If the condition under study is very serious or emotionally charged, it may be important to offer counseling resources to individuals bearing a disease-related gene. Other issues, such as confidentiality protection, are also especially critical for this type of study. See below for further discussion.

Donors who are the subjects of ongoing, prospective studies, where identities are traceable and the investigator intends to track the subjects through continuing contact for years into the future. Where tracking will occur, subjects have a much higher level of participation in the study (e.g., repeat visits, testing).

Confidentiality and Privacy in Genomic Research
Each person’s DNA sequence includes health and other information about them, their families, and their ethnicity and geographic groups. Technological advances mean that it is now cheaper and easier than ever to sequence and interpret genomic information. It is important to consider how best to ensure that the individual’s privacy is respected. While laws and policies exist that serve to protect the privacy of individual’s genomic information, there is ongoing debate as to whether further measures are needed.

Identifiable Populations: Ethnically, geographically, and linguistically identifiable populations present particular concerns with regard to privacy, stigmatization, and discrimination, since the ability to protect the privacy of these individuals or groups participating in research is diminished. For small communities or groups, relatively few numbers of family lines may make it especially challenging to protect participants’ privacy, even if research samples are de-identified. Depending on the community that the researcher aims to work in, approval to conduct the research from the authorized representative(s) of the community and/or group may need to be obtained prior to consenting individual subjects.
Involvement of Family Members: Genomic research may reveal new information about the research subject's health; in addition, the heritable nature of genetic information raises implications for the subject's relatives. Information about family members not involved in the study may be indirectly obtained through the research subject. Furthermore, genomic research using family pedigrees that can trace disease history may reveal family members who are carriers of a disease or will be affected themselves. These indirect results pose an ethical conflict between a possible duty to warn research subjects' family members and the protection of subjects' privacy.

If an investigator intends to obtain identifiable private information about the subject's family members, the family members may be considered human research subjects. In such instances, we will consider the necessity and/or appropriateness of a consent process for these "secondary subjects." Also, if the subject will be given genetic or genomic test results, the subject's consent to contact family members may be required.

Ethical Considerations Related to Risks of Genomic Research

Though there are many positives related to engaging in genetic research, genetic testing has potential downsides such as genetic discrimination, loss of anonymity, third party issues, and psychological impacts. Please find information below regarding ethical considerations and risks to participation in genomic research.

Privacy Issues Related to Participants:
- Researchers often need to put information on participant's genotypes/phenotypes into public scientific databases
- Although only anonymous data are submitted to specific databases, participants might still be identifiable by their relatives in the case of finding a rare disease or a rare mutation
- It is unclear where future technology may lead and if samples will always be anonymous

Psychological Issues Related to Participants:
- Finding out information about their family (ex: biological relatedness)
- Finding out information about their health (implications regarding inherited diseases or acquired diseases)

Employability and Insurability Issues Related to Participants:
- Discrimination issues as a result of genetic information
- Information discovered that can influence insurers decisions

Third Party/Secondary Participant Issues:
- Third Parties/Secondary Participants include family members, and groups that are geographically, ethnically, and linguistically similar
- Private information about third parties is now out there without their consent because the genome can reveal information about people related to the participant who provided the sample.
- This could put third parties at legal risk should their genomic information be used in legal investigations
- This could related in private medical and health information about a person, to now be publicly accessible
General Issues
- Ethical issues have also been raised by the increasing use of genetic variation screening, both in newborns, and in adults by companies. It has been asserted that screening for genetic variations can be harmful, increasing anxiety in individuals who have been found to have an increased risk of disease.

IRB Related Issues/Questions Regarding Ethical Practices and Study Design
- IRB Principle - Respect for Persons
  - Respect for Persons is about protecting the autonomy of all people and treating them with respect and allowing for informed consent
  - What did the donor/subject know and agree to regarding genomic research?
  - What is unknowable regarding risks (identifiability, future technologies, etc) and is it relevant/important to the participant and the study?

