# Part I
# Introduction to Genetic Testing

Chapter I

# Executive Summary

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Chapter 1

# Executive Summary

## Occupational illness and genetic testing

### *The problem of occupational illness*

Occupational illness cost the U.S. economy over 850,000 workdays in 1981. * Diseases and other medical conditions associated with the workplace range from minor skin rashes to cancer. Some experts estimate that exposures to hazardous substances at work may play a role in 5 percent of all cancers. one substance-asbestos-is at the center of litigation over claimed illness that could result in insurance payments in the tens of billions of dollars over the next three or four decades. A large asbestos company has had more than 16,500 lawsuits filed against it and, as a result, has filed for reorganization under the Bankruptcy Act. Clearly, occupational illness has a serious and far-reaching impact not only on society as a whole but also on individuals who face impaired health and shortened lifespans.

What steps are being taken to mitigate this problem? Scientific and industrial response has varied: environmental and biological monitoring, engineering controls, personal protection devices, and modified work practices are among the techniques used today.

And on the horizon is an emerging technology –genetic testing–that may prove useful in reducing occupational disease, especially disease arising from exposure to two main workplace hazards: chemicals and ionizing radiation. That new technology—its potential applications and its limitations, its current state of development, and its legal, ethical, and social implications—is the subject of this report.

Genetic testing, as used in the workplace, encompasses two types of techniques. Genetic screening involves examining individuals for certain inherited genetic traits. Genetic monitoring involves examining individuals periodically for environmentally uced changes in the genetic material of certain cells in their bodies. The assumption underlying both types of procedures is that the traits or changes may predispose the individuals to occupational diseases. (Changes in the germ cells--egg and sperm-could result in birth defects in offspring but such reproductive effects are not part of this study.)

Although this technology is still in its infancy, it has the potential to play a role in the preven - tion of occupational diseases. It is technologically and economically impossible to lower the level of exposure to hazardous agents to zero. However, if individuals or groups who were predisposed to specific types of occupational illness could be identified, other preventive measures could be specifically directed at those persons. This is the promise of genetic testing. At the same time, however, the technology has potential drawbacks and problems. For example, the ability of the techniques to identify people who are predisposed to occupational illness has not been demonstrated. In addition, some people are concerned that its use could result in workers being unfairly excluded from jobs or in attention being directed away from efforts to reduce workplace hazards.

While it may be too soon to be able to answer many of the questions raised by genetic testing, it is not too soon for society to begin to consider them. The technology is developing, and some major companies have used it to a limited degree, Many more companies have expressed an interest in using it in the future. Moreover, genetic testing is one of a number of technologies that purport to identify people, both in and out of the workplace, who face an increased risk for disease. Policy decisions made on issues raised by genetic testing are likely to be relevant to the issues raised by those other technologies. Thus, the Committee on Science and Technology of the House of Representatives requested an assessment of genetic testing in the workplace.

*The number of lost workdays is based on a survey by the Bureau of Labor statistics which acknowledges that the figure understates the amount of occupational illness because the survey does not adequately reflect chronic diseases and those with long latency periods

## *Health hazards in the workplace*

While there are many different kinds of hazard ous substances or physical agents in the workplace, this report focuses on chemicals and ionizing radiation. It is for these two categories of hazards that genetic testing has been used and that some data exist for evaluating the scientific validity of such tests.

Virtually all chemicals are hazardous, if a person is exposed to a sufficient degree. Chemicals may be irritating, toxic, mutagenic, teratogenic, and/or carcinogenic. Moreover, the hazard of working with chemicals is compounded by the likelihood of multiple exposures to one or more chemicals over time. Exposure to more than one chemical may result in a synergistic effect—damage greater than the additive damage of the individual exposures,

The exact number of hazardous chemicals found in the American workplace is unknown. An Environmental Protection Agency (EPA) inventory lists more than 55,000 different chemicals in commerce, most of which are hazardous at sufficiently high exposure. Chemicals are found not only in companies that produce them but throughout the manufacturing sector, The National Institute for Occupational Safety and Health estimated that 8.9 million workers in the manufacturing sector were exposed to hazardous chemicals in 1980.

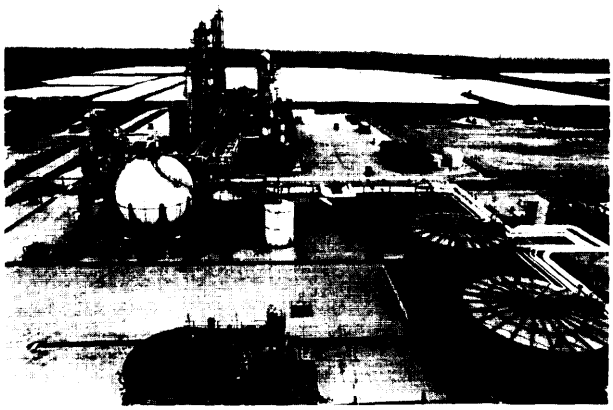

*Photo credit: Off/cc of Technology Assessment*

Chemical manufacturing plants sucn **as** the one shown produce hazardous chemicals to which workers may be exposed

Ionizing radiation is energy in the form of waves or particles that produce certain charged particles in passing through matter. X-rays are a well-known example of ionizing radiation. This radiation can harm exposed individuals or their unborn children, For the exposed individual, the principal risk is that he or she may develop cancer. For unborn children, the principal risks are childhood leukemia and birth defects.

Occupational exposures to ionizing radiation (above natural background levels) occur in many fields, such as the health professions, nuclear fuel mining and production, industrial testing, and 1aboratory research. Estimates of the number of exposed workers have varied from 750,000 by the Committee on the Biological Effects of Ionizing Radiation to 1.1 million by EPA.

