Privacy Issues in Biomedical and Clinical Research

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Preface

In 1993 the National Research Council's Board on Biology established a series of forums on biotechnology. The purpose of the discussions is to foster open communication among scientists, administrators, policy-makers, and others engaged in biotechnology research, development, and commercialization. The neutral setting offered by the National Research Council is intended to promote mutual understanding among government, industry, and academe and to help develop imaginative approaches to problem solving. The objective, however, is to illuminate issues, not to resolve them. Unlike study committees of the National Research Council, forums cannot provide advice or recommendations to any government agency or other organization. Similarly, summaries of forums are precluded from reaching conclusions or recommendations, but instead, are intended to reflect the variety of opinions expressed by the participants. The comments in this report reflect the views of the forum's participants as indicated in the text.

For the first forum, held on November 5, 1996, the Board on Biology collaborated with the Board on Agriculture to focus on intellectual property rights issues surrounding plant biotechnology. The second forum, held on April 26, 1997, also conducted in collaboration with the Board on Agriculture, was focused on issues and obstacles to a broad genome project with numerous plant and animal species as its subjects.

After discussions with the National Cancer Institute and the Department of Energy the Board on Biology of the National Research Council agreed to run a workshop under the auspices of its Forum on Biotechnology entitled "Privacy Issues in Biomedical and Clinical Research" on November 1, 1997. Participation by representatives of the U.S. Department of Energy, U.S. Department of Agriculture, National Institutes of Health, and Congressional staff suggests that this

issue is important to many federal bodies. Scientists from industry, academe, and federal agencies shared their experiences in human genetic research.

The organizers want to stress the forum was not intended to cover the full gauntlet of issues concerning Genomics and the Privacy of Medical Records. The emphasis of this forum was to look at pending legislation in Congress (Fall, 1997) and consider, if enacted as written, how this would affect genetic research. The broad language of this legislation written to protect the individual could inadvertently restrict research intended to help these same individuals. Scientific progress requires the sharing of information for the validation of results and the dissemination of gained knowledge to be effective. Other issues which were touched upon in this forum but not fully explored include; the trust of individuals involved in genetic studies in the manner their genetic information could be used, the practice of the generalized "linking" of particular ethnic groups with specific genetic traits, and the potential for positive *and* negative impact on the quality of life by having knowledge of one's genetic potential. These and other issues which have come upon us in the age of genomics require separate, focused efforts to explore their potential effect on society.

At the conclusion of the Forum on "Privacy Issues in Biomedical and Clinical Research" we invited participants to write their thoughts about the issue to be included in the appendix. One person, Mr. Frederick Anderson, responded and his comments can be read on pp. 35-39.

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise in accordance with procedures for reviewing NRC and IOM report approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the NRC in making the published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The content of the final report is the responsibility of the NRC and the study committee, and not the responsibility of the reviewers. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals, who are neither officials nor employees of the NRC, for their participation in the review of this report:

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While the individuals listed above have provided many constructive comments and suggestions, it must be emphasized that responsibility for the final content of this report rests entirely with the authoring committee and the NRC.

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Chair
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The National Academy of Sciences is a private, nonprofit, self-perpetuating society of distinguished scholars engaged in scientific and engineering research, dedicated to the furtherance of science and technology and to their use for the general welfare. Upon the authority of the charter granted to it by the Congress in 1863, the Academy has a mandate that requires it to advise the federal government on scientific and technical matters. Dr. Bruce M. Alberts is president of the National Academy of Sciences.

The National Academy of Engineering was established in 1964, under the charter of the National Academy of Sciences, as a parallel organization of outstanding engineers. It is autonomous in its administration and in the selection of its members, sharing with the National Academy of Sciences the responsibility for advising the federal government. The National Academy of Engineering also sponsors engineering programs aimed at meeting national needs, encourages education and research, and recognizes the superior achievements of engineers. Dr. William A. Wulf is president of the National Academy of Engineering.

The Institute of Medicine was established in 1970 by the National Academy of Sciences to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health of the public. The Institute acts under the responsibility given to the National Academy of Sciences by its congressional charter to be an adviser to the federal government and, upon its own initiative, to identify issues of medical care, research, and education. Dr. Kenneth I. Shine is president of the Institute of Medicine.

The National Research Council was organized by the National Academy of Sciences in 1916 to associate the broad community of science and technology with the Academy's purposes of furthering knowledge and advising the federal government. Functioning in accordance with general policies determined by the Academy, the Council has become the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering in providing services to the government, the public, and the scientific and engineering communities. The Council is administered jointly by both Academies and the Institute of Medicine. Dr. Bruce M. Alberts and Dr. William A. Wulf are chairman and vice-chairman, respectively, of the National Research Council.

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Introduction: Privacy Issues in Research

In January 1996 the journal *Science* reported a dilemma plaguing the Centers for Disease Control and Prevention (CDC) in Atlanta. For a decade a group of biologists there had been collecting blood samples from people for eventual use in genetic research, and by 1996 they had some 17,000 samples of DNA, an invaluable archive that could help researchers understand the connection between genetics and the development of various diseases. But no one was allowed to use the archive. As *Science* reported, the CDC was "concerned that its original procedures for obtaining consent fall short of today's standards."

If it were an isolated event, the CDC's predicament would be unfortunate but not particularly worrisome to anyone outside the small group of scientists involved. But the situation is not unique. In labs around the country genetic researchers find themselves face to face with ethical and legal quandaries concerning the collection, analysis, and dissemination of genetic information. As the potential benefits of genetic science have grown, particularly in the diagnosis and treatment of disease, so have the worries about possible abuse, and Congress and a number of state legislatures have begun looking into regulating the flow of genetic information.

To date, much of the discussion has been driven by people concerned about genetic discrimination—the misuse of genetic information by insurance companies, employers, and others to make decisions based on a person's DNA—and so most of the policy debates have centered on how to ensure the privacy of genetic information in medical records and to protect people from such discrimination. But there are other issues as well. In particular, biomedical researchers—not insurance companies or employers—are by far the biggest consumers of genetic information, but relatively little attention has been paid to them and to the sorts of

policies that should be put into place to regulate research that involves human genetic information.

On November 1, 1997, the National Research Council's Board on Biology brought together a group of scientists and other experts to discuss the policy issues raised by the ongoing revolution in genetic science. The primary reason for the workshop, called "Privacy Issues in Biomedical and Clinical Research," was the worry that federal legislation intended to ensure the privacy of genetic information in medical records could have unanticipated—and damaging—consequences for research. But the discussions at the workshop also identified a number of other problems and potential problems concerning genetic research. For example, in universities and research hospitals an important safeguard against the misuse of genetic information generated by research is the institutional review board (IRB), which must review and approve all research affecting humans; workshop participants identified weaknesses that hamper IRB review of genetic research protocols.

The following is a synopsis and synthesis of the workshop's proceedings. It identifies the main concerns of scientists and others involved with genetic research, it pinpoints particular pitfalls that policy makers should be aware of, and it offers suggestions for the sorts of policies that would allow biomedicine to continue its recent history of dramatic advances.

The Potential—and the Threat—of Genetic Information

In the spring of 1997, teams of researchers in Houston and New York City reported a discovery that may eventually lead to better diagnosis and treatment of several deadly types of tumors, including brain, breast, and prostate cancer. The two groups, one at the University of Texas Brain Tumor Center and the other at Cold Spring Harbor Laboratory and Columbia University's College of Physicians and Surgeons, found that a particular gene on chromosome 10 is turned off in certain malignant tumors. Apparently, when it is working properly, the gene produces a protein that acts as a brake on tumor growth, helping to prevent potentially cancerous cells from turning malignant and multiplying out of control. But sometimes a mutation deletes the gene from a cell and removes that line of defense. With this information, the researchers hope to devise diagnostic tests that will identify, for example, which prostate tumors need particularly aggressive treatment. Eventually, if scientists can develop compounds that mimic the action of the protein made by this gene, the finding could lead to potent new anticancer drugs.

The discovery of this gene, like countless other biomedical advances made each year, hinged upon the ability of researchers to test DNA from hundreds or thousands of tissue samples, looking for a shared genetic flaw. This ability, which did not exist little more than a decade ago, has made it possible for scientists to trace the causes of any disease that has a genetic basis or component, from Huntington's disease and sickle-cell anemia to heart disease, most forms of cancer, and Alzheimer's. To date, the genetic underpinnings have been identified for only a small percentage of these diseases, but the breakthroughs are coming faster and faster, as scientists accumulate more knowledge and develop increasingly

powerful tools for analyzing genetic information. Once the relevant genes are identified, biomedical researchers will have a better understanding of how and why the diseases occur, be able to develop more sensitive and accurate diagnoses, and eventually offer more effective treatments. In the future, researchers hope to use gene therapy to treat and even cure some diseases.

In short, genetic research promises to deliver the most revolutionary improvement of medicine since the discovery of antibiotics, and perhaps the most revolutionary ever. But this advance comes at a price with which many people are uncomfortable: the power of prophecy. Reading a person's DNA has the potential to peek at that person's future. In some cases the prophecy is dead certain. If, for instance, you have the genetic alteration associated with Huntington's disease, then you know that once you reach your 30s or 40s or 50s, your brain will start to deteriorate, you will lose control over your movements, and within another ten to twenty years you will die. In other cases, the predictions are not sure things but instead are statistical statements indicating a predisposition. If, for instance, you are a woman and have an altered version of the BRCA1 gene, your chances of getting breast cancer increase four to seven times more than average. Theoretically, once the relevant genes have been tracked down, genetic analysis should offer probabilistic information about a wide range of afflictions, from how likely you are to suffer from depression or develop cancer to what your risks are for having a heart attack. The predictions, being statistical in nature, would not foretell the fate of any given individual but would be reasonably accurate in estimating, say, how many people out of a thousand with a particular gene would develop diabetes.

That sort of power has tremendous potential for abuse. If an insurance company learned that a woman has the mutated BRCA1 gene, it might refuse to offer her insurance even if she has no prior history of breast cancer. If an employer learned that an applicant was at risk for serious depression, it might look for someone else for the job.

And unfortunately, this is not just a potential problem, **Paul Billings** of the Department of Veterans Affairs in Grand Prairie, Texas, told the workshop. "Genetic discrimination arising from genetic information available from medical records exists in the United States, and there are real losses and vulnerabilities associated with the participation in genetic research and genetic testing." In the early 1990s **Billings** published the first evidence of genetic discrimination in insurance and employment matters, and he has now reviewed more than five hundred cases of people reporting discrimination based on genetic information. The degree of this discrimination has not yet been quantified.

"The primary type of genetic discrimination arises from insurance contract issues," **Billings** said. "The second most common comes when employment benefits are considered . . . The results for some individuals of participation in genetic testing have been uninsurability, unemployability, the lessening of certain other life prospects, and financial instability."

