CHAPTER 3

THE CHALLENGE OF GENETIC INFORMATION IN WORKER STUDIES

Key Points:

- **Genetic information gathered—intentionally or unintentionally—through worker studies presents unique challenges because it may reveal genetic information about a potential disease or other trait not yet expressed that could have significantly harmful consequences on the subject's future employability, insurability, and/or socio-economic status.**

- **A challenge specific to the use of tissue samples is that DNA is, at least in theory, a unique individual identifier and could be used to identify the donor.**

- **Genetic testing or screening should never be mandatory, especially in the workplace. Ideally, when genetic screening or testing is to be carried out, counseling is essential if the test results may entail choices or economic consequences for the person tested and his or her family.**

Are Genetic Studies Really Different?

Genetics and biomedical technology have opened vast new avenues for research and can provide mankind with much needed diagnostic and therapeutic tools. But, where human life and dignity are at stake, technology cannot be left on its own to govern ethics, nor can health technology, practices, and procedures be left to the vagaries of economic forces and personal interests, fears, or vulnerabilities. Efforts must be made to mitigate the risks to subjects so that the safety and rights of individuals are adequately protected.

Institutional Review Boards (IRBs), researchers, and other stakeholders must ensure that genetic information and genetic research are introduced into workplace studies in ethically acceptable ways. Additionally, it is also important to allay fears and to reassure the public that adequate controls exist to prevent abuses of genetic information and unacceptable practices.

When used properly, this knowledge will be vital to achieving better worker health and disease prevention. Along with these positive effects, however, are concerns about who will have access to personal genetic information and how it will be used. Therefore, these advances will be accepted only if they are applied in accordance with evolving regulatory guidelines and within accepted ethical principles including respect for persons, justice, and beneficence (see Chapter 2).

Because the genetic code is passed from parent to offspring and is partially shared with all relatives, every genetic test has the potential to involve knowledge about many individuals in addition to the subject. Perhaps even more important is the fact that genetic information may reveal a potential disease or other trait not yet expressed that could have harmful consequences on the

CASE STUDY

BERYLLIUM: TO TEST OR NOT TO TEST

A company that uses large quantities of beryllium in manufacturing semi-conductors learns that several workers exposed to the dust and fumes of machining beryllium are susceptible to chronic beryllium disease (CBD), which slowly hardens the lungs and may lead to death. There is no treatment. The company has always adhered to federal standards for a minimum amount of beryllium dust. Nevertheless, a recent incidence of new cases of CBD suggests that for a small group of persons (perhaps 1% to 8% of the general population) who are genetically susceptible there may be no "safe" threshold for beryllium. There is no substitute for beryllium in making semiconductors. There appears to be no way to further reduce the already low level of beryllium in the plant, and there is no evidence that further reductions, if possible, would protect genetically sensitive individuals.

The company believes that genetic testing of employees would enable susceptible persons to find other work before they developed CBD. (State law prevents pre-employment testing, but allows routine physical examinations after hiring.) The union disagrees. The union would rather see routine monitoring of all workers for the early signs of CBD, arguing that monitoring is more likely to ensure a safe workplace and also to protect people's rights to work. The company argues that monitoring will detect susceptible individuals too late, after an inevitable decline in lung function has begun. This pits individuals' autonomy (rights to decide about their work) against the duties of institutions (employers, state) to protect vulnerable parties.

What should be done?

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subject's future employability, insurability, and/or socio-economic status.

While it is correct to assume that the traditional, ethical guidelines used in worker studies also apply to research using genetic information, concerns about the use of genetic information extend beyond those found in traditional worker and workplace studies. For example:

- Genetic information may affect an entire family, rather than just the individual.
- Genetic discoveries may be predictive of future adverse events in an individual's or family member's health (but also may be inconclusive).
- Genetic information and exposure to workplace conditions may have a direct negative impact on the subject's employability insurability, and socio-economic status.

Therefore, those involved in genetics research, testing, or screening have an even greater responsibility and requirement to protect the subject's privacy. As part of the informed consent process, researchers must ensure that the individual is fully aware of the potential health, employment, and social risks and that the subject's participation is truly voluntary.

Researchers, institutions, policymakers, IRB members, and other health care workers must understand the importance of ensuring that genetic information is collected, used, and protected in an ethically and legally acceptable manner. These groups and individuals should also be aware that controls must be actively used to help prevent abuses of genetic information and unacceptable practices, or may even prevent the collection of some genetic information.