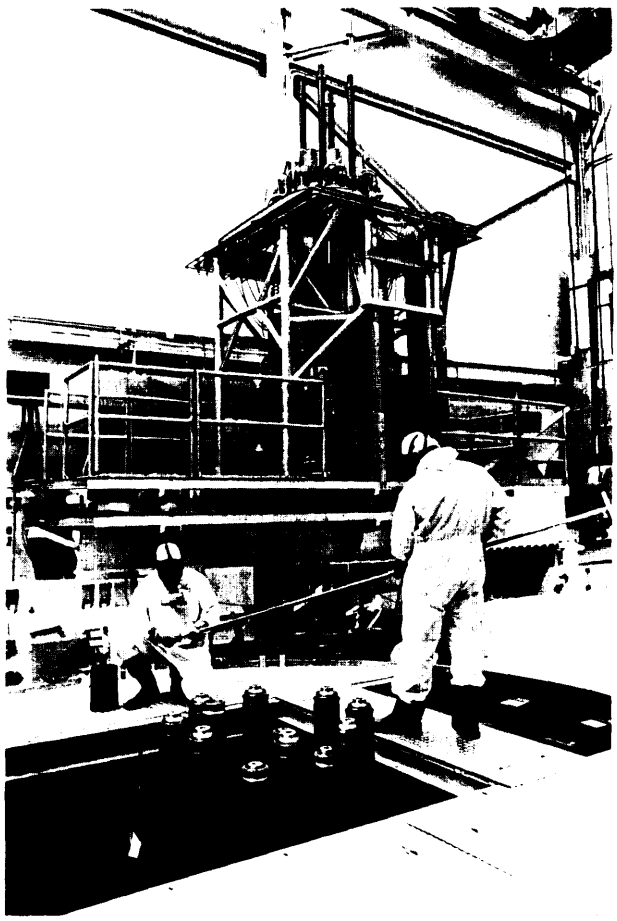

*Photo credit; Department of Energy*

Protective clothing worn by employees in nuclear power generating facilities to avoid radiation exposure

## *The use of genetic testing for the prevention of occupational disease*

The problem of occupational diseases resulting from exposure to chemicals or ionizing radiation can be addressed in many ways. These include lowering exposure levels through engineering controls, physical and biological monitoring of exposure levels, medical screening and monitoring of workers, and individual protective devices. Genetic testing falls within the category of medical screening and monitoring.

### THEORETICAL FOUNDATIONS

Genetically determined individuality is a fact of life. People differ not only in such obvious physical characteristics as height, facial features, and skin color, but also in ways that can be determined only in a laboratory, such as by blood type or types of proteins found in blood serum. Variations in some characteristics or traits result from the interaction of many genes; variations in other traits result from variations in a single gene that controls that trait. The probability of any two people (except identical twins) being exactly alike is astronomically small.

Genetic variability is also a factor in the differing reactions of people to environmental stresses, which include disease-causing agents such as bacteria, viruses, and chemicals. For example, some people have a deficiency in an enzyme called glu - cose-6-phosphate dehydrogenase (G-6-PD). The production of this enzyme is controlled by a single gene, and the deficiency is caused by a variant form of the gene. The deficiency usually is harmless. However, if these people take certain drugs for malaria or eat fava beans, they may suffer from acute anemia, due to the destruction of their red blood cells. Thus, G-6-PD deficient individuals are at a higher risk of illness than other people when exposed to those environmental stresses. Some scientists have postulated that people with G-6-PD deficiency may also be at increased risk of disease in workplaces where they are exposed to chemicals that are similar to the antimalarial drugs.

Many factors besides genetic makeup can cause an individual to be predisposed to illness from environmental stresses. Some of these are age, sex, preexisting illnesses, nutritional status, personal habits (such as smoking), and prior exposure to the environmental factors.

prior exposure is particularly important for the purposes of this report. If the environmental factor is a chemical, it may be in the body at levels at which even slight additional amounts could cause illness. In fact, the prior exposure may already have begun the disease process even though the disease may not yet have manifested itself in overt symptoms.

These considerations lead to the concept in occupational medicine of unequal risk. People who differ according to age, sex, medical history, nutritional status, lifestyle, genetic makeup, or prior exposure to hazardous agents might differ in their risk for future illness when exposed to hazardous agents in the workplace. Some may be at increased risk; in other words, they might have a higher probability than others for developing a condition, illness, or other medically abnormal status. Theoretically, it should be possible to identify such people if the risk factors could be reliably identified and if the factors could be demonstrated scientifically to be correlated with an increased risk of disease. In some cases, however, depending on the disease mechanisms involved and the state of scientific knowledge, it might be possible only to identify groups at an increased risk of disease. In other words, the group as a whole might have a higher risk compared to other groups, but it would be impossible to predict which individuals in the increased risk group might develop the disease. Genetic testing is a collection of emerging techniques that may eventually permit the identification of individuals or groups at increased risk to certain occupational diseases.

### DETECTION OF INCREASED RISK IN INDIVIDUALS OR GROUPS

The term genetic testing applies to several techniques used to examine workers for particular inherited genetic traits or environmentally induced changes in the genetic material of certain cells on the assumption that the traits or changes may predispose them to illness. It has been used by some manufacturing companies and utilities for medical evaluation and by others for research.

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There are two inherently different kinds of testing, genetic monitoring and genetic screening, whose results can be used in the workplace for different purposes.