The Human Genome Project

Seven years from now, if all goes as planned, scientists will have mapped out every last bit of the human genome—that is to say, they will have written out all of the genetic information that describes how to construct a human. And when that Human Genome Project is complete, it will offer doctors and medical researchers a powerful tool for understanding the human body and mind.

Each cell of our bodies carries 23 pairs of chromosomes, which together hold approximately 100,000 genes along with control regions for turning the genes on and off and also large sections that have no known function. Each chromosome is a long, twisted double strand of deoxyribonucleic acid, or DNA, which in turn consists of millions of the chemical units called base-pairs arranged like letters in a sentence. The base-pairs—which come in four varieties, denoted A, C, G, and T—are the alphabet of the genome, with thousands of them spelling out a single gene. By learning the precise sequence of base-pairs, one can identify not only the gene but the protein that the gene tells the body how to make. Since proteins are both the building blocks of and the construction tools for the body, a compendium of all the genes in the human genome will offer a blueprint, or at least a materials list, for assembling a person.

The Department of Energy began the Human Genome Project in 1986 and was joined by the National Institutes of Health in 1990. The purpose of the HGP is to sequence every one of the approximately 3 billion base-pairs that make up the human genome. To date, about halfway through the projected 15-year schedule, only about 3 percent of the genome has been sequenced, but the first several years were spent mostly in preparation and the actual sequencing has only recently begun in earnest. Experts predict the project will be finished not too long after its scheduled completion date of 2005.

Even now, with only a fraction of the project finished, researchers are rapidly identifying genes involved in various diseases: diabetes, cardiac abnormalities, various cancers, a form of epilepsy, early-onset Alzheimer's disease, and many more. When the entire human genome is mapped, such identification will become much easier and faster. Hopefully, a simple genetic test could allow doctors to learn what maladies a patient is at risk of developing as he or she gets older and to prepare for them or perhaps prevent some of them altogether.

Not surprisingly, such discrimination, or the fear of it, has made many people leery of offering up their own DNA for testing. The fraction of people who should have genetic testing but avoid it for fear of reprisal is not known. **Vicky Whittemore** of the National Tuberous Sclerosis Association feels fear of discrimination is widespread among those who belong to her association. "The thing that I hear from our members in terms of genetic privacy and all of the issues that are being discussed here is fear—fear of discrimination, fear that release of their medical information or genetic information will have an influence on their eligibility for life insurance, health insurance, or how it will impact them

in their jobs." And, **Whittemore** said, although her association has been successful in recruiting victims of tuberous sclerosis and their family members to take part in research, she has found that the fear sometimes overrides the patients' desire to help find a cure or treatment for the disease. "In the families that I talk to there have been a few who have refused [to take part in genetic research] because of the fear of that information getting out to the public."

Such worries are just one part of the public's uneasiness with genetic testing, said **Paul Berg**, chairman of the Beckman Center at Stanford Medical Center. "In addition to the concern that the results of genetic testing could be used to deny health care coverage, there are other issues that concern many people. One of these is the psychological impact of knowing of their predisposition to serious disease. One frequently hears, 'How am I going to deal with knowing that I have a predisposition to such and such? I have to worry about my children, and how to deal with my sister who carries the same gene.' And so on and so forth. There are all these emotional issues. Health care is important, but this other issue which is a little harder to put your finger on, is out there. It seems to me that the privacy issue is not only whether somebody else will know, but how the tested individual is going to deal with it?"

The public uneasiness may be understandable, but it is also exaggerated by the tendency of scientists and others to focus on genes to the exclusion of the other things that go into making a person. So perhaps, said **Shirley Tilghman**, a molecular biologist from Princeton University, the best approach will be to remind the public that although genetic research is an incredibly powerful tool, it is far from omnipotent. "Genes do not determine who we are," she said. "Genes are essentially a blueprint and on that blueprint many, many different houses can be built. I think there is an enormous danger as we head down this road towards defining ourselves by our DNA sequence that we will leave the impression with the public that you are who your genes are. You are not who your genes are. It is a much more complicated dynamic than that, and I think the public acceptance of knowing more genetic information will be directly proportional to the degree to which they understand that basic underlying fact."

Can We—and Should We—Ensure Genetic Privacy?

Faced with the specter of people unable to get insurance or jobs because of their genes, state legislatures around the country have begun passing laws to prevent this sort of genetic discrimination. Such efforts are admirable, the workshop members agreed, but they can unwittingly go too far. In particular, when legislators move beyond banning genetic discrimination to trying to establish some sort of genetic privacy, their efforts are likely to run into complications.

The idea itself is beguiling: set up a wall around a person's genetic information so that no one can access or exploit that information without the person's express consent. But ensuring genetic privacy is not as simple—or as desirable—as it sounds. The workshop participants described several dilemmas.

One practical difficulty is that it is nearly impossible to say where "genetic" information stops and other medical information begins. "There is no feasible operational way that you can carve genetic information out of the medical record for purposes of rational legislative or regulatory oversight," said **David Korn** of the American Association of Medical Colleges. "You just cannot do it. And yet so much of the public debate has been focused on these terms as though they were in fact discrete and unambiguous elements that could be grabbed, bounded and managed. I think the more we continue to go that route, the more confused and impassioned this debate is going to be."

Vicky Whittemore of the National Tuberous Sclerosis Association offered a concrete example of what Korn was talking about. "You cannot walk into a doctor's office and get a genetic test for tuberous sclerosis," she said, noting that one of the genes that causes tuberous sclerosis was identified only last August. So it is not possible for a person's medical file to contain "genetic" information about the presence of the disease, at least in the sense of a genetic test that

pinpointed the faulty gene. "However," she continued, "if I am diagnosed with tuberous sclerosis clinically because I have had an MRI of my brain, an echocardiogram of my heart, and I have had a skin exam, then that information is in my medical record. And the words 'tuberous sclerosis' written in my medical record are genetic information. So, with respect to laws being proposed to separate genetic information from medical information, in many cases that is impossible, without going back and erasing the words 'tuberous sclerosis' out of my medical record wherever they appear." In short, much of the standard information in medical records is actually genetic in nature, although little of it today actually derives from genetic testing.

At first glance, it might seem possible to guarantee privacy for only that information which comes directly from testing a person's DNA and leave other medical details, even those with genetic implications, alone. But that too is impractical, for a different reason.

As researchers learn more and more about the genetic contributions to disease, that knowledge will become an increasingly important part of treating disease. For example, **Edward Penhoet** of the Chiron Corporation in Emeryville, California, spoke of "the progress which is being made in identifying tumors very carefully from a genetic point of view so that when we treat the tumors we will have the maximum amount of knowledge available to us for that treatment." A doctor might know, for instance, that breast tumors in women with one particular genetic mutation would shrink rapidly when exposed to Drug X, while tumors in women with a second mutation would shrug off Drug X but respond well to Drug Y. Thus the results of the genetic test would need to be an integral part of the medical record.

"The more information the better if you are trying to treat an individual patient," **Penhoet** said, "but it seems to me that we are spending a lot of time creating barriers to the truly valuable aspects of this which will come in the near term when we are able to describe each person in much greater detail and therefore customize treatment to individual people in a way that makes treatment much more effective for a variety of different diseases." Regulations that wall off a certain amount of information in the name of genetic privacy would "compromise our ability to address the truly more important issue, which is how you use all this information to develop medical treatments which are much more specific, much more targeted, and therefore much more effective."

More generally, **Korn** said, the urge to create a right to genetic privacy betrays a lack of understanding of how the American system of health care and biomedical research operates. "I think of the system as one in which there is a set of overlapping, interlocking activities among which there has got to be a very low impedance flow of information in order for the system to work." Anything that blocks that flow of information, such as strict regulations regarding the use of human genetic data, will inevitably hurt the effectiveness of both research and medical care, he said. "I think people don't understand the degree to which both

The Dark Side of Genetic Privacy

Frederick Anderson, an attorney with Cadwalader, Wickersham & Taft in Washington, D.C., offered a perspective on the problems of genetic privacy quite different from those of the biomedical researchers at the workshop. As genetic information becomes more plentiful and more precise, he said, it will become much more valuable and much more coveted. Passing laws that give an individual total control over his genetic information would create enormous tensions between the individual and the people and groups that would like to—or might even need to—get access to that information.

"I predict black markets in information," **Anderson** said. "I predict squabbles between spouses because the husband or wife never reveals the condition that they by law are entitled as an individual in a rights-based culture to keep secret. They haven't shared with their family. They haven't shared even with their own physician, with whom they are thrust into an adversarial posture because of the kinds of laws we are drafting. And they certainly haven't shared that information with their insurers or their employers."

"The fact is, though, we as human beings in a society need to have that information available to precisely that list of role players with whom we are not willing to share the information." Spouses will want to know before they decide to have children if their partner has a genetic disease. Doctors will need as much genetic information as possible to perform the best treatments. And that information will inevitably go into the medical record, which insurance companies and employers will demand to see.

"So," **Anderson** said, "we are going to end up coming back to some kind of socially acceptable way to have the information shared, including with insurers." Simply creating a right to genetic privacy is a recipe for decades of legal wrangling, which would keep lawyers like Anderson busy but would not be in the best interests of anyone else.

the American health care delivery system and the vast array of medical research have to have access to records and samples and other archival patient materials. So, with the best of intentions, some of these state initiatives begin with a call for preventing discrimination in the health insurance market specifically and then move on to large statements about disclosure of information that simply would tie everything up in knots. It would be like throwing sand in the gears if such language were applied as articulated. It just won't work, and I think the problem is that the people trying to do these things don't understand how the system works."

Creating a right to genetic privacy will come at a price, **Korn** concluded, and that price will be to hamper the nation's system of medical care and research. "The issue then is where you draw the line between a low impedance free flow of information and a very high threshold barrier to inappropriate leakage, and that point has not been well defined in the public discourse." Up to now, he said, the debate has generally been presented as a choice between two extreme positions.

"Either you don't want any barriers, which I don't think is politically viable, or you want barriers thrown in all over the place, which will bring the whole system to a halt." Ultimately, he said, finding the best solution will depend upon understanding the system and the various tradeoffs involved, debating those tradeoffs, and finding a balance between the desire for genetic privacy and the desire for continued improvement in the nation's health care system.

Handling Genetic Data in the Laboratory

In the summer of 1996, just as laboratories around the United States were gearing up to begin sequencing the human genome in earnest, a sudden realization threatened to bring things to a halt. For years, since the start of the Human Genome Project, researchers had assumed that the DNA they would be studying would come from a large number of sources—so large that it would be practically impossible to identify any given bit of DNA as coming from a particular person. But as the time for serious sequencing approached, genome researchers noticed that almost all the DNA they would be working with was copied from the DNA of just four donors, three men and a woman, and the identities of at least a couple of them were known because they worked at two of the labs providing the DNA for the sequencing effort. To make matters worse, at least two of the four were apparently not told that their genetic sequences were to be made public, so they had never given their consent to this use of their genes. Of these two, one had since died, so scientists could not go to him and ask for belated consent.