The Use and Limits of Genetic Testing: Defined

The collection and use of genetic information can be categorized as either research or non-research (see Chapter 1). Typically, genetic information is considered ***non-research*** when it is applied in a clinical setting to diagnose and to treat an individual with a specific condition. ***Research*** efforts collect data from subjects in an effort to establish cause-and-effect relationships and contribute to general scientific knowledge. Misuse of the information obtained through genetic research has the potential to adversely affect the individuals tested.

Early in 2000, to limit the possibilities of adverse effects to federal employees, President Clinton issued an executive order titled "To Prohibit Discrimination in Federal Employment Based on Genetic Information" (see Appendix E). Included under this order, federal agencies may not: (1) collect, request, or otherwise require genetic information from an employee; (2) may not discharge or refuse to hire an employee based on genetic information it may have; (3) may not classify or segregate employees based on genetic information; nor (4) disclose protected genetic information except under specifically permitted instances. The following terms, applicable to genetic testing, are defined in the executive order (refer to Appendix E):

Genetic test means the analysis of human DNA, RNA, chromosomes, proteins, or certain metabolites in order to detect disease-related genotypes or mutations. Tests for metabolites fall within the definition of “genetic tests" when an excess or deficiency of the metabolites indicates the presence of a mutation or mutations or identifies the genotype.

Genetic monitoring means the periodic examination of employees to evaluate acquired modifications to their genetic material, such as chromosomal damage or evidence of increased occurrence of mutations, that may have developed in the course of employment due to exposure to toxic substances in the workplace, in order to identify, evaluate, respond to the effects of, or control adverse environmental exposures in the workplace.

Genetic services are health services, including genetic tests, provided to obtain, assess, or interpret genetic information for diagnostic or therapeutic purposes, or for genetic education or counseling. If genetic information and/or tissue samples obtained during the administration of “genetic services” are also used to verify, validate, or collect additional data to support a clinical or research procedure, that additional use of the genetic information falls within the definition of “research,” and the protections of human subjects research should be applied.

Furthermore, because terms relating to genetic **research** are also often used interchangeably, they must be interpreted within the context of the physician’s or researcher’s activities and intentions, and the more general definitions of research and non-research should be used to determine when the protection of humans subjects research should be applied.

Two terms closely associated with genetic **testing** are **presymptomatic** and **susceptibility** testing. **Presymptomatic** testing refers to identification of healthy individuals who may have inherited a gene for a late-onset disease and, if so, who will likely develop the disorder if they live long enough. Presymptomatic testing is generally associated with clinical situations in which physicians collect genetic information with the intent of treating or counseling the individual subject or patient. Although **susceptibility** testing may also be used in the clinical context, it is often used to screen healthy individuals to identify a genetic predisposition that may put them at increased risk for a genetically caused disease (e.g., chronic beryllium disease). In the context of the workplace, screening may allow researchers to characterize the predisposition of the subject to specific workplace hazards. Susceptibility testing also poses social and economic risk to the subject when the privacy of the subject is not maintained or testing is not voluntary.

Researchers may have the option of obtaining either **specific-use consent** or a **blanket consent**. **Specific-use consent** permits limited additional research only in study topics specified in the initial informed-consent documents. **Blanket consent** allows broad use of collected materials without obtaining additional informed consent from the research subjects. Subjects who agree to either a limited or blanket consent must also be advised

that they may cancel or withdraw their consent at any time in the future or be advised when and if this is not feasible.

When Does “Testing” Become “Research”?

Genetic testing may initially be performed to diagnose, treat, or counsel an individual subject. Since the original intent is not to generate or contribute to general knowledge, the procedure is not initially considered “research.” However, if the subject’s private genetic information and/or tissue samples will also be used to validate or to improve a procedure or test, or if the information obtained during the “test” is to be used in a subsequent study designed to add to generalizeable knowledge, this constitutes human subject “research” and an IRB review is required ***before*** sample collection and testing are begun.

Regardless of the initial intent of the collection of genetic data, researchers and all study stakeholders must understand that improper use of genetic screening data in the workplace can expose individuals to risks that affect their employability, insurability, autonomy, livelihood, and family relationships. Researchers must also be aware of the fact that tissue samples collected and stored for non-genetic purposes still possess genetic information and must be protected from potential misuse in the same manner as stored medical data or records of genetic test results.