Genetic monitoring involves periodically examining a group of workers by collecting blood or other body fluids to assess whether genetic damage has occurred in certain cells. This damage may indicate exposure to a hazardous agent, such as a carcinogenic chemical or ionizing radiation. It may also indicate the possibility that the exposed group will be at an increased risk of developing disease, most likely cancer. The procedure focuses on the risk for the exposed group as a whole because there is no evidence to suggest that it could be used to identify which individuals in the group are at increased risk. If the scientific validity of genetic monitoring were fully established, it would have potential as an early warning system, by indicating that exposures to known or suspected carcinogens are too high or that a previously unsuspected chemical should be viewed as a potential carcinogen,

In contrast, genetic screening, when used in the workplace, is a one-time testing procedure to determine if a person has particular genetic traits, regardless of whether the person has been exposed to a hazardous substance. The traits are identified through laboratory tests on body fluids, usually blood. Some scientists have hypothesized that these genetic traits might predispose an individual to adverse health effects in the presence of particular chemicals. While normally not harmful, the traits theoretically may make the individual more susceptible to blood-damaging chemicals, pulmonary irritants, oxygen deprivation, or other physical or chemical stresses in the workplace.

In sum, genetic screening has the potential to determine individual susceptibility to certain hazardous agents, It may be that, in time, genetic monitoring also will be able to determine individual susceptibility; however, currently it appears only to have potential for assessing a chemical's effect on an exposed population as a whole, Because of this distinction, screening could be used to exclude genetically susceptible individuals from jobs where they would be exposed to hazardous substances, whereas monitoring would most likely indicate a need to lower exposure levels for a group exposed to a previously unknown hazard.

## POTENTIAL BENEFITS AND RISKS

Although genetic testing is still in its infancy, its advocates believe that it might be able to play an important role in the prevention of occupational disease. It is technologically and economically impossible to attain a no-risk workplace by lowering the level of exposure to hazardous substances to zero, However, if individuals or groups who were predisposed to occupational illness because of past exposure to hazardous substances or particular genetic makeup could be identified, preventive measures could be taken by the company or the workers themselves. In addition to the obvious and significant benefits from preventing serious illnesses, there could be indirect benefits, such as a reduction in the costs associated with occupational illness for employers, employees, and society. These costs include medical, insurance, and legal expenses; time lost from work; and disability or unemployment payments.

The use of this technology, however, raises several questions. Can the techniques truly predict an association between genetic makeup or genetic damage and disease? How much of the variation in risk can be attributed to such predisposing genetic factors and how much to variation in environmental exposure? Since many of the genetic traits sought in screening happen to be distributed unevenly among some races and ethnic groups, could the use of the tests result in discrimination on the basis of race or national origin? How will the availability of the tests affect the employer's responsibility for maintaining a safe workplace? How might these procedures affect efforts to reduce the level of hazardous substances in the workplace? If the tests are predictive, to what degree should society protect high-risk individuals or groups, at what cost, and who should bear that cost?

# Findings

Because genetic testing is an emerging technology, there is insufficient evidence to assess many of its potential benefits, risks, and impacts. However, this report does examine the degree to which it has been used, the current stage of its development, expected future developments, and various legal, ethical, economic, and policy issues that it raises. This examination provides the basis for a discussion of the broader social issues and the options for possible congressional action.

## *Survey of the use of genetic testing*

There have been conflicting accounts about the extent of testing and the use of the results. None of the accounts examined by OTA was based on a rigorous, scientifically valid survey. Therefore, in order to reduce the confusion and speculation and to provide necessary data for policy analysis, OTA surveyed major U.S. industrial companies, utilities, and unions about their use of this technology.

The survey was conducted for OTA from February 25 to June 8, 1982, by the National opinion Research Center (NORC), a nonprofit survrey research corporation affiliated with the University of Chicago. NORC sent confidential questionnaires to the chief executive officers of the 500 largest industrial companies and 50 largest private utilities in the United States and to the presidents of 11 major unions representing the largest number of employees in these companies. Of the 366 (65.2 percent) organizations responding, 6 (1.6 percent) were currently using one or more tests, 17 (4.6 percent) used-some of the tests in the past 12 years, 4 (1.1 percent) anticipated using the tests in the next 5 years, and 55 (15 percent) stated they would possibly use the tests in the next 5 years. Of the 17 organizations that have tested in the past 12 years, 5 are currently testing. None of the four responding unions reported any testing.

For each type of test, companies were asked about the circumstances under which the tests were done (that is, routinely, for research, or for other reasons) and how employees were selected. Respondents generally tested routinely or for other unspecified reasons. Testing for sickle cell trait was most often based on ethnicity; for other types of tests, employees were selected on the basis of job category. No organization reported basing a genetic test on an employee's sex.

The 18 respondents who are testing or have tested took various actions based on the results. The most common action reported—by eight organizations —was informing an employee of a potential problem. Five organizations transferred employees. Two companies suggested the employee seek another job, and one changed or discontinued a product.

In evaluating the results of the survey, several caveats must be considered. The most important of these are:

- Since the questionnaire instructed respondents to include any instances of testing, pos - itive responses can include isolated cases as well as long-term testing programs.
- The questionnaire was not structured to provide information on the numbers of workers tested.
- Results of this study are more representative of the larger companies in this survey than other groups, since more large companies responded than did small ones.
- Since approximately one-third of the population did not respond and the number of organizations testing is very small, any generalizing of these results to the study population as a whole is not warranted.

## *The state of the art*

This assessment took a two-stage approach to analyzing the scientific data available on genetic testing. First, the laboratory tests themselves were evaluated to determine their reliability and validity, Then the available studies were evaluated to determine if there is a correlation between the genetic damage or trait in question and an increased risk for disease. **None of the genetic tests** evaluated **by OTA meets established scientific criteria for routine use in an occupational setting. However, there is**

**enough suggestive evidence to merit further research.**

## GENETIC MONITORING

The concept of monitoring workplace populations for genetic damage from chemicals or ionizing radiation is well grounded on a theoretical and experimental base. Ionizing radiation and a wide range of chemicals cause damage to the genetic material in experimental animals and, in some cases, humans. This damage may result in mutations, which are changes in the genetic information. The consequences of increasing the mutation rate of a population are not well understood, but mutations have been implicated in several diseases, most notably cancer.