- IRB Principle - Beneficence
  - Beneficence is about the philosophy of maximizing benefits for the research project and minimizing risks to the research participants
  - Is the proposed use of the sample and subsequent information from the sample intended to answer an important question that could improve human health? for the participant? for others?
  - Is the use of the sample (or collection of a new sample) an efficient use of resources?

- IRB Principle - Justice
  - Justice is about ensuring reasonable, non-exploitative, and well-considered procedures are administered fairly. This includes the equal and fair distribution of costs and benefits to potential research participants
  - Will the risks of use and the benefits of the information derived from the research be distributed fairly?
  - Could the use result in group harms or other consequences beyond those anticipated risks already communicated to the donor/subject?
  - Are there plans to include other donors/specimens in the study? Is anyone left out by not collecting new samples or by only collecting/using certain samples?
  - Does the study design pose risks that require more thoughtful consideration than those solely to the primary participants?
  - Can anything damaging/stigmatizing/marginalizing to discrete and insular groups occur as a result of this research?

Considerations of IRB Principles Regarding Individual Rights and the Common Good
- The traditional paradigms for subject protection often emphasize individual autonomy at expense of the principles of beneficence justice
- Many of the limits on the use of data/specimens that have been imposed to address historical imperatives related to prior unethical acts may punish everyone via opportunity costs and diminished autonomy to participate in additional research
- Given conditions of scarce resources, the expense of collecting new data and specimens is a relevant and needed consideration
- We must consider how we responsibly use and re-use data in order to maximize good and decrease burden for many participants
- When additional samples are not collected, and when older samples are not used - this creates an unequal distribution of risks which reduces the balance of the principle of justice
● If we only use samples from certain populations, we leave others out and end up with representations that don’t represent all, and it’s unfair
● Research exceptionalism - treating research decisions so differently that it reduces autonomy for participants by imposing what we think the privacy boundaries should be instead of engaging the participants in what they also think is acceptable. This sometimes gets in the way with how people want to contribute altruistically.

Considering Risks in Context and Not Overestimating/Underestimating Risks
● IRB’s currently evaluate and sometimes monitor data security plans
● In order to re-use samples/data, the IRB requires broad consent, specific study consent, or special conditions to waive consent (rare in genetic research)
● Unauthorized re-identification of samples and data is already prohibited and there have been no verified cases of research related re-identification
● The likelihood and magnitude of harm from the genetic research must already be identified in context and balanced against individual and global benefits derived from the research.
● Overestimating risks can be harmful because it can
  ○ Obstruct important research that could improve health
  ○ Slow important research to the point that critical answers are delayed and people suffer unnecessarily
  ○ Prevent re-use of existing specimens/data requiring collection of new specimens/data - which can be a waste of scarce resources, unnecessary risks to new donors/subjects).

● Underestimating risks can be harmful because it can
  ○ Directly harm your participants (including third party and relevant groups)
  ○ Negatively influence your data and results
  ○ Inhibit your data from being use to contribute to generalizable knowledge

● Discussing Identifiability and Re-Identifiability
  ○ IRBs already require researchers to discuss re-identifiability
  ○ IRBs already ask that researchers provide information about what other information is available that could be used in conjunction with this data, to re-identify a person and discussion as to if it is reasonable that re-identification would happen
  ○ Could a statistical expert say “the risk of re-identification is very small that the information could be used alone or in combination with other reasonable available information.”

