LIFE SCIENCES, TECHNOLOGY, AND THE LAW SYMPOSIUM

UNIVERSITY OF MICHIGAN LAW SCHOOL
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WELCOME AND INTRODUCTORY REMARKS

MATT MOCK: Good Morning! My name is Matthew Mock and I am Editor-in-Chief of the *Michigan Telecommunications and Technology Law Review*. Welcome to our Symposium: Life Sciences Technology and the Law. Before we begin I would like to take a moment to thank our sponsors for their generous support. This event is made possible by donations from the following members of the University of Michigan family: the Law School; the Life Sciences, Values and Society Program; the Life Science Institute; the Business School; the Office of the President; the Office of the Provost and Executive Vice President for Academic Affairs; and the Chemistry Department. I want to thank all of these members, and any of their representatives who are in attendance today.

And now, without further ado, I would like to introduce our opening speaker. Dr. Alan Saltiel received his A.B. in Zoology from Duke University and his Ph.D. in Biochemistry from the University of North Carolina. In 1984, after a distinguished postdoctoral research fellowship, he moved to The Rockefeller University as Assistant Professor. In 1990, he joined Parke-Davis Pharmaceutical Research, and was later promoted to Distinguished Research Fellow and Senior Director of Cell Biology at Parke-Davis. He was named Adjunct Associate Professor of Physiology at the University of Michigan School of Medicine in 1990 and was promoted to Adjunct Professor in 1994. In 2001, Dr. Saltiel moved to the newly created Life Sciences Institute at the University of Michigan as Professor of Medicine and Physiology. In 2002, he was named director of the Institute and John Jacob Able Professor in the Life Sciences. He has received numerous awards, including the Rosalind Yallow Research and Development Award from the American Diabetes Association, the Herschel Award, the John Jacob Able award from the American Society of Pharmacology and Experimental Therapeutics, and was elected to honorary membership in the American Society of Clinical Investigation. He has served on a number of advisory panels and editorial boards, including the *Journal of Biological Chemistry*, *Endocrinology*, *Diabetes*, the *Journal of Clinical Investigation*, and others. He has nine issued

patents and has published over two hundred original papers. And now it is my pleasure to introduce Dr. Saltiel.

[Applause]

DR. ALAN R. SALTIEL: Thank you very much Matthew. It's really a pleasure to be here and a pleasure to be at this conference with you. I want to thank all of you for coming, on behalf of the Life Sciences Institute, and to welcome you to the law school and to this important conference. I think we have in front of us what promises to be a very interesting day. I'm particularly impressed by the wide range of perspectives that we'll hear from today, scientists, lawyers, legal scholars, university administrators, and biotech industry representatives.

I want to start off the symposium by telling you a little bit about the Life Sciences Institute. The make-up and the mission of the institute are germane to today's activities because we are planning a new kind of academic endeavor that will bring together different scientific disciplines to bear on important scientific questions, particularly in the field of medicine. Our institute will consist of faculty drawn from a variety of disciplines. These will include chemistry, structural and computational biology, genetics, cell biology, and physiology.

Our building plan includes open architecture, with big labs that are designed to facilitate maximum interactions. Our hope is that the faculty who reside in this wonderful space will seek out collaborations and find synergistic ways to attack problems such as diabetes, cancer, inflammatory disease, and other problems in medicine. I'll give you one example from my own field, diabetes. I can see a situation in which geneticists will hunt for genes that endow susceptibility to diabetes, and then collaborate with cell biologists and biochemists, and possibly even chemical biologists and chemists to try to design molecules that might attack the proteins that are responsible for this kind of disease. Thus, what we are hoping to build is an exciting endeavor, with potential for impacting in a basic way human health.

This kind of approach that we're planning to take typifies a situation in which we follow the science wherever it leads. We plan to do this despite the boundary crossing that's involved in this kind of process. This is really what the new scientific problems of our area demand, the ability to focus on the complex diseases and diseases that are very difficult, particularly those associated with aging.

Now just as today's scientific problems require a variety of perspectives, so do contemporary legal, social, and ethical problems that have emerged as a result of our new, enhanced understanding of the processes of life. Indeed, some of the very basic tenets of our social fabric are challenged by today's scientific progress. You're taking up some of these

issues today, and I applaud you for this. Scientists acting alone surely cannot resolve or necessarily even identify these seismic shifts. Similarly, a discussion by lawyers and legal scholars surely need scientists to be involved, because the implications of discoveries that are made in science can't really be understood or appreciated without the involvement of the actual discoverers themselves. Finally, we all know that university administrators and legal scholars and business leaders have a crucial role to play in putting new discoveries to practice in the real world. Thus, if you take a look at all of this together, I think it's clear that we must have a dialogue across the disciplines and across the settings of our social institutions, including law, policy and business itself, if we're able to keep pace with our scientific progress in the laboratory.

Again, as I mentioned before, I applaud the planning that's assembled such a diverse and exciting stellar group to talk about life science, the technology, and the law. I wish you a tremendous day. I hope you have a very productive and rewarding symposium. Thanks very much, Matt.

[Applause]

INTRODUCTION

Thank you Dr. Saltiel. Good morning. My name is Larry LaVanway, and I'm the Executive Editor and Conference Chair for the MTTLR Volume Nine. I want to thank Dr. Saltiel for taking the time to speak here today. We really do appreciate it. And now I'd like to present our keynote speaker.

Dr. Philip Reilly is President of the American Society of Law, Medicine, and Ethics, and currently sits on the Board of Directors. From 1994 to 1997, he was on the Board of Directors of the American Society for Human Genetics. He's also been the CEO of Interleukin Genetics since 1999. Prior to joining Interleukin as a CEO, he held the position as Executive Director of the Eunice Kennedy Shriver Center for Mental Retardation, a not-for-profit organization in Massachusetts. He held that position until 1999. Dr. Reilly has also had several teaching positions, most notably an Assistant Professor spot at Tufts University School of Medicine, and another Assistant Professor position at Harvard School of Medicine, and an Adjunct Professor position in both legal studies and biology at Brandeis University. Dr. Reilly is a member of the American College of Medical Genetics, the Massachusetts Bar Association, and the American Association for the Advancement of Science. He has served on many national committees chartered to explore public policy issues raised by advances in genetics and is frequently asked to comment on

these topics by the national media. He's an author of four books and has published more than one hundred articles in scholarly journals. His most recent book, *Abraham Lincoln's DNA and Other Adventures in Genetics*,[1] published by Cold Harbor Spring Laboratory Press, has been chosen by the city of Ann Arbor's reading program for its book of the year for 2003. On a personal note, I know it happens to be a good read for both the scientist and the layperson. Dr. Reilly also holds a B.A. from Cornell University, a J.D. from Columbia University, and an M.D. from Yale. It is my pleasure to present our keynote for the 2003 MTTLR symposium, Dr. Philip Reilly.

[Applause]

DR. PHILIP R. REILLY: Good morning. It's a pleasure to be with you this morning to explore that interface between science and law that was so appropriately referred to by the first speaker. As you know, C. P. Snow, five decades ago, wrote articles about the so-called two cultures. I think that concern about the divide between those who create knowledge and those who apply it, is as great as ever.

In thirty minutes, I cannot possibly hope to ground those of you who are nonscientists in the facts upon which I would build the argument that we are, in fact, in the midst of the revolution of knowledge in biology, and particularly genomics and proteomics. So to some extent you'll have to take that for granted.

But I'm guessing that many people in the room are nonscientists. So I thought I would take just a couple of minutes to try and transfer to you some of my sense for the magic of our understanding of DNA. After all, what other symbol in modern science has become as iconographic as the double helix? Almost everybody, literate American, I think if you say double helix, an image comes to their mind about that coil that Francis Crick's wife sketched out fifty years ago as the first symbolic representation of the DNA molecule. So just before I get into my talk, just think about this for a second. You began life as a single cell, the union of a sperm and egg, each a vector carrying information—approximately 3.2 billion letters of the DNA molecule. A molecule that uses an alphabet that's only four letters long. You write your briefs or read your casebooks with a language of twenty-six letters and yet you've been created through an evolutionary scheme that needed only four letters to create things as exclusive as yourselves. So how might that be? Well the answer, in part of course, is that the message is very long, 3.2 billion letters is a lot of letters. And unlike our alphabet where three Ts or three As or three Gs wouldn't mean very much, in the language of

1. PHILIP R. REILLY, ABRAHAM LINCOLN'S DNA AND OTHER ADVENTURES IN GENETICS (2000).

DNA repeat sequences of information can, in fact, carry a message out into the cytoplasm to help make a protein, which is what makes us function.

There's a lot of really fascinating things about the DNA molecule. Just think about how you pack 3.2 billion letters of information in a single cell. The packing ratio of the DNA molecule is about seven thousand to one. When you think about it as a layman, you think of a string, when in fact it's this huge bunch of spaghetti at the microscopic level. And somehow it behaves in a very orderly fashion. It's really quite astounding. In fact to me, a never-ending source of wonder. Think about, for example, the fact that in just nine months you go from a single cell to a well organized infant of about ten trillion cells. And from the moment you're conceived you have all the genetic programming you need to make it through adolescence itself, a miracle. And to go onto age and middle age and reproduce yourselves. It's all right there in the first cell.

One of the reasons that we're here today is that we now have the ability to ask exquisitely refined questions, not only about your DNA but pretty much anybody's DNA. And, in fact, one of the underlying themes that I'm not really going to discuss is that the cost of acquiring genetic information, be it about corn or people, or the way the drug works in the body, is falling very, very rapidly. So one of the silent barriers to dealing with the information is disappearing.

Just a couple of other reflections. DNA teaches us some wonderful things about humanity. One thing it teaches us is that we're all so alike. So if I take the DNA from any two people sitting in this room and compare it, on a sequence level you're 99.9% alike. Well why are you so much smarter and better looking than the people sitting next to you? Well the answer, of course, is in part the environment, but in part the 0.1%. This 0.1% of 3.2 billion is 3.2 million. So we're both profoundly alike and profoundly different at the DNA level, which is to me a source of great mystery, actually. And maybe some day someone will figure out a way to use the fact that we're 99.9% alike to break down the lingering nineteenth century stereotypes of the colonial era that described and set the archetypes of race in the Western world, which from a biological perspective is not completely meaningless, but has much less meaning than it should have.

So what I want to do is try to proceed with some reflections very closely keyed to the remarks made in the brochure of the symposium, actually that describes it, and wonder if together I could help set the stage for the more important work that comes later, which is the work of the three panels, which I think promises to be very interesting. So this is what those who've created this conference wrote in their brochure. You

can read it, I'll just paraphrase it. Just the notion of a revolution, if you will. A notion that even legal thinking would be profoundly challenged by advances in the life sciences. I wrote at the bottom of this slide, "Do you agree or disagree?" And probably what I should've also added is, "Do you feel you're ready to agree or disagree?" Back to my question about the divide between science and policy makers. I, at least, agree that it is a revolution. And I could've put a lot of different messages up on this slide, but I tried to keep at least the first one to you.

Trying to imagine how a lawyer might see it. It is a fact that in one year in the late '90s, more bills were introduced into the nation's state legislatures about the regulation of genetic information than any other single topic. More than 650 bills at one point by one count. Now most of them did not become law and most of them, I would argue, were dealing with problems that had not yet manifested. But still I think this is a profound reflection of the way the public has begun to perceive the power of this information. I could've put up another slide. There has been, for example, a profound effect on thinking about genetics in the world of modern art. I'm involved in editing a series of books now about the role of the DNA molecule as an icon in modern art. It's almost impossible to see a TV show or read a journal article where there isn't some often-humorous reference to the power of genes and often a misleading one.

But on a less legally-focused area, it's true, genetic information is affecting aspects of human existence that are the most closely held to us, in our emotions and our hearts, how we reproduce, the very food we eat, and perhaps most importantly for the lawyers, how we take the measure of one another. And one of the themes I'd like to introduce is this notion of how we value information and what it means, and how it impacts what we perceive about other people.

The last statement on the slide is a bit controversial. There are many scientists that would disagree with that. But I actually still think that in the nature/nurture argument, and clearly it's not an argument because everything is genes unfolding in an environment, that we still tend to underestimate, in some cases, the roles genes play. That's a politically incorrect statement, but I actually think it's going to turn out to be true.

So what are some of the things we'll be able to do? And I'm glad there's some scientists here to keep me honest. I'm actually highly confident about every single one of the assertions I'm going to make in the next two slides. I think there is almost no chance that these won't come to pass. Many have come to pass already. And each one of these I think you could quickly, and I'll try to do so, raise some interesting legal or constitutional questions about the ability to assess reproductive risks for

many diseases and intervene and perhaps neutralize them. Then I have these letters PGD, which stands for Preimplantation Genetic Diagnosis.

So imagine, for example, an Ashkenazi Jewish couple both of whom are carriers for the Tay-Sachs disease, who are opposed to first trimester abortion, for ethical reasons. They could theoretically—in fact it's being done—they could engage in the technology of in vitro fertilization. If you're not infertile, we use the same technology then. To have a single cell, out of an eight cell pre-human embryo, tested to see whether that embryo pre-implanted, would be destined to have Tay-Sachs disease or not. And if it was not, then implant it, and guarantee the parents that if the child came to term Tay-Sachs disease would be one problem in life that it would not have. That's very simple when you're talking about a disease as devastating as Tay-Sachs disease, which is uniformly fatal by age five or six and a terrible disorder. But what happens when we can assess risks, whatever they are, for much more uncertain, or much less certain, categories of risk, such as learning disability and things like that?

Our ability to greatly expand the assessment of newborns, by that I mean a DNA-based analysis, which is currently biochemically-based analysis and will be DNA based in the next decade. Currently every baby born in the United States and much of the Western world has a test. All the people in this room born in the United States who are under the age of thirty-five have had their blood taken and have been tested for genetic disorders. You just don't know it because your memory traces don't go back that far. And we are going to expand that list of disorders. Currently, in Massachusetts, it's gone from five to thirty. I could easily imagine it being three hundred. Again, the issue is what's a genetic disorder? What is the right of the state to have the information? By the way, all this testing is done pursuant to mandatory state law, with some religious exemptions in certain states. Most exemptions citizens don't know about anyway and they're not imposed. This ability to identify a potential for risk in advance is an ability that gives people a lot of concern because it might have an impact on how, again, we measure other people. In this case, in schools, by the insurance industry or the workplace. There's been a lot of discussion about that and I won't get into it here.

The stem cell controversy that you've followed in the halls of Congress and elsewhere relates very much to the right to life controversy and how we value human life before it exists independently. It's just one of the areas that I think we're going to see a lot more debate about in the future.

We already have created animals that are in fact pharmaceutical, that are bioreactors. Genzyme, for example, in Massachusetts, has a herd of goats that "makes" human proteins. Female goats secrete milk and can be very easily extracted from the milk and scaled out and purified. And a lot cheaper in the long run than building a very large building.

One other area that I'm particularly interested in and has lots of international implications—huge debates underlie every one of these statements that I'm making to you—we're now seeing the first real evidence published in the leading scientific journals that the per hectare yield of basic grains, things like soy, corn and rice, is benefited if certain genes are moved into those genomes and then into seeds of those crops to confer resistance to pesticides. That has huge implications for debates over saving remaining rain forest, as well as issues that will be addressed later, perhaps about intellectual property, things like that.

I think it's very possible in the next ten years that we will have created an industrial setting, a line of pigs, that are excellent donors of humanized kidneys to humans. This year, in the United States, sixteen thousand people will die waiting for a kidney transplant. And I'm not suggesting that the science is solved yet. We have lingering concerns about porcine (pig) retroviruses, and the ability to really trick the human immune system into believing that it's getting a human kidney, when in fact it's getting a pig kidney. Imagine what folks like Peter Singer will have to say about this, and animal welfare people. It's okay to eat them, but apparently you can't take their kidneys and put them into your bodies. There's now a company called Genetic Savings and Loan that, frustrated with the lack of successive cloning dogs at Texas A&M, has decided to do it commercially and make genetically engineered dogs available for your household. John Sperling has done this work and he's got infinite resources, since he's the founder of the University of Phoenix, one of the largest degree granting institutions in the United States.

And what if your dog was really smart? I know you all think your dogs are smart, but what if your dog was really smart? What if, for example, you could ask your dog to carry a rose across the restaurant to a very attractive woman you'd like to meet, and he would do it perfectly? I suggest to you, read Dean Koontz's book *Watchers*.[2] It's a delightful meditation upon what happened if you really had a dog that was so smart you could name it Einstein. Koontz is apparently pretty good as a science watcher, especially since the book was published in '88.

But on a more serious note, the challenge for you today is to, as future lawyers and policy makers in the United States coming out of a great school like this, is to think about these three great areas in which it

2. DEAN R. KOONTZ, WATCHERS (1997).

will be the lawyers, the ethicists, and the elected officials, who take what the great scientists hand off to them and, hopefully with a dialogue with those scientists, begin to continue to craft the appropriate rules for the use of these very powerful technologies.

I wonder, even at an institution like this, how many law students who have taken criminal law are really aware of the unbelievable impact that DNA technologies have on the criminal justice system. It is profound, indeed. I don't have time here to get into it. There are other people in the room, like David and Richard who are quite expert on it. But it's really to me very astounding. Not so much the notion of the introduction into evidence of tissue analysis that confirms the identity of two samples, but the evolution of large scale DNA databanks. Throughout our society, with an ever expanding scope for the number of individuals who are covered by those banks, to the point where I would probably not be surprised if a decade from now it's routine to take DNA evidence—or have the right to take DNA evidence—from any person in the United States who's arrested. It's approaching that situation in the United Kingdom already.

Again, an area that's particularly close to my current work in the biotech world, there are some amazing regulatory issues that will emerge as we begin to understand why some drugs work in people and some drugs don't. As an internist who used to take care of people with diabetes, and heart disease, and hypertension and things like that years ago, I knew when I gave somebody a drug, as I started to manage their chronic disease, that there's about a two out of three chance I'd get roughly the desired response that I wanted. And for one third of the patients, I'd be trying another drug two or three months down the line. Now why is that? Well it's because the drug is given to people who each have a different genetic background. There are other reasons. It could depend on what other drugs you're taking, how old you are, how well your kidney works, whatever it might be. But basically your genetic profile changes that. So one of the things I think we're going to see in the near future—and I actually don't think it's going to happen in the FDA first, I think it's going to happen in the United Kingdom first because of their national health service—is the demand for pharmacogenetic information. The demand to have that information and incorporate it into decisions about prescribing and decisions about payment and reimbursement. In my humble opinion, it will not be the pharmaceutical industry that drives this forward, it will be the payers. And I'm already seeing that. I've been knocking on the doors of pharmaceutical industry for about five years, with little success. I started knocking on the doors of the payers, telling them about this, and the doors were open quite widely and my little

company now has two research agreements that are not with wonderful companies like Pfizer or Merck. They're with Kaiser Permanente and United Health Group, the people who pay the bills. There are huge legal issues lurking about, and certainly huge regulatory ones.

And a very interesting topic, especially at a great university like this, is to explore whether there is still even a boundary between academia and industry. In Boston I'm convinced, there is not. I don't think I can find a professor in the medical schools I move through that doesn't have an industrial relationship. And I don't say that because I think it's a bad thing. I actually think it's a very good thing, but I don't think we as an academic society have come to terms with it yet, and I'm glad to see you have a panel that's going to explore some of those issues.

Other topics that might, if you had three days instead of one day, deserve equally a panel are some of the ones that I just mentioned, which I won't repeat because you've heard me say them. I'm going to list some more here. These are new, and I've deliberately tried to key a couple of these to legal thinking. Something as basic as the principle of confidentiality, you've probably covered it for thirty minutes in tort law or family law, may be totally rewritten as a legal concept by genetic information. Because unlike most medical information, genetic information is familial. If I have a mutation that I inherited that confers an increased risk of colon cancer, my brother has a one in two risk of having the same mutation. If I'm the first to discover that, do I have an ethical duty to disclose this to my brother? Does the physician have an ethical duty to disclose it if I decide that I don't want it disclosed? Could he override my request to be honored on the principle of confidentiality? Now if you think that's a purely theoretical or fanciful hypothetical, let me assure you that that's wrong. There's already been, some of you may know, two State Supreme Court cases, one in Florida and one in New Jersey, that have addressed exactly this issue—lawsuits that grew out of an individual with a disease who sued a physician because that physician had treated a parent with the same disease and a warning had not gone out to the next generation. The two State Supreme Court decisions are antipodal. One says that the principle of confidentiality should be honored. And the other one says that the risk inferred from the genetic information, the risk of cancer, was so great that there was a duty to warn the transcendent principle of confidentiality. I personally am highly confident that the notion of confidentiality, as it currently exists in state common law, will be rewritten in the next decade by genetics. The more genetic tests there are, the more standards of care there are, the more breaches of standard care there are, and the more lawsuits there are. It's amazing to see how carefully the plaintiffs bar reads medical journals to see the latest developments in the

possibility for genetic testing. I get calls from the plaintiffs bar about this stuff all the time.

A harder one to get our fingers around but something that is actually bothering me a great deal, you could say for selfish reasons and you'd probably be right, is the effect of the economic downturn on the very exciting biotechnology industry. Largely because some of the best minds in America have moved out of academia into industry, back and forth, and there's over a thousand biotech companies working to become the engines of new medicines and new devices to prolong your life and make you healthier. It has been astounding to see the impact of a downturn in the capital markets on those engines. Those engines are sputtering at best and many of them are failing. It is impossible to quantify the loss to you individually and to your generation and your children's generation from discoveries that will be delayed and developments that will not be implemented, or will be implemented a decade later than they might have been, because of a change in just the way our capital and our economy flows.

I think another interesting one that would have made a good panel is how academe will see itself when called upon to get involved in either the defensive or, let me be so bold as to suggest, the offensive use of bioterrorist weapons in coming years. It is, after all, a relatively small number, a few thousand individuals in the United States that have the knowledge to do that and most of them are situated in academe or academic-like settings within pharmaceutical companies.

I think it's wonderful that we have people like David Kaye here, and others, to think about the impact in the criminal law that I alluded to earlier. DNA can do one thing in the criminal law, it can establish the identity of two samples and place an individual somewhere in space, rarely in time. It's possible to determine time only if linked to other things like the decay of a corpse or something like that. But what about a day—think about it from a jurisprudential point of view—when by analysis of the DNA sample you might also be able to infer phenotype. Phenotype, for a word that some of you might not know, is what you can see when you look at me or you look at your neighbor. It's the product, the end of a lifetime of gene and environmental interactions. I'm just imagining this for a moment, let us assume that, and I believe we will, that we identify relatively common polymorphisms, gene variance, that predispose to alcohol abuse. I would not be at all surprised if within the next decade, it was fairly well established that about ten percent of severe alcoholics in our society have a strong genetic driver. If we have a really easy test to identify that polymorphism, how would that impact on sentencing in vehicular manslaughter cases or in parole decisions? It will

be impossible to sequester that kind of knowledge from those kinds of decisions. And maybe it shouldn't be. I'm not implying that it should be, but I think we have to weigh how it would be used.

Imagine a day not so long from now when behavioral geneticists working with biochemists and psychologists ask to get a DNA sample, with the appropriate consent from a thousand people that have been convicted of drunk driving and a thousand people that have never had a drink—or have never had a violation. And you look at the distribution of a certain gene variant in the two, to determine if one variant is much more common than the others. Is that coincidental or is that a biomarker—does that allow us to infer and with what degree of precision can we map that genetic variation to a phenotype? I'm not saying we're going to be able to do a good job of it. I am saying it would be irresistible to investigate the question.

There've been really profound changes in the law already by advances of genetics, and I could think of no better one than to recall that twenty years ago there were tens of thousands of cases litigating paternity in the United States, and they've virtually disappeared. They just don't happen anymore. Why don't they happen? Because the DNA evidence is so powerful in identifying the putative father. Twenty years ago we could exclude using HLA typing, red cell enzymes, things like that. We could say he's definitely not the father. But now with the exception of identical twins, we could say essentially he definitely is the father. Paternity lawsuits don't happen anymore.

Another area where genetics and law are coming together is in one of the most problematic areas of malpractice law, the so-called brain-damaged baby cases where everyone is uncertain of the cause, but everyone assumes the obstetrician. There are thousands of them in the United States each year. I've been telling the insurance industry for years to do a full genetic analysis of every child involved in such a lawsuit. And based on my experience, I think that it may not sound like much to you, but we're talking about twenty to fifty million dollar damage awards. Probably on the order of five to ten percent of the cases the child actually has a genetic disease that was present at conception, which is really the cause of the set of problems that has directly led to the lawsuit.

And I'd like you to consider today, either with your panels or separately, some of the broad constitutional questions involved in the state's right to know things about you through your DNA. And I've alluded to a couple of these earlier. But aren't we heading toward universal sampling of DNA on entering into the United States? That actually wouldn't surprise me at all, given the recent events. Or what about universal sampling at birth? You already have compulsory newborn screening, which is in

fact universal sampling at birth. It's just that the laws weren't created for that purpose. They were created to ask whether their child had a rare genetic disorder. And the laws don't say you can save the DNA. Actually it's dried blood, it's not DNA. But now State Departments of Public Health are starting to save hundreds of thousands of DNA samples. DNA is not quite as stable as is implied by *Jurassic Park*, but DNA is a remarkably stable molecule. You can take a dried blood sample, put it on a filtered paper disk and let it sit in the basement at room temperature for twenty years and do a DNA analysis quite easily, actually. Ed McCabe, from UCLA, has published papers showing you can diagnose single gene disorders on very old DNA samples that are collected at birth.

And what about the application of routine DNA testing under a public safety doctrine? I think I've timed my last few minutes to just give you one fascinating example. If you flew across the United States in a commercial airliner in the mid-90s, say from New York to San Diego, you would, for a period of that flight, have been handled by two air traffic controllers, two brothers, who were at fifty percent risk for a disease called Huntington's Disease, and their employer didn't know it. Huntington's Disease is an incurable neurological disorder onset in mid-life—some of you know it as Woody Guthrie's Disease. One of the first things you could lose in Huntington's disease is the ability to track an object on a screen. I actually got called from the physician of the two brothers and he said, "Wow, what am I supposed to do about this, should I call the airport where these guys work?" Back to the principal of confidentiality and privacy. And you can maybe decide what should've been done in that case.

So there's some of the thinking again, tracking your three panels, which I think you've put together so nicely. Some of the specific things. I think the FDA has failed to address the issue of pharmacogenetics as a true regulatory problem. I think it ought to catch a little grief for that. The Department of Agriculture has not done enough pre-market safety evaluation for dispersing genetically engineered products in the field. We're definitely going to rewrite in the next few years our federal guidelines for human subject research. They were written in the early '70s, at a time when all we thought about was danger of putting a new compound into your body. But now with genetic testing, there's a new set of concerns about information that are not adequately addressed in the guidelines. And then you have some of the tragic deaths recently, inevitable in a new therapy, that call into question the risk benefit for subjecting children, particularly, to new therapies.

And one of my favorite ones, and I have yet to see a single article in any law, science, or medicine, in any journals on this topic (and we'll see

if I can make the argument to you quickly), is about the role of genetic information in the workplace. One of two great pillars of regulating the workplace in America are, of course, the Equal Employment Opportunity Commission, which is charged with implementing the Americans with Disabilities Act and has certain definitions of disability—the third one says if I, the employer, regard you as disabled and discriminate against you, you can claim protections of the act. The EEOC has interpreted the third definition in the guideline, written in '95, to say that if I discriminate against you, my employee, because I learn that you carry a gene that might predispose you to breast cancer later on, and I'm concerned with the costs associated with that, you can sue me. Of course that means that under the EEOC interpretation that all 285 million Americans are disabled, because each one of you carries several mutations that you don't know about. So on the one hand you have this body of law—a small body of law or regulation—that's saying genetic information should not be abused in the workplace. On the other hand, we have a slowly developing body of knowledge that says some people aren't really genetically predisposed to occupationally related disease. Berylosis, contact with the metal in berylium used in aircraft manufacturers, is an example. Under the Occupational Safety and Health Act, people are entitled to the safest possible workplace. If people are entitled to the safest possible workplace, then should you not be offered a genetic test if it really could identify people at high-risk for a disease in that workplace? And how does that fit, or how will that fit, ultimately with the principles that say you shouldn't be forced to undergo certain testing and things like that?