There are two major types of genetic monitoring methods-the established cytogenetic methods which detect major structural changes in chromosomes and the newer noncytogenetic methods, which detect damage to the DNA (deoxyribonucleic acid). The noncytogenetic methods, for the most part, are still in experimental stages, but eventually could lead to faster and less expensive monitoring methods.

The detection of chromosome damage using cytogenetic techniques is a fairly complex procedure. It requires skilled laboratory technicians and is often labor intensive. But if laboratory variables are kept constant, chromosome damage can be determined reliably.

There are two stages involved in the assessment of genetic monitoring. The first determines whether the agent actually causes the genetic damage in a manner such that increasing dosages of the agent gives increasing amounts of damage (dose-response). The second stage of the analysis asks whether the observed genetic damage actually will predict an increased risk for disease, If good scientific evidence is available to support both stages of the analysis (this is, that the hazardous agent causes genetic damage, and that this damage predicts an increased risk for disease), then the assumption can be made that the agent causes disease. OTA found that there are some studies where a dose-response relationship has been established, but there are few studies showing a correlation between genetic damage and an increased risk for disease.

A large number of studies on workplace populations, using cytogenetic techniques, have been done, but there are several factors which make the interpretation of these studies difficult. In very few cases has the level of exposure of the workers to the hazard been documented, making the establishment of a dose-response relationship impossible. Also, it is fairly well established that other factors such as age, smoking and drinking habits, nutritional status, and the presence of disease can cause differences in the level of chromosomal damage. Because most studies have not taken these factors into account, there is a large variability in both exposed and unexposed populations. When exposed populations are studied, rarely is there found more than a twofold increase in damage over the average of the unexposed population. Thus, given the variability of the unexposed population, interpretations of these studies are difficult. Finally, it is not known whether chromosomal changes in blood cells reflect the presence of chromosomal damage in internal organs.

Studies done on populations exposed to ionizing radiation, including atomic bomb survivors in Japan, are less equivocal than those for chemical exposure, mainly because radiation exposure levels are more easily documented. The evidence does show an increase in chromosomal damage with increasing dose of radiation. This damage, though, has not been correlated with an increased risk for disease with one exception. Extensive studies on the bomb survivors have shown clear dose-related increases in both chromosomal abnormalities and various cancers for these populations as a whole. Yet there seems to be no correlation between the frequency of chromosomal abnormalities for a given individual and his or her risk for cancer.

Currently, genetic monitoring has the potential for use as a biological indicator of exposure to workplace chemicals or ionizing radiation and could aid in the identification of hazardous agents, The correlation of induced genetic damage with risk for disease has been shown statistically only for the Japanese population exposed to ionizing radiation from the atomic bombs, For people exposed to hazards in the workplace, more information is needed to elucidate other environmen-

tal and genetic factors which may contribute to increased risk for disease.

GENETIC SCREENING

Differential susceptibility to chemicals has been predicted, in part, from differential reactions to drugs, which have been extensively documented. Explicitly defining this genetic differential susceptibility is not yet possible given the current state of knowledge; however, some data do exist on a few genetic traits, implicating them in susceptibility differences to certain chemicals. The list probably represents only a small percentage of the genetic traits involved in responses to chemicals. This report examines the following traits: glucose-6-phosphate dehydrogenase (G-6P-D) deficiency, sickle cell trait, alpha and beta thalassemia trait, NADH dehydrogenase deficiency, serum $alpha_1$-antitrypsin (SAT) deficiency, aryl hydrocarbon hydroxylase (AHH) inducibility, slow v. fast acetylation, human leukocyte antigens (HLA), carbon oxidation, diseases of DNA repair, and several other less well-characterized genetic traits.

OTA found that most tests for identifying these traits are accurate and reliable, but only when applied to subgroups already suspected of having the trait at a relatively high prevalence. Because the predictive value of these tests is low when used in the general population, studies using these tests could be seriously flawed. In fact, the predictive value of the test, which is based not only on accuracy but also on the prevalence of the trait in the population, will only be high when the prevalence of the trait is high,

There is some suggestive evidence, from adverse drug reactions and illnesses resulting from exposures to chemicals, that associations may exist between certain traits and risk for disease from particular occupational exposures. This report reviewed occupational studies on several genetic traits and found that the data were not extensive enough to draw any conclusions on the correlation between given genetic traits and risk for disease. On the other hand, the data are suggestive of these correlations, and research seems indicated for attempting to determine these relationships.

## *Genetic testing and the law*

Genetic testing raises legal questions related to workplace safety and employee rights. Although the law generally has not dealt with genetic testing, many existing legal principles are directly applicable to the issues raised by this technology. Moreover, employers and unions could negotiate mutually agreeable solutions to the problems raised by genetic testing. Unions, however, have no legal duty to bargain over such issues or to take special steps to protect workers who might be at increased risk.

The employer has the legal responsibility for workplace safety. Failure to meet the responsibility can result in costly judgments or civil or criminal penalties against the employer. This responsibility would not require the employer to use genetic testing, even if it were highly predictive of future illness. If the employer chose to use a highly predictive test, it would probably be negligent if it ignored the results and placed employees in a high-risk rather a than low-risk environment. However, recovery of damages by such an employee who developed the predicted illness would probably be barred by the “exclusive remedy” provision of workers’ compensation laws and possibly by the doctrine of assumption of the risk, if the employee had been informed of the risk. If the risk had been concealed from the employee, recovery probably would not be barred under workers’ compensation laws, and the employer would face the possibility of punitive damages.