● Practical Risks to Consider, Plan for, and Not Over-Estimate.
  ● Security breaches by bad actors or accidental
  ● Concerns about intentional misbehavior of researchers (unlikely)
  ● Changing social norms about privacy and self-disclosure
  ● Context-specific differences in the boundary between public and private space
  ● Notations of theoretical (dignitary) harm to individuals and groups

Risk Mitigation Strategies
● Data Discipline and Data Protection
  ○ Collect the minimum amount of data necessary to answer your question
    ■ Make reasonable efforts to limit data/PHI to the minimum necessary to accomplish intended purpose
    ■ Don’t collect the information if you don’t need it
  ○ Does everyone on the research team need access to all of the data?
    ■ Implement user based access restrictions appropriate to role and expertise.
  ○ Coding data in confines of data collection.
  ○ Keeping data anonymous when possible
○ Use data security measures that is appropriate to the sensitivity level of the data and as outlined in the approved IRB application
○ Ensure all software is updated and current

● Applicable Laws, Regulations, Policies, and Expectations
○ Understand the laws and regulations: GINA, HIPAA, NIH, and 45 CFR 46 all provide varying degrees of protection regarding genomic information and how it can be used.
○ See Appendix B for detailed descriptions of individual laws, regulations, policies, and expectations.

● Informed Consent Process and Forms
○ Accurately informs participants of exactly what they are and are not agreeing to so that they can autonomously make their own decisions regarding their participation
○ Identifies risks and mitigation strategies so that participants can make informed choices

● Public Perception and Public Communication
○ Public notices regarding how information is used or will be used
○ Provide additional information to participants after data is used.

● Awareness regarding changing landscape of data identifiability
○ Understand the role that your (or others) access and expertise play in re-identification
○ Understand and communicate that technology evolves and we cannot predict if samples will be re-identifiable in the future.

● Identifying boundaries among private and public spaces and articulating how the boundaries of your research engage or do not engage those environments.

Benefits of Participating in Genetic Research
● Participating in genomics research is an opportunity to support scientific exploration of the genome and to help to understand, prevent, detect and better treat disease.
● Often, only through the recruitment of large numbers of participants from different populations can major scientific advances be achieved. In some cases, research participants may also gain some individual benefit, such as diagnosis of a disease or access to a treatment in development.
● A wide range of genomic research studies need participants, each with different levels of involvement, and it is important to understand the scientific purpose of any study and any potential personal benefit or risk from participation.
● Receipt of results and information about themselves, family, and others that may help with health issues in the future, treatment plans, or generall life planning
● Providing insight into their own, their family’s, and others’ conditions
● Understanding the differences between inherited and acquired diseases
● Contributing to the knowledge base regarding the mitigation of, treatments of, and cures of varying diseases

Investigators need to address factors that may affect the rights and welfare of their study subjects (as outlined above), explain their thoughts on these problems and how they plan to handle the issues, as well as how they plan to communicate them to subjects. This should be reflected in both the protocol and the consent documents. Details are noted below.

Discontinuing Study Participation:
Participants have the right to withdraw from a research study at any time. However, there are likely to be practical limits on the ability of participants to withdraw samples, genomic data, or health information that have been contributed to a biorepository. The potential limitations of withdrawing samples and data from research should be discussed in the consent form and as part of the consent process.
For genomic studies that involve bio-banked samples and/or storage of associated data in unrestricted or controlled-access databases, complete withdrawal of samples and data may not be possible once samples or data have been distributed to other laboratories. However, it may be possible to withdraw samples or data from future distributions. In such circumstances, the consent document and the informed consent process should include a full explanation of the extent to which withdrawal of samples or data is possible and what the process is.

**Protections for Subjects: Laws, Regulations, Sponsor Expectations, and Common Practice**

*The Genetic Information Nondiscrimination Act (GINA)* prohibits health insurers and employers from requesting or requiring genetic information from an individual or an individual's family members, and further provides legal protection against discrimination on the basis of a person's genetic information.

*The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule* establishes protections to maintain the confidentiality of patients' individually identifiable health information. In 2013, as required by the Genetic Information Nondiscrimination Act, the Privacy Rule was modified to establish that genetic information is health information protected by the Privacy Rule to the extent that such information is individually identifiable, and that HIPAA covered entities may not use or disclose protected health information that is genetic information for underwriting purposes.