So I think there's an interesting law review article. A little bit forward-looking but not impossibly so, because after all we've had our first lawsuit brought by an Iowa Federal District Court two years ago, brought by a collection of a group of employees who complained because the employer coerced them, allegedly, into undergoing genetic testing because of a spate of disorders that appeared among those small, collective individuals. It's the *Burlington Northern* case, if you want to read about it.[3]

We certainly are going to have a lot more regulatory challenges in the insurance industry, I think. I don't really think it's going to be in the health insurance industry because most of us either get government insurance, are uninsured for economic reasons, or get group health. But I do think that a very interesting issue for the future, which will certainly generate law review articles, is what would happen if the long-term care

3. Bhd. of Maint. of Way v. Athena Neurosciences, Inc., No. C01-4012 MWB, 2001 WL 788738, at *1 (N.D. Iowa Apr. 27, 2001).

insurance industry, the most rapidly growing sector of insurance in the United States, designed to appeal to the aging population, ever got its hands on a test that really did predict risks of Alzheimer's disease, because that's what destroys the bottom line in these retirement communities that are sort of promising to take care of you until you die. Everybody who runs those committees, I think, worries about people with Alzheimer's disease, because they are so expensive to care for and they've contracted to pay for it. I was approached a couple of years ago by a company in Florida that asked if there was a way we could screen our applicants for Alzheimer's disease. And from the insurance perspective it makes perfect sense. I mean we exist in an equity-based system. We don't exist in an insurance system where we all pay in the same amount and all get the same care. We exist in a different kind of system. In fact I'm fond of remembering about five years ago Americans were asked two questions in a poll. The first question asked whether you think everybody should have access in America to life insurance at a reasonable premium? Eighty-five percent of the people said yes. But a few questions later you were asked if you would be willing to pay ten percent more in your premiums so others could get access to life insurance? And eighty-five percent said no. So that's the problem. The problem isn't just the insurance industry. The problem is also the consumer of the insurance product. And you've been looking, while I've been talking, about some of these other issues.

Back to the last part of my talk. The third panel, I think, is on technology transfer issues. As somebody who has moved into the biotech industry, there is nothing I care more about than the care and feeding of the universities. They're incredibly important to the industry. I always feel a sense of great pride and accomplishment when I convince a good investigator in a place like Michigan or anywhere to agree to collaborate with us, as a sponsor. I think it's important to remember that neither the universities or government have remotely near the resources needed to capitalize on their knowledge. This may be one of the most fundamental issues of all: we generate far more information than we utilize currently, in the United States. We have got to address that issue. Indeed the Federal Government twenty years ago or so, said we are going to figure out a way to move discoveries out of NIH and into the marketplace. There are websites that list patents available at low costs, if you're willing to develop them. So how are we going to do that? That's a big issue I think, and even more pressing in an economically stagnate society. There may be a need to create new sets of relationships.

So in closing, my last slide, what I think are really some of the great questions that lurk even above and beyond what we're talking about

formally here today—they're medical questions again. But they're ones that I hear about when I go around the country and the world. There's this tremendous sense, which is probably correct, and I'll have to elaborate a little, that we are entering a new kind of eugenic era, and not one in which its state is driven by government, but it's actually driven by consumers. If I had more time I would tell you how certain birth defects that were very common thirty years ago in certain societies have almost disappeared because the society, however inchoately, decided that it was an undesirable phenotype. Well that may've been good for the easy cases but there are harder questions. But it's when consumers are clamoring for this information that it creates a different set of ethical policy problems than when it's being proposed from the top down.

Now what is the impact of this knowledge on the whole notion of how we treat people with disabilities. Because on the one hand we are introducing and implementing technologies that are unarguably disvaluing certain people, or at least the same phenotype of certain people who also exist.

As I move to the last two, which are really economic questions, I can tell you there's very ample evidence in the Third World (China or India, for instance) that there is deep suspicion about what we're doing with our technologies. China enacted a law (or rule) recently that said you can't move DNA samples out of the country for research purposes. You can go very easily to groups within the umbrella of the United Nations and find great concern about terms that may be alien to them, like biocolonialism. Nevertheless, the fact remains that we do do research, a lot of research, a lot of genomic research in special populations around the world, that we do take the knowledge back and largely, not exclusively, confine it to societies in the West. How would you feel about that if you were a young physician in Thailand knowing that all the knowledge is really going to flow back to Europe, Japan, and the United States?

Hopefully what I've done is set the stage for the more important work of the panels. I look forward to listening in throughout the morning and hope you have a great day. Thanks very much for listening.

[Applause]

PANEL I
THE LIFE SCIENCES IN COURT

MATT MOCK: I want to thank Dr. Reilly for his remarks. And I do want to mention that I was just told that all of the royalties from Dr. Reilly's book that we presented earlier go to charity. So if you have any interest, please seek it out.

And now I'd like to introduce the moderator for our first panel of "The Life Sciences in Court." Professor Richard Friedman is the Ralph W. Aigler Professor of Law at the University of Michigan. He earned a B.A. and a J.D. from Harvard. He was the editor of the Harvard Law Review, and Doctor of Philosophy in Modern History from Oxford University. And he teaches Evidence here at the University of Michigan, among other courses. Professor Friedman.

PROFESSOR RICHARD D. FRIEDMAN: Thank you Matt. Well, this is a wonderful program that you're going to hear. I think the editors have assembled a terrific dream team of scholars, able to comment on life science technology, particularly DNA in the courtroom. We're going to go in alphabetical order. Let me just introduce all the speakers first.

First in the center there is David Kaye, Regents' Professor at Arizona State University, who is really one of the great scholars of the time on the scientific use of evidence, among other distinctions. He's been the editor for a long time of the *Jurimetrics Journal*.

Then Jay Koehler, who has a couple of long titles, from the University of Texas, where he teaches at both the business school and the law school. Of course, his advanced degree is in neither business nor in law, but in behavioral sciences. He teaches particularly Behavioral Decision Theory, and he's written a series of very illuminating articles on DNA evidence in the courtroom and the misapplication and misunderstanding of it.

And finally my colleague Rick Lempert, who bears the wonderful title of Eric Stein Distinguished University Professor, here at the University of Michigan. He's on loan to the National Science Foundation as a Division Director and we hope he'll come back soon. Rick is a profound scholar, not only in evidence, but in sociology—he's former chair of our Sociology Department. I might mention that Rick was on the 1992 NRC Panel, considering DNA evidence in the courtroom. And David was on the 1996 panel. And neither Jay nor I've been on either of the panels.

So I'm going to turn it over to David, who'll first give an overview of DNA issues, with the history of it, and then give some attention to emerging issues. David.

DAVID H. KAYE: For the next ten minutes, I propose to give a broad overview of some of the issues that arise with the use of DNA evidence in the legal system. There are, as Dr. Reilly indicated, a wide variety of uses for DNA-based technologies, and Professor Lempert will be saying more about some of these matters. I am going to focus on the criminal applications.

Postconviction Relief

DNA evidence gained prominence in regard to post-conviction relief.[4] Case after case, now over 123, of exonerations of convicted offenders have changed the political landscape for capital punishment and criminal justice. The possibility of postconviction DNA testing has raised a plethora of legal issues as well.[5] Because these matters have been highly visible, however, I shall simply leave them for later discussion.

Admissibility of DNA Profiles

Over the past decade and a half, the admissibility of DNA testing for identity has proved quite contentious.[6] This history began with a period of relatively uncritical acceptance of DNA evidence. Next, the ensuing mobilization of the criminal defense bar culminated in some successful challenges to pretrial handling of DNA samples, to the methods used to analyze the samples, and to population genetics models used in calculating how rare specific DNA types are.[7] This certainly entered the public consciousness with the O.J. Simpson trial.[8] This second period was followed by renewed acceptance of the calculations in the courts.[9] Today, still newer analytical techniques are coming into use.[10]

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4. *See, e.g.*, EDWARD CONNORS ET AL., U.S. DEP'T OF JUSTICE, CONVICTED BY JURIES, EXONERATED BY SCIENCE: CASE STUDIES IN THE USE OF DNA EVIDENCE TO ESTABLISH INNOCENCE AFTER TRIAL (1996); Paul C. Giannelli, *Impact of Post-Conviction DNA Testing on Forensic Science*, 35 NEW ENG. L. REV. 627 (2001).

5. *See, e.g.*, NAT'L COMM'N ON THE FUTURE OF DNA EVIDENCE, U.S. DEP'T OF JUSTICE, POSTCONVICTION DNA TESTING: RECOMMENDATIONS FOR HANDLING REQUESTS (1999); Seth F. Kreimer & David Rudovsky, *Double Helix, Double Bind: Factual Innocence and Postconviction DNA Testing*. 151 U. PA. L. REV. 547 (2002); Karen Christian, Note, *"And the DNA Shall Set You Free": Issues Surrounding Postconviction DNA Evidence and the Pursuit of Innocence*, 62 OHIO ST. L.J. 1195 (2001).

6. *See, e.g.*, 1 MCCORMICK ON EVIDENCE § 205(b), at 759–62 (John W. Strong ed., 5th ed. 1999).

7. *See* David H. Kaye, *DNA Evidence: Probability, Population Genetics, and the Courts*, 7 HARV. J.L. & TECH. 101 (1993); Kathryn Roeder, *DNA Fingerprinting: A Review of the Controversy*, 9 STAT. SCI. 222 (1994).

8. *See, e.g.*, Nell Henderson & Marc Fisher, *Prosecutors Build DNA Case Against Simpson: Odds are Astronomical that Bloodstains are Someone Else's, Lab Chief Testifies*, WASH. POST, May 12, 1995, at A1 (detailing the statistical analysis of DNA evidence in the O.J. Simpson trial).

9. *E.g.*, 1 MCCORMICK, *supra* note 6, § 205(b), at 762.

10. *See* NAT'L COMM'N ON THE FUTURE OF DNA EVIDENCE, THE FUTURE OF FORENSIC DNA TESTING: PREDICTIONS OF THE RESEARCH AND DEVELOPMENT WORKING GROUP (2000); David H. Kaye & George F. Sensabaugh, Jr., *DNA Typing: Scientific Status*, *in* 3 MODERN SCIENTIFIC EVIDENCE: THE LAW AND SCIENCE OF EXPERT TESTIMONY § 25–2.0 (David L. Faigman et al. eds., 2d ed. 2002).

An example of the early, uncritical acceptance of the evidence comes from Texas. Brian Kelly was accused of murdering a sixty-three-year-old woman.[11] He had been dating the woman's daughter, who lived with her mother. The mother and her truck disappeared one night. Kelly was seen that night driving the truck. He was seen selling the mother's jewelry. The body was found in the desert, and there were stains with DNA left in the mother's bedroom, which linked Kelly to the crime.

The trial court held a hearing on whether the DNA identification procedure was generally accepted in the scientific community, that being the standard for the admissibility of evidence in Texas. At this hearing, the prosecution produced two biology professors, a molecular biologist, and a "physical scientist with the FBI."[12] One of the witnesses said that his book, *Molecular Cloning*, was "the technical 'Bible' of the field."[13] The court observed, with a touch of skepticism, that "[h]e claimed to have written over 100 research papers, some of which have been published in various journals."[14] In contrast, the defense put on one witness, John T. Castle, the owner of Castle Forensic Laboratories in Dallas. His qualifications consisted of "a Bachelor's degree in chemistry and [certification] to teach life and earth sciences in public schools."[15] He testified that "radioactive technology," which was involved in determining the size of the DNA fragments, "was too new to be generally accepted in the scientific community."[16]

Needless to say, the court found the evidence admissible, and the ruling was upheld on appeal. Such outcomes tend to be cited by later courts, as establishing general acceptance of scientific validity, despite the one-sided nature of the hearings. In time, however, defendants enlisted much more impressive experts. In *People v. Castro*,[17] for instance, highly reputable scientists discerned several difficulties with the DNA testing performed by Lifecodes Corporation. The court agreed, after six weeks of hearings and what it called "a piercing attack upon each molecule of evidence," that "the testing laboratory failed in its responsibility to perform the accepted scientific techniques and experiments in several major respects."[18] The court may have found it easier to reach this conclusion

11. Kelly v. State, 792 S.W.2d 579 (Tex. Ct. App. 1990).
12. *Id.* at 583.
13. *Id.*
14. *Id.*
15. *Id.*
16. *Id.*
17. 545 N.Y.S.2d 985 (Sup. Ct. Bronx Cty., 1989).
18. *Id.* at 996. After the court's pretrial ruling to admit some, but not all of the DNA evidence in the case, one of Castro's attorneys, Barry Scheck, was quoted as saying that "[i]t is our view that DNA-based evidence should not be used in court proceedings at all." Lauren Shay, *DNA Evidence Questioned*, A.B.A.J., Oct., 1989, at 18.

because two of the scientists involved in the case happened to be at a scientific meeting at Cold Spring Harbor. They arranged for most of the expert witnesses to meet without any lawyers being present. The resulting consensus statement acknowledged that there were problems with the DNA tests performed in the case.[19]

Around this time, the National Academy of Sciences convened a panel to report on the status of forensic DNA technology. The committee issued a comprehensive report in 1992.[20] It proved difficult for some observers to digest. Headlines in the *New York Times* reported, *Labs' Standards Faulted: Judges are Asked to Bar Genetic 'Fingerprinting' Until Basis in Science is Stronger*.[21] The same day, the *Wall Street Journal* reported *Use of DNA Evidence in Court Endorsed*.[22] The next day, the *Times* printed a story under the secondary headline, *Time's Account in Error: Report Urges Strict Standards, But No Moratorium on DNA Fingerprinting for Now*.[23]

An issue that the report raised but did not resolve was a debate among population geneticists about calculations concerning the probability that an unrelated individual would match a DNA type from the crime scene. Although no statisticians or population geneticists served on the committee, the report proposed a compromise solution (the "ceiling principle") that infuriated several population geneticists who thought it was overly conservative or crude.[24] The committee did not state that the standard computations were incorrect, but its pointed recognition of the fact that there was a scientific controversy made many courts hesitate to admit the evidence. In response to concerns voiced by the FBI and others, a second panel was appointed. Before this committee issued its report, one of the more prominent members of the first panel (and the originator of the ceiling principle), Dr. Eric Lander, together with

19. *See* Roger Lewin, *DNA Typing on the Witness Stand*, 244 SCI. 1033 (1989).

20. COMM. ON DNA TECH. IN FORENSIC SCI., NAT'L RESEARCH COUNCIL, DNA TECHNOLOGY IN FORENSIC SCIENCE (1992).

21. Gina Kolata, *U.S. Panel Seeking Restriction on Use of DNA in Courts*, N.Y. TIMES, Apr. 14, 1992, at A1. This was not the first time that this reporter mischaracterized the views of experts. *See* Andre A. Moenssens, *DNA Evidence and Its Critics—How Valid Are the Challenges?*, 31 JURIMETRICS J. 87 (1990) (discussing Gina Kolata's claim in *Some Scientists Doubt value of 'Genetic Fingerprinting' Evidence*, N.Y. TIMES, Jan. 29, 1990, at A1, that "[l]eading molecular biologists say a technique promoted by the nation's top law enforcement agency for identifying suspects in criminal trials through the analysis of genetic material is too unreliable to be used in court").

22. Joe Davidson & Jonathan M. Moss, *Use of DNA Evidence in Court Endorsed*, WALL ST. J., Apr. 15, 1992, at B6.

23. Gina Kolata, *Chief Says Panel Backs Courts' Use of a Genetic Test*, N.Y. TIMES, Apr. 15, 1992, at A1.

24. Peter Aldhous, *Geneticists Attack NRC Report as Scientifically Flawed*, 259 SCI. 755 (1993).

Dr. Bruce Budowle, an FBI chemist, published an article in *Nature* with the provocative title, *DNA Fingerprinting Dispute Laid to Rest*.[25] Impressed with Lander's apparent change in stance (he had testified for the defense in *People v. Castro* and published several critical articles), the courts took notice.[26]

The second panel issued its report in 1996.[27] It reaffirmed the usefulness of forensic DNA technology and concluded that the ceiling principle was unnecessary. At the same time, it proposed certain refinements to the standard computation for special situations. Courts were reassured,[28] and debates on DNA evidence shifted to other issues.[29]

Inferring Phenotypes

Dr. Reilly noted the possibility of inferring phenotypes from DNA samples. Down the road from me, at the University of Arizona, is a Dr. Brilliant, who has advertised for research subjects to give DNA samples to develop a system for predicting hair, eye, and skin color from an individual's DNA.[30] Not long ago, an official at the National Institute of Health's National Human Genome Research Institute claimed that inferring ancestry from a DNA stain could amount to "racial profiling."[31]

Acquiring DNA from Suspects

Government efforts to acquire samples from suspects have spawned a variety of legal issues. One is consent. Nearly ten years ago, Ann Arbor police went about asking black men for blood DNA samples to find a serial rapist thought to be African-American. And they did not destroy

25. Eric Lander & Bruce Budowle, *DNA Fingerprinting Dispute Laid to Rest*, 371 NATURE 735 (1994).

26. *E.g.*, Lindsey v. People, 892 P.2d 281 (Colo. 1995); People v. Miller, 670 N.E.2d 721 (Ill. 1996) .

27. COMM. ON DNA TECH. IN FORENSIC SCI.: AN UPDATE, NAT'L RESEARCH COUNCIL, THE EVALUATION OF FORENSIC DNA EVIDENCE (1996).

28. *E.g.*, State v. Morel, 676 A.2d 1347 (R.I. 1996).

29. *See, e.g.*, Jonathan J. Koehler, *On Conveying the Probative Value of DNA Evidence: Frequencies, Likelihood Ratios, and Error Rates*, 67 COLO. L. REV. 859, 861 (1996); Richard Lempert, *After the DNA Wars: Skirmishing with NRC II*, 37 JURIMETRICS J. 439, 453 (1997).

30. http://www.ahsc.arizona.edu/opa/news/feb03/dna.htm.

31. Kathy Hudson, *The Human Genome Project, DNA Science and the Law: The American Legal System's Response to Breakthroughs in Genetic Science: Keynote Address*, 51 AM. U. L. REV. 431, 442 (2002). One group of researchers have identified markers that are said to be extremely accurate in classifying individuals as being of European, African, and Asian descent. Tony Frudakis et al., *A Classifier for the SNP-based Inference of Ancestry*, 48 J. FORENSIC SCI. 771 (2003). The constitutionality of the practice is considered in Edward J. Imwinkelried & D.H. Kaye, *DNA Typing: Emerging or Neglected Issues*, 76 WASH. L. REV. 413 (2001).

the samples. After the rapist was caught attacking a fourth woman, one man who had given blood sued for the return of his samples. Today, his refrigerator contains the two vials pried from the police by a court order.[32] Concerns also have voiced about the possibility that police will obtain samples from health care providers or tissue archives.[33]

DNA Databases and Databanks

Convicted offender DNA databases have been established in every state. Several states have laws that require DNA to be provided after arrests or indictments.[34] However, the battle in most state legislatures at the moment involves expanding the list of offenses. The 1992 National Academy report suggested that DNA evidence would only be useful in rape and homicide cases and that states should not include other offenders in their databases. However, it soon was discovered that DNA taken after convictions for burglary and breaking and entering were leading to convictions in rape and murder cases. In Florida, hits in rape investigations doubled after aggravated battery became a collection crime. In the United Kingdom, by 1999, there was a five percent chance of developing a DNA profile in property crimes, particularly car theft.[35] Many car thieves, it seems, leave a cigarette butt or other such souvenir in the car. That may change in time as criminals become more familiar with biology.

Constitutional challenges to convicted-offender databases generally have been unsuccessful. Nonetheless, the Supreme Court has had several opinions in the past two years that have undermined, to some extent, this line of cases.[36]

The ultimate DNA database would embrace the entire population. Such a database would have many advantages over the current system, which is resulting in a set of DNA databases drawn largely from racial minorities.[37] But even with extensive privacy safeguards, having

32. Accounts of the case include Alice Robinson, *DNA of Innocent Rape Suspects Will Not be Kept*, MICH. DAILY, Nov. 21, 1997, at 5, and Jack Leonard, *Using DNA to Trawl for Killers*, L.A. TIMES, Mar. 10, 2001, at A1.

33. The application of the Fourth Amendment to such practices is discussed in D.H. Kaye & Michael E. Smith, *DNA Identification Databases: Legality, Legitimacy, and the Case for Population-Wide Coverage*, 2003 WIS. L. REV. 413 (2003), and Imwinkelried & Kaye, *supra* note 31.

34. *See* D.H. Kaye, *The Constitutionality of DNA Sampling on Arrest*, 10 CORNELL J.L. & PUB. POL'Y 455 (2001).

35. *See* Kaye & Smith, *supra* note 33, at 416 n.9.

36. *See id.*, at 442–445; *see generally* D.H. Kaye, *Two Fallacies About DNA Data Banks for Law Enforcement*, 67 BROOK L. REV. 179 (2001).

37. *See* Kaye & Smith, *supra* note 33, at 450–459.

everybody's DNA in a databank is, as one of my colleagues says, "creepy." This vision, whether appealing or shocking, remains futuristic.

PROFESSOR RICHARD D. FRIEDMAN: Thank you very much, David. And among other factors, for brevity, staying within the time. So now Jay Koehler. We're moving down the alphabet and moving down the technological chain to transparencies.

PROFESSOR JONATHAN J. KOEHLER: I'd say we're moving down in many other respects as well. It's actually remarkable for me to be here with this panel. Three of the most famous scholars in advanced evidence are around me, Rich Friedman, David Kaye, Rich Lempert, and there's me from the business school with a degree in psychology at Texas. It's not hard to spot the imposter.

What I want to do is show a couple of overheads. I was shamed into doing this yesterday when I found out David had a fancy Power Point presentation. But I just want to start off by offering a couple generalities about the juror.

The typical juror is a white Protestant with some college, married, owns their own home, works in manufacturing, retailing, education, health services. In this sense the typical juror does represent the typical American. There's a lot of talk about how Americans are able to avoid jury duty, but actually the typical juror does look like the typical American. And if I can just expand this profile a little bit, based on my own experience and very little data, I would say that the typical juror can balance their checkbooks fine but they find algebra confusing; they've never heard of a standard deviation or a confidence interval; they can follow elementary logic on familiar matters, but they're prone to thinking anecdotally; and they attach too much weight to information that's very vivid, very graphic, but unreliable, uncertain, or incomplete. As far as their attitude about statistics goes, I think the typical juror is, on the one hand, impressed with people who have statistical knowledge. On the other hand, they don't really trust statistics very much. Everybody knows you can lie with statistics.

Okay, and I want to contrast the juror with the statistical thinker. The statistical thinker, we all know these guys, they were the ones who made exhibits for the annual science fair and they excelled in math as kids and their hobbies include things like puzzles and playing chess in the high school chess club. They went to college where they majored in biology and chemistry and math. Some of them went on to become accountants and medical researchers and engineers. The person who has the statistical mind frame, who has this sort of background, is somebody who believes his team will lose to the first place team today. Statistical thinkers believe that because the team that's in first place is probably better

than their own team and, as much as they'd like to think that their team is going to win, they're realistic and they think, "Well, the odds do favor the first place team." I'd go so far as to say the statistical thinker wonders whether his will be one of the fifty percent of marriages that ends in divorce. He doesn't want that to be the case but he knows that fifty percent of the people who get married ultimately get divorced. He knows that everybody who gets married loves their wife, loves their husband. He knows that everybody does all that. And so did he. And so he wonders, "Well, I began by estimating my own chance of divorce at fifty percent, and now I'll adjust that figure for the individuating features that I know about myself." Maybe he's super-religious and would therefore be particularly unlikely to get divorced. Still, he does assume that the fifty percent base rate probability for divorce applies to himself. In a legal context, the statistical thinker believes that the defendant is probably guilty, even before he's heard any testimony. After all, the prosecutor wouldn't have gone to all this trouble if he didn't have some pretty good evidence against the defendant. So he comes in to the trial as a juror thinking, "Sure, I think he's guilty. The odds favor it. Also, I'm aware of the fact that most defendants are ultimately convicted." So these are the kinds of things that influence the statistical thinker's mindset.

Now the law may not want jurors operating as statistical thinkers in every aspect of jury duty. They may not want, for example, jurors to come into the courtroom thinking that the defendant is guilty. But I would argue that the law *does* want jurors to be statistical thinkers in at least some respects, and specifically, I would say that they do want jurors to be statistical thinkers when it comes to evaluating the probative value of evidence. And more specifically still, when it comes to understanding the probative value of DNA statistics. I think the law prefers to have jurors that are sometimes able to adopt a statistical mindset. The kind of people who, as the famous statistician Fred Mosteller might say, understand that it's easy to lie with statistics, but it's easier to lie without them. So statistical thinkers want to have the data so they can see for themselves how well the data support the claim.

Okay, so I've obviously over-generalized these stereotypes, but I'm trying to make the point that I think there's a difference between the typical juror and the statistical thinker. And it worries me because I think the typical juror is not well equipped to handle statistical evidence at trial. And we do know something about how the typical person thinks about statistics at trial. Now, I'd like to review a couple of those studies with you.

First of all, how do people in general and jurors in particular assign weight to statistical evidence? Well, studies in psychology and law

suggest that people tend to underweight statistical evidence, relative to its true value. Its true value is described by a likelihood ratio or some other technical measures that we may talk about if we have a little bit more time. We know that jurors aren't sensitive to variation in statistics as much as the normative theory says they ought to be. So, for example, if a juror is told that a defendant suspect matches DNA evidence that's found in a crime scene, and the match is such that it occurs for one in a hundred people, the juror is likely to be somewhat impressed with the evidence. Now if you tell the juror "Actually the DNA occurs in one in a thousand people, not one in one hundred people," the juror is unlikely to be any more impressed by the DNA evidence. The jurors might change his or her estimate of the chance that the defendant is the source of the DNA a little bit, but not by as much as the mathematical theory that underlies probativity requires.

We know from some studies that I've done and that others have done that jurors and laymen aren't very good at combining probabilities. For example, suppose you're told that a DNA profile occurs in one in a million people. It's a very rare DNA profile. And then let's say that the lab makes mistakes one time in a thousand. How likely is it that this defendant is not the source of the DNA? In order to figure this out, you've got two things to think about. First, you've got to think about how rare the DNA profile is. You've got to consider the possibility that maybe it's just a coincidental match. This chance is one in a million. And then you've also got to consider the possibility that the match occurred because the lab makes mistakes every now and then. This possibility is one in a thousand. It turns out that people aren't very good at combining those two numbers. What they tend to do when they have a very extreme DNA match probability like one in a million is to disregard the error rate number. They think, mistakenly, that the one in one thousand error rate is swamped by the extremity of the DNA profile statistic (which is one in a million). That is, they think that if the DNA profile is extremely small, then we don't have to pay attention to the one in a hundred error rate. Now, we know that there's a problem with this kind of thinking, because when you just provide people with the one in a hundred error rate, they actually are a little nervous about the DNA evidence and they think, "Well, maybe this isn't the guy after all. One in a hundred is a one percent chance of a mistake and, even though the odds strongly favor that a mistake wasn't made, I'm not so sure I'm willing to convict beyond a reasonable doubt." But when people are also provided with a one in a billion match probability, now they are much more willing to convict beyond a reasonable doubt. We observe a difference between these two scenarios even though, from a mathematical standpoint, there's really

very little difference between them. Strangely enough, there's very little difference between having a match probability of one in a billion plus an error rate of one in a hundred, and just having an error rate of one in a hundred in a situation where you're not even sure what the coincidental match probability is. The reason they're very similar is that if there's a mistake, if the suspect is not the source of the DNA evidence, it's not because of coincidence, it's because of a lab error in both cases. Anyway, it turns out that's a hard idea for people to grasp intuitively, probably understandably so.

And other studies have shown that the way the DNA evidence is presented actually makes a difference to people. Some of these changes don't make any difference from a math standpoint; they're just different ways of saying half full, half empty. Yet these different ways of presenting the DNA statistics can make a big difference, in terms of how probative people think your match statistic is.