Under the Occupational Safety and Health Act of 1970 (OSH Act), the Secretary of Labor is empowered to promulgate standards that protect all employees from toxic substances to the extent that the standards are directed toward a significant risk to health and to the extent that they are technologically and economically feasible. These standards can, among other things, set maximum exposure levels, require personal protection gear, and require various medical procedures. The feasibility requirement may leave some percentage of exposed workers at risk, depending on the circumstances of the particular hazardous substance and industry. Of those workers at risk,

some may be genetically susceptible and others may be at increased risk because of genetic damage. An open question is whether the courts would allow a standard designed to protect a very small number of susceptible individuals or would invalidate it on the grounds that it failed to address a significant risk because of the small number of workers involved.

The OSH Act and regulations thereunder neither prohibit nor require genetic testing. However, the Secretary of Labor has broad authority to regulate employer medical procedures as long as the regulation is related to worker health and meets the feasibility and significant risk requirements. Therefore, the Secretary could require genetic testing in its various forms, if the techniques were shown to be reliable and reasonably predictive of future illness. The Secretary also could regulate the use of genetic testing, but only to the extent that the regulation was related to employee health. The act grants no authority over rights or conditions of employment per se and no authority to protect applicants for employment from discrimination.

State and Federal laws place few restrictions on how medical exams or testing procedures may be conducted in the workplace and what the employer does with the resulting information other than the requirements that the procedure not be negligently performed and that the employee be informed of potentially serious health risks. Submission to medical exams, which include various tests, can be a valid condition of employment. As a result, employees or applicants would have no right to refuse to participate without jeopardizing their job. Moreover, participation in research can be a valid condition of employment. How much the employee needs to be told about the research is unclear, except in two cases. If the research were federally funded, subjects must understand the risks and other aspects of the study and consent to them, A few States require research to be reviewed by special boards in order to protect the interests of human subjects, and these boards may require informed consent.

With respect to the data generated by genetic testing, there are few requirements regarding confidentiality except in the State of California. But employees have a right of access to medical records under Occupational Safety and Health Administration (OSHA) regulations and unions have a similar right under a recent decision by the National Labor Relations Board. This access could help prevent abuse of genetic testing. However, those who face the greatest risk of being denied employment because of their genetic makeup—job applicants—would not have access to the test results.

For those applicants or employees who were subject to some adverse job action because of their genetic makeup, Federal and State antidiscrimination statutes may offer some relief. However, they do not deal specifically with genetic screening except for a few State statutes that prohibit employment discrimination on the basis of certain genetic traits, usually sickle cell trait.

Title VII of the Civil Rights Act of 1964 prohibits discrimination in employment based on race, color, religion, sex, or national origin, In addition to intentionally discriminatory actions, neutral employment practices that have a disparate impact on a protected group may violate title VII. Some types of genetic screening, such as for sickle cell trait, would have a disparate impact; therefore, an adversely affected genetically susceptible employee in one of those classes would have a prima facie case of discrimination. Then, the employer would have the burden of justifying the screening program by demonstrating its relation to legitimate job requirements or business needs. It is presently unclear whether using genetic testing to screen out employees who might become ill in order to avoid the cost of engineering controls is a business necessity. Nor is it clear whether the employee's capacity to perform the job without a risk of future illness is a legitimate job requirement. However, it is clear that any job selection method must be predictive of the characteristic for which it allegedly selects. Since the ability of genetic screening to identify workers at increased risk for disease has not been demonstrated, a program that had a disparate impact on the employment opportunities of the classes protected by title VII probably would violate that act.

The Rehabilitation Act of 1973 prohibits employment discrimination against otherwise qualified handicapped people by employers who are

Government contractors or recipients of Federal assistance. Virtually all of the States have similar statutes, and the State laws usually offer broader protection to handicapped people. These statutes offer a greater potential than title VII for aiding the employment opportunities of genetically susceptible individuals; however, for those laws to be applicable, two currently unresolved legal questions must be settled in favor of the employees. The first is whether or not a particular genetic makeup is a handicap. If not, these employees would have no rights under these laws. If it is a handicap, the next question is whether employment may be denied to handicapped individuals on the basis of a reasonable probability of future illness. If the courts were to rule that future risk of illness was not a legitimate area of inquiry for employers, the Rehabilitation Act and similar statutes would prohibit adverse job actions on the basis of genetic makeup. If risk of illness were recognized as a legitimate concern, the employer would have the burden of showing the genetic screening techniques were reasonably predictive of illness. Even if the employer demonstrated this, however, it might have to accommodate the "genetically handicapped" employee anyway. But such accommodation probably would not require the installation of expensive engineering controls to lower exposure. *

### *Ethics of genetic testing*

Because genetic testing is relatively new and has not been widely used, there is little direct experience on which to make judgments regarding its use, Nor are there direct legal precedents. Under these circumstances, it is appropriate for policymakers and others involved in decisions concerning this technology to look to ethical principles for guidance.

Ethics may be defined as the study of moral principles governing human action. These principles, or general prescriptive judgments, create moral duties that guide action in particular circumstances. Sometimes, however, the principles conflict in their application and provide no clear guidance. Then, difficult choices must be made. Such is the case with genetic testing in the workplace.

Genetic screening and monitoring are not inherently unethical. The tests are morally justified to the extent they enhance worker health in a manner consistent with established ethical principles. Whether or not they are consistent with these principles will depend on how the tests are done and how the information is used.

Ethical principles regarding the duties of company medical personnel toward workers are often conflicting or not well established. Therefore, they offer little specific guidance about the manner in which tests should be conducted with the exception of procedures done for purposes of medical research. In cases of research on humans, ethical principles are well established and provide for the rigorous protection of individual rights and interests.

Ethical principles constrain how the results of genetic testing may be used. In the absence of a significant correlation between genetic endpoints (traits or evidence of damage from exposure) and disease, it would be unethical for the employer to act adversely to the employee's interests, such as by denying him or her a job.