The Risk–DNA is an Identifier

Genetic information is sensitive because it discloses information about individuals that can be embarrassing or even harmful if revealed outside of the research or medical environment. A challenge specific to the use of genetic information is that, in principle, it is not possible to remove the individual “identifier” from tissue samples.

The advances that have occurred in human genetics during the past 20 years have revolutionized knowledge and understanding of the role of inheritance in health and disease. Catastrophic single-gene disorders, certain behaviors, and predisposition to some diseases such as some cancers and heart disease, as well as individual susceptibility to some materials and conditions—as found in workplace exposures—may be inherited.

An individual’s genetic information may be of interest to a wide variety of individuals and organizations. Insurers and employers may want to use it as a predictor of future illness, to determine future health-care costs, or to determine the ability to perform a job. Family members, educational institutions, or the courts may also want access to genetic information. There have been cases where genetic information has been used to deny medical benefits to retirees having illnesses with a known genetic basis. Cases of insurance and employment discrimination based on genetic information have also been reported.

Within the worker community, concerns about the potential for loss of health care and life insurance or for discrimination in employment are real. The problem is further compounded by the fact that genetic samples are, by their very nature, identifiers. The

combination of these forces, and the possible economic consequences to the worker-subject, make workers a vulnerable population with respect to genetic or other medical information, samples, or data when collected as part of a worker health survey or worker study.

Counseling and Informed Consent

As in other worker studies, voluntary informed consent is essential for projects that involve genetic information. Informed consent for any study must be obtained if the specimen can be linked to the person from whom it was taken. Furthermore, subjects should be informed of possible future uses of the specimen, whether identifiers will be retained, and, if so, whether individuals will be re-contacted about new developments concerning their health care.

In a research or health study situation, elements of an informed consent process include an explanation of:

- The experimental nature and purpose of the study.
- Why the individual is invited to participate, and that the participation is voluntary.
- The procedure.
- The discomforts and risks (if any) of the test to both the individual and the family.
- The uncertainty of the results of the test for prediction and accurate genetic counseling.
- The possible benefits to others and to science.
- The confidentiality of records identifying the test individual.
- Whom to contact for questions about research or in the event of a research injury.
- The right of the individual to withdraw at any time, although data and/or samples may not always be able to be withdrawn.
- The possible future uses of blood and other tissue specimens obtained.
- When and for how long personal identifiers will be retained with the specimens.
- When and if individuals may again be contacted about new developments concerning genetic information or their health care.

Adequate genetic counseling is important before any genetic testing, screening, or research occurs. Ideally, counseling should continue when results, choices, and outcomes are explained. If, however, the results and conclusions obtained through experimental or investigative research are not ***clinically validated***, disclosure of test results to the research subject becomes ethically and legally problematic and, in some cases, may be prohibited by regulation. These, as well as other conditions of the research, must be included and disclosed to the subject as part of the informed consent process (see Chapter 2).

Genetic Research Means Additional Challenges for the IRB

Individuals who participate in worker studies are protected by the Common Rule, which requires that all research involving human subjects that is supported, conducted, or

regulated by federal agencies must be reviewed by an IRB. IRBs are responsible for protecting the interests of the research subjects. Because the use of genetic research is a relatively new and rapidly developing research tool and because of the personal, economic, and social impact genetic research and testing results may have on the well-being of subjects, IRBs must add the science and ethics of genetics to their expertise and area of responsibility. In addition to its usual responsibilities, IRBs must be assured that researchers will adequately explain to participants how genetic information and tissue samples will be used and maintained, to what extent the information is protected, and, if applicable, how it may be used in subsequent research.

Many effective safeguards to protect the confidentiality of research subjects are available. As discussed previously, the Federal Privacy Act of 1974 protects health, research, and other records held by federal agencies. Additionally, recommendations to restrict the use of genetic information in health insurance and in the workplace have been developed by the National Human Genome Research Institute (NHGRI) and many professional societies.

Currently, several state and federal laws restrict some access to genetic information by health insurance carriers and employers. Comprehensive federal protections, however, are not in place, and the U.S. Congress has been considering stronger federal legislation. Researchers, IRBs, and other worker-study stakeholders should remain alert for new or revised legislation that could significantly affect how worker-study data are used and controlled. Furthermore, there are those who feel that genetic screening or testing has no place in the workplace or workplace studies.