This posed a dilemma. Researchers had worked for years to prepare large libraries of clones—identical copies of short stretches of DNA—from the genomes of these donors, and it would be time-consuming and expensive to do it over with other donors. On the other hand, the four donors might some day face unpleasant consequences. "Their redundant DNA would be out there for anybody to look at and draw conclusions from," noted **Shirley Tilghman** of Princeton University. "If an insurance company finds out it is this guy's DNA that is largely in GenBank, looks up this guy's DNA and finds he has 27 recessive alleles and is going to be a big-time problem with early onset Alzheimer's," the donor could find it impossible to get health insurance.

At the same time, some genome workers worried about the political correct-

ness of the DNA libraries. Being mainly from staffers at genome laboratories, might the selection of DNA be seen as elitist? Would some people wonder why there were three men and only one woman contributing DNA? Was the set of donors diverse enough? "There was sensitivity to how it would be publicly perceived, who was selected," said **Raymond White** from the University of Utah.

So the choice was made to work out an agreement between DOE and NIH for such libraries and to phase out use of those with known donors. "It was painful," recalls **Tilghman**, who served on the council that made the decision. But it seemed necessary to get fully informed consent from the donors and make sure that their identities remained secret.

Pieter de Jong of the Roswell Park Cancer Institute in Buffalo, New York, described the process for collecting a new set of DNA. Advertising in Buffalo in newspapers and on radio, he and his colleagues attracted five or six hundred willing donors. They took the first ten male and ten female volunteers who were okayed by genetic counselors. Each of the twenty gave a blood sample and was paid a small amount of money—in cash, so there would be no paper trail leading to the donor. "The blood samples entered into my laboratory with a number on them rather than a name," **de Jong** said. "Numbers were taken off and replaced by our own lab numbers. No records were kept about this correlation, so there was no way for us to go back to knowing which twenty people they were." Then two donors, one male and one female, were selected at random to supply the DNA to make the libraries of DNA clones. The only record of who took part in the study is twenty sealed envelopes, each containing a consent form with the signature of one of the donors. The result of all this secrecy is that it would be practically impossible for anyone, even the researchers, to learn whose DNA was analyzed for the Human Genome Project. "The best chance of revealing the identity of the donors is through the donors themselves," **de Jong** said. "They know they have a 10 percent chance that they eventually were the people who delivered the blueprint which is part of the genetic database."

As this tale illustrates, the field of genome research is still so new that researchers sometimes find themselves making up the rules as they go along. Many of the issues that genome researchers face are either not covered at all under existing policies or else are regulated by policies that were intended for very different sorts of research and are not appropriate for genome work. More specific standards will need to be developed to deal with dilemmas created by the new genetic technologies.

Consider, for example, the difficulties that genome researchers face in trying to comply with the Privacy Act of 1974. The Act forbids government agencies (and their researchers) from maintaining secret files of any type on individuals, noted **Sherri Bale**, a genetic researcher at the National Institute of Arthritis, Musculoskeletal and Skin Diseases, but genetic research demands a certain amount of discreteness. "We are supposed to allow people to see the records kept

on them," she said, "and that is an issue because there are certain pieces of information that in my consent document I tell people they will not see." For example, genetic testing may reveal that a child was not fathered by the man who believes he was the father. **Bale**—along with many other researchers—does not reveal this information, and she tells her subjects before the experiment that she will not reveal it. "I think it is a good decision," she said, but it is "a little bit in conflict with the Privacy Act because the misattributed paternity information is in my research record, and I don't open that research record to the individuals who I am supposed to allow to see all their records."

In general, a literal reading of the Privacy Act would seem to imply that any withholding of information from the records of any government researcher is illegal. Yet because this record often contains sensitive details that are not relevant to the medical care of the patient and whose release could actually harm the patient, researchers like **Bale** take a less-than-literal reading of the Act.

The Clinical Laboratory Improvement Amendments of 1988, or CLIA, offers a different set of problems for genetic researchers. To ensure the clinical value and a minimal quality of precision and accuracy of clinical lab work around the country, the Act imposes standards on all clinical laboratories. This includes the mandatory testing and periodic on-site inspections. Because research labs are not intended to provide information for use in clinical care, few worry about or are even aware of the CLIA regulations. But this means that, by law, they cannot provide to patients the genetic information generated from research testing.

"This is a very big issue where I am from," **Bale** said, "whether or not we can release this kind of information even to the patients themselves. People in the research labs are ignorant of or just tend to ignore the fact that the CLIA regulations are there, and in some cases information just goes out. In some cases it goes into the medical chart, in others it goes to the research chart. In some cases it goes directly into the hands of the referring physician and in others the hands of the participants themselves.

Not releasing the results of genetic tests to the subjects is not an attractive option, **Bale** noted. "A lot of people come into these studies because they want to know what their mutation is." If the research results would be kept secret, many people will not participate in the study. Furthermore, there is a tension between the Privacy Act and CLIA, the former demanding that nothing be kept from the subjects and the latter demanding that certain things not be released. Research labs generally cannot become CLIA certified because of the expense and difficulties posed by an array of requirements intended for clinical laboratories.

Yet another challenge for genetic researchers is the consent form that subjects must sign in order to take part in an experiment. The guidelines and requirements for consent forms were not designed with genetic experiments in mind, and researchers find themselves scrambling to meet these mandates. "We are required," **Bale** noted, "to tell everybody that their participation is voluntary and they can withdraw at any time," but what does "withdrawal" mean when the

Archived Data

One particularly sticky genetic privacy problem concerns what to do about archived data. "The national bank of archived human tissue is vast," said **David Korn** of the American Association of Medical Colleges, "and institutions that have a long history—Yale, the Massachusetts General Hospital, Hopkins—may have over 1 million archived cases. Not samples, but cases with multiple samples that are all basically accessible like an archaeological dig, if you will." And all of these records are potential sources of information for genetic researchers looking to understand a particular disease.

Unfortunately, almost none of these samples were obtained with a consent form that would allow such genetic research to be done on them. How, then, can this vast bank of information be put to use?

The case of the National Health and Nutrition Evaluation Survey (NHANES) offers one answer. "The NHANES III story," said **Sherri Bale** of the National Institute of Arthritis, Musculoskeletal and Skin Diseases, "is that between 1988 and 1991, 7900-plus subjects ages twelve and up had white blood cells stored on them, and between 1991 and 1994, another 9500 subjects had white cells frozen on them, and 8200 cell lines have been established already and are stored." These cell lines can be used for, among other things, extracting DNA and doing genetic research, so the researchers who collected the data and samples wished to make it available to genetic study. Unfortunately, when the study began, no one had thought to ask the donors to consent to such genetic testing.

The Centers for Disease Control and Prevention (CDC) decided that the samples could still be made available for genetic research if they were "anonymized." So, **Bale** said, "we have gotten to the point of trying to define what this new verb 'to anonymize' means. The definition that the CDC staff has come up with is that anonymized samples are those where no one, including the staff of the CDC, is ever able to link the results of a genetic test or any kind of test done on DNA back to the survey participant." To this end, the samples will be made freely available but identified only by race, sex, and ten-year age groupings. These data will be useful to researchers who wish to study how common various alleles, or versions of a particular gene, are in the population. If researchers want further information, such as disease status or exposure to possible carcinogens, they will have to come up with a research design that guarantees that the anonymity of the data will be kept intact. As for detailed information on the subjects, such as would appear in a medical record, that will not be provided, as it would theoretically make it possible to identify the donors.

In general, anonymization seems to be the only way to make archived material available to genetic researchers short of contacting the original donors and asking them to sign new consent forms, a process that, in most situations, would be prohibitively expensive. It is not an ideal solution by any means, as it limits researchers to a small percentage of the information they could glean from these archives, but no one has come up with an acceptable alternative. "There has been a tremendous amount of discussion on this, as you would expect," **Bale** said, "and this was the only solution that [NIH's Center for Human Genome Research] and [the National Cancer Institute] would allow."

researcher may have already sequenced the person's DNA and put it into a database? "Do you destroy the sample? Do you destroy the information that you have already gleaned from the sample?" As **Susan Rose** of the Department of Energy commented, the option of opting out of an experiment makes no sense after researchers have isolated or even published the subjects genetic sequence. "That is another example of something that was written for a biomedical situation where somebody is on a therapeutic drug or something like that. The idea of checking in and out when the DNA sequence taken from your sample has been published is an example of something that doesn't fit the genetics world."

Perhaps the most vexing issue facing genetic researchers is how to protect the privacy of individuals, such as those whose DNA is being used in the Human Genome Project, without compromising the research itself. The obvious solution might seem to be an approach like the one **de Jong** took in assembling the samples for the genome project's new clone libraries, when he made it practically impossible for anyone—even the researchers involved—to identify who provided a particular genetic sample. Such "anonymization," however, is not suited for most genetic research. Workshop participants agreed on this point more than perhaps any other issue, and several of them explained in great detail the value of maintaining a link to the medical records of the donors of genetic information.

"In our research now it has become very important to be able to go back to the individual who gave the original tissue sample," said **Vicky Whittemore** of the National Tuberous Sclerosis Association. Working from DNA provided by a number of people with tuberous sclerosis, researchers have recently identified two genes that cause the disease. Now, **Whittemore** said, scientists want to go back to the medical records of the individuals that supplied the original samples and correlate the symptoms each has with the genetic mutations they have. In this way the researchers can learn more about how the particular mutations produce the disease and, eventually, come up with ways to treat it. But if the original samples had been stripped of all identifying information, it would be impossible to do this.

In the same vein, **David Korn** of the American Association of Medical Colleges argued that for many types of studies it is vital to have longitudinal data—information that is accumulated over time, usually years or even decades—and that this is impossible if the data are made anonymous by destroying links to the subjects' identity and medical records. Suppose, for instance, a researcher studying a collection of tissue samples from breast tumors has discovered a particular genetic marker (a stretch of DNA used to identify genes) that seems to be associated with the tumor. If the researcher knows the identity of the donors of the samples—which may be a decade or two old—he can follow the progression of these patients' tumors over time and look for correlations between the marker and the development of the disease, perhaps discovering a way to predict its course ahead of time. Without identification, the archived tissue samples have much less value.

"Anonymization decisions mean irreversible disruption of linkage," **Korn** noted. "No one will ever be able to restore that link." In some studies, such as the Human Genome Project, this may not be a problem, but in others "it really means that you are destroying the utility of the material. Without having the ability to get the additional correlative or follow-on information that may, in fact, already exist, you are severely truncating the significance, the interpretability, the impact of whatever it is that you are measuring. People have to realize what the trade-offs are on these kinds of decisions."