For example, to this point, I've used a particular format when describing the DNA profile. I've been saying "Imagine you have a frequency of, say, one in a thousand." But there are other ways to describe this DNA match statistic. Before doing so, let me set the scenario. Suppose a person has been murdered and there's blood under the victim's fingernails that matches blood from a suspect. And the match is such that the observed DNA profile occurs in one in every one thousand people. Okay, when you describe it that way, when you say it occurs in one in every one thousand people, people will realize pretty quickly that it's not unique, even in a small city such as Ann Arbor. If it occurs in one in every one thousand people, there's a bunch of people here in Ann Arbor, including forty or fifty people here at the University, who would match. So it's not terribly impressive, relatively speaking, to describe a match probability of one in a thousand that way.. However, let's say you describe it this way: if the suspect were not the source of the blood evidence found underneath the fingernail, there's only one chance in a thousand that he would match. Okay, now that sounds like you got the right guy. If he weren't the source, the chance he would match is just one in a thousand. By the way, you can make it sound even better by saying if he weren't the source, the chance that he would match is .001. People are more impressed with that way of presenting the statistic. And yet, from a mathematical or probative value standpoint, each of these statistics is identical.

Jurors are even more impressed with a match statistic when it is described as what is known as a likelihood ratio. This term is sneaking into court more and more. Everybody on this panel, I think, has written about likelihood ratios and most of us think that it's a terrific way to describe the probativity of statistical evidence. But what I worry about is how people

who are not familiar with the term understand likelihood ratios. That is, it may be a terrific scientific tool, it may be a great way for scientists to communicate with one another, but, in the end, what is important is what jurors take away when we give them a likelihood ratio that describes the probative value of evidence, and whether they understand it the way we understand it. This is the way to describe a likelihood ratio associated with that one in a thousand DNA match statistic: it is one thousand times more likely that the suspect would match if he were the source than if he were not the source. Or you could say: it is one thousand times more likely he would match if he were the source, than a randomly selected person. So it *sounds* like the likelihood ratio is giving this one thousand to one ratio to estimate the chance that the suspect is the source which, if true, would translate into a 99.9% chance the matching suspect is the source. But this isn't actually what's being said. You can't conclude that there's a 99.9% chance somebody's the source of a one in a thousand profile. You can't say that because each of the forty or fifty people in Ann Arbor who matches would then also have to have a 99.9% chance of being the source. There's something strange about that translation. It can't be that the suspect has a 99.9% chance to be the source, just because he matches this one in a thousand profile and so too does some administrator at the University of Michigan. By this logic, the administrator would also have a 99.9% chance of being the source because he or she is also among those who match. Likewise, hundreds or thousands of people in Chicago match and, by this logic, each of *them* would have a 99.9% chance of being the source. As should be clear, it can't be that each of hundreds or thousands of people have a 99.9% chance of being the source. One cannot translate the one in a thousand match statistic into a probability that the suspect is the source just by subtracting that from one. And yet we know that people commonly do that.

I do want to keep my comments brief. Let me mention one other form of statistics. Well you might say let's just go the frequency route. It's the most favorable to the defendant. If you say one in a thousand, you know people are less likely to make that 99.9% error when you tell them one in every thousand people would match, but lots of other people in the city would match. If you describe it that way, you don't get as many people jumping to the 99.9% conclusion. But why is it that we're describing the statistic as one in a thousand anyway? Why didn't I describe it as say *two* in *two* thousand? What difference would that make? Well it turns out it does make some difference. When you describe a one in a thousand as two in two thousand, then people think, "Hey, what about the other guy?"

[Laughter]

And so people are a little less impressed with one in a thousand described as a two in two thousand. So that's a little hint for defense attorneys out there. On the other hand, the prosecutors have an even larger advantage, if you're willing to go this route, prosecutors to be. If you're willing to describe your numerator as a fractional value. So suppose that instead of describing the statistic as one in a thousand, you describe it as point one out of a hundred. Point one out of every one hundred people would match. It turns out that that's extremely impressive to people. Why? Because people focus on the numerator and think wow, not even a person. Point one is so little that they disregard the denominator and say "wow, that's got to be him. Only point one out of every hundred would match, I'm impressed!" We actually collected data on that and sure enough, we got that effect.[38] It's a very strong effect for fractional numerators.

I should also mention that I'm worried, aside from these kinds of presentation issues, about more fundamental issues related to how people understand statistical information. It's not clear to me, for example, that people understand that a rare DNA match is more impressive than a less rare DNA match. A law student at Texas, who was in one of my classes, gained access to four jurors who had just served in a capital murder trial, in which the jury convicted. That case involved DNA evidence. In that case, blood matching the victim was found on the suspect and one in twenty people shared that profile. And so the law student gave each of the four jurors a scenario where he said suppose that you've got some blood, let's say it's underneath the fingernails of a victim, and that blood matches the suspect. And the match probability is one in a hundred. So one in every hundred people would share that DNA profile. And he asked the jurors, "How likely do you think the person is the source?" One of the four did say ninety-nine percent. So this juror made that kind of a mistake that I alluded to before where there's a temptation to just subtract the match profile from one to figure out the probability somebody's the source of the DNA. And that's obviously not the right calculation because then one in every hundred people would have a ninety-nine percent chance of being the source. And that can't be right. The other three jurors estimated the chance that the suspect was the source of the DNA was one percent. So what they most likely did was translate the one in one hundred match probability to a probability that the suspect is the source. This suggests that if we told them the match probability was one in a million, they'd say the chance the suspect is the

38. Jonathan J. Koehler & Laura Macchi, *Thinking About Low Probability Events: An Exemplar Cueing Theory*, 15 PSYCHOL. SCI. (forthcoming 2004), *available at* www.mccombs.utexas.edu/faculty/jonathan.koehler/articles/2004_Psych%20Science.pdf.

source is one in a million. And in fact those three people did not convict in the hypothetical scenario. Their argument was that it just didn't seem like that was his DNA.

These were four jurors who actually had served on a trial where they heard DNA testimony. So this is the real deal and I'm really worried about whether people can understand DNA statistics. I'm not too hopeful about it. And on that pessimistic note, I'll stop. Thanks.

[Applause]

PROFESSOR RICHARD D. FRIEDMAN: The other pessimistic note, I'm wondering if I should temper the congratulations I offered Jay last night on finding out he's engaged to be married.

PROFESSOR JONATHAN J. KOEHLER: Yeah, I'm not a statistical person.

PROFESSOR RICHARD D. FRIEDMAN: You're not a statistical person, okay. Let me just say before we move to Rick, usually the DNA evidence isn't presented alone. In other words, in almost every case, there's other evidence, so that the defendant is going to look more likely to have committed the crime than are those other people in Chicago with the same profile. But it's the combination of the DNA evidence with the other evidence that's part of the problem here. I suppose the only type of case in which the DNA evidence would be practically alone in proving identity would be one in which the DNA evidence is quite powerful. But still it doesn't relieve the problem of the juror misunderstanding.

Okay, so now on to Rick Lempert, who is going to talk about the effect of DNA evidence on science and on scientific evidence in general, and some emerging issues.

PROFESSOR RICHARD O. LEMPERT: Thank you. Those of you in the audience who are not lawyers probably are not familiar with the dreaded overtones in the student law journal world of the word "preempt." When a student works for six months on a note for a law review but before it can be published some other law journal publishes a story on the same topic, suddenly all that work is for naught. The law review withdraws the piece because it has been "preempted."

I knew when I came here that my co-panelists were David Kaye and Jay Koehler. I'm not trying to be polite when I tell you that in my view David is our nation's preeminent authority on the statistics of DNA evidence, and Jay is the leading student of how DNA statistical evidence is received by jurors. So I thought that although this is a panel of three people who had done work on DNA evidence, I would stay largely away from that topic and talk about other issues. I didn't tell Philip Reilly that that was what I was going to do, and he gave a presentation which has a remarkable similarity to what's in my notes. So I'm going to scramble

and say a bit more about DNA than I thought I would, and probably a bit less about some of the other areas. Though I will talk about those also, Philip has in large measure preempted me.

Let me begin with DNA. DNA evidence has had a substantial impact on our justice system. DNA evidence is absolutely terrific evidence. It's the best identification evidence that we have today, at least in terms of its science base. Fingerprint evidence also seems to be extraordinarily good evidence, but although it has been around much longer, it has not been studied in the degree to which DNA has. Also there is considerable subjective variation in standards for making claims about fingerprint evidence, and there has been no official promulgation of fingerprint identification standards, at least no court-sanctioned regulation that I know of.

DNA is marvelously probative evidence. As such, it has cast, in recent years, interesting light on our criminal justice system. We have, for example, learned about the large number of factually innocent people who have been convicted of homicide or rape. We also know that those shown to be innocent have to be the tip of an iceberg since only people alive today, with crimes for which DNA was preserved, can be in this group. Thus, these "DNA acquittals" say a number of things about our criminal justice system, which we should take to heart.

The first is that these acquittals emphasize how fallible any human decision making system is. The second is that they indicate sources of fallibility. One recurring flaw, that would surprise no one who has studied criminal identifications, is the fallibility of eyewitnesses. The confirmation of this fallibility suggests that those courts which resisted allowing psychological experts to testify before juries about the weaknesses of eye witness testimony were in all probability too skeptical about the value of such experts and may have helped work an injustice by barring their testimony.

A more surprising aspect of the DNA acquittals is the number of people who confessed to charged crimes who have been proven innocent. We think we don't have coerced confessions in this country because we've gotten away from the rubber hose, beatings, and the like, but we see in these acquittals the reality of psychological coercion. There have also been acquittals in which the apparent cause of the mistake has been perjury by police or others. So again, thanks to DNA, we have this light on the deficiencies of the system that we should be taking to heart.

In the past, the system has resisted taking these things seriously. It's only in the last few years, almost through shame, that a consensus seems to have emerged in the prosecutorial community that if DNA evidence is

available and a credible claim of innocence can be made, testing should be allowed. Some courts have now said this. But in the early days, the same prosecutorial establishment that was using DNA evidence to convict people and claiming, in good faith, that DNA was terrific evidence, were arguing, when it came to using DNA evidence to reverse convictions, that we should let things rest and not reopen cases. Perhaps because there have been so many other scandals in our criminal justice system, there has been no cry of outrage over this, but there should be. A prosecutor's task is to do justice, not to secure convictions. Something is wrong with the system when prosecutors subordinate protecting the innocent to not just securing but maintaining convictions.

Recently in Virginia, an issue has arisen that I find fascinating, for what it says about official attitudes. A man was executed by Virginia, although he claimed throughout the process that he was innocent. Apparently, before DNA tests were available seriological samples were tested and found inculpatory, but with limited probative value. Now the relatives of the man executed want to test the crime sample DNA to show that he was innocent of the crime for which he was executed. The state, including the State Supreme Court, has denied the request to test. One of their arguments, as reported in the press, was that if the test results were exonerative, they would discredit our system of capital punishment. Hello! I mean isn't this exactly what we want to know? Shouldn't we seek to learn how well we are doing in separating the innocent from the guilty in order to decide if we wish to maintain a system of capital punishment and to decide what protections to require if we do. Shouldn't capital punishment systems be discredited, as the system was in Illinois, if it leads the state to kill the innocent? As a social scientist and as a lawyer I deplore a system in which political preferences can override proper evidentiary value.

I also want to emphasize something implicit in Jay's remarks. Today, in most cases where we use DNA evidence, we can honestly say that if the suspect's DNA matches the evidence (crime scene DNA) we are virtually *certain* that the evidence DNA came from the suspect (or an identical twin). The probability of a match, if someone else is the source of the evidence sample is, in most cases, infinitesimally small. Although to claim that the defendant is certain to be the DNA source is a slight overstatement, given the findings Jay reports, I think it is a better way of proceeding than our current presentation of random match probabilities. If told the match was certain, I think, jurors could take better account of error in the testing that yielded the match and of the possibility of dishonesty in evidence collection or reporting than they are likely to do if they get random match probabilities like one in ten billion thrown at

them. The important point, and this has been my hobbyhorse from my first involvement in DNA as a member of the NRC Committee, is that the limits of the probative value of DNA evidence are not set by the frequency of random matches. Rather, they are set by the quality of the technical work and the honesty of the people who are involved in collecting, preserving and analyzing DNA evidence. The probability of a misidentification from these error sources is, in the typical case, far higher than the probability that a misidentification occurs because two people have DNA that is identical at all tested loci.

Let me just give you two examples from a case I'm sure you're familiar with: the O.J. Simpson case. There were two items of DNA evidence that seemed compelling because they showed that Nicole Simpson's blood was on O.J.'s possessions. (I am speaking from memory here, but I think what I say is accurate.) One item was a bloody sock found in O.J. Simpson's bedroom, which was reported to have had Nicole Simpson's blood on it. The evidence was highly incriminatory. But there was a problem for the prosecution's case. That is that if you take a sock, which is like a tube in that it has four sides. There was blood on the inside and outside of one side and on the inside of the other side. Obviously the blood must have splashed on the outside of the sock, soaked through to the inside and then been deposited on the inside of the other side of the sock. But if you're wearing a sock, blood will not go through your ankle to come to the other side. The prosecution's theory was that when O.J. took the sock off, it was still damp so when it flattened down on the floor, there was a transfer of blood from the inside of one side of the sock to the inside of the other, thus accounting for the blood on the three sides. The defense, to counter this, presented an expert witness who testified that given the time it would have taken O.J. to get home, the blood would have clotted sufficiently so that the transfer of blood would not have occurred—or could not occur to the degree that it did. The defense theory was that the transfer happened when a police officer, who contrary to police procedures had retained a vial of Nicole Simpson's blood, poured blood on one side of the sock when it was lying flat on the floor and it soaked through to the other side.

Now I don't know which story is true. I tend to believe the state's theory more than I do the defense theory, despite the expert testimony. But I certainly believe that the chance that a cop poured blood on the sock was far higher, even if it was as low as one in a hundred or one in a thousand, than the chance that that blood did not come from Nicole Simpson, if it matched her DNA.

Another bit of highly incriminatory evidence in the O.J. case was that in O.J.'s van, there were very, very small flecks of blood identified

as coming from Nicole. This evidence too appears to be strong evidence of O.J.'s guilt. The problem here is that the L.A. police came directly from the crime scene to the van. At the crime scene, they were involved in examining Nicole Simpson's body, and it is hard to imagine that they did not get some blood on them. There was so little blood in the van that they had to use a technique, called PCR, to amplify what there was for analysis. It's entirely conceivable that an accidental, unintentional transfer of blood would have left samples of Nicole's blood in the quantity found. Again, I would not say it is more likely than not that the blood in the van was due to accidental contamination, but it is far more likely that there was inadvertent contamination of the van, with Nicole Simpson's blood, than that the blood came from somebody other than Nicole with matching DNA. Yet the evidence was presented so that the jury would think its incriminatory value was defined by the very low random match probability and not by the far higher probability that there was accidental contamination. Thus we have to be very careful about DNA evidence, despite its many virtues.

Another aspect of DNA evidence, which in my mind has been all to the good, is that because of its tremendous incriminating power, the need to ensure that DNA testing is reliable has been driving standards for forensic laboratories in general. The first moves toward accreditation of forensic laboratories were driven by the critiques of DNA and the awareness of how misleading DNA based errors could be. This does not mean, however, that laboratories cannot err in DNA analyses. Early proficiency tests revealed errors. The response of the laboratories to tests that showed erroneous reports is instructive. They said something like, "Yes, it's true, we made a mistake, but we've corrected that problem. The mistake will never happen again." It may be true that they corrected a problem, but this doesn't mean there cannot be other problems. Within the last week, there was a story in *The Washington Post* reporting that several hundred DNA identification cases were going to be reopened in Texas because of sloppy laboratory conditions. If before the story broke you had asked a DNA scientists whether that degree of malfeasance was possible, I think most would have replied that it couldn't happen anymore in the DNA world. In short, DNA is far more reliable than other forensic identification evidence, but DNA scientists like other forensic scientists systematically overvalue the virtues of their science by ignoring the inescapable deficiencies of humans.

As interesting as the fact that DNA drove standards for forensic laboratories, is my sense that DNA analysis is the very rare case where the law also drove the science. Thus, controversies about DNA statistics led scientists to empirically examine population genetics and related

issues sooner and in greater depth than they would have if they were not interested in presenting the evidence in court. It also led to the rigorous testing of hypotheses about genetic variation and probabilities of allele combinations which might not have occurred as soon if the evidence did not have to be admissible in court. This was in part due to the involvement in litigation of leading scientists, with quite different perspectives on the value of DNA evidence as well as to attempts by the FBI to legitimate DNA evidence by promoting the appointment of two National Research Council panels on the topic. It is a shame that equally eminent scientists seldom get as deeply involved in establishing the validity of other techniques of forensic science. I expect that, as with hair or handwriting comparisons, this is often because the scientific basis of the evidence is so weak as to not be scientifically interesting.

Before leaving the topic of DNA, let me also mention the complexities one gets into when considering felon DNA databases or DNA databases in general. Despite some disagreements, there seems to be a consensus that at a minimum, it is appropriate and legal to take DNA from convicted felons, including felons convicted of crimes other than rape and murder, and to put the DNA profiles in a database that can be checked when DNA is recovered from a crime scene. These databases are becoming much more important tools of criminal identification, as PCR techniques allow us to develop cold hits in crimes other than rape and murder. For example, analysis of the DNA left by saliva on a cigarette butt can identify a robber, a burglar, or auto thief.

There is disagreement, however, on whether arrestees should be vulnerable to having their DNA taken and profiled for inclusion in databases before they are convicted of a crime. Important value questions are raised. If, as there is good reason to believe, police are more likely to arrest members of some racial groups than other racial groups, then taking DNA from innocent arrestees means there is a racial bias built into vulnerability for future prosecution.

Also a good case can be made that all of us should be equally vulnerable. None of us should get a free ride on crime. Perhaps we should use the blood samples taken from all hospital-born babies at birth and build a DNA database that includes all of us. But that's not where we are. Today, I think, most people would not allow this. A universal DNA databank violates our sense of privacy. What we have instead is an "every dog gets one bite" rule. You've got to commit a crime or at least be suspected of it. I suspect that many people are untroubled by a policy of taking DNA from arrestees because they believe both that an arrest is suspicious, and they are not going to be arrested. People, in other words, are perfectly happy putting the "other's" DNA in a database, particularly

if their image of the "others" who are arrested is black, Hispanic, or otherwise clearly different from them. But if we allow arrestees to have their DNA entered into databases in part because we don't think we will be affected, it raises serious moral issues.

For the moment, however, let us put aside the problem of arrestees and accept the "one bite" principle: people should not be included in DNA databases, unless they deserve it because they have committed felonies and so show they are not law-abiding citizens. Now consider the following situation. There has been a rape. DNA evidence has been secured and run against a database without yielding a match, so we know the offender is not in the database. Suppose, however, that of thirteen places tested, someone in the database matches on ten. We know this person is not the criminal, but we also know there is a very good chance that some close relative of the person in the database is the criminal. What do we do then? Do we ignore the evidence and tell the local police only that there was no match. To do so might let a rapist rape again or a murderer kill again. Or do we tell the police to get DNA samples from the felon's father and brothers. In this case the father and brothers are effectively in the database even though they have not in the past been apprehended for a crime. More importantly, if we allow these identifications not only are some people not protected by the "one bite" rule but the racial and other biases of felony convictions built into the database because of the overrepresentation of blacks and Hispanics in the criminal population are enlarged so that proportionately many more never-convicted blacks and Hispanics are vulnerable to DNA identification. This problem is exacerbated if an arrest is sufficient reason to acquire a DNA sample for database storage.

Because of this, my strong inclination, except for one consideration, is that we all should have our DNA in the databases. Let's be fair; no one should get a free ride on crime. I don't care whether you're a first time offender or you've gotten away with five crimes, or a convicted felon. If you rape somebody, I want you caught, and I want a world in which people are deterred knowing that if they commit a serious crime they are likely to be immediately identified. But here is my problem (which I admit may just be paranoia about a future world that may never exist). Recall the movie *Casablanca*? The movie turns on the presence in Casablanca of a leader of the anti-Nazi resistance named Viktor Lazlo. He must leave Casablanca to continue his work and the Germans, working through the apparatus of the Vichy French government, are determined that he will stay in Casablanca or die. In one scene Lazlo and several other members of the French underground are at a secret meeting. If they were found, they would surely be arrested and would probably be shot.

Somehow the police get wind of the meeting and they stage a raid. At the last moment the plotters realize their danger. Everybody flees and gets away. No doubt the police frantically chased them (the movie doesn't show this, but it is reasonable to suppose) but they didn't catch any. So the Casablanca underground lived to fight on.

With everyone's DNA on file, however, there would be a different ending. The police would save their breath. Rather than give chase, they would take the glasses the people were drinking from and the cigarette butts in the ashtray, and they would run DNA analyses, arresting or shooting those whose DNA matched. So in creating a universal database, we would be creating an ability to follow everyone, for good or for evil, that we have never had before. It is important to consider even such low probability scenarios, as we think about how we're going to treat DNA in the courts.

Now let me briefly address some areas where Phil has in some measure preempted me. First, it is important to realize that DNA evidence is not confined to criminal cases, and is only going to get more important in civil and regulatory law. The use of DNA to establish paternity has already been mentioned. DNA analyses today dispose of most disputes about paternity, so the obligations that arise out of paternity now turn largely on genetic testing. The number of genetic tests and the number of adults seeking genetic testing has increased markedly in recent years, and a new profession, genetic counseling, has arisen to help people with issues related to genetic tests, including coping with unwelcome results. It turns out that genetic counselors are learning, in a not insignificant number of cases, that a child being tested is not the child of the person who thinks he is the father. What should a genetic counselor do in this situation and what legal liability will arise if the counselor tells or fails to tell what she has learned? Suppose a father or mother asks. Must the counselor then reveal what she has learned about paternity?

Another issue that the court has to confront is the genetic counselor's responsibility to persons other than those tested. Suppose, to take an extreme case, that one identical twin tests positive for the breast cancer gene. The test results would alert the other twin to closely monitor for the development of cancer and might even lead her to decide on a prophylactic mastectomy. If for some reason the tested twin refuses to share her results with her genetically identical sister, does the counselor have an ethical obligation to do so? Will the counselor be vulnerable to a law suit for breaching confidentiality if she tells the twin sister? Or, might the sister sue if she is told and preferred not to know? Alternatively, if the genetic counselor does not tell and the twin sister develops breast cancer, will the counselor be held liable for a failure to warn?

Genetic tests also have a role to play in adoptions and tracing family histories. In Argentina, during the "Dirty War," many people were killed and their children were adopted by others. Mary Claire King, an American geneticist helped trace through DNA testing the relationship of these adopted children to their grandparents and other blood relatives. Thus, the children could be returned to their extended birth families, though there parents were dead. But were the children better off than they would have been had they been left to grow up with their adoptive families? That's a question DNA cannot answer.

Genetics may also help decide immigration questions. Relatives of people living in a country often get immigration preferences. Suppose there's a dispute, as has happened in England, about whether a claimed filial relationship is real, with the INS arguing it is phony. DNA can be used to determine if the claim of relationship is a valid claim.

Consider also the potential relevance of DNA evidence to issues of responsibility and the issues that a deeper understanding of the genetics of behavior might raise. One can imagine, for example, that we learn that some people have uncontrollable impulses to drink alcohol or to act violently. How do we deal with responsibility for criminal actions that are in part attributable to genetic propensities? Is this going to be the new Twinkie defense? Indeed, maybe we'll learn there's something to the Twinkie defense. Perhaps we will identify a rare mutation which means that for a small number of people sugar releases inhibitions and stimulates violence. What do we do if a genetic test reveals that a man charged with assault shortly after he devoured four Twinkies had this mutation?

When we turn from crimes to torts, we find all sorts of implications for law in the new genetics. Phil gave the example of using genetic evidence to show that a condition like cerebral palsy was not due to harm a doctor might have caused during the delivery. But genetic evidence cuts both ways. It may show that some damage is genetic in origin, but it may also show that it is not. In the latter case, there may be a strong impetus for a jury to attribute a baby's condition to malpractice when it was caused by something else, like the womb environment, which is not the subject of expert DNA testimony.

I have been asked to finish. So I'll just provide a catalog of other issues that I would discuss in further detail if I had the time. One can imagine a new tort of releasing genetic test results without proper counseling. It can be psychologically devastating to learn one has a disease like Huntington's. If someone is told she has the gene for Huntington's but is not properly counseled, does she have a cause of action? Does someone who does not want to know whether he has the HD gene have a cause of action against a relative who informs him of her test results,

when they mean that he has an elevated risk of having inherited the HD gene? Additional issues are raised by the genetic testing of children. Do parents have authority to test their children's DNA for diseases like HD for which there is no known cure? May a genetic tester be sued by a child for complying with the parents' wishes? Other tort cases are likely to grow out of pharmacogenetics, allergies to GMO crops, destruction of native crops by the transposition of DNA genes, and the like.

Another area crying out for legal regulation and fraught with the potential for litigation is insurance. Can a company deny insurance because a person refuses to allow DNA testing on privacy grounds? If insurance companies are allowed to collect DNA samples, will there be limits on what they can test for and with whom they can share results? Will companies face liability if they don't disclose to the applicant health-relevant genetic information? If insurance companies are not allowed to insist on genetic tests, how will they deal with the moral hazard problem which will arise if people use their own genetic test information as a basis for deciding whether to purchase insurance? Also, will we have different rules on genetic testing for health and life insurance? States have begun to tackle some of these issues, particularly denial of coverage and genetic privacy issues, but state laws are a patchwork and much remains to be done.

Employment is another sector in which genetic tests raise legal issues. Can a company, for example, use DNA tests to determine whether an employee can work with chemical or biological factors? May it screen initial hires genetically and exclude those who are most susceptible to alcohol addiction, if it is worried about shop floor safety, or breast cancer, if it wants to minimize health care costs? Intellectual property issues abound; we'll have a whole panel on that later. DNA and biotechnology will play an important role in regulatory law. It can, for example, provide new ways to test the purity of certain products, and recombinant technology allows genetic markers to be inserted in bacteria that facilitate the tracing of non-point sources of pollution. Contracts issues include the question of who owns DNA samples. If somebody provides a DNA sample and it turns out that its special properties allow a large medical payoff, who gets the benefit of the intellectual property? Finally in almost all areas the law will face the problem of seeking to resolve complex issues by appeal to the judgment of nonscientist judges and juries. How can we educate them when DNA is used in court? This list is by no means exhaustive though I fear I may have exhausted you. Thank you.

[Applause]

PROFESSOR RICHARD D. FRIEDMAN: Thank you, Rick. I want to open it up to the floor for questions in a bit. But let me pose the first one, which ties into comments by all the panelists.

The question of juror understanding. Jay presented some depressing data on this and Rick has presented one possible way out, which is basically for the defendant to concede that the DNA samples come from the same source. But if the defendant doesn't concede that, is there a way out? Is it possible that the technology will be sufficiently good, soon enough, that we can say we can do without all the statistics? That's one possibility. Or should we at least say that the proponent of the evidence, most often the prosecutor, doesn't have to present statistics? In other words, is it plausible to say we can just avoid this whole issue, effectively by brute force because the evidence is so good? Or will that soon be a possibility? Anybody want to take a crack?

PROFESSOR JONATHAN J. KOEHLER: Well I think most of us agree that a chance of a coincidence when the numbers are as extreme as they typically are, is so small that it probably won't even happen in our lifetime.

PROFESSOR RICHARD D. FRIEDMAN: Right. But yet we still go through this exercise, right? And I'm wondering how we can avoid that.

PROFESSOR JONATHAN J. KOEHLER: Well, I mean the lawyers should probably talk more about it. I have told defense counsel that I think the best way to focus the jury's attention on the possibility of error is to simply concede there's no chance of coincidence whatsoever.

PROFESSOR RICHARD D. FRIEDMAN: Yeah, right.

PROFESSOR JONATHAN J. KOEHLER: And then the only statistic you're talking about is the chance that this could've been an error and maybe the one percent chance or whatever chance you were able to introduce for error will be sufficient to make a few jurors think, "I'm not convinced beyond a reasonable doubt." But lawyers aren't willing to give that up. They're not willing to concede that there's no chance of a coincidental match because then they lose one issue on appeal. And so instead we hear lines like this, where an expert will say "there's a ninety-five percent chance that ninety-nine point three percent of the people in North America don't have this DNA profile." This is very typical testimony. But I just can't imagine a jury doing anything sensible with a ninety-five percent chance that ninety-nine point three—so— . . .