When tissue or blood samples are collected during workplace studies, privacy concerns can be protected adequately by removing traditional identifiers from samples. Although IRBs may, in principle, approve the use of samples for genetic characterization when "identifiers" are removed, individual IRBs differ as to what they will allow as an identifier or what consent language may be required. (For guidance on the control of human tissue samples, see Appendix F, "Issues to Consider in the Research Use of Stored Data or Tissues," prepared by the Department of Health and Human Services, Office for Protection from Research Risks.)

Regardless of the level of control and protection provided through legislation, acquiring genetic information must be undertaken with due regard to the general principles of the Common Rule: benefiting individuals and families—not doing harm, offering autonomy of choice after counseling, and facilitating personal and social justice.

Disclosure and Confidentiality

Disclosure and confidentiality issues pose significant ethical problems for researchers conducting worker studies using genetic information. Because of the possibility of harm from disclosure to institutional third parties, utmost care must be taken to protect confidentiality.

Guidelines for disclosure and confidentiality:

- All test results relevant to a worker's health**C** and clinically validated**C** should be available to the subject.
- Test results should be communicated in a timely manner.
- Test results not directly relevant to the subject's health may be withheld if it appears necessary to protect a vulnerable party or if prescribed by law. This information is still subject to the rules governing confidentiality and privacy and this should be explained to subjects in advance.
- The wish of individuals and families **not** to know genetic information, including test results, should be respected.
- Results of presymptomatic or susceptibility tests should be kept confidential from employers, health insurers, schools, and government agencies. People should not be penalized or rewarded for their genetic makeup.
- Registries should be protected by the strictest standards of confidentiality.
- Subjects should understand, however, that the Federal System of Records may legally permit researcher to have access to personal, identifiable genetic information.

Some ethicists feel that employers, insurers, schools, government agencies, or other institutional third parties should not be given access to test results even with the individual's consent.

Many important research hypotheses involving variations in genes or in gene expression can be investigated efficiently and quickly by using specimens stored in repositories. The use of stored DNA is often restricted by the apparent reluctance of many IRBs to approve studies requiring access to these tissue specimens. This reluctance may be attributed to the IRB's concern over the potential for misuse of genetic information or the IRB's lack of familiarity with and understanding of how individual privacy can be assured. To the extent that this reluctance is scientifically informed, one might simply view it as evidence that the IRB system works well. If, however, an IRB's refusal to approve a study is based on an inadequate understanding of the protections provided or the goals and risks of the proposed research, the refusal may be counterproductive. In either case it appears likely that concerns about the confidentiality of individually identifiable data weigh heavily on IRB members, and education about risks, benefits, and limits of genetic testing should be provided to all IRBs.

In developing policies about the protection and control of DNA specimens, IRBs may consider the following factors:

- Will subjects be protected from possible discrimination by employers and insurers, etc.?
- Will the subjects be protected from any significant harm?
- Will the research findings potentially benefit any of the individual subjects?
- Is there the possibility of multiple uses of the same sample in different and unforeseen research projects?

- What are the advantages and disadvantages to individuals, researchers, and society of removing all identifiers from samples?

It is important to again point out that Congress, state legislatures, and other agencies continue to struggle with legislation to control access and use of both electronic medical data and genetic samples and information. New or revised legislation could affect and limit the use of genetic data and samples regardless of the conditions of a limited or blanket consent. (See Appendices E and F for the President's executive order and the Department of Health and Human Services, Office for Protection from Research Risks, for examples of current federal directives and guidelines.)

Other suggestions for maintaining and protecting tissue samples include:

- DNA samples should be stored only so long as they can be of benefit to the individual or for the purpose for which they were collected. After this time, the DNA samples should be destroyed. If identifiers are used that link the identity of the subject to other records, those links should also be destroyed when the data are no longer needed.
- Except for forensic purposes or instances when the information is directly relevant to public safety, institutions should have no access to the samples without the donor's consent.
- Insurance companies, employers, schools, government agencies, and other institutional third parties may be able to coerce a subject's consent. IRBs should carefully consider not allowing access to samples, even with the individual's consent.

In summary, the research community must make certain that effective, state-of-the-art security measures are developed and in place to ensure the confidentiality of genetic and all identifiable data relating to research participants or donated samples. Professional organizations should develop standards, policies, and procedures for the handling of subject and patient-identifiable information.