An even more important reason not to anonymize genetic data may lie in the emerging field of predictive medicine. As **Barbara Handelin**, a genome consultant for private industry, explained it, predictive or prognostic medicine will tailor treatments for a particular patient according to that patient's genetic makeup. To that end, she said, researchers are now trying to understand such things as "why people respond or do not respond to certain drugs or to certain kinds of therapy, why people have adverse reactions to drugs, and how we can better define cancers." So doctors of the future may speak to their patients like this: "I want to give you this drug but before I do we are going to have to do some kind of genetic profiling on you because we know that there are three groups in the population and if you are in Group X you are going to have a very bad reaction to it so clearly I am not going to give it to you. Furthermore, I am not going to give it to you if you are in Category A because we know that people of the A profile simply don't get much therapeutic benefit from this drug."

The promise of this sort of medicine is hard to overstate, **Handelin** said. "We could produce a rational delivery of diagnostics and therapeutics. We would overall save medical dollars spent. We would give medicine to people who really benefit from it and not give it to people who would be harmed by it, and, also, we would develop new drugs that would address the reasons why some people don't respond to the drugs that we already have. We would also be able to stratify patients into groups according to how much time and money we need to spend monitoring them, for example, for a certain future disease."

But developing such a genome-based medicine will demand a tremendous amount of information correlating genes and diseases. "We would need to study large populations of people. We would need to access a lot of the archival material that Dr. Korn just referenced in order to study lots of individuals, to understand the variability that impacts on all these aspects of how we develop disease. Then we would need to correlate those genetic profiles with exhaustive clinical information. It is of no use just to have the tissue. We have to be able to connect the tissue with as much information as we can find out about that person, with the exception of things like your name and address, telephone number, e-mail address. Everything else about you, we want to know. We would need outcome data. We would need drug history. We would need to be able to put all that information together into some really large informatics capability to be able

to make complex analyses, to be able to draw conclusions and associations between genotypes and a whole bunch of clinical information."

"It is not just the good of the researcher in this case," added the University of Utah's **Ray White**, "but it is really the public good that is at stake."

For these reasons, many workshop participants agreed, wherever possible genetic data should be maintained not anonymously but with identification that will allow researchers to get further information on the donors. However, until the extent of the threat of genetic discrimination is known, several participants suggested that modern encryption techniques might offer a way out. **Carol Dahl** of the National Cancer Institute summed it up this way: "Are there technologies out there that will enable us to encrypt information to allow us to use it in a prospective way for studies in research while protecting that information from incorporation into medical records and from insurance companies gaining access? Clearly encryption is not perfect, but there are industries out there in defense and banking that have spent a lot of money trying to make it as secure as possible." If such encryption technologies were put to work in genetic research, she said, "we might be able to actually protect patients in research studies rather than looking for legislative ways of solving our problems."

Institutional Safeguards

The first line of defense against misuse of genetic information garnered from research will always be the researchers themselves. In designing and carrying out their experiments, scientists try to make sure that their subjects are protected, and in general they do a good job. But because individual researchers cannot be expected to spot all the potential pitfalls of a project, universities, research hospitals, government labs, and many corporate labs supply a second line of defense: the institutional review board, or IRB.

"Any research that is federally funded or that is being done for submission to the FDA must by law be reviewed and approved by an IRB," noted **Leo Whelan** of the legal department at Mayo Clinic. And in general, **Whelan** said, the IRB approach seems to work well, allowing local oversight of research that can be tailored to local conditions. "It has been very effective in determining what type of review is appropriate, determining what the risks are, addressing those risks, and advising the researchers on appropriate ways to handle the confidentiality and privacy issues, which often have to be tailored to the research. For example, if you are involving minors in genetics research, a whole host of new issues come up. When you have a family linkage study as opposed to a study dealing with individuals, when you are dealing with patients from your own institution versus a population of samples coming from a variety of different institutions—these pose very different sets of issues."

Despite the apparent effectiveness of IRBs at Mayo, however, many workshop participants thought that the IRB system as a whole needed improvement if it is to be effective in protecting the subjects of tomorrow's increasingly powerful and sophisticated genetic research.

One major concern is that IRBs are only as good as their members, but many

institutions put too little effort into supporting and compensating IRB members, which makes it difficult to retain the people best suited for the job. "Where more and more responsibility is being put on IRBs, you have to remember these are non-paid slots, voluntary, and a lot of time is required," said **Pearl O'Rourke** from NIH's Office of the Director, who recently moved from the University of Washington, where she served on an IRB. While there, O'Rourke found that many clinicians were hesitant to serve on the IRB because it represented 8 hours a month of their time that weren't billable hours. "I also found that as a physician I could sway any vote because community members and others [on the IRB] did not have a clue about genetic information. I also felt that in terms of the local interests as soon as you have NIH or any federal moneys on a grant there is the bias that you have to okay this project because it is good for the institution." If IRBs are to be effective, she said, institutions must find some way to reward or "validate" service on them. "It cannot just be this volunteer, non-paid, 'Oh, yeah, I can do it' thing."

Besides attracting and keeping good members, IRBs must find some way to keep up-to-date on the areas of research that they are considering, and they do not seem to be doing a good job of that now. "Professor Mildred Chou at the University of Pennsylvania and I have published a study of IRBs in the J*ournal of Investigative Medicine* focusing on a genetic issue," said **Paul Billings.** We concluded that most IRBs were seemingly poorly informed about much that was going on at the national level or in states about the social, ethical and legal issues surrounding genetics." One potential solution, **Billings** suggested: "It might benefit IRBs substantially to have some sort of network of communication, and sharing of information, that apparently is not present currently. IRBs should be informed of research findings, board reprints, commissions and other sources relevant to their deliberations."

Finally, **David Korn** argued that although the local character of IRBs may have advantages, it also carries a cost. "There may be two or three thousand IRBs extant in the country right now, and every one of them is on its own in trying to interpret a particular research proposal and determine what standards it needs with regard to authorization or this or that or the other." This lack of standardization means that similar research projects performed at different institutions may be evaluated quite differently and placed under quite different constraints. The result is that researchers never quite know what to expect.

"We hear all kinds of scare stories from institutions around the country where research proposals involving issues of genetic information and data privacy have been sitting in the local IRB for up to 2 years while these people sit and have talmudic discussions about whether it can or it can't or what should be done and what shouldn't be done," **Korn** said. "Mr. Whelan's IRB may be an excellent, well-functioning IRB. But many of them are troubled by these issues and don't really know where to go. So, I think that a federal standard that provided some clarity would be useful."

The closest thing to a federal standard on genetics research now available is a set of IRB guidelines published by the Office for Protection from Research Risks (OPRR) in 1993. It was intended to serve as an educational tool for researchers and members of IRBs, said **William Dommel** and **Melody Lin** of OPRR.

The OPRR's process is not entirely satisfactory, **Korn** said. "Those guidances almost have the effect of rules. Once they are issued IRBs tend to pay very, very careful attention to them." But because the guidelines were not intended to serve as policy, they did not go through a formal rule-making process with public input and debate. "I am not trying to make more work for the government," **Korn** said, but it would be useful if OPRR or perhaps some other agency would go through such a formal process, with input from the public, to set out policies that IRBs across the country should follow.

Sheri Alpert of George Mason University explained her concern about the IRB review process. "The current regulations only require an IRB to look for risks when information is identifiable to an individual or affects an individual. This does not protect the privacy of an identifiable group that may be ideal for the study of a particular genetic disease." The group may not want to be associated with, or known as high probability carriers for a specific "disease gene." Simply being recognized as a member of that group has the potential to affect their privacy, whether as an individual they carry the gene or not. "I would say the regulations need to be strengthened or re-examined as more and more genetic analysis occurs that is specifically identifiable to an ethnic or social group that has a genetic dimension."

But if IRBs have their shortcomings, they are clearly much better than no review at all—which is precisely what a great deal of genetic research in the United States may face. "Well over half of all the dollars spent in the United States in the pursuit of genetics-based research is spent today by private industry," mainly by pharmaceutical and biotechnology companies, said **Barbara Handelin**, a private genome research consultant. "Those research protocols that are not done in collaboration with an academic institution and not funded by federal moneys are not subject to IRB review." Drug companies are required to get IRB approval for any research that will be submitted to the FDA in support of a new drug, but that still leaves a great deal of private-industry research uncovered by IRBs. "Mostly what ends up in an FDA filing is preclinical and clinical research," **Handelin** said. "Basic research typically does not end up in an FDA filing."

Non-profit organizations may pose a similar problem, said **Vicky Whittemore** of the National Tuberous Sclerosis Association. "As a non-profit we give out a significant number of research dollars, as do many other non-profits. We require our researchers to submit IRB approval for our applications, but I don't know how widespread that is among non-profits, and it raises the issue

of how much clinical research is actually being done on patients with non-IRB approved protocols. I don't know."

If private companies and non-profit organizations are to conduct genetic research, some workshop participants said, they should hold their researchers to the same standards that federally funded scientists are held to, and that implies review by IRBs or something comparable. "I think that it is incumbent upon the industry to do its own homework," **Handelin** said, "and I would hope that that can be done in the absence of new and burdensome regulations, that industry gets it together to take a much clearer look at the need for external review of research protocols that are being conducted by and funded by companies. I think that this industry actually should be held to a higher ethical standard than many other industries because we deal in and are given the privilege of dealing in some of the most vulnerable aspects of our society."

What, If Anything, Should the Federal Government Do?

While the immediate impetus for the workshop was the worry that ill-considered federal legislation could harm genetic research, participants at the meeting were not necessarily asking that the federal government stay out of the issue altogether. Indeed, as **Anne Phelps** of the Senate Committee on Labor and Human Relations noted, "A lot of [Congress's involvement] has been at the request of the research community and the genetics community. They came to Congress and said, 'You need to act.'" But act how? Much of the discussion at the workshop centered on the question of what the federal role should be.

Some participants, particularly **Paul Billings,** thought that the federal government should play little if any role, given current conditions, in the areas of genetic privacy and genetic discrimination in health insurance. Because health insurance is primarily regulated at the state level, Billings argued, the individual states have more experience and are better equipped to legislate. "I would suggest that federal legislation should only be directed at reducing the stranglehold that the ERISA exemption has had on the states' ability to legislate in areas of genetic discrimination, and to ERISA, the Employees Retirement Income Security Act of 1974, imposed federal regulation on insurance plans offered by companies to their employees and thus preempted much of what states can do to oversee such medical coverage. Congress should return to the states much of their traditional ability to regulate health insurance, including issues of genetic discrimination, **Billings** said. Otherwise, it should stay out of the area for now, "except to rectify gross inequities of state legislation."

Billings said that if states were given this power they would be unlikely to pass legislation that would harm research. There has been no negative impact arising from the genetic discrimination legislation that was passed in California on the conduct of clinical or basic science in that state."