PROFESSOR RICHARD D. FRIEDMAN: Right. So one answer that now both of you have presented is that the defense lawyer should just be smarter by conceding the one issue. But if they're not doing it, I'm wondering what the law can do. Any other thoughts from David or

Rick on this? Or the technology? As I say, will the technology bail us out by getting us to the point we can say you know what, we don't want to hear it, this is the same DNA, assuming there's no lab error?

PROFESSOR DAVID H. KAYE: Two things come to mind. First, in the cases where courts were concerned about the method of computing probabilities, many courts wrote that it would not be permissible for an expert to report a DNA match without an accompanying statistic to indicate how significant this finding is. One reason that courts gave for this conclusion is that the 1992 NRC report stated that it is not scientifically acceptable to report a match without assessing the probability of a random match. The courts construed this to preclude admissibility of all purely qualitative testimony about a DNA match. I think that this makes no sense. Once it is established that DNA typing allows an exquisite degree of differentiation among individuals, it may no longer be necessary to report that degree of differentiation down to six decimal places. Rough statements, like "this is a very rare type" should suffice.

Second, in most cases it should be possible for an expert to give an opinion that the defendant is the source of the DNA in question. The chance that even a full sibling would match at 16 STR loci, for example, must be less than one in a million. As early as 1994, Daniel Hartl, a population geneticist known for challenging the usual computations of matching probabilities, submitted an affidavit stating that "to a reasonable degree of scientific certainty," a DNA sample came from a specific defendant.[39] Thus, when the probability computed in a given case is small enough, FBI analysts now report that the defendant is the source of the DNA.[40]

PROFESSOR RICHARD O. LEMPERT: I think the FBI policy is all to the good so long as it is clear that the claim presupposes no fraud or error. I have a couple of additional comments. One is in defense of the 1992 NRC report. One of the interesting things about being on that panel was that information about DNA evidence was changing so rapidly in the course of our writing the report that it was almost overtaken by scientific advances before the ink on it was dry. One of the problems with courts is that they're used to looking at authority, and often the older the authority the better. However, for a science that changes as rapidly as DNA, that's exactly the wrong policy.

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39. State v. Bloom, 516 N.W.2d 159, 160 n.2 (Minn. 1994); *see also* People v. Hickey, 687 N.E.2d 910, 917 (Ill. 1997) (given the results of nine VNTR probes plus PCR-based typing, two experts testified that a semen sample originated from the defendant).

40. Bruce Budowle et al., *Source Attribution of a Forensic DNA Profile*, 2 FORENSIC SCI. COMM. (July 2000), *available at* http://www.fbi.gov/hq/lab/fsc/backissu/july2000/source.htm.

I stand by what we said in that report on the issue David raises as of the time we wrote it. But relatively soon after the appearance of the report, what we wrote was no longer the best advice that a group of scientists could give a court, though the random match probability should be calculated for internal purposes. I think the FBI (and this is also done in Britain by some scientists) is right to report only that the defendant is the source of evidence DNA when the probability that the DNA came from someone else (including close relatives) reaches a certain low level. We probably need a court judgment about what that threshold probably should be.

Lawyers, however, like to win, and, unfortunately, sometimes they like to win more than they like to do justice. Each side has its incentives to keep using DNA statistics. The prosecution has an incentive to present random match statistics because if Jay's work is right it may be more persuasive than simply reporting a unique match and allowing the focus be switched (as it should) to the error probability. The defense, on the other hand, clutching at straws may dwell on statistics in the hope of confusing enough jurors so that the jury can't reach a decision.

Confusion may, however, also hurt the defense. Suppose a match is found but it is reasonable to think that there is a one in five hundred chance of laboratory error or police malfeasance. A defense attorney might think it silly to offer this information, for it seems little is to be gained from admitting a match with such a small error probability. But the defense may be misreading the evidentiary strength of this information because implications of a probability like this depends tremendously on the other evidence in the case. If the other evidence is itself incriminatory, as Rich suggested is usually the case, the defendant will lose and deserves to lose. But if the other defense evidence is strong, for example, an alibi that seems reasonably solid, an error rate of one in five hundred might well justify an acquittal. But the jury may not appreciate that DNA evidence, including error probabilities, must be read in the context of all the other evidence, and may even think it means that there is only one chance in 500 that the defendant is innocent.

PROFESSOR RICHARD D. FRIEDMAN: All right, thanks. Let's open up to the floor. I have enough questions to keep us going if there aren't any. I'd rather hear from you folks.

PROFESSOR RICHARD O. LEMPERT: [INAUDIBLE—TOO FAR AWAY FROM MIC. NUMBER 2:02 ON VIDEO]

PROFESSOR RICHARD O. LEMPERT: That is a really interesting question. I have several things to say about these issues. First, when people think of universal population screening, they are usually thinking about extracting from the blood samples that are taken from newborns

for state-mandated genetic testing, a profile of the loci used in identification databases, and storing these profiles in a searchable database. An interesting side issue is that for identification purposes all that is needed are the profiles of these loci, which were chosen in part because they seem not to code for any known traits. Yet the police often keep the whole DNA sample on file, from which a wide range of genetic information, with no implications for police work, can be extracted. There is a real question whether we should allow this.

I sit on the advisory committee for the Community Genetics program of the Michigan Department of Public Health. Recently we learned that the blood samples collected from newborns for genetic screening are kept for something like twenty-one years and then destroyed. The question we were asked to discuss was whether researchers should be given access to these genetic samples. They are tremendous resources for understanding disease, particularly if we can follow people through their lives and see what happens to them. In our discussion of the issue there was general agreement, indeed it went without saying, that if researchers were to be allowed access to these resources, the access would have to be anonymous, since the sample donors had not given informed consent to research uses. People thought that if there was total anonymity, the informed consent issue was solved. But if we ever establish a universal DNA database, we will not be able to give anonymous genetic samples to researchers. There will always be the chance that a person could analyze the alleles used for identification, and if she had access to the universal database, determine who is the source of the sample. So all sorts of problems that one doesn't usually think about arise in this area.

My other quick point is that even though we don't have universal DNA databases, in some areas, for some crimes, there is tremendous police coercion on large numbers of people, none of whom would be conventionally called a suspect, to give DNA samples for identification. So in a sense, we are creating local DNA databases to investigate crimes. Indeed the very first DNA identification case in the United Kingdom, with the marvelous name, *Regina vs. Pitchfork*, grew out of such a situation.[41] It was a case involving two rape murders near a village in rural England, which unfortunately for the perpetrator, was near the laboratory of a pioneer in DNA genetic analysis. The police tactic was to demand that every male in the village area give a DNA sample. The interesting thing is that none of the samples matched. But then it turned out that one person had had a buddy give a sample for him. Sure enough, when that person's DNA was later tested, it matched the DNA left at the crime

41. Craig Seton, *Life of a Sex Killer Who Sent Decoy to Take Genetic Test*, TIMES (London), Jan. 23, 1988, at 1.

scene. Of course, at this point one hardly needed DNA evidence to identify the perpetrator.

PROFESSOR RICHARD D. FRIEDMAN: You mentioned blood samples. My impression is that with newborns you wouldn't take blood and that when they do the databases, it's usually from a swab.

ANSWER: In newborn testing in Michigan, and I think elsewhere, they take between three and five dots of blood, which are placed on a card, and stored. They are used immediately to do a series of tests, in Massachusetts it's thirty, in Michigan the panel is, maybe, twenty-five, but the panel is increasing all the time. The cards with blood are kept for 21 years.

QUESTION: [Inaudible].

PROFESSOR RICHARD D. FRIEDMAN: Yeah. Rick said you know it's a marvelously powerful tool to have the universal database, the concern being that it could be used for ill. My own personal feeling, I'm curious what others feel about this, is that's true of all governmental information. Information the government has is particularly powerful information but we'd have to develop, as David indicated in the slide, strong privacy protections. But my goodness, it would mean no first crack—no opportunity to commit a crime before your DNA has been collected—which is what a felon database allows. I'm curious whether others on the panel have comments.

QUESTION: [Inaudible].

PROFESSOR DAVID H. KAYE: If we are going to have a universal law enforcement database, the only practical way of doing it at present is something that Dr. Reilly has suggested, which is to use newborn screening and slowly build the database over time. It could be structured so that the police do not handle the blood samples, for these contain information that would be problematic. The identifying loci that the FBI now uses involves thirteen or more STR markers. These are no more meaningful than a passport photograph or a Social Security number. They are essentially random noise in the genome. One could add to the newborn disease screening done for public health purposes, by force of law and without informed consent, an additional test for the identification markers. That one test result could be transmitted to a single database without any law enforcement personnel ever handling a sample.

This system would need to be supplemented to include immigrants and perhaps visitors. The details are by no means worked out, and the public might well reject the concept at the present time. But twenty years from now, perceptions and fears may change. Certainly, the technology for creating identifying profiles at low cost will improve.

PROFESSOR RICHARD D. FRIEDMAN: Thanks. Other questions?

PROFESSOR JONATHAN J. KOEHLER: I'd like to see proficiency testing in all areas of forensic science. So I don't know if your database was concerned, per se. But I'd like to see the experts tested, that is provide the expert with samples of known matches and see how often they correctly say match. No non-matches and see how often they correctly say no match. Then we get a sense of their error rate and then we introduce that.

PROFESSOR DAVID H. KAYE: Some forensic scientists recognize the need to gather data that would justify claims about probabilities or frequencies. Researchers in New Zealand have collected fragments of glass from roadways to determine how common or rare various features of broken glass are.[42] In *United States v. Nichols*, one of the Oklahoma City bombing cases, an FBI tool mark analyst referred on cross-examination to a study of the individuality of drill bits, but the study never was completed.[43] In response to defense challenges to handwriting and fingerprint identifications, a few experiments and statistical analyses have been conducted.[44] Thus, there are forensic scientists who are interested in doing such studies, but far more should be done.

PROFESSOR RICHARD D. FRIEDMAN: We're over time. I only have time for one quick question. Gentleman in the back.

PROFESSOR RICHARD D. FRIEDMAN: Can you speak up please?

AUDIENCE MEMBER: [Inaudible 2:16] How do we ensure that defendants have counsel? Lawyer training?

PROFESSOR RICHARD D. FRIEDMAN: Yeah, that's a serious problem. Any comments? I'll just say, if I may, one way of looking at it is it's one more complexity among many others that defense lawyers have to deal with and you can view it as just a part of what in many instances is the inadequacy of the assigned counsel, particularly in capital

42. K.A.J. Walsh & J.S. Buckelton, *On the Problem of Assessing the Evidential Value of Glass Fragments Embedded in Footwear*, 26 J. FORENSIC SCI. SOC'Y 55 (1986); *see also* S.A. Coulson et al., *Glass on Clothing and Shoes of Members of the General Population and People Suspected of Breaking Crimes*, 41 SCI. & JUST. 39 (2001); J. McQuillan & K. Edgar, *A Survey of the Distribution of Glass on Clothing*, 32 J. FORENSIC SCI. SOC'Y 333 (1992).

43. No. 96-CR-68 (D. Colo. Nov. 10, 1997). Trial transcript available at www.courttv.com/archive/casefiles/Oklahoma/nichtranscripts/1110am.html (last visited 11/29/03).

44. Susan R. Poulter, *Presidential Showcase Program on Expert Witness Law*, EBLAST: THE BULL. OF LAW SCI., & TECH., Oct. 1999 , *at* http://www.abanet.org/scitech/eblast/oct99/2oct99.html#expert (describing a talk by FBI laboratory director Donald Kerr).

cases, and the whole range of problems that they face. But does anybody else want to offer a quick comment on it?

PROFESSOR JONATHAN J. KOEHLER: My quick comment is that I think it's the responsibility of your law schools. It shouldn't be the government's responsibility. I think your law schools should offer some sort of training in scientific thinking and statistical thinking and probabilities. I know that's not what you're in law school to do. Part of the reason you went to law school was so that you didn't have to do that kind of stuff. But I think it should at least play some minimal role in your training, because science is now playing such an important role in the courtroom that it's important to understand scientific theory and the statistical underpinnings of it.

PROFESSOR RICHARD D. FRIEDMAN: I think that's a good way to end. Okay. Thank you very much to the panelists. Thank you to the audience.

(Applause)

MATT MOCK: Thank you very much Professor Friedman and thank you members of Panel I. We're going to break for an hour. We'll be back around 1:10. Panel II will be "The Regulations of Life Sciences."

PANEL II
THE REGULATIONS OF LIFE SCIENCES

INTRODUCTION

MATT MOCK: Alright, welcome back everybody. I would now like to introduce the moderator for our second panel, The Regulations of Life Sciences. Dr. Joel Howell is the Victor Vaughan Professor of the History of Medicine at the University of Michigan, where he also holds appointments in the departments of Internal Medicine, History, and Health Management and Policy. He received his M.D. at the University of Chicago, where he stayed for his internship and residency in internal medicine. At the University of Pennsylvania, he was a Robert Wood Johnson Clinical Scholar, and received his Ph.D. in the History and Sociology of Science. Dr. Howell has been a faculty member at the University of Michigan since 1984. He is Co-Director of the University of Michigan Robert Wood Johnson Clinical Scholars Program and Director of the University of Michigan Program in Society in Medicine. He has written widely on the use of medical technology, examining the social and contextual factors relevant to its clinical application and diffusion,

analyzing why American medicine has become obsessed with the use of medical technology. He has also written and spoken widely on the history of human experimentation, especially the policy implications of that history.

His current research is an attempt to analyze the implication for health policy of factors that have both contributed to and slowed the diffusion of medical technology into clinical practice, using both the sociology of knowledge and a comparative approach. His most recent book is *Technology in the Hospital: Transforming Patient Care in the Early Twentieth Century*, published by Johns Hopkins University Press.[45]

Dr. Howell's research has been recently supported by the Robert Wood Johnson Foundation Investigator Award in health policy research, and by a Burrows Wellcome Fund Award in the History of Medicine. He was recently named to the University of Michigan's Society of Fellows. It is my pleasure to present Dr. Joel Howell.

[Applause]

DR. JOEL D. HOWELL: Thank you very much. We're in for an exciting afternoon. It's a fascinating topic and we've got three wonderful speakers. And before we get to it, let me just say a couple words about how things are going to work here. Each of the speakers will talk for about fifteen minutes, I've been told, and then we will throw the discussion open for questions. I understand the morning session ran over a little bit. This session will end at two-thirty. Hopefully, that will still leave us plenty of time for ample questions.

Our first speaker this afternoon is an old friend, Rebecca Eisenberg, who I've had the privilege of knowing for some time. I once had the experience of listening to her try to argue me out of a position for about two hours on a car ride through a dark Virginia countryside. At the end of the ride I was still sure she was wrong but I couldn't think of a single way to attack her position.

Rebecca's a graduate of Stanford University and the University of California, Berkeley, where she was Articles Editor of The California Law Review. She served as law clerk for Chief Judge Robert Peckham on the U.S. District Court for the Northern District of California and subsequently practiced as a litigator. She teaches courses in patent law, trademark law, and torts, and has taught courses on legal rights and regulation of science and legal issues in the human genome project. In fact, Rebecca, I think that the NIH Director's office probably has a direct line to you at all times, when these issues arise. She just recently came back from the 1999–2000 academic year as a Visiting Professor of Law,

45. JOEL D. HOWELL, TECHNOLOGY IN THE HOSPITAL: TRANSFORMING PATIENT CARE IN THE EARLY TWENTIETH CENTURY (1995).

Science, and Technology at Stanford. She's received grants to support her work from the Ethical, Legal, and Social Implications of the Human Genome Project, for the United States Department of Energy. She's played an active role in public policy debates concerning the role of intellectual property and biomedical research. As a member of the advisory committee to the Director of the National Institutes of Health, the panel on Science, Technology, and the Law of the National Academies, and the board of directors of the Stem Cell, Genomics, and Therapeutics Network in Canada. In short, I can think of no one who is better qualified to address the issues that we'll be starting off with today. I present Professor Eisenberg, the Robert and Barbara Luciano Professor of Law.

PROFESSOR REBECCA S. EISENBERG: Thank you very much. This is an absolutely huge topic and I was told that I could really talk about whatever I wanted. So I decided to focus my remarks on the regulation of research in the life sciences, which is also, of course, a huge topic. Life sciences research is extensively regulated by the government, which provides multiple entry points for addressing the concerns that advances in the life sciences provoke about ethics and health and safety. Advances in life sciences research have been the focus of recurring public policy debates in different government venues over ethical issues and the appropriate form and scope of government responses to the concerns that are raised. This generates lots of public discussion about emerging areas of research that push ethical buttons—especially, in recent years, in matters that touch upon the politics of abortion, such as embryo research and the derivation of embryonic stem cells. Sometimes we've seen government intervention in research, although rarely do we see outright prohibitions against research in any particular category. More typically, government regulation of life sciences research has the effect of bureaucratizing certain policy choices and values choices, and handing them over to the scientific community for administration. We see this pattern over and over again, in different particularized settings.

Life sciences research evokes strong feelings among the general public, both good and bad. On the positive side there is hope for relief from disease and afflictions, for new scientific breakthroughs that will prolong and improve our own lives and the lives of our children. On the negative side are fears about bringing upon ourselves unanticipated consequences, anxiety about human meddling in the natural order of things, concerns about loss of reverence and respect for human life. Or simply fear that we will act too quickly upon too little knowledge. Government

regulation often provides a stage for expressing these hopes and fears, and a bureaucratic apparatus for addressing and managing them.

One circumstance, more than any other, that inevitably involves government decision makers in oversight and regulation of life sciences research is the dependence of much of life sciences research upon government research funding. In recent years, private funding has overtaken public funding for biomedical research in monetary terms. But public funding remains extremely important, especially for elite scientists doing fundamental research in academic laboratories. This public funding comes with numerous regulatory strings attached. Universities and other recipients of government research funding are accountable for how they use these funds. Government-funded biomedical research is subject to regulation on a broad range of topics, including protection of human subjects, the use and containment of hazardous substances in the laboratory, the protection and dissemination of research results, and the introduction of new products to market. Some of these regulations have arisen in response to particular notorious episodes in biomedical research that initially provoked widespread public debate, like the Tuskegee Syphilis Study that led to further regulation of informed consent in human subjects research, the initial experiments with recombinant DNA technology that led to the formation of the Recombinant DNA Advisory Committee, or birth defects in children born to mothers who took thalidomide that expanded the scope of FDA regulation. But after the shouting is over, in each of these areas, what has emerged is bureaucratic institutions that are substantially within the control of the scientific community itself. This is true of institutional review boards, to oversee protection of human subjects and informed consent in research within hospitals. It is true of the Recombinant DNA Advisory Committee to review research proposals within NIH. It is true of the delegation to FDA of authority to keep new drug products off of the market until they have been proven safe and effective. Some of these institutions are deliberately set up to include lay participation, to provide a broader range of voices on ethical issues, and to involve some people who are not co-opted by their own professional stake in seeing the research move forward. But members of these review boards sit alongside scientific experts, who typically outnumber them and whose expertise, inevitably, skews the discussion towards the concerns of the scientists. And so, although the mandate of an institutional review board or the Recombinant DNA Advisory Committee may include attention to ethical issues, the mechanism itself, over time, starts to look more and more like another layer of professional peer review.

Non-experts have a larger voice in regulation of science at the legislative level. They have a larger voice before Congress. Congress makes broad choices about legislative appropriations for publicly-funded research and exercises some control over the terms of grants, although the more fine-grained choices about priorities and how to allocate funds among competing proposals are generally left to funding agencies, like NIH, that are substantially within the control of the scientific community. On the whole, public funding of research has been a very welcome form of regulation within the scientific community, despite the strings that are attached to it. Biomedical research, in particular, has benefited greatly from the high hopes of the public for future medical breakthroughs expressed in the political process through lobbying by disease advocacy groups for more funding of research on particular problems. This may not be a perfect system for deciding how to spend federal research dollars, but it is a system that has generated substantial increases year after year, for many years now. Sometimes the research community bristles at a particular legislative allocation for something that they think is a political distortion of scientific priorities, such as the formation of a National Institute of Alternative Medicine, to cite a recent example. Or sometimes they grouse about overallocation of funds to the study of particular diseases relative to spending on fundamental research that is not disease specific.

Perhaps in their dreams, researchers would prefer to enjoy the same growing levels of public funding without any legislative guidance as to how they should spend the money. But the two go hand in hand. The extraordinary legislative largesse that biomedical research has enjoyed, relative to other worthy fields of scientific inquiry, like physics and math, is a direct result of the political effectiveness of the disease group advocates, who have pleaded successfully for more funding for their particular causes. And the research community doesn't complain too much because for the most part, they have been quite successful at exercising control over how funding agencies spend their appropriations through mechanisms that are within the professional control of scientists, such as peer review of grants. To return to the example I mentioned earlier, when Congress decided to create and fund a National Institute for Alternative Medicine, within the NIH, the inevitable upshot has been that these funds are used for peer reviewed empirical tests of remedies like Echinacea and St. John's Wort, and glucosamine-chondroitin. Peer review goes far to ensure that public research funds are ultimately deployed in accordance with the priorities and methodological commitments of the scientific community, within broad constraints set by Congress.

Sometimes, however, legislative control does not stop at writing out checks with broad directives about how to spend the money. Sometimes Congress, or even the Executive Branch, sets limits on how the money can be spent that are a little harder to work around. Sometimes they seek to prohibit the use of federal funds for particular types of research, like Congress's ban on human embryo research a number of years ago, or President Bush's more recent ban on the use of human embryonic stem cells derived after August 2001, in federally-funded research. This sort of move—an outright prohibition on what you can do rather than an affirmative provision of funds for a particular purpose—is far more frustrating for scientists, particularly when it cuts off government-funded academic scientists from use of an emerging technological platform like human embryonic stem cells that is likely to have implications for a broad range of problems. And it has been much harder for the community to figure out ways to work around. This type of prohibition is actually pretty rare, and so far has arisen primarily in areas touching upon abortion or the values implicated by abortion and the status of human embryos.

But the scientific community is bristling at it and sometimes questions not only its wisdom, but also its legitimacy. Scientists argue that a restrictive approach to federal funding of embryo research, for example, has set back fertility research considerably, by effectively excluding fundamental research on fertility of the sort that the government might pay for, but the private sector generally will not. Some research is done, of course, in private fertility clinics, but it is not the sort of rigorous, peer-reviewed, fundamental research that is most respected in the scientific community and that has been so productive of advances in other fields. This is a fair criticism of the choice to withhold federal funding for research in a particular area: it chokes off university research, with the effect of slowing the kind of applied research that private investors are willing to pay for. In other words, withholding federal funding not only limits the total amount spent on research in a particular field, such as fertility research, but also limits the character of research that is likely to be done, by limiting the involvement of academic scientists who rely on public funding and relegating these fields to the private sector. The private sector is very effective at carrying out certain kinds of research projects that are within site of profitable endpoints, like drug development. But it is less effective at funding and performing "upstream" research of the sort that has flourished in academic institutions with public funds. Even though the private sector has been extraordinarily forward-looking in biomedical research, funding upstream research that

is far removed from product development, there is still a significant loss to upstream research from withholding federal funds in an area.

The historical importance of government-funded academic research to biomedical advances is a powerful argument for maintaining federal funding in areas of biomedical research that we want to promote. This argument often wins, but it doesn't always win. The academic biomedical research community is very well represented in Washington. It has the backing of organized disease group constituencies, and together they lobby hard for federal funding of things like stem cell research that promise to advance fundamental knowledge of human health and disease, and they are often successful. They win so often that it seems illegitimate to them when they lose.

Indignant scientists are arguing that it is irrational to withhold federal funding from ethically controversial areas of research, such as stem cell research, that Congress has not chosen to prohibit entirely. If stem cell research is ethically repugnant, why not prohibit it entirely? If it is not so repugnant as to justify an across-the-board prohibition, then why not fund academic scientists to perform the research in the public sector? They note that the paradoxical consequence of withholding federal funding from research that is not prohibited entirely, such as embryonic stem cell research, is that controversial research still goes on in private labs, behind closed doors, under conditions of trade secrecy. It is pursued for profit, outside of public oversight, rather than in the public and academic sector, where the ethical issues that it raises could get more fully vetted and explored by researchers and institutions that are publicly accountable and motivated to advance knowledge rather than to make a profit.

A wiser government might well be investing more public research dollars in embryonic stem cell research right now. However, it is not irrational or illegitimate or inconsistent to withhold federal research dollars from an ethically controversial field just because the federal government has not taken the stronger step of prohibiting the research entirely. We need to make collective political decisions about whether and how far to regulate controversial fields of scientific research, and we don't always agree about the underlying ethical constraints or the force of competing ethical imperatives. At one end of the spectrum, many of us might agree that certain areas of research are completely ethically unacceptable. We might choose to prohibit entirely, for example, research that poses untoward risks to human subjects or that uses human subjects without their consent. But prohibiting research entirely is a very heavy-handed step that we do not want to take unless there is widespread consensus that there is something really wrong with allowing it to proceed. We also value free inquiry and we particularly value progress in biomedical

research. We therefore want our government to think long and hard before issuing an outright prohibition against research that could prove fruitful, at least in advancing human understanding and perhaps also in advancing human health.

At the other end of the spectrum is research that seems so good and so valuable to so many of us that we're actually willing to tax ourselves so that we can subsidize it in the public sector. Much, but not all, biomedical research falls under this heading. There is nothing that we value more than our lives and our health, and if publicly-funded research offers real promise of prolonging our lives and improving our health, we want to encourage it. We're even willing to pay for it, even in times of fiscal belt tightening.

But it stands to reason that some kinds of research are going to fall in the middle of this spectrum. They are not so unambiguously unethical as to call for the extraordinary move of an outright prohibition against research by anybody (or perhaps those who find the research unethical to enact a prohibition), do not command enough of a political consensus, but still ethically controversial enough that we cannot reach political agreement to subsidize the research. For the moment, that seems to be where we are with human embryonic stem cell research in the U.S.: we neither forbid it entirely nor subsidize it without restrictions. And the result is to drive much of this research to private funding sources.

I wish that the political forces in favor of the research were more persuasive to the government. But I don't think the current stalemate is inherently irrational or improper. It is a pragmatic compromise. But if the terms of a pragmatic political compromise are to have democratic legitimacy, then it's important to have the competing arguments fully vetted in public, in the political process. And for that reason, I find it a little troubling that the current compromise position on the use of human embryonic stem cells in federally funded research was not worked out in Congress, but rather imposed by executive fiat, in the form of President Bush's decision that it is okay to use preexisting embryonic stem cell lines, but not to create new ones. That's not a call that the President ought to be making. It belongs to Congress, as a more broadly representative body that is more accessible to lobbying on all sides of the issue and can conduct public hearings that give it a full airing. So when we disagree sharply about competing ethical imperatives, I think the issue calls for broad public discussion, not a resolution that's imposed by the Chief Executive.

I may have gone over my allotted time, so I'm going to stop here.

DR. JOEL D. HOWELL: Thank you very much. [Applause]

We will now move on to hear from Rosemary Quigley. Rosemary Quigley is Assistant Professor of Medical Ethics and Health Policy at Baylor College of Medicine in Houston. She serves on the National Institute of Health Directors Council of Public Representatives, sitting on the Council's Working Group for the Protection of Human Subjects in Research. She served on the Advisory Committee to the Director Working Group on Oversight of Clinical Gene Transfer Research, so she's had a quite a bit of experience in this area.

At Baylor she teaches in the first-year medical student and residency programs, as well as in the Ph.D. program, and Philosophy. She serves on the Ethics Committee and Case Council Service at the Methodist Hospital, working specially on implementation of medical decision-making policy. Her research interests include the protection of human research subjects and adverse event reporting in clinical research, the impact of genetic information, and the prospect of gene transfer research in patient care, as well as regulatory and constitutional issues involving intellectual property, professional standards and disability.