**Certificates of Confidentiality:** When dealing with sensitive data, the NC State IRB may require that the investigator obtain a "Certificate of Confidentiality" ("CoC"). Certificates of Confidentiality are issued by the National Institutes of Health (NIH) to protect identifiable research information from forced disclosure. CoC’s allow the investigator and others who have access to research records to refuse to disclose identifying information on research subjects in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. However, there are limitations to this protection (e.g., it does not apply to any state requirement to report certain communicable diseases, or to legal or ethical requirements for researchers to report child abuse to appropriate authorities, etc.)

For more Information regarding laws, regulations, policies and more, please see Appendix B

**Considerations for return of research results and incidental findings**

The IRB recognizes that plans for returning results either directly related to the research or incidental findings revealed during the course of the research will by necessity vary between individual studies, therefore uniform requirements are neither appropriate nor desirable. Nonetheless, there are several important points that investigators should consider in making the decision to return results and in the devising and implementing plans to return results. Unless it is an obligatory part of the research design, participants should be provided with the option to choose whether or not they wish to be informed of the results of the study or of incidental findings. This should be clearly indicated as an opt-in or opt-out selection on the informed consent document.

Determining what results to return to participants. If it is decided to return research results or incidental findings, the investigator must determine what results they will give back to the participant. In making this determination, the investigator should consider the following:

- The strength of the evidence linking the mutation (or other genetic finding) to a disease phenotype. What is the penetrance of the phenotype? Is there consensus among experts in the field that the finding is linked to disease?
● Whether there is a clinically validated, independent test that can be used to verify the results.
● Whether there is an action that the individual can take as a result of learning this information that will modify their risk. Are there other important actions that might be taken as a result of learning this information, e.g., family planning?
● Whether there are serious consequences to the individual of not learning and/or acting on the information.

The strongest case for returning results or incidental findings would be a mutation that was indisputably disease causing, had 100% penetrance, could be independently verified and for which an action would prevent serious health consequences. On the opposite end of the spectrum are findings for which the evidence of disease association is weak, there is no independent test and there is no action to be taken to modify risk. Most fall in between these extremes, and there is no clear consensus as to what mutations would be considered most reportable. Furthermore, as more studies are conducted new mutations will be found, new tests and therapies will be developed and the evidence for particular associations may strengthen or weaken Therefore, the reportability of specific findings is a moving target.

Should an investigator deem it appropriate to return either research results or incidental findings to a participant, the plan must provide for adequate counseling and access to resources such that the person is fully informed as to the implication of the findings. In general, this will depend on the expertise of the investigator and the research team. If the results being returned are outside the expertise of the investigator, it may be desirable to include additional persons with expertise. If there are significant implications for family members, or for family planning on the part of the participant, the use of a professionally trained genetic counselor may be an important and desirable part of the plan. The investigator should also consider whether they will provide additional confirmatory testing to the participants, whether they are willing to test family members, and how the cost for such testing and counseling will be covered.

The return of individual research results (IRRs) and incidental findings (IFs) from genomic research is an issue of interest among researchers, ethicists, sponsors, policy makers, research subjects, and others. As indicated above, when conducting clinical research studies, scientists may discover new health-related information about volunteers who have chosen to participate in the studies. This raises the question of when and how it is appropriate for the scientists to share such research findings. Currently, the only federal law regarding return of individual genetic testing research results and incidental findings is the Clinical Laboratory Improvement Amendments of 1988 (CLIA), which sets quality standards for all laboratories performing clinical testing. CLIA prohibits the return of individual research results to study subjects unless the tests were physician-ordered and the results were obtained in a CLIA-certified laboratory.