Other researchers disagreed, however. **David Foster** of Genzyme Corporation in Cambridge, Massachusetts, described how the Massachusetts legislature was close to passing a law that would have crippled certain types of research in the state. "They have been at this [writing genetic discrimination legislation] for two years, and now that some of our key research folks, like Massachusetts General Hospital, are starting to review legislation which is actually ready for passage, they have discovered that it would shut us down. When the research folks look at this and think it through, they are dumbfounded. They cannot believe that state legislatures would pass certain things that would really prohibit a lot of the research that we take for granted today."

As observed by **Eleanor Kerr** of SmithKline Beecham, "it is a mixed bag out there." California legislators may have done their homework and produced a reasonable law, but other legislatures have not. "The danger here is that without federal legislation states are racing ahead. You saw a list of ten bills in Congress. There are literally hundreds on the state level. I think about twenty states have now passed statutes. There are states that have passed statutes, that have repealed them and passed new ones. We are not just dealing with California."

For that reason, many of the workshop participants seemed to want the federal government to step in. "I think one of the hopes of the research community," said **Raymond White** of the University of Utah, "is that reasoned legislation at the federal level might actually supersede a large number of local efforts which might not be so well thought through and might, in fact, be damaging to local groups."

A second argument for federal involvement was that even if all the states passed reasonable legislation, there would still be fifty different sets of regulations. "One of the concerns about approaching this state by state," noted **Leo Whelan** of the Mayo Clinic's legal department, "is that it is very easy to conceive of a situation where samples are collected in one state under full compliance with that state's laws and then the researcher later hopes to collaborate with a researcher in another state but is unable to do that because of differences in the two states' laws. That could be a very significant problem."

Or, **White** said, consider the nationwide cancer-genetics network that the National Cancer Institute is now planning. "Can you imagine trying to share records not only between states but to merge and provide access to records at the national level if each state, each community, each principality has its own set of regulations which you must satisfy in order to create a merger? I think that the effort would be effectively gutted were that to come to pass."

If the federal government is to get involved, what should it do? Perhaps the first and most important thing, some workshop participants said, was to keep the issues of genetic discrimination and access to health care separate from the policy issues surrounding genetic research. Because genetic research produces information that, if leaked, could lead to a research subject losing health insurance, there is a natural tendency to put genetic research and genetic discrimination into a

National Health Care

When the discussion turned to protecting people from genetic discrimination in health insurance, several workshop participants suggested that the best solution would be to reform the entire national health-care system. "I urge that we not disintegrate this discussion of privacy and privacy law from the fact that health care financing is significantly broken in the United States," said **Paul Billings** of the Department of Veterans Affairs in Grand Prairie, Texas. "By fixing that, we would change this discussion enormously. The losses that research subjects might face as they enter into medical research would be changed if these willing individuals did not face the chance of losing their ability to finance health care."

A number of forum participants felt we would be facing fewer issues in genetic research if our health care system wasn't based on a system of voluntary private optional health care.

Even if the country does not move to such a system in the short run, advances in genetic research and medicine may leave it no choice in the long run, argued **Frederick Anderson**, an attorney with Cadwalader, Wickersham & Taft in Washington, D.C. In the future, he predicted, people will be able to foresee quite accurately, through genetic tests, what their life expectancy and health problems are likely to be. On the other hand, given if it is possible for people to keep that genetic information to themselves, it will put insurance companies at a huge disadvantage. "As a cynical lawyer," he said, "I predict individuals will choose their life insurance and health insurance in such a way as to deal with one's condition, which twenty years from now they will know quite accurately, so that the insurers will be bankrupt and will have to spread risk over the largest possible pool, and that will be a national health insurance scheme."

Billings, citing a study from the University of Utah that found people with genes predisposing them to breast cancer did not modify their insurance choices, thought Anderson was being too pessimistic. "There isn't much evidence that adverse selection will occur in pools with this [genetic] information. There are lots of other factors that go into why people buy insurance and how much they buy."

"If I were 40 years old," *Anderson* replied, "with three kids, and in receipt of a genetic profile that says that I am at a 75 to 80 percent chance of being very ill and dying between fifty and sixty years of age, I think it would be irresponsible of me not to take that information into account in the health care that I purchase and the life insurance that I purchase. I would be astonished if, as studies come out over the years, people in resounding numbers insist on ignoring this information."

single box. Then setting policy becomes a matter of weighing the benefits of genetic research against the costs to the people involved. That is the wrong way to go, **Billings** said. "I don't think we want to set up a situation where we are balancing people's access to health care—that is, research subjects' eventual access to health care—against scientific freedom and the conduct of scientific research." Instead, the two issues should be addressed separately.

Although the first of those two issues—how to prevent genetic discrimination, particularly against the subjects in genetic research—was not officially on

the workshop's agenda, the participants did discuss it and offer suggestions. Some argued that the best solution was a national health care system. [See box, page 24.] Others thought that since national health care is such a controversial topic, it makes more sense to look for solutions that fall short of that. **Cynthia Kenyon**, a researcher at the University of California, San Francisco, offered one possibility: "Since the primary risk that the individual volunteers face is loss of health insurance, why not have the government guarantee to provide health insurance to every individual that is subject to genetic testing?" Since genetic research is for the common good, she said, it makes sense that the country protect those people who might be hurt financially by participating in genetic research.

Or the risk to research subjects might be dealt with by laws preventing discrimination on the basis of genetic testing. "The health insurance law that passed last year does prohibit genetic discrimination in health insurance in certain instances," said **Phelps**, the Senate staffer. It also set a precedent for the proper way to think of a genetic predisposition, she said. "There is social significance and awareness attached to the legislation as well. One of the key elements was the language saying that a genetic predisposition to a disease is not a diagnosis of a disease. It is not a pre-existing condition, and that is as much a social statement as it is a legal one."

Many workshop participants did not believe that concerns about genetic discrimination could be dealt with by trying to establish some sort of right to genetic privacy. Too much genetic information is already in people's medical records, and the amount of such information will increase dramatically in coming years. Yet people's medical records are not private now, at least not in any practical sense, and that isn't likely to change soon. "I truly do not believe that we have the political capacity in this country in the short term to secure medical information to the point where people who worry about privacy will ever be comfortable," said **David Korn** of the American Association of Medical Colleges. "There are too many necessary folks rummaging through the files."

"The key question," **Whelan** said, "is whether you have information generated by the research getting into the medical record. If it does go into the medical record, then the privacy risk really becomes significant because the medical record—for all the protections afforded it—is often shared with health insurers, life insurers, and employer owned benefit plans. If the person ever becomes party to litigation, it is often disclosed, and there are a number of other means for disclosure of the medical record."

But, **Korn** said, if genetic information generated in research is never passed along to a subject's medical record or to the subject, it should be possible to keep it private. "I really do believe that we could secure the research database," he said. "There is no reason why any external entity should be entitled to forcibly get into a research database and poke around in it." And this, most workshop participants agreed, is a step that the federal government should take, and take quickly.

Current Genetic Discrimination and Privacy Legislation in the 105th Congress

Irene Stith-Coleman of the Congressional Research Service reviewed the current legislation (Fall 1997) pending in Congress which had the potential to affect biomedical and clinical research. This legislation can be grouped into 3 area's: legislation devoted to the privacy of medical records, legislation devoted to the prevention of discrimination from the use of information in medical records, and legislation devoted to the more specific regulation of how to perform genetic research (see Table 1). According to Stith-Coleman, "Three bills are more generic in terms of medical information privacy, 9 bills are more specific to disclosure, use and protection of genetic information, and one bill, Domenici, which is quite comprehensive in addressing specific considerations while doing genetic research."

"There is a continuing debate as to the most appropriate strategy in dealing with the issue of genetic discrimination or issues of medical record privacy." According to Stith-Coleman, "a hearing by the Senate Labor Resources Committee was supposed to be focused on general medical privacy, but the discussion evolved into something that focused on genetics, much like today's deliberations. So the verdict is still out as to which strategy will be used to address this issue"

"Domenici's bill is quite comprehensive in addressing research considerations, so I will spend most of this time highlighting some of the provisions pertaining to this bill," said Stith-Coleman. The bill has provisions that would require anybody who would be collecting tissue to provide so-called "vital" information, as well as provide certain rights to the test subjects. The tissue collector must inform the subject what the expectations and implications are for the genetic tests. The individual has rights to rescind consent anytime before the analysis is initiated, and this would include the right to order the destruction of any identifiable DNA sample as well as the right to examine clinical records. "In addition," said Stith-Coleman, "there are provisions for civil penalty if these rights are violated."

There are "re-transfer" controls which would apply in cases of discontinuation of the activities pertaining to the protocol under which the tissue was obtained. "If a researcher is planning to transfer the tissue, or if the services for which the tissue was obtained are ceasing for some reason, information would have to be provided to the subject. The subject would have to give the consent for the tissue to be transferred, or if he or she elects to have the tissue destroyed, the researcher would have to honor this decision. If the researcher holding the sample attempts to locate the 'donor' and doesn't get a response, the tissue may be destroyed, placed in a 'tissue-archive' or transferred to another facility."

"Also within the Domenici bill," said Stith-Coleman, "there are provisions for

"I'm certainly not a legal scholar," said **Eugene Carstea** of the Saccomanno Research Institute in Grand Junction, Colorado, "but it seems that trouble arises when research information is added to a patient-participant's medical record.

Such a policy could protect the subjects of genetic research, thus making the public more comfortable with such research and allowing researchers to recruit

TABLE 1 Genetic Discrimination and Privacy Legislation in the 105th Congress[1]

Medical Information Privacy
H.R.52 (Condit)[2]
H.R.1815 (McDermott)
S.1368 (Leahy)

Use and Disclosure of Genetic Information
H.R.306 (Slaughter)/S.89(Snowe)
H.R.328 (Solomon)
H.R.2275 (Lowey)/S.1045 (Daschle)
H.R.2215 (Kennedy)
H.R.314 (Stearns)
H.R.2198 (Stearns)
H.R.2216 (Kennedy)
S.422 (Domenici)

[1]Text and status of these bills can be accessed at www.thomas.loc.gov.
[2]H.R., House of Represenatives. S., Senate.

defining the responsibility of the IRB or similar Board that is overseeing genetic research. The IRB or Board must determine whether or not the sample is essential to the project, and balance the benefits to society versus the risk to the subject from which the tissue is being obtained. The protocol must contain adequate safeguards to protect the subject, though those safeguards are not specified. The protocol must also require informed consent as well as written authorization from the subject from which the tissue is being obtained."

"In addition, there is a prohibition of including genetic information in the clinical record unless the subject authorizes it. One additional provision that the protocol must have is the person obtaining the tissue must provide a reasonable method of disclosing to the family of the subject information pertaining to the risks associated to the genetic information."