Professor Quigley received her A.B. in English Literature from Harvard College and her Law and Public Health Degrees right here at the University of Michigan, where she was also the Book Review Editor of the Michigan Law Review. She clerked for Judge Carmen Lopez of the U.S. Court of Appeals for the First Circuit. Professor Rosemary Quigley, Assistant Professor of Medical Ethics and Health Policy at Baylor.

PROFESSOR ROSEMARY QUIGLEY: Thank you very much.

What I'm going to be focusing on today is adverse event information and how intellectual property issues come into play, in terms of the safety of clinical research. It seems that in these debates about who owns clinical trial data and human body parts that the public interest in medical research has been considered, the industry's interest in this research has been considered, but rarely have the interests of the research participants been considered in these debates about intellectual property. And I would assert that they might actually have interest in this as well, given that they're the ones who are giving their bodies, often experiencing the adverse events, and they might want their fellow research participants or potential research participants to have the information about their adverse events and about other goings on in clinical trials before they make decisions about enrolling in these trials.

From the literature standpoint, there's been a growing discussion about the commodification of biological materials, specifically human tissues and their cells, genetic sequences, fragments of genetic sequences, as well as the potential for sale of organs. This has become a

hot topic ever since the *Moore* Case when we took cells from someone without telling them we were going to use them for commercial development. In that case, the patient did not win for various reasons, but since then we've wondered—do people who contribute to the advance of medical research have any stake in what they contribute?

Private interests have increasingly been assigned ownership of body parts or biological material once it has been removed from the body. Once that happens, the participants rarely have any claim to their data or their fluids anymore. Even the case law has essentially supported the commercial stake in that kind of information. It hasn't really advocated for even the public interest, let alone the research participant interest. And there are people who think, especially in medical research where there is a history of exploitation of research participants, that this has the potential for subordination of people who are giving of their bodies, who might not have full information about an investigation of a new therapeutic research substance. And this has been discussed actually very thoroughly in a book by Peggy Radin, *Contested Commodities*.[46] She talks more about body parts than she does about research, but I think a lot of her concerns are about the potential that there will be an underclass of people who need the benefits of medical research and thus sign up for these trials, which is applicable to the research context.

Professor Eisenberg has talked a good bit about the new emphasis on oversight of some areas of clinical research. One of these areas is financial conflicts of interest. This primarily concerns industry's influence on setting research priorities. It's not clear whether participants in research want to know about how much control industry has over research, how much their investigators, often their own personal physicians, are also influenced by what industry has them do in the conduct of clinical trials. But there is a kind of emerging consensus that we need better regulation of this.

In terms of informed consent, there is a debate, particularly about adverse events and whether these participants who are in research should get real-time information about the experience of adverse events in clinical trials, given that they might need that information to appreciate whether they're having an adverse event or whether they will suffer injury in the trial. Some people think that this action might skew the performance of the trial, if you give them too much information about the risks or the history of adverse events in the trial, that more people will notice adverse events or report adverse events. And that that this might ultimately have the effect of undermining research or even that compliance with more research regulation will force industry to pull out

46. MARGARET JANE RADIN, CONTESTED COMMODITIES (1996).

of pursuing certain research products. There have been demands for public and participant disclosure for adverse event information, but the industry has actually made a claim that this sort of information is proprietary and that is mainly what I'm going to focus on.

Just to give you an idea of what a serious adverse event is, this is the definition from the National Institutes of Health: "[A]ny event occurring at any dose that results in any of the following outcomes: death, a life-threatening event, in-patient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect."[47] I'm focusing on serious adverse events because that's what some of the proposed regulation focuses on. There are lower grade adverse events that happen in research and it's possible that some of this movement toward public disclosure of this information could ultimately cover a broader range of adverse events.

Issues with adverse events are very complex. Often investigators don't know how to report them exactly. They're supposed to say whether they're related or unrelated to the research product, whether it was an anticipated or an unanticipated adverse event. And also the occurrence of adverse events, many times, is a result of the underlying disease that the research participants have. It may not be related to the therapeutic agent or potentially therapeutic agent that's being tested. So it's very hard to parse out what events are actually relevant to the research protocol.

Dr. Reilly made a reference to this case this morning, and I'm going to talk about it mainly because it raised the issue of gaps in serious adverse event reporting. It involves Jesse Gelsinger in a gene therapy trial at University of Pennsylvania. Many of you have probably heard about this case. Gene therapy, in general, has not gone especially well. Even the success that it has seen, particularly in the trials of SCID in infants, has recently had a setback. Some children with that trial were cured of the Severe Combined Immune Deficiency Syndrome, but at the same time, two or three years down the line two of the people who got the gene therapy have now developed a form of cancer, a form of leukemia actually. So those trials are on clinical hold now. And essentially that was the only shining light in the history of gene therapy research and that now seems to be slipping away a little bit as well. That said, this trial was going forward and it was a trial for OTC deficiency. Jessie Gelsinger was eighteen; he was receiving an adenoviral vector product by hepatic artery infusion. There were many problems with this trial, as it turned out in the end. The consent was a little bit misleading. It didn't disclose the serious history of catastrophic events in the animal studies and

47. Department of Health and Human Services, 66 Fed. Reg. 57970, 57975 (Nov. 19, 2001).

information about adverse events earlier in the trial. The trial had, at one point, been put on clinical hold by the FDA, that means the Food and Drug Administration stopped the trial because of safety concerns. And then it got started up again. And there is some evidence that Gelsinger and his family were misled about early evidence of the efficacy of this gene transfer protocol. There were adverse event reporting violations in this case. Earlier in the trial, there had been significant toxicities, resulting in elevated liver enzymes and inflammation, hospitalization of some of the research trial participants. In reports to the Food and Drug Administration, the investigators stopped flagging these serious adverse events, these toxicities. They had been doing that and they stopped doing that, apparently because they didn't want to be put on clinical hold again. And then Jesse was the eighteenth person enrolled in this trial and he died of respiratory distress and massive organ failure. They're still investigating why that was, but you know even if he did die from some previously unknown condition that this gene transfer product caused because of his own susceptibility, there still were major ethical gaps in the administration of the trial.

I'm going to talk mainly about gene therapy. What's the deal with these oversight mechanisms? Professor Eisenberg talked about some of them. The NIH, National Institutes of Health, oversees federally funded research. Their Recombinant DNA Advisory Committee, the RAC, reviews all these research protocols. They review novel gene therapy protocols publicly. A lot of industry people who do the gene transfer research actually do submit their protocols to the RAC for public review because it's part of what they think will endear them, I think, to the overall funding community. And it does get thorough scientific review. So for federally funded research in this area, public disclosure of research information is routine. There are some studies, though, that do not receive federal funding. All these trials are reviewed by the FDA, but the FDA has, to this point, viewed that kind of information as proprietary and thus not publicly disclosable. And again the FDA is the entity, generally, that has the power to impose the clinical hold and stop a trial as it proceeds.

At the time of the Gelsinger case, up to seventy percent of adverse event reports were not being made to the National Institutes of Health per the requirements. As a result, a working group was established to reevaluate what exactly was going on with adverse event reporting oversight in these trials. I was actually on this working group. We did revise. Trials had been able to go forward without final review from the RAC. At one point, we kind of rearranged so that they would have to get final sign-off from the NIH RAC in order for the trials to go ahead. Also, the

FDA and NIH had, until now, different definitions for what was a serious adverse event and for what was a related adverse event. The definitions were slightly different, which of course drove scientists nuts in terms of having to report those adverse events. And the working group, in general, emphasized that there should be public discussion of adverse events, that this sort of information should not be termed trade secrets or proprietary, and in fact that the data, especially in terms of gene therapy, should be disseminated in an analyzed, interpretive form.

And what kind of data were they talking about? Well, complete descriptions of the events; the actual incident that caused the adverse event; other clinical observations relevant to the protocol; the gene delivery method used; the vector type; the dosing schedule for the trial; how it's being administered: is it being administered through an aerosol or through an artery; and then the names of where the trial's being done and the investigators.

So the NIH went ahead with this, which they had the ability to do because some cohort of the protocols that they review are publicly funded and so the public maybe should have access to that data. The FDA had this idea that all that information was proprietary for the industry protocols that weren't subject to the public review. The FDA changed its mind and decided at least for gene therapy and for xenotransplantation that, in fact those protocols were under such scrutiny in the public that there should be public disclosure of adverse events and of those complete protocols. In terms of the xenotransplantation—I was hoping that I would be the first person today to say porcine retroviruses, but Dr. Reilly beat me this morning. There have been big setbacks in xenotransplantation research as well. But it's worth noting that xenotransplantation also probably covers a cohort of stem cell research because some of those cells in the stem cell research are cultured in animal products. And so this research might be constituted as xenotransplantation regulation as well. So the FDA said, we're going to write a rule that we're going to publicly disclose the protocol, the amendments to the protocol, annual reports about the protocol and all the serious adverse events. Then in terms of the adverse events, they essentially wanted the industry to begin to say these are our consent forms, these are the kinds of setbacks we've had. Industry got furious about this. They said that if we had this kind of information disclosed, where the clinical studies were, what the biological products are that are being used, what the regulatory status of the research is, that other competitive biotech companies would be able to streamline their protocols, size up the competition as to where they were compared to where a competitor was, and essentially skip ahead and avoid the costs of some of the initial investigation of research materials,

and also make decisions about abandoning and or pursuing a research agent based on others' costly finance. The FDA justifies this rule, essentially by saying that these are serious ethical and scientific issues. The decision-making process on these trials should be transparent. These types of information should not be considered confidential and proprietary.

This is a big change from the FDA's position. In this case, it only applies to gene transfer and xenotransplant research. At the same time they might extend it to other types of protocols. There's no reason why it should be limited to those types of research necessarily. There are other types of research that are under just as much of a public eye, that are just as risky, including chemotherapy research and vaccine research, so maybe they're just starting here to make the process more transparent. But ultimately, I believe that the rule should probably be applied to a broad range of research trials that the FDA has control of for reviewing.

Industry objects to these rules also on very precise legal grounds. Essentially they think this action is "arbitrary and capricious" under the federal law, under the Freedom of Information Act, and as well a violation of the Federal Trade Secrets Act. Essentially, if a public official discloses information that they get in the process of regulation that could be considered confidential, it would be a potential violation of the Federal Trade Secrets Act. They also say the FDA lacks authority under the Food, Drug and Cosmetics Act to regulate in this area. The FDA thinks, broadly defined, we are supposed to act in the public interest and in the safe development of drugs and so public disclosure of this sort of information comes within those auspices. And then industry's big power argument is that the disclosures would violate the Takings Clause of the Constitution.

So my question: is this a trade secret? Are adverse event reports trade secrets or confidential information? The Freedom of Information Act argument is not the strongest argument. The Freedom of Information Act (FOIA) might not even apply because it addresses requests from the public for disclosure by an agency and here, the agency essentially wants to disclose. But that body of case laws is actually pretty helpful in finding out where we might go in terms of deciding what the status of adverse event information is. Is an adverse event a trade secret? Actually, Public Citizen has filed most of the suits in this line of cases, trying to get clinical trial data publicly disclosed. The definition that the D.C. Circuit came to, in this case, was "a secret commercially valuable plan, formula, process, or device that is used for making, preparing, compounding, or processing of trade commodities."[48] Nobody thinks that an

48. Pub. Citizen Health Research Group v. FDA, 704 F.2d 1280, 1288 (D.C. Cir. 1983).

adverse event or an adverse event report is something that's involved in the processing or in the development of a product for marketing. It's a different species of information altogether. So under the current case law, an adverse event report is probably not a trade secret. Under FOIA, there is a question, and this is number two of the definition, if it's a commercial product or commercial information, which it probably is, it's probably information the industry needs to progress through the research approval process. But the courts need to decide, under the D.C. Circuit test, if disclosure causes substantial harm to the competitive position of the person from whom the information is obtained. In most cases, industry has made kind of conclusory assertions about whether there is substantial harm. There's not a lot of proof out there about whether public disclosure would cause a competitive harm, and so there are times when the courts have said they don't find this argument compelling. We actually think that the clinical trial data should be publicly disclosed. At the same time, there are times when they have seen evidence of one company trying to get a jump on another company, based on the public release of data. But that's sort of where the test has been.

The most recent case in this line of cases is *Public Citizen v. FDA* from 1999.[49] And I just want to raise this because in some of the case law, there has been a balance described between the public interest in having this information disclosed and the private interest in protecting industry's competitive edge. In that case, they actually decided that some of the information was not publicly disclosable.[50] But at the same time, the majority of that court said they don't even think that the public has an interest in having this information disclosed, which was against existing precedent.[51] Judge Garland of the D.C. Circuit concurred in this result, but he also said that denying a necessary balance means that even if disclosure were the only way to prevent the loss of human life, that would count for nothing as against a showing by a company that disclosure would cause substantial harm to its competitive position.[52] And in his opinion, he sort of revived the idea that there is a substantial public stake in this kind of information that ensures the safety of clinical trials, as they go forward.[53] So I think this is an unsettled issue and that recent decisions of the D.C. Circuit have reinvigorated the question.

I'm just going to tell you what the current status is, as I close. The NIH guidelines were amended to promote the reporting of adverse event information in gene transfer trials. The FDA rule that I referred to was

49. Pub. Citizen Health Research Group v. FDA, 185 F.3d 898 (D.C. Cir. 1999).
50. *Id.* at 907.
51. *Id.* at 903–05.
52. *Id.* at 907.
53. *Id.* at 907–08.

open for comment—it was closed for comment just over two years ago—and the FDA has taken no final action on the rule. Notably, this rule for openness and transparency was proposed during the Clinton Administration. It was inherited by the Bush Administration. The FDA did not have a director for a while, so it is in limbo and I would not be surprised if it doesn't come out of limbo for some time. But I think there are outstanding issues on serious adverse event data, and whether patients might benefit from having this kind of information when they're enrolling in trials. We don't know if they'll be deterred from enrolling in trials, based on receipt of this information. But I think there is potential for future litigation in this area, certainly if these rules go forward at some point industry will sue.

I encourage all of you to not necessarily go to work for the law firms that are going to represent the industry, although they might have a good argument in some cases. But you might consider representing the participants in these research trials, as they might also have an interest in their own human experience. And I think the more the investigators in industry detach the experience of the adverse event from the actual participants, who give of themselves to advance research, I think we're losing something in terms of what kind of benefit we're trying to derive from clinical research for society broadly. Thank you very much.

[Applause]

DR. JOEL D. HOWELL: Thank you very much. That was a fascinating presentation. We're going to move on to a third presenter, for a third perspective from a third institution. Reverend Clayton Thomason is Assistant Professor in the College of Human Medicine at Michigan State. His position in Spirituality and Ethics in Medicine is a very interesting appointment. It's a joint appointment between the Department of Family Practice and the Center for Ethics and Humanities in the Life Sciences. Reverend Thomason's responsibilities include directing courses in spirituality of medicine, directing a mentoring program of professional development for medical students, as well as teaching bioethics. He's also an Adjunct Professor in the Michigan State University Detroit College of Law, where he teaches Bioethics and the Law. He serves on the Human Subjects Committee, the IRB, and the Michigan Department of Community Care in the Michigan Public Health Institute, and was appointed by our then Governor, John Engler, in 2000 to serve as the bioethicist on the Michigan Commission for the End of Life Care, and served as Chair of that commission which released its report to the governor and the legislature in 2001 and eventually resulted in legislation being enacted in January of 2002.

Professor Thomason has studied bioethics at the Kennedy Institute for Ethics at Georgetown University and the Hastings Center in New York. He's published and taught in the fields of biochemistry, bioethics, law and spirituality, including works on issues of law and aging, spiritualness and ethics of AIDS care and the use of advance directives in health care. His current work focuses on spiritual assessment in medicine, the role of virtue in professional development, public policy in end of life care, and the role of spiritual values in bioethical decisions. Reverend Clayton Thomason.

PROFESSOR CLAYTON L. THOMASON: Thanks very much. I want to thank you and the student organizers of this conference for doing important work here and say how privileged I am to be part of this very august panel. Going last allows me the opportunity of knowing where the other panelists have been and being able to incorporate by reference some of the details of the material that both Professors Quigley and Eisenberg have already discussed.

What I would like to do this afternoon, as briefly as I can (and I will endeavor mightily to stick to my fifteen minutes and give us time for some discussion), is to step back a little from the sort of specific examples that we've been looking at today and think analytically about why this is so hard. Why in these public policy discussions is it so difficult to adequately capture and address the regulatory environment of biotechnology, particularly with regard to the human genome? I want to suggest three conceptual models—three ethical categories of ways in which law responds to these challenges in the human genome. They are ownership, stewardship, and privacy. These are arguments by analogy, we'll notice, in which we're frequently trying to figure out how old law that used to work just great for other things that we know about well can apply to something new, in the form of a new technology.

I want to think first about a model that we might think of as the model of *ownership*: can life be patented? This is a central question that Professor Eisenberg has written very importantly and helpfully about, from my perspective. But it is nonetheless an ownership model, a model that applies to property. So we have to ask *whether* and *how well* it applies to genetic material, to the moral and legal status of DNA and RNA, to animal models, to human models. Without much review here, you probably already know the general outlines of the purpose of patents. The United States Patent Office issues them in order to confer a *right to exclude* others from competing with you in the invention, distribution, or production of your widget—of a thing, a product. And the goal is to encourage the time and money invested in research and development. The three criteria of novelty, non-obviousness, and human

invention are particularly significant with regard to human genomic material because of how difficult it is to get these criteria to fit exactly. We know pretty well how to apply these criteria to manufactured products—the kind of products that you can hold in your hand and look at and sell in boxes at the hardware store. But it requires some argument by analogy to make them fit genetic material. So for example, in the realm of genetic patenting, novelty is most clearly seen (from the viewpoint of those who rely on genetic patents) when considering something like transgenic organisms, which we've heard about already today.

In transgenic modification, you may know, a gene or a segment of genetic material is transferred between species. So a gene typically found in a species of bacteria that codes for the production of a toxin—a kind of pesticide, for example—could be spliced into the DNA of a corn crop. You can get corn plants that have a built-in pesticide. There's no naturally occurring species of corn that has that ability, so that looks new. That's a new product, that's novel. And the same can be said for animal models as well. The distinction is harder to make with specific genes. If the gene is simply sequenced and then isolated from the natural environment, the question becomes whether it represents something new, or is an isolated form of the gene simply a found object? Is it an *invention* or a *discovery*? There is a long history of allowing patents to be granted for products of nature that have been isolated or purified. Since the purified state is not seen in nature, it tends to be conceived of as a new entity.

The *non-obviousness* criterion is again a challenge in that it requires that we have new advances, not just technical tinkering or modifications of existing products. Thus, some would argue that the insertion of a gene into an organism to improve the overall health or the productivity of the whole organism, for example, is now obvious to specialists in the field. Since the technology has already been developed that allows it to happen in the first place, by this view, only the first event of gene splicing would become patentable and it's up to the Patent and Trademark Office to determine the level at which that distinction is going to be made.

The most interesting and difficult challenge has to do with whether something is a *discovery* or an *invention*. Products of nature themselves can't be invented by humans. They can only be discovered. So the heart of the issue revolves around this distinction. You wouldn't expect somebody to be granted a patent on crude oil, for example. Or on minerals, because they preexist—they're products of nature that are found. But an individual who creates a product *from* something—a plastic developed from crude oil, for example—deserves a patent for being an invention. It

is important to distinguish this from the novelty criterion. Mother Nature, if you will, can be thought of as the original inventor by that criterion, while the human invention criterion requires a human intervention that is given credit for the invention. For example, in the case of the Harvard Onco-Mouse, the genetic manipulation that was performed on the whole mouse was sufficient for the Patent and Trademark Office to classify an entire animal—and its offspring—as an invention for the first time. This is a frame shift. This requires a new way of applying an old and well-established form of law to a new technology. Or in another example, Dr. Anand Chakrabarty's petroleum-eating bacterium that he had genetically modified to be sprinkled out on oil slicks and gobble them up, metabolize them, was finally recognized as an invention after some eight years of struggling his way through the court system.

If we think, then, about some of the effects of this ownership model of genetic patents on three categories of work, the first would be how does issuing patents on genetic material affect *research*? Well we've already heard this afternoon that scientific and medical research requires this kind of free flow of information. There is this expectation that there is a kind of collegiality and openness and objectivity among researchers. The concern about trade secrecy is that openness and collegiality becomes perceived as a risk to the proprietary trade rights of patent holders.

Secondly, there is concern among clinicians that in clinical medicine, patents on naturally occurring mutations, for example, might prevent physicians from having ready access to the therapeutic information they need in order to treat a disease that's caused by that naturally occurring organism. Or again, that patents on fragments of genes might impede the progress of research. Or again, those patents may actually increase the research and development costs of important therapeutic modalities that would otherwise be marketed.

Finally, Professor Quigley described for us some of the commodification arguments and concerns. Whether or not patenting genetic material, patenting human gene sequences, represents somehow a *commodification* of life. Does it take into account some kind of argument about the intrinsic worth or value of human life, or does it assign a merely instrumental or a merely commercial value to life? And again you can see that the models hold just fine for widgets. We feel relatively sure about commodifying crop plants, for example. We feel relatively comfortable about owning livestock and animals and animal products. We start to get a little bit fuzzier about what it means to own their genetic material. And then as we move into the realm of human genetic

materials, we come up against some limitations about our perceptions of what property is and what is appropriate to own or not to own.

So I want to suggest that that takes us to a second category of ways in which we can think about genetic materials. And that's a *stewardship* model. Let me just think briefly with you about this ethical category that I want to impose on a number of ways the law responds to these technologies, by thinking about *duties* and *obligations*. What kinds of duties and obligations come with these new technologies? With new knowledge? And duties and obligations to whom? Again, I want to use this ethical category of stewardship to encompass things like the obligations and duties that are owed to others through tort law, for example, that lead to actions in wrongful death or negligence or medical malpractice.

We've already heard now twice today about Jessie Gelsinger's case, which is a terrific example of the application of that kind of legal cause of action to a novel situation in which someone dies in the course of genetic research. And yet the law works pretty well to take account of the kinds of special relationships that had been developed in the Gelsinger case. Between, for example, doctor and patient, or between researcher and subject. We might also think about the ways in which special relationships engender special obligations. Those might include parent and child relationships and the whole realm—that we haven't quite touched on yet—of reproductive technologies and the ways in which those challenge the parent/child relationships that we're used to using to structure family and personal life.

Then we might think of statutory or regulatory obligations that have been imposed on, for example, human cloning and stem cell research. We have highlighted some of those for you today, such as the regulation of research involving human subjects through the "Common Rule" that Professor Quigley has guided us through a little bit today.[54]

A third kind of stewardship obligation to others has to do not simply with obligations to individual, identifiable others, but obligations we recognize to whole populations and to generations yet to come, to putative persons who aren't yet here. And so we have a whole scheme of environmental regulatory mechanisms that seeks to think about those kinds of stewardship obligations we might be said to have to the human genome itself or to the biosphere at large. This is another way in which we have to try to expand our thinking about the kinds of obligations that count when we're regulating genetic technologies.

I don't think I need to talk much more than Professor Quigley already has about protection of human subjects through federal regulation. It might be worth just noting for a moment, though, the status of human

54. *See* 45 C.F.R. § 46 (2002).

cloning bans. Currently, both reproductive and therapeutic cloning have been banned by statute in both in Michigan and Iowa. There is a reproductive cloning ban currently in California, Louisiana, Virginia, and Rhode Island. There is a federal bill that passed the House once and stalled in the Senate in 2001 and just passed the House again last Thursday, that would impose criminal fines and imprisonment as well as civil penalties for attempts at human cloning, as well as the kinds of research banned by executive order that Professor Eisenberg reminded us of this afternoon. This is all an example of the kind of vigorous debate addressing a range of issues that I would categorize as stewardship arguments.

Finally, and very quickly, I will just mention the third category having to do with privacy. Privacy concerns are not so much other-referential but self-referential. If patents have to do with exclusionary rights of ownership against others, and stewardship has to do with our obligations to others, privacy has to do with protecting one's own autonomy. In moral terms, privacy concerns the protection of my autonomy interest in myself, in my own body, extending to my own information. So for our purposes, it concerns who owns genetic information and who has rights to know information resulting from genetic tests. How about the police, the military, employers, insurance companies? It gets scarier and scarier the farther along that kind of list you get, right? How about law schools or universities? Do they have a right to know about the results of your genetic tests? Or should pharmaceutical companies own your health or genetic information? How about the possibility of economic benefit to either you or your family? I must quickly suggest that this is another category that we have to take into consideration, whether or not you would allow your DNA be used for research purposes.

Then how shall we protect genetic privacy? What would happen if you lost control of how your DNA is used? We have some existing kinds of laws that attempt to accomplish this, including potentially, at least, some provisions of the Americans with Disabilities Act that might offer some protections against genetic discrimination in the workplace, for example (though they haven't been tested very well in the courts). HIPAA, of course, the Health Information Portability and Accountability Act, is going into final effect next month and it will be interesting to see exactly how that plays out. There's the ELSI (Ethical, Legal, and Social Implications) program within the Human Genome Project at NIH that's addressed this at the federal level. Thirty-seven states, including Michigan, have state laws against genetic discrimination in health insurance. Twenty-four have state laws about genetic discrimination in employment, including Michigan.

In closing, I might suggest opening the discussion by considering some questions about what kind of protection we should afford genetic information, who should own it, who should have access to it, and how it should be used. How will we balance the public and private interests in genetic privacy, stewardship, and ownership? Thank you very much.

[Applause]

DR. JOEL D. HOWELL: Okay, the floor is open for questions. I'm going to take executive privilege here and say we'll extend this session by a few minutes, since we did get started a little bit late, but not by too long because we want to give adequate time to the session to follow. Would anybody like to take a stab at answering one of these questions or asking another question of your choosing?

AUDIENCE MEMBER: Hi. I work for a biotech spinout, called HandiLab, and have to work with the Federal Government on many levels, with NIH, SPIR grants, FDA, the Center for Medicare & Medicaid Services (CMS). And I'd like to hear from the panel a little bit more on some of your thoughts about the FDA—how it has new leadership and its role. My question is: do you think the FDA and the CMS have overlapping and in some ways duplicative mandates when trying to decide safety and efficacy?

PROFESSOR REBECCA S. EISENBERG: I'm not sure exactly what kind of a product your company produces. I think there are interesting overlaps in the roles of FDA and other agencies. And I think that we traditionally understand the role of FDA as being about protecting the patients, protecting the health and safety of patients. I think the role of FDA intertwines with NIH and with the patent office, for that matter, in more complex ways than that, surrounding generating information, motivating firms to invest in certain forms of R&D that generate socially valuable information. So yes, of course, these are not distinct. We think of the core mission of FDA as about health and safety, the core mission of NIH as about promoting investments in research and development. But these are overlapping missions and it's not surprising to see that there are some overlap in the kinds of oversight that these two agencies engage in. Maybe Rosemary can respond to your question. . . .

PROFESSOR ROSEMARY QUIGLEY: Well I was actually going to add that I think the FDA and people generally are concerned about research protection. The FDA hasn't had enough of a mandate to review the ethical content of research. I think to the extent that there is overlap, there are some other entities within the government that are starting to assume responsibility for that particular oversight, the Office of Human Research Protections in the Secretary of HHS's office is probably the best example. But whether it's the FDA or whether it's the OHRP office,

they don't have enough resources to find out—I mean from my perspective and from many people's perspective—if research is being essentially conducted up to code. And there's also not really high quality information exchange between researchers broadly and the FDA, about why, for example, the FDA might need more information in one case but not in another case. If there could be more discussion, I think, with the agency and with the research community about that, there might be a way to streamline the FDA responsibilities. And when you have to report to more than one entity, as you do adverse events for some instances, you have to report to both NIH and FDA, or at least you have to for certain kinds of research. You know, that creates use of resources that could be better utilized, in terms of promoting safety.

DR. JOEL D. HOWELL: Other questions?

AUDIENCE MEMBER: You've mentioned various kinds of information that could be released, adverse effects but also protocols. And then there's the "who" question of who receives the information. Certainly the potential participants need as much information as they can get, but I'm not sure about the competing company. So what I'm driving at is, is it reasonable to ask whether there can be different levels or shells of disclosure?