In the hypothetical case of a strong correlation between genetic endpoints and disease, the morally correct course of action is significantly less clear. For screening, the employer might justify excluding susceptible workers from certain jobs on the grounds of benefiting the employees. on the other hand, employees might claim that they have the right to decide whether to assume the risk. Whether or not genetically susceptible people are entitled to protection from discrimination or compensation for harm depends on which of several theories of justice is chosen. For monitoring, the most ethically feasible course of action for an employer would be to inform the workers of adverse findings and to reduce worker exposure, Failure to do so would be inflicting harm, and it is unlikely that the group would consent to assuming this risk.

### *Economic evaluation of genetic testing*

Genetic testing in the workplace has potential benefits and costs to workers, employers, and so-

*()'1'.1 is conducting a study on the use of engineering controls to enhance worker safety and health.

ciety as a whole. The magnitude and distribution among the sectors of society of these benefits and costs will help determine the desirability of this approach to improving occupational health. Two techniques of economic evaluation-cost-benefit and cost-effectiveness analysis—are methods for collecting, organizing, and presenting evidence about the benefits and costs of alternative courses of action so that choices can be better informed. They are systematic approaches to examining the tradeoffs among the different kinds of consequences–for example, dollar outlays today v. improved levels of health 5 years hence—stemming from a decision.

The usefulness of economic evaluation rests on its ability to improve decisions. Even when economic analysis is severely limited by uncertainties about the magnitude, direction, or value of certain consequences, as with genetic testing, it can still be a useful exercise. The identification of key areas of uncertainty, for example, can be used to set priorities for further research, Thus, economic evaluation can be used to dissect and examine alternative strategies in order to understand their underlying assumptions and uncertainties.

In the case of genetic testing, rigorous economic analysis of the costs and benefits is not possible because of the lack of knowledge about the association between test results and risk of disease, the numbers of people to whom testing could be applied, and the amount of occupational disease that could be prevented, If additional information became available, economic analysis could provide a rough sense of the benefits, burdens, and tradeoffs associated with genetic testing programs.

# Congressional issues and policy options

**ISSUE: What actions could Congress take with respect to genetic testing in the workplace?**

**OPTIONS:**

*A. Maintain the status quo,*

Congress could choose not to take any action to stimulate, constrain, or regulate genetic testing. This would allow private parties to continue research into the merits of the technology. Constraints on its use would develop through court rulings in lawsuits between these parties or by negotiations between companies and unions. Interested congressional committees could continue their practice of holding oversight hearings to raise the issues for public discussion.

The primary argument supporting this option would be the view that congressional action would be premature. The technology is not being widely used, and it is primarily in the research phase of its development. In addition, there are existing constraints on its potential misuse. These include the possibility of lawsuits and adverse publicity. Finally, much of the important information necessary for legislation is unavailable because it is unknown. For genetic screening techniques, this information includes the number of workers who might be genetically predisposed to disease, the extent to which they might face adverse employment actions, the availability of other employment opportunities, and the cost of safeguarding these workers. For genetic monitoring techniques, this information includes their predictive value, the extent to which they might be used, and the costs associated with either using or not using them.

The arguments against this option relate to how society controls an emerging technology. Many policy decisions will need to be made with respect to genetic testing, and arguably Congress is a better forum for doing so than the courts or private parties. Congress can gather all information and viewpoints and then balance the conflicting interests. In addition, while the courts often play a major regulatory role for any technology, they are limited in their ability to encourage the development of a technology in a positive manner. However, Congress can do so by providing funds for research or other incentives.

*B. Stimulate the technology's development and use.*

Congress could stimulate the technology by providing money for research on the techniques, for epidemiological studies to determine associations between genetic endpoints and disease, and for basic research on the cause of occupational disease in general, If genetic testing could be developed to the point where the tests are predictive of an individual's or group's increased risk of occupational illness, their use could result in a number of direct and indirect benefits. The principal direct benefit would be a lower incidence of occupational disease among workers. They and their families would be spared some of the pain, cost, and emotional trauma that accompany illness. In addition, employers would save some of their direct and indirect costs of occupational disease-employee time lost from work, insurance premiums, legal fees, and monetary damages assessed in lawsuits. Society would benefit through the greater health and productivity of its work force. A major indirect benefit of developing this technology might be a greater understanding of the causes of occupational disease and disease in general.

The principal argument against this option is the concern about the potential misuse of the technology and about potential adverse impacts. Some of these concerns relate to unfair employment discrimination and attention being directed away from other ways to address occupational diseases. These concerns might be dispelled by regulation to direct the technology's development in socially desirable ways. In fact, if the tests were highly predictive of future illness, OSHA could require their use and constrain how they were used, so long as those constraints were shown to enhance worker health and were not directed merely toward prohibiting unfair employment practices.

Another drawback to this option is the fact that there is no definitive information on the amount of occupational disease that could be prevented by genetic testing, even if the tests were reliable predictors of disease. Similarly, there is no information on what it would cost to develop the tests to the point of clinical usefulness.

*C. Prohibit the use of genetic testing in the workplace.*

The principal reason for prohibiting genetic testing in the workplace would be concern over its potential misuse, particularly at its current stage of development where its ability to predict future disease has not been demonstrated. This potential for misuse probably would be greater for genetic screening than genetic monitoring because the former is targeted toward identifying individuals at increased risk while the latter focuses on groups at increased risk. However, concern exists that employers might use either type of test to exclude individuals from jobs. Existing law may offer protection in some circumstances, but there are many questions to be resolved. The collective bargaining process could be used by unions to negotiate protection for workers, but the primary focus of bargaining has been economic matters. While health matters have also been important, little, if any, negotiating has occurred with respect to genetic screening. In addition, most of the work force is not unionized. Moreover, these remedies are not helpful if a susceptible person does not know why he or she was denied a job. Finally, while ethical principles provide guidance for the proper use of this technology, it is difficult to know if they are being followed.