There are other bills in addition to Domenici which concern genetic research. "The Stearns bill provides for the requirement of a report to be submitted to Congress by the National Bioethics Advisory Commission" said Stith-Coleman. "The report should set standards with respect to the acquisition and retention of genetic information, how it would be obtained and stored, and the report must be submitted within 1 year after the enactment of the legislation."

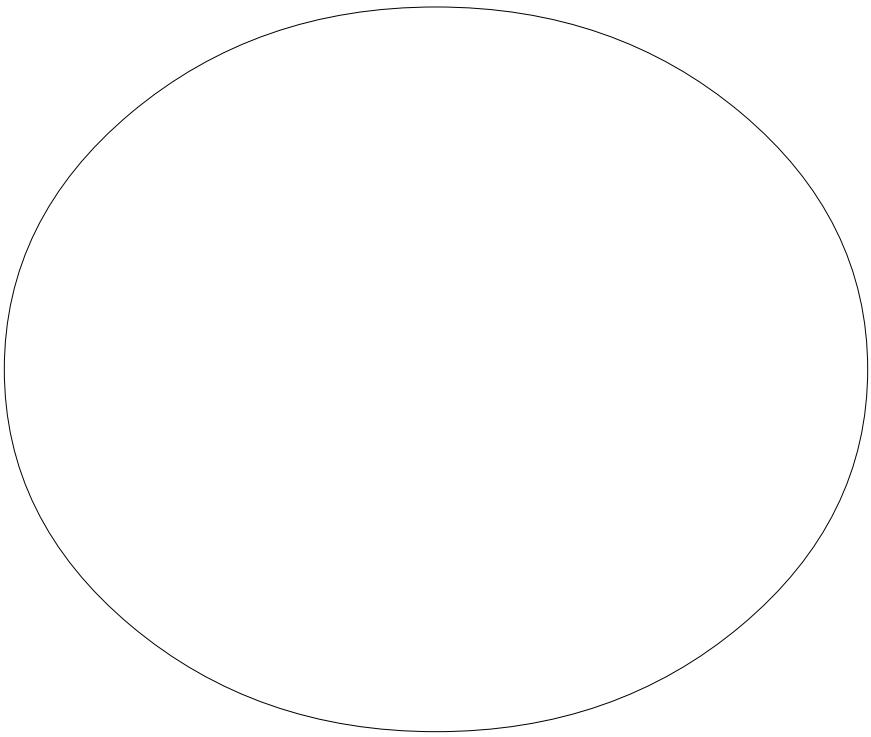
the large numbers of volunteers they need. "Any institution doing human subjects research should have a stiff confidentiality policy in place," **Korn** said. "Public flogging might be a good thing for violators, and I would say that I think the Feds have to oversee this. I don't think anybody else has the credibility to at least try to assuage some of the public anxiety.

"I am not a big government person philosophically, but I don't know who else can do this. In return for a policy that met standards, the Feds could give to the institution—not the individual, not the project, but the institution conducting human subjects research—a blanket protection of its human subjects research database modeled on the certificate of confidentiality."

The certificate of confidentiality is a federal credential designed to let researchers keep information about their human subjects secret from people outside the lab. "It was enacted back in the 1970s to permit studies of drug abuse in returning Vietnam veterans, who clearly weren't going to play if they figured they were going to get arrested for talking to the researcher, and was subsequently broadened in the late 1980s to include any biomedical or behavioral research that might generate sensitive information about individuals." In theory, **Korn** noted, the certificate of confidentiality may not be a perfect safeguard. "I know that people will say that if a court wants information and a judge issues a subpoena, nothing will stand in the way." But, he added, "it has been twenty-two years or more that the certificate has been used, created for studies of a criminal activity, and to my knowledge it has never once been challenged successfully. I am not sure anybody has even tried to challenge it."

If institutions doing genetic research could be given such protection, it would guarantee a near-absolute privacy of genetic research data. "Now, nothing will work perfectly, and you can never prevent an individual scientist from acting like a jackass," **Korn** said, but "the system should work very hard through education and reinforcement to try to prevent such behavior." Then people could volunteer for genetic experiments confident that their genes would not be used against them, and medical research could continue providing the rapid advances that people have come to expect.

APPENDIXES



APPENDIX
A

Program and Discussion Questions

Congress has begun to draft legislation to help ensure the privacy of general medical records. At the same time the issue of whether information obtained by the emerging medical technology of genetic testing should merit protection through specific legislation is being discussed. Although no federal legislation has been passed, pending privacy legislation includes such things as specific language that should be used in obtaining informed consent, which signatures should be obtained when releasing results of medical tests to third parties, etc. In the desire to protect people from unwanted intrusion of their medical records, the broad language of these potential laws may affect biomedical and clinical research, and the use of genetic testing in this research.

After discussions with the National Cancer Institute and the Department of Energy the Board on Biology of the National Research Council has agreed to run a workshop under the auspices of its Forum on Biotechnology entitled "Privacy Issues in Biomedical and Clinical Research." Experts from a variety of sectors affected by human genetic research will assemble for an open exchange of views in a neutral setting. Congressional staff and advocates for legislation addressing genetic privacy and discrimination will discuss current legislative initiatives. Researchers and health care providers from government, academe, and industry will share their perspectives on these issues and discuss concerns arising from the legislation. This forum will be held on Saturday, November 1 from 8:00 am until 1:45 pm.

Forum questions:

1. What are the key concerns that the legislation hopes to address?
2. How does the legislation address these concerns?

3. To what degree does this legislation create new concerns for the biomedical research community?

Format:

The format will be a roundtable discussion with several speakers introducing issues for group discussion to promote an open exchange of views among NAS members, federal agency administrators, industrial scientists, and university researchers.

APPENDIX
B

Agenda

7:30 am	Light Breakfast
8:00	Welcome Ray White, Ph.D. *University of Utah, Salt Lake City*
8:15	Panel One: Public Concerns About the Use of Genetic Information Vicky Whittemore, Ph.D. *National Tuberous Sclerosis Association & Alliance Genetic Support Group* Paul Billings, M.D. *Veterans Administration Hospital, Grand Prairie, Texas*
8:45	Discussion
9:15	Coffee Break
9:30	Panel Two: Current Safeguards Used to Maintain Privacy in Genetic Research Leo Whelan, JD *Mayo Clinic - IRB Member* Sherri Bale, Ph.D. *NIAMS, NIH - IRB Member for CDC* Pieter de Jong, Ph.D. *Roswell Park Cancer Institute, Buffalo, NY*

10:00	Discussion
10:30	Panel Three: Informed Consent and Research Sue Rose, Ph.D. *Department of Energy* Gene Carstea, Ph.D. *Saint Mary's Medical Center, Grand Junction, CO* Barbara Handelin, Ph.D. *Handelin Associates*
11:00	Discussion
11:30	Working Lunch
12:15	Current Legislation Related to Genetic Research Irene Stith-Coleman *Congressional Research Service, Washington, D.C.*
12:30	Discussion
12:45	Panel Four: Researcher Concerns About Restrictions on Genetic Research Ray White, Ph.D. *University of Utah, Salt Lake City* David Korn, M.D. *Stanford University and Senior Vice President, AAMC* Eleanor Kerr *SmithKline Beecham*
1:15	Discussion
1:45	Wrap up
2:00	Adjourn

APPENDIX C

A Comment by Frederick R. Anderson

Our society's initial attempt to resolve issues of privacy in biomedical and clinical research is off to a poor start. We are drafting statutes to create many new rights for research subjects and new duties for biomedical institutions. Perhaps it was inevitable that we would focus on defining privacy and property rights for research subjects, because our law already contains a vast arsenal of private rights to protect individuals from community coercion. Democratic government uses the engine of political struggle between competing factions to power law making. We have a rich and evocative language for rights-based public discourse that can be quickly mobilized when the interests of society and the individual appear to be about to collide.

We are justifiably proud of a political heritage that includes federal and state bills of rights, statutes to protect groups within our society from discrimination and to provide them the opportunity to succeed, and, yes, an already-impressive body of law and practice to protect research subjects and patients from institutional abuse. Yet we live in a time when rights-based approaches sometimes overwhelm community interests. We need to restore the balance between individual rights and social responsibility in the policies we adopt, including, as David Korn put it, selecting the right "equipoise" between protecting the privacy and rights of research subjects and patients, on the one hand, and the need for data that will enable biomedical research to advance, on the other.

At present, our lawmakers may be on the verge of a proliferation of rights that may delay striking the optimum balance for years and may impede biomedical research with little gain in the protection of individual research subjects. Worse, the current rights-based political discourse seems to drive stakeholders

apart, exaggerating—perhaps even on occasion creating—differences that could be reconciled if we placed somewhat less emphasis on rights to privacy and property and more emphasis on opportunities for shared responsibility in relieving genetically-based human suffering.

This perspective has practical implications for current legislative debates about the rights of research subjects. Legislation can be drafted that strikes an appropriate balance and lays the foundation for incentive-based cooperation between research subjects, families and genetically-related groups, researchers, care providers, insurers, employers, and family planning counselors.

My plea for balance between rights and responsibilities may perhaps be dismissed as the idealistic musings of a disaffected attorney. I must sound positively disloyal to others of my ilk whose bread-and-butter, like my own, is rights-based statute-drafting, regulatory representation, and litigation. Yet, the case can be made on purely practical grounds that the course on which we have embarked will fail, and that eventually we will want to strike a more publicly minded "equipoise" between individual rights and the overall community interest. Let me elaborate.

Some stakeholders, including some researchers, seem intent on erecting a legal wall with genetic information about individuals on one side of the wall, and insurers, employers, researchers, medical caregivers, and even spouses, children, and other family members on the other side.* At the conference, Susan Rose stated that "privacy does not exist," i.e., cannot be guaranteed. I believe that individual genetic information (especially for research purposes) can be kept confidential and that practical measures can be put in place to ensure confidentiality, at least so far as our current genetic database is concerned. However, as time passes, the amount and value of genetic information will assume enormous proportions. At some relatively proximate time in the future, after (1) a substantial number of the estimated 4,000 genetic diseases is mapped, (2) genetic predisposition to disease and injury is better understood, and (3) a significant part of a person's ordinary medical care becomes genetics-based, the pressure to use this wealth of information in health care delivery, family planning, employment decisions, and life and health insurance will be overwhelming. Statutory prohibitions against the use of a large genetic database are unrealistic and will engender abuse, covert markets in information, litigation to vindicate (or abrogate) rights, and an intolerant climate for additional research. We cannot pursue the genetics revolution while simultaneously erecting legal barriers to its practical use.

I agree that genotype and phenotype are not deterministically linked by rigid cause-and-effect. A person's genome never will be to a person what a blueprint

*To summarize for emphasis: an individual may refuse genetic testing; may permit it but ask not to be told the results; may receive the results but not have to act on it; may deny or subsequently withdraw access to test results and samples to anyone; and may bargain financially without limit for the use of test results and bodily samples.

is to a house. Still, a major (if not the major) goal of genetic research is to increase the statistical correlation between genotypical and phenotypical attributes. At some point in the future (and where genetics research is concerned, the future always arrives sooner than expected), the practical value of genotypical information will be overwhelming. At that time, it will become morally indefensible not to use that information in making health care, family, and estate planning decisions for oneself and one's family, and accurate use of that information by employers and insurers cannot continue to be called "misuse" or "discriminatory."