PROFESSOR ROSEMARY QUIGLEY: Well I do think it would be possible to have a mechanism by which potential enrollees in research get information that isn't otherwise publicly disclosed. But I think the way the environment is right now, industry doesn't necessarily want to give information to the potential enrollees, who they really need to get enrolled in this research so that it can be done and so they can move through the approval process, and they don't really want to tell some of the investigators either. Investigators often only have the research data for their own site, they don't have the data for research being conducted in other sites. So there might be limits on how much a physician who's enrolling their patient in a trial knows about the safety of that information. That seems so egregious, given the fiduciary responsibility there. So I think they've kind of jumped at public disclosure because they're not getting anywhere in the interim level of just getting better informed consent.

PROFESSOR CLAYTON L. THOMASON: There is a real conflict between a theory of informed consent for human research subjects and the protection of confidential or proprietary information. Putting a gag order on subjects in a research study that would prevent them from disclosing information that had been disclosed to them runs counter to the whole thrust of the last half-century of development of informed

consent doctrines that are about full and open disclosure. So I think that that hasn't been adequately explored or resolved in any sense yet.

DR. JOEL D. HOWELL: I've always wondered about one type of disclosure, but I haven't been able to convince anybody to do this study. It would be very interesting to see what would happen if patients being enrolled for clinical research studies asked to see the proposal, if they said at the end of the consent process: "That's very nice, now may I please see the grant that you've written for this protocol." Once the grant is funded it's probably FOIA-able, it's publicly available, so would the investigators be willing to share it with the patient?

PROFESSOR REBECCA S. EISENBERG: Yeah, I don't know.

PROFESSOR ROSEMARY QUIGLEY: After the new drug application is approved it would be.

DR. JOEL D. HOWELL: It would just be interesting to see what would happen to researchers when subjects said I'd like to see the research protocol please. I would guess that most researchers would say no, and we might then wonder what that means about full disclosure and openness. The gentleman here, I believe, had a question and once again I'm going to keep talking until you get the microphone.

AUDIENCE MEMBER: It was kind of on the same topic, actually. And since I work for a large pharmaceutical sponsor in the area, I guess—

PROFESSOR ROSEMARY QUIGLEY: Do you want to meet outside afterward? [Laughter]

AUDIENCE MEMBER: I'd be happy to touch base about anything afterwards. I have some of the same concerns about—I can at least speak about personal experience—if I had access to the data of my competitors, I know it would be most helpful. You know it might not be helpful to them. And I think it's a very important process to work on, the informed consent process that has some inherent intentions built in. I think that a lot of the information that is mandated to be disclosed to the investigators brochure through all the past studies, all the information that does go to the regulatory agency. So I guess just the comment that I had not heard that, specifically for gene therapy, not all concepts are needed for public disclosure. I definitely have some real concerns about it. I just want to add my comments there.

PROFESSOR ROSEMARY QUIGLEY: I think there really are commercial concerns. I didn't mean to say that those weren't valid. But there are people who also think that if there was public disclosure and people heard what's going on with other research that research might become more efficient and the research might be expedited and that people might not make the same safety mistakes in other trials that

they're making now. And whether that will ultimately deter investment in biotech and have some downstream adverse effect on progress, there's no answer to that question.

PROFESSOR CLAYTON L. THOMASON: One of the principles behind the openness and sharing of research protocols in the first place is to prevent duplication of efforts, so that you do not have to reinvent the wheel, over and over again, as well as allowing scientific validation of the research by others.

PROFESSOR REBECCA S. EISENBERG: Yes, I think that the interest of the companies and the interest of patients are at odds here. The patients stand to benefit from the information that you're presenting to the FDA being fully vetted by competitors. That's good for patients, right? The competitor might reanalyze the data in a way that would draw different conclusions and that would allow their doctors to make better choices for them. Now you don't want that, from your own perspective as a pharmaceutical firm, you'd rather be in control of the information that goes out to doctors about the effects of your products. And so sharing the information is going to make those products less profitable for you, which is going to make you less motivated to invest in developing those products and generating information about them. So I think I come out at the same place that Professor Quigley does. We have a bottom line, unanswerable question: do we place more value on having a greater incentive to invest in drug development by making it more profitable, or do we have a greater public interest in making sure that such knowledge as we have about drugs is widely disseminated to permit people to make the best choices about what drug products to use? And that information may be adverse to the interest of the sponsor.

DR. JOEL D. HOWELL: We have time for one more question, in the far back.

AUDIENCE MEMBER: I just wanted to say that it seems to me that, to some extent, the whole FDA system is inconsistent with the notions that you're talking about. If we were actually talking about trying to facilitate this kind of sharing of information, and I agree, that companies like Pfizer and HandiLab could benefit from information that's come out of studies from other companies, but in fact the FDA doesn't facilitate, it regulates. And that's a very different thing. So if we created a system and went back and stopped worrying about looking at compliance and looking at confidentiality of data and rather looked at a way in which that data could be shared efficiently, we would eliminate some of the cost of the big drug companies to putting these products on the market. And it's that cost that causes them to be competitive. So by reducing the cost to market, they would be less inclined to be so proprietary about

the data in the first place. So if the FDA, in fact, became a funding agency and not a regulatory agency, that might actually help.

PROFESSOR REBECCA S. EISENBERG: At the end you said a funding agency. Generating the data is costly. If we want the data, that's costly.

AUDIENCE MEMBER: Yes, but it's the FDA that requires that the data be generated in the first place. So they've created this very cumbersome and very expensive system and then they criticize the companies who are forced to use the system. When in fact, if we put all of that energy, and time, and money into a system that allowed sharing of data—so some sort of central review and funding of trials—and allowed the patent system, in fact, to protect the proprietary positions of the company, that might be more efficient.

PROFESSOR REBECCA S. EISENBERG: I'm not sure if I get exactly what you have in mind, but if you want the data, then you've got to get companies to incur the cost or else the data doesn't get generated. I guess you're saying have the FDA fund the data collection.

AUDIENCE MEMBER: Exactly.

PROFESSOR REBECCA S. EISENBERG: But that doesn't make the cost go away. That just means the cost has to be borne by taxpayers instead of by drug companies. It doesn't make it any cheaper.

AUDIENCE MEMBER: The drug is cheaper in the long run.

DR. JOEL D. HOWELL: And it may have the potential of encouraging the funding of studies of drugs that are not new. As a clinician, one of my greatest frustrations is fighting with trainees who want to use the latest, greatest drugs. Why? Because the new drugs are well advertised and well pushed. One rationale that is often given is based on studies about relatively new concepts, such as diastolic dysfunction. Older, less-expensive, quite effective drugs like hydrochlorothiazide might or might not work for diastolic dysfunction. We don't know, because nobody's studying them. And nobody's studying them because there's no money to be made running that study. And so, perhaps, if the funding of drug studies had more to do with the funding of those studies that would be the most beneficial to patients, rather than the most benefit to the bottom line of the companies, we would have a different pattern of drug studies.

I want to thank very much the three presenters in this session for giving us a wonderful session. Lots of food for thought and I think the fact that we haven't answered all the questions is a very good sign rather than a bad sign. Thank you.

[Applause]

MATT MOCK: I just want to echo those sentiments. As long as we're this close to being on schedule, we're going to stay on schedule, so at a quarter till.

PANEL III
THE EVOLVING ROLE OF TECHNOLOGY TRANSFER

INTRODUCTION

MATT MOCK: Our third panel is "The Evolving Role of Technology Transfer." I'm sure this will be an interesting panel. I would like to introduce once again Professor Rebecca Eisenberg, who is the Moderator for the panel and we'll leave it at that. She is the Robert and Barbara Luciano Professor of Law, here at the University of Michigan Law School. Professor Eisenberg.

PROFESSOR REBECCA S. EISENBERG: Thank you very much, Matt. This panel focuses on a topic that has been a great professional fascination of mine for many years, and that's technology transfer, or the movement of research discoveries from public and academic laboratories out to the private sector for commercial development. And one of the reasons I'm particularly pleased to be moderating this panel is that the people who do this stuff have had really interesting career paths. It's inspiring to look at what they've done, particularly for people who are beginning your careers. You see people who start off doing one thing, change their mind completely, do something else, and then it turns out that they have a combination of backgrounds that uniquely suits them for doing yet another really cool and interesting thing. So they're sort of fun to introduce, just to go over their biographies with you a little bit.

Our first speaker is Carl Gulbrandsen, who is the Managing Director of the Wisconsin Alumni Research Foundation, which is I think, the great granddaddy of the university tech transfer offices. Wisconsin was one of the first universities to get into the business of patenting technology and licensing it for commercial development. Dr. Gulbrandsen received both his Ph.D. in Physiology and his Law Degree from the University of Wisconsin at Madison. He has practiced law in the areas of patent prosecution and patent litigation. Prior to becoming Managing Director of WARF, he was the general counsel of Lunar Corporation and Bone Care International. He went from there to be the Director of Patents and Licensing at WARF, where he is now the managing director. Dr. Gulbrandsen.

DR. CARL GULBRANDSEN: This is kind of an unusual position to be hidden behind a projector here and try to talk. I'm usually walking around when I'm talking, but I'll try to do this.

So I'm going to talk a little bit about technology transfer because that's one of the things that WARF does. One of the issues that we deal with is what do we mean when we say technology transfer? My chancellor tells me what WARF does is a very insignificant part of technology transfer at the University of Wisconsin. And he's serious about that. The biggest technology transfer that any university is engaged in is graduating students and moving them into the market place. University staff also engage in publications, presentations, conferences, all these things transfer technology that's occurring at universities. Industry sponsors research on campus. They send their scientists to work with our scientists. That results in technology transfer. Our faculty love to consult with industry and that also results in technology transfer. There's transfer among scientists from universities of biologic material and ideas, and among scientists at universities and scientists in industry, both ways, of materials and ideas. And this is informal technology transfer. That's what's been going on for as long as academia has been around.

Then there's the licensing of IP that I'm going to talk about. Ken will talk about startups. And as I said, I understand where my position is in life, when my chancellor tells me that what I do is a very insignificant part of technology transfer at the University of Wisconsin, Madison.

As a manager of a technology transfer office, we have a number of constituents and a number of expectations, and we're always sensitive about that. I just throw these out as things to consider; I'm not going to address all of these issues, at least specifically. I will address some of them indirectly. But you know the first constituency that we have, since we are a public university, is the taxpayer, the public. And there is a generalized expectation of the public, that the research should be done to benefit the public. The Federal Government is probably our largest investor, at the University of Wisconsin, Madison, and probably here, at Michigan. And as the largest investor, they have expectations of us. When they give us money for research, there is an Act in place, that I'm really not going to talk much about. It's the Bayh-Dole Act. That Act lays out a uniform patent policy for federally funded inventions and an expectation, if we decide that we're going to handle these inventions, as to how we're going to handle them and what we're going to do with it. There are expectations built into the Bayh-Dole Act, and to other federal laws governing funding, that the technology ultimately is commercialized, used to benefit the public and will advance research. I think the Bayh-Dole Act probably, to a good measure in response to Dr. Eisenberg's work, was just recently

amended in the prelude to indicate that this act would not be used to frustrate research. Something like that?

PROFESSOR REBECCA S. EISENBERG: I had nothing to do with it, but thank you.

[Laughter]

DR. CARL GULBRANDSEN: And the university, as an institution, has expectations regarding its technology transfer offices. More and more today the expectations of the universities are that they're going to get money in return for the transfer of technology. And it's particularly a dear expectation now when all of our states are in deficit and everyone is scrambling as to how they're going to replace the state dollars that aren't going to be coming to the university.

Technology transfer today, more and more, is being used for faculty retention or recruitment. It's become a relatively recent phenomena that on the way to recruitment interviews, faculty stop off at the technology office to find out how you handle their intellectual property, if they generate any.

Faculty and staff, once they get hired and start to work, they have their expectations and they're constituents of ours. We treat them as customers, just like we treat industry as customers. Faculty expect us to commercialize their invention, so if they disclose something to us and we take it, there's an obligation on our part. And, of course, they want to make money from it. Money both for their research, but money to supplement their salaries. They love to have consulting arrangements with industries and they look at the technology transfer offices to help facilitate that through their licensing agreements.

State government, more and more, is looking at the universities as sources of economic development and I'm sure Ken will talk more about that. And then industry, what does industry want? Industry wants access to new technology. They don't want to pay double for it. They don't want to be unduly hampered with red tape when they come in. They want things to be facilitated. And they certainly want a competitive advantage.

A little bit about WARF. WARF is the exclusive patent management agency of the University of Wisconsin, Madison. We're an old organization. Actually we're seventy-eight years old now. We were established in 1925 by Professor Harry Steenbock, a professor of agricultural biochemistry. And we are a tax-exempt, not-for-profit corporation. Why was WARF founded? There was another professor that preceded Steenbock by the name of Babcock. Babcock, who was a famous Wisconsin graduate, discovered a technique for measuring butter fat, which at that time Babcock felt should be dedicated to the public. He did not believe in

patents, particularly patents on academic discoveries. And so he published his butter fat process. He did not bother to try to protect it. And the invention was actually misused. There were a number of companies that advertised that they were using the Babcock technique for butter fat measurement, when in fact they weren't. It ended up giving his technology a bad name. He always regretted the fact that he didn't do something affirmative to try to control the use of that technology.

Well when Steenbock came on the scene, he remembered that story. Of course Babcock was his dean and made everybody aware of the fact that he was upset about what had happened to his discovery. So in 1924, Harry Steenbock discovered that if you irradiated animal tissue with ultraviolet light, you increased the Vitamin D content of that tissue. Now take note that this is 1924. At that time, Quaker Oats came along and offered Steenbock nine hundred thousand dollars for that invention—in 1924! And Steenbock, being a lot smarter than I'll ever claim to be, turned them down. He went to the university and he said I have a particularly valuable invention that I want to protect. I don't want the same thing to happen to my invention that happened to Babcock's invention. I also think that we can use my invention to fund my research. So I'd like you patent it and license it and bring the money back to fund research in my laboratory. And the university—unfortunately for the university or fortunately for the university, however you want to view it—turned to Harry and said, "Harry, we're an academic institution, we don't get involved in commerce. And we have no vehicle, no authority to do this. If you want to sell your invention to Quaker Oats, sell it. But frankly, you're hired here to work in your laboratory and get back to work."

So Steenbock being a stubborn Dane, a very persistent Dane, got together with eight of his friends, all alumni at the University of Wisconsin, Madison, and each threw in a hundred bucks. We carry nine hundred bucks on our books today, still, as the dues paid in for WARF. They founded Wisconsin Alumni Research Foundation. Steenbock assigned his technology to WARF and over the next ten years they made fourteen million dollars off that invention. That was in the twenties and the thirties. He also controlled how that invention was being used. The beer industry came to him and said they'd like to use that invention and he said no. The cigarette industry came to Steenbock and said—we'd like to use that invention; we'd like to make healthy cigarettes.

[Laughter]

And he didn't license to them. So he recognized there was a way to control the technology. And if you look at the early records of what they did, they actually did control the technology and they persisted very hard

in making the technology widely available and in fact eradicated rickets, which at that time was a significant problem.

WARF has a very simple mission. Our mission is to support research at the University of Wisconsin, Madison. And we do it in two ways, we do it by transferring inventions from the lab bench to the marketplace and, hopefully, when we do that we can bring some consideration back that is used to fund further research. We also have an endowment that has been built up over the seventy-eight years of our existence, starting with the seed that Steenbock gave us. And at the end of each year, we take what income we receive off of patenting and what income we receive off of investments and we give the university a non-restricted gift, which in recent years has been in the range of thirty-five to forty-five million dollars.

I thought what I would do is give you a more current example today of the types of things that a technology transfer office can get faced with. And so since Dr. Eisenberg talked about human embryonic stem cells, it'd be appropriate if I talk a little bit about human embryonic stem cells. People don't like the term "breakthrough technology" but I'll call it that. In 1997 Dr. James Thompson, at the University of Wisconsin, Madison, came to WARF and disclosed that he had been successful in culturing what he called human embryonic stem cells. This was not a serendipitous discovery. He'd been working on it for some seventeen years. He started first in the field of mouse embryology, and then he moved over to the Oregon primate center and started working with monkeys. Then he came to the Wisconsin primate center at the University of Wisconsin, Madison, and continued his work, succeeding in about 1994 with culturing primate embryonic stem cells in Rhesus monkeys. He then duplicated that work with Marmoset monkeys—these two species of monkeys are farther apart in lineage than is the Rhesus from the human.

So he figured since he was successful with both of these species of monkeys, he would be successful if he had the opportunity to do it in humans. Unfortunately, at that time the Federal Government prohibited the use of any federal funding for work with human embryos, which he needed to derive these cells. So at that point, he was in a fix as to what to do and WARF wasn't smart enough to fund the research. So a company by the name of Geron came along and said—in fact three days after he published his article on the monkeys—they've had a pool of money and would like to fund the research to do this in humans. And Geron has some rights, as a consequence of that.

WARF now has two U.S. patents. One covering primate embryonic stem cells generally and one covering human embryonic stem cells. And

Jamie Thompson got his face on the cover of Time Magazine and had a private dinner with Dustin Hoffman. How great is that?

[Laughter]

So what is the use and promise of embryonic stem cells? Well, it'll probably surprise many people to learn that ninety percent of what we know about early human development is inferred from studies done with mice. You can't work with human embryos, so work in the mouse embryo is a good platform that is well understood and well used and a lot of work has been done on that. There's a lot of research that has been inferred from mouse research to what early human development is. But this is a cross section of a mouse embryo and a human embryo about the same day, same time, same stage in development. The colors on this slide represent various tissues and you can see that they have relatively similar tissues but the shape is quite different at this stage. I will tell you from a physiological standpoint, the physiology at this early stage at the seven-day stage is also quite different. At this stage, the human embryo releases a hormone to set up the uterus for implantation in the embryo. The mouse doesn't have this hormone at all, and it uses a completely different scheme to get itself implanted. So you can see that that's just one example. There's probably a number of examples that makes it risky to infer too much from the mouse embryo to the human. Well with human embryonic stem cells, for the first time, we have a window of opportunity to look at one stage of development and see what factors cause an undifferentiated cell to become a more specialized tissue cell.

Research, of course, is just a basic understanding; it is a great promise. But there's also promise for drug development, drug discovery. Molecular switches that turn genes on and off. I'll give you just one example. Now that's a picture of human heart cells that have been derived from the human embryonic stem cell. That meeting of those cells occurs in the petri dish. And there's a coordinated contraction, which is quite remarkable. Electrophysiology done on those heart cells shows that they're very, very consistent with an absolutely normal human heart tissue. As far as we know, there are no human heart stem cells. But the human embryonic stem cell gives us an almost infinite supply of human heart cells that we can apply drugs to and do drug screening or toxicity studies, something that's not available today. Today you do your early screening on animals, which may or may not be similar to humans. You hope that at some point you'll get into a clinical study with a human being, but you aren't going to do the early studies on human hearts. I can speak from personal experience, I used to do heart research. Once in a while I could do research on a human heart, but it was always a diseased human heart. You didn't take a normal human heart and do research on

it. So that's just one application of the technology that hopefully will be quite useful.

The most hyped indications for it, of course, are disease treatment, self-therapy. And we could go on forever on that. But there is legitimate promise with some of it. It's quite a ways away. But truly the most practical near applications of this is with the research. There's a patent controversy about this. You know Wisconsin Alumni Research Foundation owns these basic patents covering human embryonic stem cells and people question—do these patents obstruct research? Do they frustrate development? I had to appear in the Senate, in front of Senator Harkin and he asked me if there was any reason why he shouldn't move to rescind these patents. Now I don't know that a U.S. Senator can do that, but I wasn't going to argue with him at that point.

[Laughter]

I tried to convince him that that wasn't smart to do. You know as a technology transfer office and as a patent lawyer, we have some basic assumptions that we work from. I have a basic assumption that university patents encourage innovation. They provide some incentive to our inventors. They facilitate publication. Patents themselves are a publication. We never try to hold up publication at Wisconsin. We use the provisional patent system very readily to make sure that our academics can publish as much as they want to publish and can talk as much as they want to talk. And this helps supplement salaries of inventors. University patents help support research. They protect academic freedom. I strongly believe that. If we allowed industry simply to own the patents, industry would be setting the agenda. If universities own the patents, then universities set the agendas, it's as simple as that. And then university patents can serve the public good by guarding against abuse or irresponsible licensing. I think Steenbock realized that. Those examples demonstrate that. And I think some of what we've been doing with human embryonic stem cells demonstrate that. How am I doing?

PROFESSOR REBECCA S. EISENBERG: Well you know I'm really interested in this, so I have a conflict of interest here, but probably we are just about at your time. If you want to take another couple of minutes to finish up.

DR. CARL GULBRANDSEN: Okay, we do have an institute that has been established. We did that because we had biological concerns that needed to be guarded against and you couldn't use federal dollars when we started with this research. So we took it off campus. We still have the institute operating. We also had a high demand for the cells and we didn't want Jamie Thompson just to be expanding lines and distributing stem cells, so the institute does that.

Rebecca's talked about the President's compromise. There's arguments on both sides of the fence about whether that's good or bad. My simple-minded view of it is it threw the ball back in the laps of the scientists and at some point if the research is successful, these restrictions will be relaxed.

We have an active licensing program. If you talk about obstructing research, I will tell you that we have inter-institutional agreements with over a hundred institutions around the world, most of them in the United States. And we have distributed these cells to over a hundred and thirty research groups throughout the world, again most of them in the United States. We provide support to these research groups. And we do have ongoing, a national research project in human embryonic stem cells. We have also facilitated licensing with the PHS, the Public Health Service, so that other groups that have stem cell lines can freely make these lines available to other researchers without fear from Wisconsin Alumni Research Foundation. And yet we also protect WARF's rights to license the cells for future commercial benefit.

I just will show you this for your legal class, today's lesson on sharing has been canceled and will be replaced by a lesson on protecting intellectual property. [Laughter]

And I think that I've said enough, so I'll move on.

PROFESSOR REBECCA S. EISENBERG: Thank you very much, very interesting.

[Applause]

Such an interesting story. Our next speaker is Ken Nisbet, who is the Executive Director of the Office of Technology Transfer here in Ann Arbor, at the University of Michigan. He's had a very different career path that has also led him into the field of technology transfer. He was previously director of new business development within the Office of Technology Transfer, where he was responsible for creating new business startups with University of Michigan technology. So it's a somewhat different emphasis in his role within the technology transfer profession.

Mr. Nisbet has over twenty years of experience in the commercial sector within engineering, finance, marketing, and management roles at Ford Motor Company, Digital Equipment Corporation, and Nortel. He was a co-founder and president of Memory Bank Incorporated, which is a storage systems provider, and was a director responsible for business startups at Trinovas Corporate Technology Laboratory. He holds a Bachelors Degree in Mechanical Engineering and an MBA, both from the University of Michigan, and is active in a number of community activities, including leadership positions within the Ann Arbor IT zone,

New Enterprise Forum, Great Lakes Entrepreneurs Quest and the Washtenaw Development Corporation. Ken Nisbet.

KEN NISBET: Thank you.

I'd like to continue from Carl's presentation on the issues in running a tech transfer office to focus on the impact from and on tech transfer related to new business development and economic development. In order to do that, I thought I should define economic development. Most people would say it's growth in industry, resources and talent in a focused geographic area, and its purpose is to generate industry or jobs and improve the quality of life. Economic development can happen naturally. In fact I would argue that in most cases economic development that one can see in the Bay Area, Boston, is impacted more by natural rather than artificial stimulation programs. But there are things that you can do to stimulate economic development and we're seeing these results. So in areas that are perhaps lacking in resources, different organizations, universities, state governments, et cetera, are looking to invest resources and induce behaviors to stimulate economic development.

So today I'll talk a little bit about how tech transfer offices at universities are influenced by the linkage to economic development, and what we're doing that both help and are affected by economic development.

First, a quick little background on tech transfer, going back a bit to what Carl said. Nineteen-Eighty was a watershed date, because at that point some legislation was created that induced universities to invest in technology transfer. And in 1980 there were fewer than two hundred and fifty patents awarded to universities in the United States. In the year 2000, there were sixty-three hundred patent applications and over thirty-seven hundred patents awarded. So you can see there was a tremendous increase in that activity, a lot of investment, and some very positive results. And as Carl mentioned, with this legislation, the Federal Government not only gave universities rights to the inventions funded, they expected certain performance outcomes, and part of this patenting activity is just that. A couple of other dry statistics: in the year 2000, there was thirty billion dollars of sponsored research going on within the universities; there were thirteen thousand disclosures of inventions during that year; four thousand licenses and options, which you can equate to products and services on the market. Looking at startups, meaning new businesses that were created with university technology, there were 454 new companies founded in 2000, all with university technology. And in that twenty-year period, almost twenty-five hundred startups were created. Interestingly, many of the startups stay local to the university. They don't always stay local companies for long, depending on resources. But 80 percent are still located close to the licensor university.

And tech transfer does generate licensing revenue, which everyone likes to focus on: about $1.26 billion dollars. That money is plowed back into the university system to stimulate more research, more fellowships, education, basically to try to prime the pump and get more research and more results in research stimulated.

So why do we do this? There are a lot of benefits. And these benefits are just more than in fact the results of research. There are rewards of attracting faculty, getting a reputation for talent, attracting students, generating income, promoting economic growth. And I'll focus on that last element, economic growth.

There have been some real success stories across the country that have built over time and a lot of people have said, we should do that too. So states as Michigan have taken a look and said we would like the benefits of economic development and we'd like to utilize the resources we have within universities for that purpose. Wisconsin's a great story, because of how long they've been at it, how good they are at it, and also how actively they work together with state government. There was a study in 2002 that looked at, not just the return on investment of a college education to the people within a university system, but also the enhanced quality of life, the reputation and expertise in the area. They took a look at the spending and the income of people involved with universities, directly and indirectly, and technology transfer. They figured out that about ten billion dollars was added to the state economy, which is about 5.5 percent of the state's gross product. They figured it produced 150 thousand jobs, which is about 5.5 percent again, of the state's employment. So not an insignificant contribution to the state's economy.

Not to be outdone, our state government, the Michigan Economic Development Corporation, did a similar study and they found out that Michigan universities contributed thirty-three billion dollars. Now compare that to the ten billion dollars in Wisconsin, and I think that's because we have a bigger football stadium.

[Laughter]

No actually what they did is they took one more dimension and said let's take a look at the earnings of someone who would go through the university system and compare that to the earnings they would have if they didn't go through the university system. And that's obviously a very large number. So this is a very popular argument now with tight budgets, because they're arguing that for every dollar going into a university system is going to produce twenty-six dollars of benefits. Now I'll be honest, I don't believe all of this.

[Laughter]

But the bottom line is that there are obviously some benefits. So people now have very increased expectations of the benefits that universities can contribute to economic development. We definitely are seeing this influence in tech transfer offices. The university itself wants in fact to have economic development and they're looking to again attract talent, build their reputation and attract research. Local communities like Ann Arbor are quite interested in seeing what we can do to leverage the presence of the University of Michigan and its research and reputation, to help our town to build industry. Many more of our students coming to the university want to see benefits associated with economic activity and tech transfer, both for their own educational reasons, being able to participate in research, and thinking about their own vocational opportunities after they leave. And then obviously there's also financial implications. I'll point out that the financial returns of tech transfer pale in comparison to all these other economic measurements. So the direct result of tech transfer is not going to be a significant amount of revenue, but obviously the actual activity itself leverages a lot of other economic activity.

But a little bit of caution here. I think a good tale here is looking at Stanford, again one of the most successful universities in terms of tech transfer. In 2001, they reflected back on thirty years of operation and said that they had produced over forty-three hundred disclosures, but only 30 percent of them were successful and 70 percent were not. So when an inventor comes to you, you just have to realize that probably he's not going to be successful, yet you still have that service element of trying to help technology reach the marketplace. Of that 30 percent that were licensed and successful, only 50 percent produced more than ten thousand dollars in income. You probably understand there's a huge investment, not only in people but in patenting. So with ten thousand dollars, you are not making any money. But again, that's not the main purpose. And they also found out that only 10 percent produced more than a hundred thousand. So if the goal of your technology transfer activities is for the money, you're in for a big disappointment because you're probably not going to make money and the licenses that do make a significant return are going to be a very small minority. Nationwide, only 125 out of over twenty thousand licenses produced more than a million dollars. So there's a perception about universities and tech transfer, you're making lots of money for lots of people, but the reality is it's about a half percent of what is licensed that makes a lot of money. Meanwhile, who cares? There's a lot of great technology, helping people, stimulating and building up and increasing the resources to do some really terrific things.