The principal drawback to this option is that it is a drastic solution to the problem of potential misuse. Genetic testing does not appear to be widely used. Law, ethics, and public opinion provide incentives against its misuse. Moreover, banning its use would prevent research that might determine its usefulness in preventing occupational disease or provide basic knowledge about occupational disease.

Another argument in favor of this option would be the claim that an employee's risk of future illness is not an appropriate factor for job selection, even if screening or monitoring were highly predictive, Employees have no control over their genetic makeup and generally have no control over previous exposures to harmful agents, In addition, their increased risk would not affect their current ability to do the job.

There are at least two counterarguments to the assertion that risk of illness should not be a job selection factor. First, society accepts the proposition that immutable characteristics can be proper criteria for employment selection. Intelligence is at least an implicit selection criterion for many professional jobs and physical attributes are exceedingly important for jobs ranging from professional basketball to neurosurgery. Second, this viewpoint places the autonomy interests of the individual above the interests of society in lowering the costs of occupational illness even when it may not be feasible to take other steps, such as lowering exposure,

*D. Regulate the technology.*

This option represents a judgment that any risks presented by the technology can be controlled and that the claimed benefits will be of value to society. The option would permit research to continue, yet constrain the manner in which genetic testing is used, One type of constraint would be limitations on what job actions employers could take on the basis of test results. Another type of constraint would be a requirement that the tests meet minimum standards of scientific validity before employment decisions were made on the basis of the results. Such a statute need not specify detailed standards; it could adopt a standard such as "reasonably predictive of future illness" and allow the appropriate agency to provide details.

This option has the advantage of addressing the potential risks of genetic testing immediately and in a comprehensive manner rather than waiting for the law to develop on a case-by-case basis through the courts. Congress may be uniquely able to study the problem fully, balance competing interests, and provide comprehensive yet targeted solutions.

A possible drawback of this option is that the problem may not yet be "ripe" for congressional action. On the basis of available evidence, genetic testing in the workplace does not appear to be widespread. Moreover, there is no available evidence about: 1) the number of workers who potentially could be screened or monitored if the tests were sufficiently predictive, 2) the number who might be excluded from jobs, 3) the ease with which excluded workers could find comparable jobs, and 4) the costs of various regulatory alternatives.

*E. Encourage the development of voluntary guidelines on the acceptable use of genetic testing.*

Congress could request the National Academy of Sciences or a similar body to establish a special commission of representatives from industry, labor, academia, and other sectors of society to draft voluntary guidelines for the use of the tests, This would allow the parties most involved to make the difficult value judgments in balancing competing interests and would avoid direct governmental regulation.

**ISSUE: How could Congress regulate genetic testing in the workplace?**

**OPTIONS:**

*A, Constrain employment actions that may be taken on the basis of genetic testing.*

Congress could address many of the concerns raised by genetic testing by regulating how employers may use the results of the tests, even if they were highly predictive. The following represent some possible elements of such an approach: 1) prohibit job exclusion on the basis of genetic makeup or genetic damage, 2) prohibit job transfers because of genetic makeup or genetic damage unless the transfer were to a comparable job at comparable pay and benefits, 3) require strict confidentiality of medical information, and 4) require that employees be told the results of testing and be given counseling.

This option clearly would protect the interests of workers, preventing potentially serious consequences to individuals who have no control over the reason for the discrimination. In addition, no difficult judgment would have to be made as to how predictive the tests should be before they are permitted.

There are at least two major disadvantages to this option. First, it may be too broad, If not carefully drafted, a statute could reach genetic diseases (not traits) that do affect an employee's current ability to perform the job safely and effective-

ly. It is generally accepted that inability to perform a job, even for medical reasons, is a valid criterion for job selection. Second, if workers with certain traits were in fact predisposed to occupational illnesses and chose to ignore that information, the additional direct and indirect costs of their illnesses eventually would be borne by society. This would be the case even if employers were required to install additional engineering controls, since the costs of those controls would be passed on to society. On the other hand, if excluded workers were unable to find comparable jobs, society would bear the costs of lost productivity and possibly additional unemployment payments. The answer to the question of who should bear the costs associated with genetically predisposed or damaged individuals will depend not only on economic analyses but on prevailing political views of distributive justice.

*B. Prohibit employment decisions on the basis of genetic testing unless the employer can demonstrate that the results are reasonably (or substantially) predictive of future illnesses.*

This option places the burden on an employer to justify the claimed correlation between test results and risk of illness. The specific criteria for meeting a necessarily general statutory standard could be provided by agency regulation and case law.

There are several advantages to this option, especially when compared to option A. First, it focuses on the immediate concern of job denial on the basis of poorly predictive tests, thus protecting employees' interests. Second, it protects employers' interests in lowering their costs from occupational diseases by allowing the exclusion of certain workers when there is a rational, scientific basis for doing so. Third, it would allow research on the techniques to continue.

The principal drawback of this option is that it could be a de facto determination without a full public debate that future risk of illness is a proper job selection criterion. On the other hand, there is a substantial lack of the type of information desirable for deciding this fundamental issue at this time.

C. *Amend the Rehabilitation Act of 1973 to state that genetic makeup is a handicap and clarify whether individuals who are genetically predisposed to illness are considered to be "otherwise qualified" within the meaning of that act.*

A major advantage of this option would be working with an existing statute rather than devising an entirely new one. Sections 503 and 504 of the Rehabilitation Act deal with problems that conceptually are very similar to those posed by genetic screening. If applied to genetic screening, the act would require at a minimum that the tests be reasonably predictive of future illness.

On the other hand, this option would force legislative activity into an existing statutory framework that may not be completely suited to genetic screening. The Rehabilitation Act was designed to bring millions of handicapped people into the mainstream of American life. Genetic screening has not created a problem anywhere near the magnitude of that addressed by the Rehabilitation Act. Moreover, section 503 requires employers to take affirmative action to employ the handicapped. Congress may not wish to require affirmative action to employ people who are genetically predisposed to occupational illness, if that predisposition can, in fact, be demonstrated.