The current state of affairs is revealed in the intensifying debate over what constitutes a patient's "medical record" and what should and should not be included in it. We gave this issue serious attention at the workshop. Two observations seem in order about the genetic medical record. First, medical records seem headed down the same path as legal records. We appear to be moving into an era of formalistic, even adversarial, medical record keeping. We focus more and more on how prejudicial, discriminatory, or injurious to one's privacy interests the contents of the medical record may be, and less on how that record may best serve the patient and society. Hospital staffs, researchers, and legislators are beginning to discuss the "medical record" much the same way we attorneys discuss the "legal record," which in regulatory rule makings, trials, and appeals is the critical repository of information on which a regulatory or judicial decision must be based. Lawyers spend a great deal of time and energy sparring over the contents of the record, because the decision maker cannot "go beyond the record" in deciding important questions about life, liberty, and property. We may be headed into an era when the contents of the patients' medical record are defined by elaborate rules.

Second, recently proposed legislation on genetic information may thwart informed decision-making based on the medical record, by keeping some of the most vital data out of the record if the patient so desires. Yet where else but in the medical record should the most valuable information for the most important decisions we can make about treatment be located? A family lockbox? The black market? Word-of-mouth? We may be perversely reversing the incentives we should be creating: complete records shared with family members, care providers, researchers, family planners, insurers, and attorneys.

It became clear at the workshop that the impact of legislation drafted primarily to prevent insurers from denying coverage may "spill over" into biomedical research, with researchers swept along with insurers in being denied access to genetic data. Because of its pivotal role in the current debate, insurance deserves special mention here.

The current consensus appears to be that an insurer should be denied access to genetic information that could cause it to deny life or health coverage for an individual and/or relative whose genetic profile suggests an uninsurable risk. Commentators, including the leadership of the Human Genome Project, brook

little willingness to consider any possibility other than making denial of insurance in such circumstances strictly illegal.

Such a policy makes sense only in the short run. In the long run, the imbalance of knowledge between insureds, who will hold all the cards, and insurers, who will be denied any by law, would likely bankrupt the insurance industry. We were told at the workshop that preliminary studies of carriers of the BRCA1 and 2 genes who are at greater risk of breast cancer indicate that insureds do not purchase coverage that takes their greater risk of cancer into account. Yet assume that I am a married forty-year-old with three children and a genetic profile that suggests a 70 percent likelihood I will die in my fifties after a long and costly illness. Would it be responsible of me to purchase insurance coverage as if I had an average life and health expectancy? I would be more likely to buy the health and life insurance my condition and family needs suggested, and at very favorable rates, because my insurers would be denied genetic information that would assist them in predicting both their higher outlays for my medical care and the shorter time my invested premiums would earn a return.

As Cynthia Kenyon suggested at the workshop, perhaps national health insurance will receive support as the way to spread the financial impact of genetic risk. Dr. Kenyon suggested genetic testing could be made a condition of national coverage, thus removing the financial incentive to conceal genetic data—a boon to care providers, researchers, and others, although not necessarily to citizens as employees. Yet Dr. Kenyon's proposal for national health insurance raises numerous societal concerns best reserved for debate another day. Substituting a government program for existing market-based approaches raises questions about efficiency, tax policy, bureaucracy, and flexibility that buck the current trend toward privatizing, not socializing, social services. The nation's experience with the federal vaccination injury compensation scheme, the federal Black Lung compensation program, and other funds that have attributes of Dr. Kenyon's proposal has been expensive and troubled, to say the least.

Another possibility exists that is more consonant with the approach advocated in beginning this comment. That is to afford insurers an opportunity to develop entirely new products, in competition with each other, and in collaboration with their customers and their families, health care providers, and a new generation of family financial advisers who are sure to arise as the genetic revolution continues. If insurers can meet the challenge that is currently viewed as the most difficult to resolve, i.e., providing affordable privately financed insurance that takes account of the insured's genetic profile, then issues about access to genetic data for research, and about complete and accessible medical records for treatment and family planning, should be easier to resolve. It remains to be seen if insurers are up to this challenge. But they should be afforded the opportunity before the knowledge imbalance I alluded to earlier overwhelms the industry and non-market schemes such as national health insurance begin to receive serious attention.

At the workshop, David Korn was correct that practical, effective means exist at present to protect research subjects from stigma or penalty, through degrees of "anonymization" (my noun, not his) of medical records. If I correctly read the workshop, his position captured the desire, if not the actual agenda, of most workshop participants. As a lawyer who works in the legislative and regulatory arenas of Washington, it struck me that the various institutions and points of view represented around the table could form an effective coalition, not only to ensure that legislation and regulation do not needlessly impede genetic research, but also to advance a more cooperative, responsibility-based social response to the genetic revolution. Many of the organizations represented have their own efforts under way in support of responsible privacy measures to protect research subjects from harm. Yet the patients' groups, private and public research institutions, professional associations, companies, and agencies present represented a potential coalition whose impact could be greater than the sum of its parts.

APPENDIX
D

Participant Biographies

FORUM CHAIRS

Michael T. Clegg is Dean of the College of Natural and Agricultural Sciences at the University of California, Riverside. He is the leading student of the evolution of complex genetic systems. He is recognized internationally for his contributions to understanding the genetic and ecological basis for adaptive evolutionary changes within populations and at higher taxonomic levels. Clegg's current research interests include: population genetics of plants; plant molecular evolution; plant phylogeny; and genetic conservation in agriculture. He received his Ph.D. degree in genetics from the University of California at Davis. Clegg is member of the National Academy of Sciences and chairman of the Board on Biology.

Ray White is Chair of the Department of Oncological Sciences and Director of the Huntsman Cancer Institute at the University of Utah. He was a pioneer in developing the methods used to identify disease-causing genes. He discovered the mechanisms and, ultimately, several specific genes involved in inherited forms of cancer. He received his Ph.D. in microbiology from the Massachusetts Institute of Technology. He is a member of the National Academy of Sciences and the NRC's Board on Biology.

PARTICIPANTS

Sheri Alpert is an information privacy policy analyst for a large federal agency. She has also been researching and writing about medical privacy issues for sev-

eral years. Ms. Alpert recently completed a paper for the National Bioethics Advisory Commission on privacy issues in the analysis of stored tissue samples. She is a Ph.D. candidate at the Institute of Public Policy at George Mason University.

Frederick Anderson is a Partner with Cadwalader, Wickersham & Taft and former Dean of the law school at American University. His practice involves science, the environment, and natural resources including risk assessment and management, hazardous air pollutants. He has degrees from Harvard University and Oxford. He is a member of the D.C. and U.S. Supreme Court bars. Mr. Anderson is Chairman of the Board of the Center for International Environmental Law and was president of the Environmental Law Institute. He is the author of: *Environmental Protection: Law and Policy; NEPA in the Courts; Environmental Improvement through Economic Incentives* and numerous scholarly articles. He is a member of the NRC's Commission on Life Sciences.

Sherri Bale is Chief, Genetic Studies Section/Lab of Skin Biology, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health. She has been involved in research into the genetic basis of hereditary disorders, particularly those affecting skin and musculoskeletal systems, throughout her career. She received her Ph.D. in Human Genetics from the University of Pittsburgh graduate School of Public Health. She took her Fellowship training in Medical Genetics at the National Institutes of Health and is board certified in Medical Genetics.

Paul Berg is the Director of the Beckman Center for Molecular and Genetic Medicine at Stanford University School of Medicine. His research interests include the molecular biology of mammalian gene expression and regulation. He received the Nobel Prize for Chemistry in 1980 and the National Medal of Science in 1983. He received his Ph.D. degree in biochemistry from Western Reserve University School of Medicine. He is a member of the National Academy of Sciences, the Institute of Medicine, and the NRC's Commission on Life Sciences.

Paul Billings is the Chief Medical Officer and Deputy Network Director of the Heart of Texas Veterans Integrated Service Network. He received his M.D. and Ph.D. degrees in immunology from Harvard University. His research interests indulge social and political impacts of biotechnology. A board certified internist and medical geneticist, he is a Director of several not-for-profit organizations including the Council for Responsible Genetics.

Eugene Carstea is the Director of the Saccomanno Research Institute at St. Mary's Hospital & Medical Center. The institute maintains the Saccomanno

Uranium Miner Archive. This collection, assembled over the past 45 years, harbors tissue samples and documentation from over 17,000 uranium miners of Western Colorado and Eastern Utah. Dr. Carstea's research interests include familial susceptibility associated with the onset of lung cancer and the development of molecular markers important for its early identification. In 1997, he led a team of investigators at the National Institute of Neurological Disorders and Stroke in Bethesda, Maryland in identifying the gene responsible for a neurodegenerative disorder known as Niemann-Pick disease type C (NPC).

Carol Dahl is currently Assistant to the Director of the National Cancer Institute (NCI) in the area of strategic technologies. In this capacity she advises the Director of the NCI on technology development opportunities in support of the National Cancer Program. Prior to joining the NCI, Dr. Dahl was Program Director of the Sequencing Technology Branch at the National Center for Human Genome Research and served on the faculty of the University of Pittsburgh and the Pittsburgh Cancer Institute. Dr. Dahl received her Ph.D. from the University of Wisconsin-Madison.

Pieter de Jong is currently Acting Chairman for the Department of Cancer Genetics at Roswell Park Cancer Institute, Buffalo, NY and Associate Research Professor for the State University of New York at Buffalo. His research interests are in the area of the Human Genome initiative and its applications related to Cancer Genetics. His main contributions to the Human Genome project have focused on the improvement of large-fragment DNA cloning procedures and the preparation of the central DNA resources used for large-scale genome sequence analysis. Prior to joining Roswell Park Cancer Institute in 1993, Dr. de Jong directed the National Laboratory Gene Library project at Lawrence Livermore National Laboratory at Livermore, California. Dr. de Jong received his Ph.D. in 1982 at Utrecht State University, Utrecht, The Netherlands.

William Dommel has served the Office for Protection from Research Risks from 1979 to 1998, with positions that include Director, Division of Human Subject Protections, followed by Director of Regulatory Affairs. From 1996 to 1997, Dr. Dommel served as acting Executive Director of the National Bioethics Advisory Commission, after which he returned to the OPRR to serve as its Director of Education. In January of 1998 Dr. Dommel finished 20 years within the Office of the Director at the NIH to become an independent consultant, concentrating on issues related to biomedical ethics. He also serves as Executive Director of the National Reading Panel, within the NICHD of the NIH.