Generally it is recommended that individual research results of genetic or other genomic testing for research purposes rather than clinical reasons should not be shared with subjects or their families. For such studies, the fact that this information will not be passed on to subjects must be made clear in the protocol and consent form(s). However, if the investigator does intend to share results of genetic or other genomic testing with subjects, s/he will need to provide ethical and scientific justification for passing on such information to the subjects or family members. The NC State IRB will determine if disclosing genetic or other genomic testing results is appropriate, considering factors including:

● Clinical relevance and implications of the genetic or other genomic testing results.
● Reliability of genetic or other genomic testing results.
In addition to presenting justification for sharing results, the investigator must provide:

- A plan in the protocol outlining how such disclosure will be managed, including methods by which subjects will be informed of their results, qualifications of individuals who will disclose results (e.g., training and experience in discussing social, psychological and other non-physical risks); whether counseling will be offered, and if so, the qualifications of the counselors and who will pay such costs. This plan should also include how the investigator will minimize the risks of such disclosure and preserve confidentiality of test results.
- A consent process and document(s) giving subjects the option of receiving test results (e.g., by initialing boxes in the signature block), and providing information about plans for minimizing risks, preserving confidentiality, etc.

Subjects' "Right Not to Know"
Subjects generally retain the right not to receive information about the results of a study that reveals their genetic status. A possible exception occurs where early treatment of a genetically linked disease could improve the individual's prognosis. In such circumstances, investigators may have a duty to inform the subject about the existence of the genetic defect and advise her/him to seek medical advice. As legal opinion and policies in this regard are still evolving, an investigator should consult with the NC State IRB if such a situation arises; these situations will be handled on a case-by-case basis by the NC State IRB.

Secondary data obtained from banked specimens
Returning results from specimens that were obtained from biobanks adds additional layer of complexity. Secondary users of banked specimens have no relationship with the participant, and the participant is almost certainly not aware of the details of the study for which the specimen is now being used. For the primary investigator (the one that collected the specimen) to assume responsibility for reporting back to the participant the findings of other, secondary users would be not only extremely burdensome, but problematic. In that instance, the researcher would be vouching for the validity of another researcher's results. Therefore, unless the finding is thought to represent a serious and preventable threat to the health and welfare of the individual, the most appropriate plan may be to not return any findings.

Data Disposition: A detailed plan for data disposition must be articulated in the IRB protocol. This includes physical samples, hard copies of data, and digital data.
Appendix A: Definitions

Whole genome sequencing (also known as WGS, full genome sequencing, complete genome sequencing, or entire genome sequencing) is the process of determining the complete DNA sequence of an organism's genome at a single time. Whole genome sequencing has largely been used as a research tool, but is currently being introduced to clinics.

- Whole genome sequencing should not be confused with DNA profiling, which only determines the likelihood that genetic material came from a particular individual or group, and does not contain additional information on genetic relationships, origin or susceptibility to specific diseases.
- Whole genome sequencing should not be confused with methods that sequence specific subsets of the genome—such methods include whole exome sequencing (1% of the genome) or SNP genotyping (<0.1% of the genome).
- When an individual undergoes whole genome sequencing, they reveal information about not only their own DNA sequences, but also about probable DNA sequences of their close genetic relatives. This information can further reveal useful predictive information about relatives' present and future health risks.

Genotyping is the process of determining differences in the genetic make-up (genotype) of an individual by examining the individual's DNA sequence using biological assays and comparing it to another individual's sequence or a reference sequence. Traditionally genotyping is the use of DNA sequences to define biological populations by use of molecular tools. It does not usually involve defining the genes of an individual.

- The genotype is the part of the genetic makeup of a cell, and therefore of an organism or individual, which determines one of its characteristics (phenotype).
- A phenotype is the composite of an organism's observable characteristics or traits, such as its morphology, development, biochemical or physiological properties, behavior, and products of behavior (such as a bird's nest). A phenotype results from the expression of an organism's genetic code, its genotype, as well as the influence of environmental factors and the interactions between the two.

Exome sequencing, also known as whole exome sequencing (WES), is a genomic technique for sequencing all of the protein-coding genes in a genome (known as the exome).