*D. Require that research on employees be done according to existing Federal regulations designed to protect human subjects of research.*

The Department of Health and Human Services has promulgated regulations governing federally funded biomedical and behavioral research on humans. The regulations contain a number of provisions designed to protect the interests of the research subjects. Requiring private companies to follow these regulations in research involving genetic testing or any other kind of research done in the workplace would mitigate the potential for abuse.

*E. Require full disclosure to employees and their representatives of the nature and purpose of all medical procedures performed on employees.*

Under current law, employees and unions have access to employee medical records, but employers are not required to disclose the nature and purpose of medical procedures and how the results are used. Required disclosure of this in-

formation to the employee at the time the procedure was being performed would be a strong incentive to employers for self-regulation. If workers and their medical advisors had full knowledge of a company's medical procedures, they could take steps to prevent abuses, through negotiation or legal action. Publicity alone could prevent the worst abuses. This would also protect the autonomy interests of workers by allowing them to be part of a decisionmaking process that affects their health and economic interests. Some of the arguments against this option would be that it might be burdensome and costly for employers and that it would intrude too much on the professional judgment of the occupational medical specialist.

**ISSUE: How could Congress foster the development and use of this technology?**

**OPTIONS:**

*A. Fund research for the development of tests with high reliability and validity.*

Genetic variability and differential susceptibility to toxic chemicals are well-established concepts in the scientific literature. Currently there are many genetic screening tests which could be done in a workplace setting to detect potentially susceptible individuals. For the most part, these tests are accurate, reliable, and valid for identifying the genetic traits in question when applied to subgroups already suspected of having the trait at a relatively high prevalence; a notable exception is the test for aryl hydrocarbon hydroxylase (AHH) inducibility. Research on developing tests for those traits which are more prevalent in the population should receive higher priority because they are more likely to have a high predictive value. The only test covered in this report which falls into this category is AHH inducibility.

With respect to genetic monitoring, the notion that exposure to toxic chemicals and ionizing radiation can cause genetic damage in humans is less well established scientifically than the concept of differential susceptibility. However, there is an overwhelming amount of evidence that this is true in experimental mammals. Moreover, the impact of genetic damage on one's risk for disease, especially cancer, or on future generations is not known, yet the current thinking of the scientific community is that increased amounts of genetic damage is generally deleterious.

Alternatives are needed to the time-consuming cytogenetic tests currently in use. If genetic monitoring is to be done on a large scale, the availability of automated tests becomes important. The development of various noncytogenetic methods could be useful in this respect. Those that show promise currently include tests for detection of: mutagens in urine, alkylated hemoglobin, HGPRT mutation in lymphocytes, hemoglobin mutations, chemically damaged DNA bases, and LDH-X variants in sperm. For both cytogenetic and noncytogenetic tests, a better understanding of the factors that contribute to genetic damage in the absence of occupational exposure is needed (that is, a "normal" or baseline response) in order for the tests on exposed populations to be meaningful.

The government agencies which could be involved in these studies include the Environmental Protection Agency (EPA), the National Institute for Occupational Safety and Health (NIOSH), and the National Institute for Environmental Health and Safety (NIEHS).

*B. Fund epidemiologic studies in occupational settings directed by NIOSH or NIEHS.*

Data are most lacking concerning the correlation of genetic traits or genetic damage to an increased risk for disease. Epidemiologic studies in an occupational setting can address this problem. If these studies were to be undertaken, they must use good epidemiological practices and document exposures. Studies should only be undertaken if they are likely to yield statistically reliable data. For instance, genetic monitoring studies would require exposure levels high enough to yield a clear-cut statistical response between exposed and nonexposed groups without having to use excessively large numbers of people. Especially important would be to establish a dose-response relationship. Genetic screening studies would have to focus on genetic traits which have a significant prevalence in the population (greater than 1 percent).

Epidemiologic studies are very costly and difficult to control, especially if they run over long time periods. Some genetic screening studies could be done in a short time (1 to 3 years) once a population with the trait was selected because, presumably, the symptoms of disease resulting from exposure would manifest themselves soon after exposure. These traits include the red blood cell traits. Most of the other traits reviewed here are potentially correlated with diseases which have a long latent period, such as emphysema and cancer. To correctly assess the exposure information with the disease endpoint, much longer epidemiologic studies (10 to 30 years) are necessary.

For genetic screening, higher priority should be given to studies on traits which have a high prevalence in the population. These include SAT deficiency, AHH inducibility, carbon oxidation ability, and the association of particular human leukocyte antigens with risk for disease.

Epidemiologic studies using genetic monitoring techniques would have to be long term in order to determine the association between genetic damage and cancer. The chemicals chosen for study would have to be selected carefully. Many of the agents discussed in this report are known already to cause cancer in humans (for example, ionizing radiation, benzene, vinyl chloride), and occupational exposure to these is very low and possibly not detectable by the genetic techniques now in use.

C. *Establish a federal!y funded data bank, directed by NIOHS, EPA, or NIEHS, to be used in the stud&v of the causes of differential susceptibility to occupational disease.*

Because the study of the effects of harmful agents includes many scientific disciplines, it would be useful to have the relevant data collected in an accessible location. This computerized data bank could include not only genetic factors affecting toxicity, but developmental, aging, nutritional, and lifestyle factors as well. The data bank would include epidemiologic studies that have been or are being done in occupational settings, either governmentally or privately funded (somewhat in the same manner as EPA's Gene-Tox Program). Those ***working*** in the field of genetic toxicology could draw on the information in the bank in order to design studies and to prevent duplication of effort. The toxicology data would be of considerable value to various regulatory agencies in their standard setting.