New business creation, creating startups, is a focus area within many university tech transfer offices. Startups are a great channel for moving technology because often academic research is really too early to be interesting to established companies, and they would like to take more of the risk out of it. And sometimes the small, hungry, focused group of individuals, even though it looks like they're a risky bet, can actually be a safer bet. Sometimes a larger company, if it doesn't have the right champions, is not, in fact, the right channel for technology. Startups lead to jobs and local economic development. People like that. It fosters the growth of entrepreneurial faculty, it leads to opportunities for students, and it enhances the reputation of the university in the region. So most tech transfer offices now look at new business creations as being a good addition to the toolkit of trying to have technology reach the marketplace.

But this activity is not without cost and risk. It definitely leads to more complex conflict of interest situations, very long lead times for success, and it is very expensive to try to do this activity. It's very hard to find good talent and to keep them within the university environment. And I think it's very highly dependent on the resources that are inherent in a region. So if you're in the Boston or Virginia area, for instance, it's actually very easy to do startups. If you're in an area—you know I don't want to pick on anybody—in some city in some midwestern state, it is actually fairly difficult because the resources just aren't around you.

So very quickly I'll close on what's happened here at U of M. We've made a focused effort at trying to use startups and resources to stimulate economic development. The good news about all of these influences and some of the efforts is that they have produced a consensus of the U of M leadership that technology transfer is not just only important but worth investing in. And that, I think, is one of the prime ingredients for success. It's required a broadening of our skill sets within the office, where before we focused nearly entirely on just the licensing and protections. Now we really have a much broader focus. We have to look at business, we have to look at marketing, and we have to look at entrepreneurial skill sets. So it's a much broader skill set than we had before.

We have built a very small team of people that I call Business Formation Consultants, and they act as counselors. They screen, and they try to bring resources to our inventors. The state here has injected a lot of resources. I'm sure many of you have heard about the Life Science Corridor. They've taken the tobacco settlement monies and spread them out over time to try to stimulate new research and commercialization efforts. They've also taken some gambling money and put that into a kind of a complimentary fund to induce some gap spending. I'd like to

say that we're trying to get all the sins covered here and we'll get economic development really rolling.

[Laughter]

There's also been, I think, a real change in collaboration out of this effort—a change in attitudes. There's been a lot more collaboration among the universities and state, and also within the Midwest. There's been a lot more collaboration within the city. I think it's broken down a lot of the town problems we had before. And I think it's actually led to a lot more engagements for the alumni. Our development office likes to use me in their alumni meetings. And I love it because I'm gaining contacts and resources from people all across the country that help me do my job better.

So the bottom line is that although we have a long way to go here in Ann Arbor, we're doing pretty well. A lot of this stimulation, a lot of this investment and interest has led to some really good things. A lot more disclosures, we had 30 percent more disclosures to our office in the last year. We've done really well with startups. Talking to Carl, Ann Arbor actually is blessed with some resources which have really helped us. We had twelve startups in 2001, including HandiLab back there. We had some terrific opportunities that are going to lead toward great products and some great job opportunities. And overall I'll say that the momentum is very, very positive. We have some terrific financial rewards that may be coming, that will allow us to do the work we do and that this enthusiasm in our staff and faculty and in the community is very refreshing. Thank you.

[Applause]

PROFESSOR REBECCA S. EISENBERG: Thank you very much, Ken. It's a very interesting counterpoint—somewhat different focus or maybe a shifting focus of technology transfer in universities in the years since passage of the Bayh-Dole Act.

Our next speaker is from the other side of tech transfer. He's from the private sector. He's also had an incredibly interesting career path in a lot of different institutions. He received his Ph.D. in physics from Stanford University and was a post-doc following that at the University of California, in biophysics. He has held scientific and technical management positions at NIH, at QuantaRay, at Applied Biosystems, at Hewlett-Packard, and since Agilent Technology spun off from Hewlett-Packard, he's been with Agilent Technologies where he recently became chief scientist for the BioResearch Solutions Unit. In all of these positions he has worked extensively on systems for sensitive biochemical measurements. At Applied Biosystems he was responsible for groups that were developing novel genotyping and comparative DNA

sequencing technologies. For the past three years he's been R&D manager for the division of Agilent that develops DNA microarray solutions for gene expression measurements in bioscience research markets. Dr. Kronick.

MEL KRONICK: Thank you. For my remarks today, what I'd like to do is to give you a personal perspective on technology transfer. It's interesting that Ken mentioned Stanford; in the early seventies when I was a graduate student there the work I did for my Ph.D. thesis was patented and licensed by Stanford. I remember visiting Neils Reimers in the little trailer that he had out in the parking lot at Stanford when the licensing operation there had really just begun. And since then, in my career, I've managed to be at a few different companies, and a lot of the activities that I've personally been involved with have been the result of, in one way or another, university research which was licensed to commercial organizations.

What I'd like to do this afternoon is to focus primarily on life science applications and technology transfer, because that's the real topic we're talking about today. And my remarks will be slanted more toward comments considered most relevant to some of the issues that come up in genomics and molecular biology kinds of applications. And it probably goes without saying that these are my personal remarks, not the remarks of the company I work for.

There are three fundamental premises I want to put forward. The first and most fundamental premise is that the nature of the life science research and technology that's going on in universities today is so inherently state of the art, novel and cutting edge, that it causes a whole bunch of problems and issues to arise with licensing. I think that the newness and novelty implies, for example, that it's a long way from the time that something develops in the university to when it can become a commercializable product. That means a lot of time, a lot of investment.

My second premise is that when the invention in the university in these life science areas I'm talking about actually gets patented, the patent can actually often create a lot of confusion in the scientific and commercial areas, i.e., in the commercial marketplaces, because of the patent office's inability to really fully anticipate the implications of granting unreasonably broad patents. That's a theme I'll keep coming back to. It is something that a lot of us involved in these areas get very upset about and are very concerned about.

My third premise follows from my first two. Because of the fact that there is a long gestation time with a lot of these inventions and because of the danger of the patent office granting overly broad patents, I think the university, in doing technology transfer, must use utmost care to

make sure that the intellectual property they're responsible for gets into the private sector in a manner which really maximizes the benefit to society and, at the same time, maximizes the long-term and not the short-term benefits to the university. What we all do not want is a situation such as the one described by Dr. Stan Williams last September before the Senate Commerce Science and Transportation Subcommittee on Science, Technology, and Space. Williams was a faculty member at the University of Illinois and is now a Principal Scientist at Hewlett-Packard in Palo Alto. Williams claimed that relations between universities and corporations have rarely been worse. He commented that it was easier for Hewlett-Packard to start up a research collaboration with a university in Russia or France than one a few miles down the road in the Palo Alto. And Williams felt the Bayh-Dole Act encourages universities, when granting intellectual property licenses, to favor small companies, often started by faculty members, over larger companies that have supported much of the research. He noted that a lot of companies feel that they have been burned a lot of times in licensing deals with universities. So I think that's an attitude that we all have to work to try to change; somehow we must think through the processes so that we do not have that kind of attitude existing within the commercial side.

I want to go back to the first of my three premises about big investments being made. I want to remind everybody about all the things that a company has to do from the time it starts looking at a technology until that technology becomes a commercial product. I have often observed that the people in a university who invented something feel if they have run an experiment four times and it worked, then they think its development is done and it's ready for commercialization at a company that ought to be making it in six months and charging a very small amount of money to sell it broadly. But I think most of the companies I have worked for probably spend a maximum of maybe 20 to 40 percent of their investment in a product when they are done developing it as a technical entity. The rest of that investment—the majority—all goes into things like scaling-up manufacturing, investing in facilities, investing in quality methods, figuring out how to package the product and how to market it, creating learning tools for customers, training the sales and support people, setting up that infrastructure, doing advertising, promotion—lots of things like that. All that kind of investment is really necessary. And even just the feasibility phase of a project needs to address considerations which university researchers do not consider. We constantly amaze ourselves with the details that can slow us down, even with stuff invented internally, ideas that we are not in-licensing. You have to take an invention and see how it works in the real world where it

will be used. If you're talking about a research tool, it might be used by different people who will handle it in different ways. If you're talking about a drug, it's obvious that a company needs to understand how it works on different people or, for a plant improvement, how the plants will incorporate the invention in different environmental conditions. A company must also determine how the product works when it is made from different lots of the same raw materials, things like that. There's just a lot of nitty-gritty, difficult scientific and technical hurdles that you have to go through following the initial invention or licensing of something.

This large investment of time and money needs to be considered in the context of my second premise: that so much of this life science technology is so new that the patent office doesn't know quite what to do with it. A most bothersome thing is when you license one patent to try to get a product going and then you realize, either soon afterwards or, worse yet, later on, that you have to license three or four other things as well. The area of DNA arrays that I work in is a prime example of that. To use a DNA array, you run into intellectual property issues having to do with the enzymes and dyes that are used to label the DNA. You run into intellectual property issues with respect to how you actually make the DNA arrays. You run into intellectual property issues associated with many, if not all, of the particular DNA sequences with which you want to be interrogating on the array and the sequences could be owned by fifty different organizations. And you might then have additional IP issues associated with the ways in which you choose to actually scan the microarray and analyze the data coming off of the array. I mean it's just a lot of different organizations to work with. It's really very complicated. You have a situation which, I think, is a prime example of a principle described a few years ago in an article written by Professor Eisenberg and a former Michigan faculty member, Michael Heller.[55] They called this principle the "tragedy of the anticommons." So many people have a stake in the action that it's very, very difficult for a company to commercialize something and do it at a profit without an inordinate amount of investment and a lot of wasted time.

I think a lot of these problems have to do with, as I said earlier, the fact that technology is really very, very new. There is a wonderful article by John Barton, a professor of law at Stanford University, that appeared a few years ago in the journal *Science*.[56] Barton talked about reforming the patent system. He points out here that changes should be enacted to

55. Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698 (1998).

56. John H. Barton, *Reforming the Patent System*, 287 SCI. 1933 (2000).

shield our society from the problems which can result from broad, overly basic patents on fundamental research processes that may deter and complicate follow-on research. Barton said in dealing with this issue it's crucial to balance incentives to initial innovators against incentives to follow-on innovators. And although the point deserves further study, experience suggests that this balance is currently weighted too much in favor of the initial innovator. The problem is likely to be increasingly serious in the areas of biotechnology and computer software. Barton's article goes on to quote a Supreme Court case, *Brenner vs. Manson*,[57] which discusses the risks to the public interest that would arise if patents block off entire areas of scientific inquiry and development.

A recent example in my field of DNA arrays provides a great example. There's a patent out there now on databases of gene expression profiles. In my mind, compiling a database is a pretty obvious thing to do when you're starting to collect a lot of data. It's a little bit like the one click patent that Amazon was dealing with a few years ago.

Fortunately, I think the tide may be turning a little bit. And in fact there was a significant court ruling this week, I think on Wednesday, in a lawsuit that the University of Rochester brought against Pfizer on COX-2 inhibitors, molecules used as anti-inflammatory drugs.[58] The Rochester patent was held to be invalid, or at least not enforceable against the makers of COX-2 inhibitor drugs like Celebrex (the target of the suit in question) because of the fact that the patent really was too broad and wasn't really enabling the particular invention that Celebrex was and represented to the drug company.[59]

There are other kinds of complications which arise from bad patents. We all know that you can get a very legitimate patent which reads on somebody else's patent, because the new patent can represent a very innovative improvement of a previous invention. So you have this wonderful thing but you can't, in a strict legal sense, commercialize it unless you figure out ways of getting rights to the broader patent that dominates. At this point, interesting negotiations sometimes occur, because if your innovation really changes the rules of the game, the company that holds the dominating rights may be willing to engage with you—trade, barter, things like that. That process is reasonable. But a related issue I think goes back to the way the patent office works again. One of the things that just drives us in industry crazy is when a patent that we know about has issued with very narrow claims. Then, perhaps years later, what's called a submarine patent 'surfaces' wherein the

57. Brenner v. Manson, 383 U.S. 519 (1966).
58. Univ. of Rochester v. G.D. Searle & Co., 249 F. Supp. 2d (W.D.N.Y. 2003).
59. *Id.* at 235.

inventors have managed, through aggressive legal representation, to wear down the patent office to the point at which claims in a continuation are broadened so they cover almost everything. Frequently, in doing this, the attorneys take advantage of the insights developed during the continuing evolution of the science and the technology. In doing so, they distort what the original inventor had in mind five or ten years ago and make it seem like the inventor was far more prescient in his thinking than he probably really was. And then you're all of a sudden faced with the fact that you've invested a few years in developing something, thinking that Company X had a relatively narrow patent. Suddenly Company X owns the whole field because they were able to convince the patent examiner that the broad interpretation of the specification was really what the inventor had in mind. It is as if I had invented the wheel but now I were claiming I also had invented the automobile. So you know it's very frustrating sometimes to deal with that lack of sophistication within the patent office, which could result in such a distortion of the patent continuation process.

So I think really all of us have to work to try to improve the quality and the nature of the decisions that are made out of the patent office. And frankly, it's a very, very difficult thing to do. I think that the really good legal minds, like are present here, and scientific minds usually don't want to go to work in Washington at a low salary, looking at one patent every twenty minutes and trying to pass judgment on it. Barton made similar comments in his article, noting that the PTO service ideally should become a career rather than a stepping stone to private practice. And yet the current employees of the patent office are the individuals that really end up establishing whether a patent exists or not. I think it's a fundamental difficulty in the way the system works today. And I know that some creative ideas have come forward with regard to privatizing the system here or making it a little bit more similar to the system that works in Western Europe, where there's a comment period during the initial pursuing of the patent and where a pending patent is opened up for external comment. In Europe, a lot of people get a chance to comment during the prosecution—anybody that might have an interest in that patent can ask the patent office to look at a particular previous publication that could affect the patentability.

Taking into consideration the amount of investment required to commercialize most university inventions and the overly-broad issuance of claims on certain patents, the situation we are all in just requires a lot of sensitivity on the part of universities that are involved in technology transfer. I would say that when you, the university, are dealing with a patent for which you're lucky enough to get very broad claims—perhaps

like the Wisconsin stem cell patents that were just discussed before my talk—I think non-exclusive licensing is extremely important. The way Wisconsin's been doing it has not really upset the way in which the marketplace can work and does not really stand in the way of future developments.

I recently read an article from a nanotech trade magazine that I get called *Small Times*. The nanotechnology industry is now struggling with a lot of the issues that biotechnology has been facing over the last several years. And, in fact, the scientist Stan Williams that I mentioned before works in the nanotechnology area. In this particular article in *Small Times*, Harold Wegner, who's a partner at Foley & Lardner, a law firm in Washington D.C., made a statement that I know from my personal connections in Stanford is true. Wegner said that the initial success of licensing the Cohen-Boyer patent, one of the most fundamental gene cloning patents, was based on the very modest demands made by Stanford.[60] Stanford asked only a ten thousand dollar fee per year to have blanket research use of Cohen-Boyer patent. The patent was widely suggested to be of questionable validity but a standard form agreement was offered to everyone at this modest rate, far less than the cost of even a modest legal opinion on validity. The licensing policy resulted in the patent being broadly licensed and was definitely the biggest money making patent that Stanford has had. The second biggest one that Stanford has had, something I personally ended up being involved with when I went to Applied Biosystems, had to do with a protein labeling technology. And again it was broadly, non-exclusively licensed.

I would suggest on most of these broadly applicable technologies that the policy of the university ought to be to make them easily available. Follow more the Southwest Airlines or JetBlue model in making the transactions simple, not a big complicated negotiation. Just a few weeks ago I had a call in about something I was interested in to one of the University of California licensing offices. And I asked the person there if the university wanted to license it exclusively or non-exclusively. He said, "It's just a lot easier for us if we do it exclusively." I just think that's the wrong attitude. You have to look at the idiosyncrasies of the particular patents and issues that you're dealing with. And attitudes like that just upset a lot of people in industry who are trying to respect the value of legitimate intellectual property but also are trying to run a business.

I think the second point about exclusivity is that the university should be careful about locking up the rights too soon with any one

60. Stephen B. Maebius & Harold C. Wegner, *America's Technology Leadership at Stake if Patent Owners Control University Research*, SMALL TIMES, Jan.–Feb. 2003, at 23, 61.

party. That sort of goes along with making broad patents widely available. I talked to a few people I know in the technology transfer on the university end and on the industry end before coming here. And I think that it makes the job of people in the technology licensing office a lot easier to have the inventor be a real advocate for the patent. Tech transfer offices are motivated if somebody comes to the tech transfer office and says, "This is great, you 'gotta' get it out there." Such encouragement is clearly going to really be a very motivating thing. On the other hand, there's certain conflict of interest that exists there, especially as long as the inventor is an employee of the university. I think the technology transfer office has to look out for the university and society in a bigger sense and listen to what the inventor has to say but not be overly influenced by that. I think there's lots of room for continued creativity on the part of all to come up with licensing conditions that either do things like limit the license to a certain area of exclusivity or licensing at a very minimal cost to a company up-front and then, as the company has that license for more and more time, charging them more and more. That would encourage a company to try something, and if they like it, then they have to pay more and more. A company does not want to get into the big up-front negotiations to just try something, because then it's just not going to be worth it to go down that path.

Finally, I would just like to go back to that comment I made on exclusivity, and combine that with some of Ken's remarks. It's difficult to know when you get a very preliminary invention if it's really going to make a lot of money or not. And I think the quicker inventions are produced and get tested and tried in the marketplace, the sooner the true value of those inventions is going to really come out. It's just hard to pick winners. I think the easier everybody can make the process the better—for both the tech transfer offices and the universities so that you create situations like Carl talked about where a hundred institutions get licensed to use something in a relatively short period of time. I think that's the goal that we really ought to be moving toward. I think it'll end up maximizing the income for the universities over the long term and it'll maximize the effectiveness with which inventions get transferred to commercial licensees.

So in summary, I think that what we want to do is to recognize in some of these really dramatic new areas of biology that the patents are imprecise and broad when they're granted and that the most important thing is to figure out a way to let innovators who can build on some of this new technology have access to the exciting stuff that's coming out of universities. We do not want to set up a situation I earlier referred to as a tragedy of the anticommons. If we do, I think that we'll just end up

putting a lot of time and energy into efforts in which companies are fighting each other and universities, rather than really trying to produce more products for the common good. Thank you.

PROFESSOR REBECCA S. EISENBERG: Thank you very much. That was a very interesting set of presentations that each offer interestingly different perspectives on the issue of technology transfer. I think while I wait for some of you to frame your own questions, I'm going to invite the first two panelists to see if they want to respond to Mel Kronick's presentation, because he was offering a peek at the industry perspective on the dark side of technology transfer, the ways that things can go wrong that would have the opposite effect of the underlying goal of achieving more widespread development and dissemination of technologies coming out of universities by patenting them and licensing them to the private sector. You can have too much of a good thing, obviously. You could have patents that are covering fundamental technology that are too broad, where the underlying technology would be better utilized if broadly disseminated, or you could have technologies of the type that I think Ken Nisbet has in mind, that form the kernel of some of these new enterprises where you probably do want to have an exclusive license in order to get some new business off the ground. So how do you try to manage some of the tensions involved between the good side of technology transfer as a way of promoting investments and economic developments on one hand, and the bad side of technology transfer, that can get in the way of effective utilization and dissemination of new technologies to the scientific community?

DR. CARL GULBRANDSEN: Well, I agree with Mel. I don't think that it's strictly a university problem. I think that industry also, if they can get a broad patent, will get a broad patent. It takes people that are sophisticated and educated and understand that your market is probably better if you license it broadly. We're much better off if we get a cheap license than if we hold out for an expensive license and we never get it licensed. So our goal is to get things licensed. That's what our goal is, to get it into the marketplace and get it commercialized. The issue of stacking patents is something that all of us worry about, particularly industry worries about it. But it's not anything that's really new. I came out of the medical device industry and every time we wanted to build a new product, we had to do our literature searches and our patent screening to find out whether or not we could even make the product. And generally it involved acquiring rights from other companies or universities, it wasn't strictly universities. So this is kind of an age old problem that has been worked out in the marketplace and I can just say that in our own experience, at WARF for instance, we used to ask for reach through

rights, which means that when you license somebody with a research product and they get a great discovery on it, you want some part of that end discovery. We very rarely do that anymore because it's a waste of time. It's difficult to monitor administratively for one thing, and we'd rather just get paid. And so we license it for a low price, and as long as they continue to use it, hope that they pay us a moderate price, but then license it broadly. And at the end of the day, we'll probably do much better than trying to license it to a company and try to extract anything that they might gain from it down the road. So you know there are creative ways to approach these things. But I do think it takes people that are reasonable and don't have too high of expectations of commercial property when they start.

KEN NISBET: You know, I think the same thing. I think we agree, we have to make sure that the interests are aligned. We train our people that industry is our client. And we also have inventors on the inside who are also clients. The bottom line is that we know that there is a substantial investment required to have our technology reach the marketplace. Ten times what we put into it. And we need to have those incentives to make sure that the outside companies are willing to do it. This is not selling. They do not come in and say I'll take one of these and one of these. I mean it is really hard to match up our technology with industry. It's even more than, I think, the exclusivity issue. It's also about time. We have so many things we're trying to get out and we're servicing so many masters. If we can get more of our technologies out and leave a few nickels on the table, that's the attitude.

PROFESSOR REBECCA S. EISENBERG: We welcome any questions from you. Meanwhile I'm just going to keep asking questions. Oh yes, Jason Owen-Smith from the Sociology Department.

AUDIENCE MEMBER: Question for the panel. I'm not quite sure who to address it to, and I have a sense that you might have differing thoughts. I'm interested in how academic scientists decide to patent things. But one of the issues that runs through that is that scientists at work in academia, especially life scientists at the bench, typically aren't terribly concerned with the overlapping patent rights, the background rights that are necessary to enable someone downstream to practice their invention. So I was wondering if the technology licensing directors could speak to the role that their offices play in trying to figure out what background rights exist and if the representative of Agilent could speak to the ways in which licensing from universities may be more difficult because they're typically not directly concerned with such rights.

DR. CARL GULBRANDSEN: Well we have a professor bring a disclosure to us. There are several things we consider before we decide if

we're going to take them. First of all we look at whether or not we can protect the invention—that's not true in all cases. We handle also a lot of biological materials we don't bother to patent, or software we don't bother to patent, so that's less of a concern. But if you're talking about an invention that is of the type that you would like to patent, you want to figure out first can we protect this. Secondly, is there a market or can there be a market built for it. And then thirdly, what's the importance of this from the standpoint of the public good or use. Is it something we should invest in? Stem cells, for instance, I can tell you we've never made any money on stem cells. Whether we ever make any money on stem cells is a big fat question mark and likely we won't. But it is an incredibly important research tool, and we've decided to invest in it. So that's what we are doing. As far as looking at what background rights exist, I don't know if we necessarily do that except to determine whether this is something that we can protect.

KEN NISBET: Yeah, I just have a comment. That is very difficult. But one of my colleagues here, Elaine Brock, works in sponsored research. The time they think they have something valuable is not the best time to help commercialize it. We have to go way back and look at who were their relationships, what materials did they use, what other people were involved in helping you discover this? And at times we find that unless we give them counsel early on, there really isn't much that we can do with it afterwards. I have to admit, I don't think most of the inventors have a good grounding on all of these elements because when they first are starting their research, they are not always thinking about the end goal of commercialization. We have to help them with those options.

DR. CARL GULBRANDSEN: I would add onto what Ken said, that one of the other considerations that is on our checklist of things to look at is complications. And complications arise when they've been consulting with somebody in Warsaw or they've been working with somebody at another university and we need to deal with that university, or graduate students have come and gone and we can't find who the inventors are, those types of things. There are too many complications.

PROFESSOR REBECCA S. EISENBERG: Maybe the decision in the University of Rochester case, that was alluded to earlier, will discourage some of these broader claiming strategies or make them less effective. I want to recognize Elaine Brock, who's been negotiating sponsored research agreements for the University of Michigan for many years and has also had a lot of experience in the other direction of tech transfer, which is bringing stuff into universities from the private sector.

AUDIENCE MEMBER: Right, taking it out too. But I think one of the key differences between university technology offices and industry is

universities do not defensively patent. We don't defensively patent, so we won't take a technology and patent it just to be able to shelve it to promote a product that's closely related. So that is a key difference.

PROFESSOR REBECCA S. EISENBERG: Actually that's a nice segue into another question that I had here in my notes. Recently, the Court of Appeals for the Federal Circuit decided a case called *Madey v. Duke University*, which is a patent infringement suit against a university brought by a disgruntled faculty member who held a patent on a technology that the university had built a special lab around.[61] After a falling out, he sued the university for patent infringement. The university defended on the grounds of a research exemption, that this is noncommercial academic research. And the Court of Appeals for the Federal Circuit said basically, what research exemption? You are using this technology in accordance with your ordinary business purposes, that being noncommerical academic research, and therefore you are an ordinary infringer, and don't think you have any special exemption.[62] Is this maybe part of the other side of the coin for technology transfer: that as universities become more assertive about their own patent rights over their own technologies, they start to look like ordinary players in the patent system and they lose their special status as nonprofit users of technologies developed elsewhere? And if so, is that something that's likely to change what Elaine has just suggested to us? Will universities be able to afford not to patent defensively, if they feel more vulnerable as infringement defendants?

AUDIENCE MEMBER: I don't know if anybody in the room is looking at the *Madey* case, but it's a great example of what not to have done procedurally. And potentially calling the question might be a bad thing to have done, not only for universities, but for industry who also believe, to some extent, in the research use exemption. But I don't necessarily think it'll promote defensive patenting. But it definitely will make us treat research tools differently, particularly when we're actually using them in non-industry sponsored projects, because to the extent that the Federal Government puts millions of dollars into research, on which we're basing the potential research result on a tool that's available only commercially from somebody else and that we've been relying on the research use exemption to promote, we may end up having a lot of federal investment of money in a potential product that we can't move out because of a background right. But I'm not so sure that that problem doesn't already exist, for the reasons that Carl said; we have those problems already. If it's too complicated, if there are too many blocking patents, if we can't find the inventors, then we're not likely to try to

61. Madey v. Duke Univ., 307 F.3d 1351 (Fed. Cir. 2002).
62. *Id.* at 1361–63.

move forward with it anyway, just because we don't have the resources to be able to do that the way industry does. But like I said, the *Madey* case is not going to make great law.

DR. CARL GULBRANDSEN: I guess I've talked to Ken about this and I know Michigan—there was an amicus brief that was filed by the Association of American Universities and by the Association of American Medical Schools. Wisconsin didn't join that and I know Michigan did not join that. I don't think that the decision in the Duke case is too much of a surprise. It was a surprise for them to say that if you're using it for the business of the university, which is education, it is infringement. I think that's going a little bit far. But I think as everything happens in the law, you'll see shadings of this and probably contractions of it. It came out of a disgruntled employee suing the university. It wasn't a company suing the university. And frankly, there is kind of an unwritten rule among companies particularly in the biotech area that they aren't going to sue universities. And I don't think that this case will precipitate a lot of lawsuits. Saying that, at Wisconsin we certainly don't encourage our professors to infringe, if they knowingly are using somebody's technology. And we will negotiate for licensing position, even though the courts have said you can't sue a state university for damages on infringing intellectual property, we don't encourage infringement in Wisconsin.

PROFESSOR REBECCA S. EISENBERG: Jason?

AUDIENCE MEMBER: A follow on to the discussion of *Madey v. Duke*, does either WARF or Michigan explicitly reserve rights to use technologies they license exclusively in research, as part of contractual arrangements?

DR. CARL GULBRANDSEN: Absolutely. It's the holy cloth. We do not take that out of our license agreements.

KEN NISBET: Same here.

MEL KRONICK: Even the stuff that gets licensed out that was federally funded, the government always holds onto a license, too.

That doesn't make any difference.

AUDIENCE MEMBER: Well sometimes it can if it wants to use the technology. I've run into situations where it actually worked to a company's benefit.