- It consists of two steps: the first step is to select only the subset of DNA that encodes proteins. These regions are known as exons—humans have about 180,000 exons, constituting about 1% of the human genome, or approximately 30 million base pairs. The second step is to sequence the exonic DNA using any high-throughput DNA sequencing technology.
- 1% of the genome

DNA profiling (also called DNA fingerprinting, DNA testing, or DNA typing) is the process of determining an individual's DNA characteristics, called a DNA profile, that is very likely to be different in unrelated individuals, thereby being as unique to individuals as are fingerprints

- DNA profiling is most commonly used as a forensic technique in criminal investigations to identify an unidentified person or whose identity needs to be confirmed, or to place a person at a crime scene or to eliminate a person from consideration. DNA profiling has also been used to help clarify paternity, in immigration disputes, in parentage testing and in genealogical research or medical research.
- Although 99.9% of human DNA sequences are the same in every person, enough of the DNA is different that it is possible to distinguish one individual from another, unless they are monozygotic ("identical") twins.

DNA sequencing is the process of determining the precise order of nucleotides within a DNA molecule. It includes any method or technology that is used to determine the order of the four bases—adenine, guanine, cytosine, and thymine—in a strand of DNA.
Appendix B: Resources

Federal Laws:
Genetic Information Nondiscrimination Act (GINA):
- Generally prohibits health insurers or health plan administrators from requesting or requiring genetic information of an individual or an individual's family members, or using such information for decisions regarding coverage, rates, or preexisting conditions.
- Prohibits employers from using genetic information for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment.
- Provides a baseline level of protection against genetic discrimination for all Americans.
- Provisions prohibiting discrimination in health coverage based on genetic information do not extend to life insurance, disability insurance, or long-term care insurance.
- Provisions prohibiting discrimination by employers based on genetic information generally do not apply to employers with fewer than 15 employees.

Health Insurance Portability and Accountability Act (HIPAA):
- Remove and redact specific IDs from data sets.
  - The HIPAA covered entity must not have “actual knowledge that the info could be used alone or in combo with other info to identify the individual; any other unique identifying number, characteristic or code.
- People can get a list of covered entities regarding how their data is disclosed. This can sometimes be be “general” accounting.

Clinical Laboratory Improvement Amendment (CLIA):
- This does not apply to research - but may apply to facilities that perform research
- The Centers for Medicare & Medicaid Services (CMS) regulates all laboratory testing (except research) performed on humans in the U.S. through the Clinical Laboratory Improvement Amendments (CLIA).
- The objective of the CLIA program is to ensure quality laboratory testing.
- For entities that are covered by HIPAA but are not CLIA certified, there is a possible regulatory tension. HIPAA says patients have right to access all PHI about themselves from any HIPAA covered entity however, the Clinical Lab Improvement Amendment (CLIA) prohibits return of results of testing performed in any non-CLIA certified lab.

North Carolina Laws:
NC laws regarding screening for hereditary and congenital disorders as well as one on setting up a birth defects monitoring program (and protection of related records):
- § 95-28.1A. Discrimination against persons based on genetic testing or genetic information prohibited.
- § 130A-125. Screening of newborns for metabolic and other hereditary and congenital disorders.

NC Bills and Statutes:
- Genome Bills in NC
- Genome Statutes in NC

Federal Regulations: 45 CFR 46
- Common Rule: IRB Regulations before January 19, 2019
  - Does not address genomic research
  - Does address adequate data protection for identifiable data
  - Does address Risk/Benefits Analysis
- Final Rule: IRB Regulations on and after January 19, 2019
  - Addresses Genomic Research.
  - Requires periodic reassessments of identifiability of data
  - Discusses technology as related to generating identifiable data even in analysis
  - IRB jurisdiction: is there adequate privacy/confidentiality protections and HHS must issue guidance regarding what adequate protection means.