Daniel Drell is biologist at the U.S. Department of Energy's Human Genome Program in the Office of Health and Environmental Research. His major responsibilities have included the DOE Microbial Genome Program, Bioremediation

and Its Societal Implications and Concerns (BASIC) of Natural and Accelerated Bioremediation Research (NABIR) Program, and the Bioinformatics of Human Genome Program. Dr. Drell received his undergraduate degree Magna cum Laude from the department of biology at Harvard College. He continued his studies at the University of Alberta, Edmonton where he received his Ph.D. degree from the department of immunology.

David Foster is with Genzyme Corporation, Cambridge, MA.

Barbara Fuller is a senior policy analyst for the National Human Genome Research Institute. Her major responsibilities include initiatives regarding genetic information and health insurance discrimination, employment discrimination, and the privacy of genetic information. She received her B.A. and J.D. from the University of Maryland. In addition to her legal background, she is a Registered Record Administrator and has worked in a variety of health care settings, including hospitals and HMOs.

David John Galas is president, CEO, and chief scientific officer at Darwin Molecular Corporation in Bothell, Washington. His research interests include molecular genetics of transposition, and the mechanisms and consequences of these recombination processes; and molecular interactions of DNA with proteins, and their consequences in gene control and recombination. Galas secured all of his degrees in physics from the University of California; studying at Berkeley for his undergraduate degree, and at Livermore for his masters and Ph.D. degrees. He currently serves on the NRC's Board on Biology.

David Goeddel is Presidant, CEO, and a founder of Tularik Inc., in San Francisco. Tularik Inc. is engaged in the discovery and development of a broad range of novel drugs that act through the regulation of gene expression. The company is currently focusing on seven disease areas: viral diseases, hypercholesterolemia, immune disorders, inflammation, bacterial diseases, obesity, and cancer. Prior to Tularik Inc. he was a Genetech Fellow and the Director of Molecular Biology at Genentech Inc. He received his Ph.D. at the University of Colorado. He is a member of the National Academy of Sciences, the American Academy of Arts and Sciences and currently serves on the NRC's Board on Biology.

Judith H. Greenberg has been Director, Division of Genetics and Developmental Biology, National Institute of General Medical Sciences (NIGMS) since 1988. In this position she is responsible for the funding of grants that support research on the fundamental mechanisms of inheritance, development, and cell function. She joined NIGMS as a program administrator in 1981. Prior to that she was a senior staff fellow in the National Institute of Dental Research, NIH. She received her Ph.D. in 1972 from Bryn Mawr College.

Barbara Handelin is President of her consulting firm, Handelin Associates. She received her training at the Oregon Health Sciences University and MIT. Afterwards, Dr. Handelin was an early practitioner in the field of molecular genetic diagnostics and its application in general medical practice. She was Director of the molecular genetics laboratory at Integrated Genetics (now Genzyme Genetics) for 7 years (1987 to 1994), where she helped create appropriate protocols—both clinical and laboratory—for genetic testing for Huntington's disease, cystic fibrosis, spinal muscular atrophy, and other diseases. Dr. Handelin is currently working on a project funded by the Department of Energy's Ethical, Legal and Social Implications program which is directed at developing general principles and frameworks for review of research protocols involving use of human subjects in genetics studies.

Kathy Hudson is with the National Human Genome Research Institute, Bethesda, Maryland.

Edward Hild is a Legislative Assistant to Senator Pete V. Domenici.

Diane Isonaka has spent the last fifteen years working in the global genetics community. Prior to her position as Director of Development and Technology with Darwin Molecular Corporation, she was one of the founders and then served as the Americas Director and International Secretary for the Human Genome Organisation (HUGO); was the Manager of the Howard Hughes Medical Institute's Genome Program where, together with the NIH and the DOE, she worked to develop the U.S. Human Genome Project. She was also the Executive Director of the Utah Resource for Genetic & Epidemiologic Research, one of the first U.S. programs specifically initiated to address the complex social, ethical, and legal issues surrounding genetics research using human populations. Dr. Isonaka obtained her degree from the University of Southern California.

Cynthia Kenyon is the Boyer Professor of biochemistry and biophysics at the University of California at San Francisco. Her research interest is in developmental genetics and genetic influence on the process of aging. She received her Ph.D. degree from the Massachusetts Institute of Technology. She is a member of the American Academy of Arts and Sciences and the NRC's Commission on Life Sciences. She has also published childrens' stories that help illustrate the law of probability.

Eleanor Kerr is Senior Director, Government Relations, for SmithKline Beecham. She has been with SB for 5 years, and represents SB before Congress and the Executive Branch on a variety of health care matters, including pharmaceutical and vaccine issues, research and development issues—encompassing genomics and bioethics matters, and health care services-related issues. Prior to

coming to SB, Ms. Kerr was an appointee in the Bush Administration, serving as chief policy coordinator for HHS Secretary Lou Sullivan on all medicaid and FDA matters. She has also worked in the U.S. Senate twice, for the Senator Labor and Human Resources Committee, as health advisor to then-Senator Dan Quayle, and as a legislative assistant for women's issues to former senator Bob Packwood, and as a lobbyist for the Health Insurance Association of America.

Margaret Kidwell is Regents' Professor of Ecology and Evolutionary Biology at the University of Arizona. Her research interests include the evolution and population genetics of transposable genetic elements and their impact on genome evolution. Kidwell completed her undergraduate training in agriculture at Nottingham, UK, followed by a master's degree at Iowa State University and a Ph.D. in biology at Brown University. She is a member of the National Academy of Sciences and currently serves on the Commission on Life Sciences and Board on Biology.

Jack Killen is the Director of the Division of AIDS, where he oversees National Institute of Allergy and Infectious Disease's support of basic biomedical, therapeutic and vaccine research on HIV. He received his M.D. from Tufts University in 1975, and completed postgraduate training in internal medicine and medical oncology at Georgetown University in 1980. He is board certified in both specialties.

Michael J. Knapp is vice president for program development at the National Center for Genome Resources where he is responsible for creating the Genetics and Public Issues program, overseeing the company's external communications, managing government relations, and developing and implementing fund-raising plans. He received his undergraduate degree in economics and government from the College of William and Mary in Virginia.

David Korn is Senior Vice President for biomedical and health sciences research at the Association of American Medical Colleges and Vice President, Dean and Professor of Pathology, Emeritus, of Stanford University School of Medicine.

Melody H. Lin serves as Deputy Director of the Office for Protection from Research Risks (OPRR) at the National Institutes of Health. OPRR is legislatively mandated to oversee implementatioin of the HHS Regulations for the Protection of Human Subjects and the PHS Policy on Humane Care and Use of Laboratory Animals. OPRR is engaged in a wide range of ethical and regulatory issues relative to the involvement of human subjects in biomedical research. Dr. Lin is responsible for the management of all policy, personnel and budgetary matters of all divisions of OPRR. Dr. Lin has held previous positions at OPRR as Director of the Division of Human Subject Protection (DHSP), Chief, Compli-

ance Oversight Branch; and AIDS Assurance Coordinator/Health Scientists Administrator.

Pearl O'Rourke is in the Office of Science Policy and Planning, National Institutes of Health.

Edward Penhoet is President and CEO of Chiron Corporation. Chiron Corporation is a science-driven healthcare company positioned to combine diagnostic, vaccine and therapeutic strategies against many diseases, including AIDS, hepatitis C, and cancers. Prior to joining Chiron he was a professor of biochemistry at the University of California at Berkeley. He received his Ph.D. in biochemistry at the University of Washington. He is a member of the NRC's Commission on Life Sciences.

Anne Phelps is currently Health Policy Advisor on the Senate Labor and Human Resources Subcommittee on Public Health and Safety, Chairman Bill Frist (R-TN). She handles issues for the Subcommittee regarding public health and biomedical research, medical records confidentiality, genetic discrimination, and health care quality/insurance issues. She has served as health policy fellow to the Senate Labor and Human Resources Committee under the chairmanship of Senator Nancy Kassebaum (R-KS). Prior to this, she worked at the NIH, with her most recent position prior to coming to Capitol Hill in the NIH Director's Office of Legislative Policy and Analysis. She received her Master's degree in Public Policy from the George Washington University in 1991.

Susan Rose is responsible for human subjects activities and policies at the U.S. Department of Energy. She has been involved in these issues since the early days of Human Subject Regulations (1976) and also managed the Radon Research Program for the Department. Dr. Rose received her Ph.D. from the Catholic University of America in Medical Technology/Immunohematology.

Lana Skirboll is the National Institutes of Health (NIH) Associate Director for Science Policy. She is a neuroscientist and the author of more than 75 scientific publications. She received her Ph.D. in the Department of Pharmacology, Georgetown University Medical School, and conducted her post-doctoral training in the Departments of Psychiatry and Pharmacology at the Yale University School of Medicine. She has also worked in the Karolinska Institute in Stockholm, Sweden, in the intramural research program of the National Institute of Mental Health, and in the Alcohol, Drug Abuse, and Mental Health Administration.

Irene Stith-Coleman has served as Head of the Biomedical Policy Section of the Science, Technology and Medicine Division at the Congressional Research Ser-

vice (CRS) since 1990. Dr. Stith-Coleman received her Ph.D. from Meharry Medical College in Nashville, Tennessee. Dr. Stith-Coleman specializes in issues related to the Human Genome Project, reproductive and contraceptive technology, biomedical ethics, and women's health research.

Shirley M. Tilghman is currently Howard A. Prior Professor of the life sciences and investigator at the Howard Hughes Medical Institute at Princeton University. Working in Phil Leder's laboratory, Tilghman was the first to clone the beta-globin gene of mice and show that the gene had an intron. She identified the H19 gene in mice, an early example of parental imprinting, and showed how this gene and its regulatory elements initiate and maintain parental imprinting. Other research interests include using genetics to understand the role of the genes involved in the development of melanocytes, the pigment-producing cells in the mouse. She received her Ph.D. degree from Temple University in biochemistry. Tilghman is National Academy of Sciences foreign associate member and Institute of Medicine member, and currently serves on the NRC's Board on Biology.

Suzzane Tomlinson is the bioethics counsel and the outreach manager for the Biotechnology Industry Organization (BIO). She works with BIO member companies to prepare documents on bioethics issues impacting the industry, such as the privacy of medical information and issues of genetic discrimination. Previously, she worked at Genzyme Corporation, a biotechnology company, where she monitored the impact of health care reform on biotech drugs and devices. Prior to this Tomlinson interned in the Office of the General Counsel at the Department of Health and Human Services, the Council on Competitiveness in the Office of Vice President Quayle, and at the George Washington University's Center for Health Policy Research. Dr. Tomlinson earned her juris doctor degree from the George Washington University in Washington, D.C.

Leo Whelan is a member of the Mayo Foundation's Legal Department and advises its IRB and its researchers. He received his J.D. from the University of Minnesota.

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