QUESTION: Looking forward to the continual evolution of the technology transfer office, is that considered to be the vehicle for creating synergies for research between universities and companies? I know from a company standpoint, as I work for a company in the R&D side for over ten years, we used to look at universities a lot for these collaborations but at some point, things changed and now we go overseas, for

the most part, and look. Not just because of maybe some of the terms are better—I mean we have more control over what's generated, as far as from a property standpoint—but also costs and how much it costs to do research in the U.S. versus somewhere else. It's almost like an extension of the manufacturing issue of do you make it here or do you make it elsewhere. Now the thing is do you invent it here or do you invent it elsewhere. And how are the tech transfer offices going to react to that, to keep the pipeline open for these synergies between universities and companies to continue?

KEN NISBET: I think you have to break that question into two parts. Tech transfer offices are really interested in having technology results, our research results, being used by industry. If you really want to know about the relationships of how to engage the universities to do some work collaboratively, it's really the sponsored research group, which is separate from tech transfer typically, or corporate relations, or obviously just personal interactions that occur. And I really can't comment too much about whether we are becoming more or less competitive, but it certainly does seem, when you look at the dramatically increasing levels of research going on at universities, the chronic shortage of space, the talent drain in both directions, that it's becoming more difficult, but obviously there is a lot of good research going on. Most of that is federally funded and not as much corporate-funded. It depends on the strategic direction and intent of the university, and again the economic development aspects of that as well.

DR. CARL GULBRANDSEN: I think that there is some truth to what you say, that technology transfer offices are getting more and more involved. The university technology is at a very early stage. It always needs a tremendous amount of development before it can become commercialized. These early stages of development often are efficiently done at the university and we encourage the companies to use our talent in the laboratory. In fact we have a program in Wisconsin, that the first seventy thousand dollars of any license agreement goes right back into that laboratory, to help fund additional research in that area. So the company that pays gets that research without having to pay overhead. So there are professors like that and companies like that. But it is a recognition that university research can be cost efficient. And licenses can help drive sponsored research at universities.

PROFESSOR REBECCA S. EISENBERG: We have time for one or two more questions.

This is Larry LaVanway, a law student who's also had some experience in tech transfer.

AUDIENCE MEMBER: A couple of times during this panel a few people have mentioned that because a lot of this technology is done from the universities, it's more basic and fundamental in nature, and therefore it creates a lot more effort and investment to get it into the marketplace. And I'm wondering if newer, kind of younger, generations of researchers and people affiliated with the academia are more aware of the technology transfer option and possibly looking at more applied research in their labs, because they're aware of this option now, as opposed to just simply publishing in academic journals and going to academic symposiums. Instead of just simply publish or perish, it's maybe publish and/or patent or perish. And, therefore, the inordinate or very large amount of investment that's necessary to get this into the marketplace is maybe decreasing because new, younger generations of researchers are more aware that this is an option. Do you see a trend in more applied research because of the options for technology transfer, or is it still basic research?

KEN NISBET: I actually don't think there's a trend towards more applied research. Obviously I think people are more conscious of the work that's required to make their research attractive and are more aware of the technology transfer option. But it really stems down to what's exciting and stimulating. That's why they're at the university. Typically it is very early, very exciting research and that's what they want to do, and they'd be bored at finishing the job. I mean I saw that in industry as well. There's different kinds of engineers, different kinds of scientists. In the end, I think the answer is probably to continue to work with people and find additional resources, things like gap funding, things like finding a particular development or marketing specialist. You know, Larry, by the way, participated in an internship program we have here at the university. And in applying resources like interns towards projects to help reduce the risks and make it more attractive is a very good strategy. So in the end I don't think you can dramatically change the way research is done, but we're trying to add resources to make it more attractive and less risky for outside partners.

MEL KRONICK: I do have a sense, and I read some similar things in preparation for coming here, that the issue of tech transfer is creating a bit of a schism between different camps within universities. Some people just want to not have anything to do with the technology transfer process or any of the limitations that people place upon themselves when they have to think about the patenting system. This is in spite of the downsides such as Carl talked about in the particular example of the Vitamin D therapy. I recently read that Professor Steven Austin, who's at Princeton, says that when the subject comes up, he just doesn't want to

collaborate with people that are going to try to patent what they're doing because it just distorts what he perceives to be a fundamental value of the university system. So I think it's still an issue which universities themselves, I think, are struggling with. It's an interesting issue as well with everything going on now with regard to publications. There's a big movement now to trying to set up web-based journals that go around copyrights associated with the for-profit journals that exist out there. It's creating another interesting intellectual property controversy within the university of whether to publish freely or privately.

DR. CARL GULBRANDSEN: I think I agree with Ken. Wisconsin is very active in this area, but I don't know that there are many researchers that I have contact with, that have really changed the style of their research and are going more toward applied research. There's certainly much more interest in startups, which is a little bit different issue. It's very sporadic across the university, whether anybody's given credit for a patent or not. Most departments don't give you credit for the number of patents that you have on your resume. If you're Hector DeLuca, at the University of Wisconsin, and you've brought in a hundred million dollars, they give you credit for it. You become Chairman of the Department. But that's an unusual situation. So I don't think it's a whole lot different, other than there's more awareness today.

PROFESSOR REBECCA S. EISENBERG: Well thank you very much for a very provocative and interesting discussion.

INTRODUCTION

MATT MOCK: Thank you Professor Eisenberg and thank you very much to members of Panel III. It's a great discussion. And before I introduce our closing speaker, I want to encourage everyone to take a moment to fill out the evaluation forms that you got in your packets. Or if you need a form, please raise your hand and we'll hand you one and a pencil. You can place the forms in the metal basket that are on the table outside this room. Or if you'd like you can mail the form to the address that is on it.

And now to give some closing remarks, summing up what we've learned here today, I'd like to present Professor Lempert.

PROFESSOR RICHARD O. LEMPERT: I looked at the program and it says closing remarks four-fifteen, next event six-thirty. This gives me a lot of time to fill. But don't panic. You are going to be partly in control of the time. We certainly will not go past five, and I'm not going to speak nearly that long.

The staff of the Michigan Telecommunication and Technology Law Review have thanked everybody but themselves. So on behalf of the speakers and those in the audience, I want to thank you all for mounting this terrific conference, taking the initiative, having the idea, and proceeding. The three students that I think have done the lead work are Matthew Mock, Larry LaVanway and David Abramowitz. So I thank you very much for this intellectual feast for the law school and people in the community and around the university. Also, as a panelist who came from out of town, I want to thank Maureen Bishop who has been responsible for our care and feeding and transportation and everything else. She has done a great job. I also want to say a word with my hat on as Director of the University's Life Science Values and Society Program. LSVSP is pleased to be one of the cosponsors of this event and to have played a role from the start in talking with the staff and journal about the paths this conference might take. Many of you know about the LSVSP. Those of you who don't know us can be kept abreast of future activities of this sort by going to the University of Michigan website, following the Life Sciences link to our web site and signing on to our mailing list. If your interests change and you no longer wish to hear from us, it is just as easy to get off.

I have some remarks to make, but you all have sat through this day and I think you've heard a lot and learned a lot and we've had a lot of questions. So by way of summary, I'd like to invite people in the audience to give statements, not to ask questions. If you have any observations that you want to make, based on what you've heard today or on other concerns, here is a chance to share your observations.

AUDIENCE MEMBER: Thanks for the opportunity. I first want to say that I'm from the business school, I'm an MBA student. And I came back to school after thirteen years in industry, again in the R&D side, engineering, because I realized that most of the times technology was interrupted or innovation was interrupted, not so much because of the technology issues but because of legal or business issues. So I came back to school to understand a bit more about that. Since then I've come to understand or think of innovation more of like a parallel to a supply chain. At one time companies were highly integrated and they manufactured everything their products needed from nuts and bolts, but today they mostly buy a lot of that stuff when making it is not value added. They focus on manufacturing just the part that they're best at. I think innovation is going the same way. Products are more and more complex and no matter how big a company is it cannot invest the trillions of dollars it would take to invent everything it needs. There's just too many

bright people out there. So that's what my interest is in and how I came to this panel, because of the tech transfer side.

I think there is an evolutionary path that needs to continue or accelerate so that we get to some synergy level between universities and companies that doesn't exist right now. I think that if we add up the parts, we only get the sum of the parts and nothing greater than the sum. I think universities could be great suppliers of innovation to companies, but as was pointed out, companies need to be true to their strategies and to their stakeholders. Thus, we must continue the dialogue to figure out where are the opportunities to keep the truth and the ethics side in sight. You are a university, and you are doing research to improve the common good and to get innovation in the hands of all innovators, but you must figure out how your innovations fit the incentives of a business scheme so that companies can multiply their value and spread it through the globe.

So my statement is that I think universities among themselves are still very isolated in how they collectively market their innovations and offer them to companies that are seeking not to reinvent the wheel every time, and not to reverse engineer, and not to work around patents, but to just figure out how they can legitimately utilize innovations for their products. On the other hand, companies need to understand that in universities, in particular, the biggest value is the creativity and not try so much to push investigators or professors to deliver a product that's almost ready to market. Those are the observations that I want to bring to the table. And again, I thought the panel was fantastic. Thank you.

PROFESSOR REBECCA S. EISENBERG: I'm going to hold you all to two minutes, I should note.

AUDIENCE MEMBER: I applaud the organizers for this conference and also all the attendees because I think Ann Arbor needs more, as a community, and we all have to participate in the theme of talking about life sciences. But being an MBA student and also working for a biotech company, the role of law is so apparent to me, whether it be the deal structure between the company and university or the company and venture capitalists. When you're trying to commercialize a product and you have to go through the USPTO, and have to work to gather data for clinical trials, and have to set up manufacturing policies, and try to submit data to the Senate for Medicare/Medicaid Services, you realize the power of law. I think that it is a tribute to the organizers that we're talking. Hopefully we'll have more discussions about law and how when you're trying to commercialize a product you need to work with the university, the government, all the different players, and other companies. So I think it's good that we addressed—I mean we also talked about life

sciences and biology—that bringing that out is very important, just to realize that you can't escape law when you're trying to commercialize life sciences.

PROFESSOR RICHARD O. LEMPERT: Other comments? Well if there aren't any I'll share some closing observations with you. I didn't prepare anything in advance but just noted issues that arose during different presentations. So I will be taking you back through points that struck me in the talks and share some reactions with you.

Listening to Alan Saltiel and his opening remarks and hearing him talk about complexity (which is an important buzzword and problem area in modern biological life science research) I was reminded of what's become a mantra of mine. As some of you know, I'm now at the National Science Foundation, on leave, temporarily, to direct the Division of Socioeconomic Sciences. This is a relatively small program. I think our Directorate, which includes the Behavioral and Cognitive Sciences as well, has a budget of about a hundred and ninety million dollars when the next smallest program has half a billion dollars to spend. As you know the other sciences are often referred to as the hard sciences. That might be true, but the social sciences are the difficult sciences. That is, the problems that the social science deal with are in many ways less tractable than the problems with which many so-called hard scientists must contend. I have no doubt that given enough time and investment we're going to uncover the causes of many diseases, that we will understand the genetic structure of germs and advance pharmacogenomics among other things. I have much more doubt that we'll ever resolve satisfactorily and, without considerable clashes, debates about human embryo stem cell research or therapeutic cloning. The issues that we're trying to grasp in a forum like this are truly difficult. This is, in part, because their answers cannot be found through hard science. There is no one best patenting system for biological products, or if there is, nobody knows or can prove what that best system is in the way scientific hypotheses can be tested and proved.

At the same time, I think we've learned from these panels something else I deeply believe is true. Scientific progress and, particularly the hard science progress, has become inextricably linked with developing effective ways to deal with value and other social issues. Several forces put up roadblocks to scientific progress, such as the potential roadblock to therapeutic cloning if Congress passes certain bills now before it, and the President signs them as he says he will. We have also seen progress slowed by disputes over embryonic stem cell research, suspicion of GMOs and similar bones of contention. In short, the advance of science

depends, in part, on our resolving the kinds of issues that we have been discussing today, at least to some point of general satisfaction.

Listening to Philip Reilly, there was much I found intriguing. I was particularly struck by his interesting statistic that more bills were introduced in state legislatures across the country on the topic of regulating genetic information for insurance purposes, than any other topic. When you think of the concern with crime, with welfare and with the economy, it seems extraordinary that somehow genetic information should be at the top of the attention list of state legislatures. There are lots of reasons for this. One is that there are real problems here, though, ironically, at the time these bills were being introduced, we were far from having to confront most of them because we didn't have that much genetic information which was of use to insurers. Hence, while I think the spate of bills on genetics and insurance are aimed at real problems, they also reflect something else, fears of change and of the unknown. For a while with respect to biotechnology and now in nanotechnology, there is substantial fear of what the future holds. Some of that fear exists for good reason and sometimes one wishes the scientists advancing these technologies were a bit more fearful. Some of it is of the "person's read too much science fiction" variety. People think that dangers they can imagine are imminent or certain to happen at some time. These fears are also fed by publicity seekers, like the people who claimed to have cloned humans. But whether fears are justified or not they are real and need to be taken seriously and responded to. This is in part for the sake of those who needlessly fear and in part because even baseless fears can derail scientific progress. It is also in part because fears that are not baseless may be underappreciated by scientists or commercial exploiters of science, each of whom has incentives to ignore the dangers of low probability, high cost outcomes. We have seen possible examples of this in several gene therapy trials including, most famously, the research at the University of Pennsylvania that led to the death of Jesse Gelsinger.

Because popular fears tend to focus on outcomes that are unambiguously bad, usually extreme and easy to characterize or visualize, I think popular fears often lead us to focus on the wrong issues or the wrong aspects of issues. GMOs (genetically modified organisms and crops) are a good example. As Phil Reilly has pointed out, both here and last night at the conclusion of *Ann Arbor Reads*, GMOs may not be accepted in Western Europe, but everyday in China farmers are planting more and more GMOs, and they're doing it for a good reason. They have a large population to feed, and they're finding they have a much better yield per hectare from GMOs, than from customary crops. GMOs allow them to feed China's population, prevent starvation and save lives. Clearly

GMOs have tremendous potential for good. The problems, which has stalled the acceptance of GMOs in Europe and which gives many people pause is the fear that if we eat these so-called "frankenfoods," we will be seriously harmed. I don't think these fears are completely fanciful; in particular the danger that we may be obscuring or creating allergens which may harm a small percentage (but still a large number) of people strikes me as real. However, only limited gene transfer work has been done in food crops to date, and no widespread harm has been reported. I'm not, however, sure that immediate adverse health consequences is the danger that demands most attention, especially as those producing GMOs are acutely aware of this potential for harm and of what GMO-induced deaths would do to their markets.

Let me illustrate my point about misplaced concerns by switching the example. Some years ago, Monsanto got in big trouble through its inclusion in certain seeds of a "terminator" gene. This gene meant that crops grown from Monsanto seeds would be sterile, so those planting these GMOs would always have to come back to Monsanto for more seed. They couldn't save seed from their crops for planting. Monsanto took a lot of flack about how this would destroy subsistence farming; they were named exemplars of corporate greed, etc. Eventually Monsanto terminated the terminator gene.

I don't want to denigrate the concern about the culture and livelihood of subsistence farmers, nor do I want to claim that Monsanto is less concerned with maximizing profits than the next company, but I do want to point to another concern about GMOs, which may have considerable substance. This is the escape of GMO varieties and genes into the environment. I don't know enough about the biotechnology, but it seems to me that we might want to incorporate a terminator gene in genetically modified crops not to maximize profits but to prevent the uncontrolled spread of GMOs in the environment and cross-pollenization with native species that can then reproduce. Another example is the concern over BT corn; that is corn that has been genetically modified to produce BT, a natural pesticide. People oppose its planting by appealing to the yuck factor. Here is the yuck: do you want to eat insecticide? Behind this yuck, there is a serious issue, for the concern is not so silly that it may be dismissed out of hand. But willingly or unwillingly virtually everyone in this country who eats corn or soy beans or products made from them has been ingesting these BT products, and no clear evidence of harm has to date emerged.

My fear is that this concern for health draws our attention away from more likely harms. It is almost certain, indeed it seems to be happening already, that over the not very long run insects that feed on BT corn and

soy beans, will evolve, so that the pesticide is no longer an effective way of controlling them. If this happens what we will have done is taken an organic, natural pesticide, (one of the few that organic farms have available) which if used selectively and on a limited basis, might be useful for the next fifty or a hundred years, and shortened its effective life to perhaps ten years, before insects evolve so that they are not affected by BT, whether it comes in corn or it comes in the application of a pesticide. Again, what grabs the popular imagination and what creates the fear is not always a likely harm, and it can distract our attention from problems that should be of more immediate concern to us.

Now let me turn to regulation of life science research, and share with you several concerns. One concern is widespread within the social sciences. Because the potential dangers faced by subjects in clinical trials involving new biotechnologies and celebrated lapses in research ethics with tragic consequences (the study that recruited Jessie Gelsinger comes to mind), universities, spurred on by the federal government, are erecting higher barriers to research involving human subjects in the form of more careful Internal Review Board (IRB) examinations of research protocols. In the abstract, it is hard not to applaud this. But many social scientists complain that IRB's are applying standards designed for situations in which there may be lives at risk, to surveys and other research with very low harm potential. Standards of informed consent well suited for subjects in clinical trials where lives might be lost can make low risk social science research, like some survey research, difficult if not impossible. For example, if a survey researcher must explain why a question is being asked, answers may be so likely to be distorted that they are useless. In short, clinical models of research do not always apply in other settings and we must be wary of taking this one model and applying it across the board. More generally, this issue serves to remind us of the subtle ways in which life science research has widespread ripple effects. Ripples of life science research that are of low visibility in universities or social systems occasionally become far more salient because of the issues they raise.

It's also worth reflecting on the instinct to withdraw funds for politically controversial life science research. As Becky said, this is a questionable strategy, even from the point of view of regulation, because funding gives leverage for regulation. Funders can impose rules for how money will be spent, and the possible withdrawal of funds is a powerful incentive to meet standards. If our government is not funding human embryonic stem cell research (HESCR) or is funding too limited a set of cell lines to allow rapid progress, the research is likely to find a home in other countries or in private industry. This research will almost certainly

proceed with much less regulation, oversight and transparency than would occur if our government were funding it with a set of reasonable regulations and reasonable requirements for transparency. The problem is that official support for human embryonic stem cell research has a symbolic importance for some politically powerful groups such that they prefer the official affirmation of their values to policies that may make their concerns less likely to be realized.

This reflects a more fundamental problem which has helped shape the debate on both therapeutic cloning (i.e. cloning not designed to produce human babies but rather to produce stem cells that might be used to fight disease in the cell donor) as well as human embryonic stem cell research. I'll use the latter as my example, and simply state my position in the debates about this research. Becky referred to HESCR as morally controversial, or morally problematic. I see nothing morally problematic about the HESCR that's being proposed. I see nothing morally problematic because although it's true that this research uses and destroys human or pre-human life (depending on when one thinks human life begins) the proposed sources are embryos that were created for in vitro assisted reproduction, that were not needed for this purpose and that after a period of time in storage will be destroyed. (It is estimated that more than 200,000 such embryos are in storage today.) No human life, assuming barely visible embryos are human life, that would endure is destroyed nor, from everything we know, will any life experience pain. Created cell lines will, however, endure and will be used to find ways to preserve the lives of babies and other people and prevent their suffering and pain. The hardly differentiated embryo—no larger than the period at the end of this sentence—suffers no different fate than it would have eventually suffered, and some people's lives may be saved or wonderfully transformed. So I personally don't see any moral problem raised by HESCR unless it's the moral problem of preventing research that could save human lives.

But there are large numbers of people who feel differently. To them, the moral question is as clear as it is to me. For them, human life begins at conception, and it doesn't matter if the embryonic sources of stem cells are doomed anyway. We should not intentionally be taking their life whatever their likely eventual fate. Life in this view must be respected, and no matter how noble the aim in taking it, it cannot be treated as a means to an end, even the end of saving other lives that are not necessarily doomed.

How does one reconcile these competing views? I do not see any way. I also think we should recognize that these are both legitimate moral positions. Decent, thoughtful, moral people can hold different

positions in the HESCR debate, but by and large, they can only talk around the problem. If one side objects to the claim that the embryos used will be destroyed anyway by saying they might be adopted, the other side says it is willing to make adoption a priority and use only embryos that will be discarded, but the response seldom persuades. If responses like these don't persuade, I don't think we can persuade, and we certainly shouldn't coerce opinion change.

So what can we do to resolve these issues? I think we actually have a very good way of resolving the issues, and it's called democracy. When we have value conflicts, we can vote on how we want to resolve them. Democratic resolution works as well or better than other methods of resolving value disputes so long as it combines two things: majority rule with respect for opposing positions. Even while imposing a resolution—which is what even democracies do in the end—each side should recognize that differing positions in the HESCR debate are not silly but reflect deeply held positions by thoughtful moral people. The winning majority should not run roughshod over the minority but should require only the minimum that must happen to implement its views while maintaining maximum respect for the other's position.

Problems with the democratic solution arise when a minority has political leverage, meaning that through political pressure, its views can prevail over the majority's. It doesn't matter if the minority is the biotech industry or a "right to life" or "right to choose" lobby. Minority control tends to delegitimize resolutions and creates tensions that are difficult to resolve as well as resentment on both sides.

The Conference has raised a number of other fascinating issues. Consider the question whether people should retain ownership of body parts removed in surgery and in cell lines drawn from their tissues. One might argue that giving individuals ownership rights will not help them at all because surgeons, researchers and hospitals can always make waiving ownership interests a condition of operating, and what patient will refuse a possible life-saving operation because he wants to retain an ownership interest in an organ to be removed. Contracts for surgery will invariably be contracts of adhesion. It is, of course, not clear that we should want to give patients ownership rights in their tissues, for no matter how unique their biological material, it is the researcher's work that gives it its value. But if we do see a moral or ethical problem here—after all what is more completely one's property than one's body—traditional notions of ownership are likely to be of little help in resolving it. Rather, we must consider unbundling the concepts of ownership and the idea of property rights. We might, for example want to give people inalienable right to a percentage of profits that can be traced to research using

unique features of their tissues while not letting them exercise other prerogatives of ownership, such as blocking the use of one's property by others regardless of reasons. We must, I would argue, deconstruct traditional notions of property and reconstruct them if we are to deal effectively with the numerous issues that advances in the life sciences are likely to raise. Creative lawyering may be as important as good science in realizing the benefits of what science allows. Lawyers should do a lot more thinking about those issues.

Gene patents provide another example of policy issues that require legal and social science attention. Maybe we want to allow genetic information to be patented for some purposes and not for others, or perhaps we should allow wide open patenting with compulsory licensing. There are many points midway between total ownership with the full bundle of property rights and denying property interests altogether. Indeed as we heard today that universities and other actors are asserting or enforcing property interests that are compromises between competing values. We also have groups, like the SNP consortium, that is rushing to put information in the public domain so that it cannot be patented. The federal human genome project had similar policies and provided for the release of genetic information almost as soon as it could be ascertained.

One problem which the issue of property rights in the genome has in common with other issues raised by advances in the life sciences is that there is little consensus about the basic principles we should draw on to resolve it. Yet we need to draw on core principles if we are to get beyond self-interest and the political lobbying that goes with it. The problem is we don't have a basic consensually agreed-upon set of principles. Moral philosophy, where one might look for such principles, seems of little help because moral philosophers themselves have no agreed-on perspective. Different bioethicists draw differentially on the virtue school, utilitarianism, deontological philosophy and other perspectives. It's going to be hard, if it's possible at all, to come up with a core set of moral principles that most people, or even most philosophers, will accept.

Some questions are to be sure, easy. Today, for example, the permissibility of human reproductive cloning presents an easy question. I don't know of any responsible life scientist, social scientist, lawyer or ethicist who believes we should be creating a human "Dolly." But this is an easy question because the science itself suggests that there are tremendous risks involved. Suppose, however, these risks diminish, and experiments with primates convince us that cloned babies will encounter no more difficulty than babies that result from in vitro fertilization. What then? Surely, opposition to human reproductive cloning will not melt away entirely. Indeed it may hardly melt away at all, but it is likely that the

consensus that now exists on the issue will be shattered. Moreover, even among those who reach similar conclusions, principles that justify the conclusions are likely to differ.

The final point I wish to comment on was raised during the last panel's discussion of the challenges of managing tech transfer and the issues that arise in considering tech transfer. It is fair to say that this panel was composed of three cheerleaders for university involvement in tech transfer, and I will confess my own bias, which is that I am somewhat of a cheerleader as well. I believe it is on balance a good thing for universities to be involved in tech transfer to try to facilitate the application of university based inventions to the resolution of human problems while returning a profit to the university. But as some of the questions indicated, there are many people, particularly within universities, who are deeply concerned about the implications of tech transfer. Their concerns are not frivolous. A major concern is that research directions will be distorted and the openness associated with university-based research will diminish. There is evidence this is already occurring. At the University of California, Berkley, for example, one department in return for substantial financial support purportedly established a research agenda to please a commercial supporter and agreed to give the company an early look at all research results produced by department researchers regardless of whether the company's funds had supported their work. But even without such overt institutional commitments, commercial interests will almost inevitably effect individual research. Imagine a scientist who has a choice of working on two problems that are intellectually fascinating and practically important. One of them is perhaps a little more interesting, but the other one, if it succeeds, will make the scientist wealthy. Which topic will the scientist study? I don't know about you, but I would shamelessly choose the one that might make me rich. I don't think this choice is a sin, but in the long run and in the aggregate, such choices risk the distortion of priorities and ignoring of basic research in favor of work with more immediate financial pay off.

There's also the issue of whether universities are subsidizing private gain. Few university professors entered the academy to become rich and few have done so. But, although only a small proportion of professors have grown wealthy from their research, stories of such people circulate as do stories of professors who have subordinated teaching and scholarly duties to financial interests. Regardless of the representation of such stories or even their veracity, their circulation can do harm. Universities can lose good will and invite regulation and people less committed to academic values may be attracted to faculty ranks.

Of more immediate consequence are the effects of commercial support and interests on publication and sharing research materials. We are, I think, in the last decade or so, seeing delays in publication, pending legally protective disclosures and maintaining secrets to see if there is a commercially valuable further step that could be taken before work is publicized. There is particular concern about the effects that commercial considerations have had on the transfer of cell lines and other biological materials between researchers and laboratories. Delays in or roadblocks to research also arise out of efforts to work out the intellectual property implications of shared materials and technology. Transfers may, for example, be forestalled by disputes over "downstream" rights. As troubling are claims that graduate students are being exploited, by, for example, being assigned projects that advance a supervisor's commercial interests rather than projects that best meet the student's intellectual interests and educational needs. One even hears tales of graduates whose thesis completions were delayed so that they could continue to work on a professor's commercially promising studies. And professors who spin off companies to exploit their discoveries may hire their best graduate students rather than direct them to academic careers.

I don't want to exaggerate any of these claimed costs to university tech transfer, but I think we have to be aware that these are concerns that some university faculty voice; that they have led some faculty to oppose efforts like the University of Michigan's Life Science Initiative, and that none of these concerns is completely fanciful. Problems with excessive secrecy, publication delay, difficulties in securing or transferring biological materials and the exploitation of graduate students have all been described in the literature. So it was that when several years ago LSVSP cosponsored a forum dealing with some of these issues, we had as a theme "Facing the Brave New World." And this is what we must do. We have in the modern life sciences tremendous potential for good for the sciences, for the university and for the larger society. This potential is being realized every day, at the University of Michigan, in the state's Life Sciences Corridor, throughout the United States, and within foreign countries. At the same time, there are red flags that signal real dangers. It wasn't likely that Jesse Gelsinger would die in gene therapy, but he did. Altered genes from genetically modified corn weren't expected to be incorporated in native Mexican maize, but this has apparently happened. Lots of other untoward outcomes are not likely, but they may occur. We must work to anticipate them and try to minimize the likelihood they will come to pass. We won't always succeed. But absent horrendous bad luck, the fruits of life science research should far exceed its costs.

MATT MOCK: Thank you very much Professor Lempert. And thanks everybody for coming today. If you're registered for our banquet, it begins tonight at the Campus Inn, at six-thirty. Thanks again. Have a good night.