NC State University Regulation and Policy:
- 04.25.05 Equal Opportunity and Non-Discrimination Policy
- 04.05.06 Equal Opportunity, Title IX, and Non-Discrimination Training for Employees

NC State University policy and standard procedures:
Federal Organizations:

- The National Institutes of Health (NIH) Genomic Data Sharing (GDS) Policy:
  - Sets forth expectations that ensure the broad and responsible sharing of genomic research data. Sharing research data supports the NIH mission and is essential to facilitate the translation of research results into knowledge, products, and procedures that improve human health.
  - Investigators should de-identify human genomic data that they submit to NIH-designated data repositories according to the standards set forth in the HHS Regulations for the Protection of Human Subjects 25 to ensure that the identities of research subjects cannot be readily ascertained with the data. Investigators should also strip the data of identifiers according to the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule.
  - Although the data in the NIH database of Genotypes and Phenotypes (dbGaP) are de-identified by both the HHS Regulations for Protection of Human Subjects and HIPAA Privacy Rule standards, the NIH has obtained a Certificate of Confidentiality for dbGaP as an additional precaution because genomic data can be re-identified.
  - For studies initiated after the effective date of the GDS Policy, the NIH expects investigators to obtain participants' consent for their genomic and phenotypic data to be used for future research purposes and to be shared broadly. The consent should include an explanation about whether participants' individual-level data will be shared through unrestricted- or controlled access repositories.
  - For studies using data from specimens collected before the effective date of the GDS Policy, there may be considerable variation in the extent to which future genomic research and broad sharing were addressed in the informed consent materials for the primary research. In these cases, an assessment by an IRB, privacy board, or equivalent body is needed to ensure that data submission is not inconsistent with the informed consent provided by the research participant.
References


National Human Genome Research Institute: Issues in Genetics, “Human Subjects Research in Genomics”

National Human Genome Research Institute: Issues in Genetics, “Informed Consent for Genomics Research”

National Human Genome Research Institute: Issues in Genetics, “Privacy in Genomics”

UC San Diego, Human Research Protections Program, "Issues on DNA and Informed Consent"

PRIM&R Webinar: Forward Looking Strategies for IRBs in the Genomic Age

Washington University IRB Guidance, reviewing Studies Involving Genetic Research

UC Berkeley Genetic/Genomic Research IRB Guidance

Article: Genetic Research with Stored Biological Materials: Ethics and Practice
  ● By Leslie Wolf, Timothy Bousley, and Charles McCulloch

Article: Genomic Research Data: Open vs. Restricted Access
  ● By David Resnik

Research ethics and the challenge of whole--genome sequencing
  ● By Amy McGuire, Timothy Caulfield, and Mildred Cho

The Common Rule Canary in the Mine: How the Final Common Rule Presages A Need for a New Way to Protect Human Subject Privacy in the Genomic Age
  ● By Medical Research Law and Policy Report

Genetics researchers’ and iRB professionals’ attitudes toward genetic research review: a comparative analysis
  ● By karen Edwards, Amy Lemke, Susan Trinidad, Susan Lewis, Helene Starks, Katherine Snapinn, Mary Quinn Griffin, Georgia Wiesner, Wylie Burke, and GRRIP Consortium

IRB perspectives on obligations to disclose genetic incidental findings to research participants
  ● By Catherine Gliwa, Llana Yurkiewicz, Lisa Soleymani Lehmann, Sara Chandros Hull, Nathan Jones, Benjamin Berkman

Genomics Really Gets Personal: How Exome and Whole Genome Sequencing Challenge the Ethical Framework of Human Genetics Research
  ● By Holly Tabor, Benjamin Berkman, Sara Chandros Hull, and Michael Bamshad

Informed Consent for Exome Sequencing Research in Families with Genetic Disease: The Emerging Issue of Incidental Findings
  ● By Amanda Bergner, Juli Bollinger, Karen Raraigh, Crystal Tichnell, Brittney Murray, Carrie Lynn Blout, Aida Bytyqi Telegrafi, and Cynthia James