

Presidential Commission *for the* Study of Bioethical Issues

TRANSCRIPT

Incidental Findings in the Direct-to-Consumer Context

Meeting 13, Session 6
April 30, 2013
Washington, DC

DR. GUTMANN: Our first speaker is Dr. Thomas Donaldson, the Mark Winkelman Professor of Legal Studies at the Wharton School of the University of Pennsylvania. Dr. Donaldson is also the director of Zicklin Center for Business Ethics Research at Wharton and his book, "Ties That Bind: A Social Contracts Approach To Business Ethics" was the winner of the 2005 SIM Academy of Management Best book Award.

Dr. Donaldson is a founding member and past president of the Society for Business Ethics. In 2002 Dr. Donaldson testified in the U.S. Senate on the Sarbanes-Oxley corporate reform legislation. In October 2006 he delivered a half-day address for the Secretary General of the U.N., Kofi Annan, and the other assistant secretary generals regarding the U.N.'s reform initiative.

He was named the most influential thought leader in "Ethisphere" Magazine's 2009 ranking of 100 most influential people in business ethics. And Dr. Donaldson has written broadly in the area of business ethics, corporate governance and leadership in wide ranging publications. Welcome, Dr. Donaldson.

DR. DONALDSON: Thank you. Thank you very much. The only qualification you failed to mention is you're my boss.

(Laughter.)

DR. DONALDSON: It's important, I think.

DR. GUTMANN: I'll remind Dr. Donaldson he has tenure.

(Laughter.)

DR. DONALDSON: It's an honor to be here. What an important issue. I want to talk a little bit about current views, dominant views on how we see the responsibilities of corporate organizations, and, of course, especially with an eye to some of the organizations that are forming with respect to consumer providers.

The question that I was asked initially to address was whether or not corporate responsibility extended beyond contract. And, I'm sorry to say that the dominant view that prevails in business schools today and in economics is not very much; that is to say contract lies at the bottom of pretty much everything.

The current view of the firm rises out of traditional, sometimes called neo-classical economic theory. In the backdrop always is the conception of the market with three individuals making transactions regulated by agreements or contracts that are voluntarily entered into. From this you get something, at least theoretically called pareto optimality, a situation in which nobody can be made better off without somebody being made worse off, which is not bad. It doesn't always work that way, but that's not bad.

The firm, business organization, that's in some ways almost an afterthought. It is a way of making the market more efficient. The firm is a way to make the market more efficient. It's a way of creating incomplete contracts that are more efficient, substituting authority relations organizations. And we have a couple of Nobel prizes that have been won on that base, Coates and Williamson.

So the classical view is what I'll call now "dominant view." It also entails that corporate actors follow the law. Against the backdrop, there's a normative expectation that corporations will follow the law. This view, however, is coming under increasing pressure. It hasn't yet fallen. I predict it will fall within a decade or two, and what is coming into its place is what might be called neoclassical views. These are views that in essence say the firm is not only about maximizing return on investment for share owners, it's also about something else. And if it's a stakeholder view, which I notice is referenced in one of the readings, it basically says the corporate manager has to

understand their other stakeholders. There are customers. There are employees. There are members of the surrounding community.

Some things are owed to them. If it's a social contract view, which I am most associated with, it affects us. All these individual contracts have to be integrated with micro social contracts, that is, social contracts in effect integrating with the individual contracts, sort of holding control in a way that expands the obligations of the corporation beyond merely satisfying the interest of the owners.

Now, I've got to tell you there's been tension with the dominant view for a very long time. For the last half century, we've served as business executives, only a minority -- and a fairly small minority -- are forced to choose between the corporation is only about maximizing profit for the shareholders and the corporation is about helping the shareholders, but also about helping other stakeholders. So in reading numbers -- people in anonymous surveys -- executives choose the latter view. And this runs about 70% of the United States. By the time you leave the United States, it goes up to 80, 90, 95%. So this view -- I mean, the irony is we're still teaching this view in business schools, but there's an angst.

There's a discomfort that's been fermenting for quite some time, and I think one way of understanding the pressure on the dominant view is to see how limited the values are that hold sway on this view. Basically, you've got property, fiduciary duties; that is, duties that people have to people who give them money; economic freedom, contract, promise keeping. That's pretty much it. Fairness, justice, human rights, right to privacy; those don't figure at all in this view. And most of us understand those somehow have to figure in.

Well, I'm going to in the remaining few minutes I have focus on the

ascending views, these neo classical views, because I think they're the right ones. And let me say a little bit about social contract approach and its implications for incidental findings. The idea of the social contract is you could have micro social contracts. People can agree inside an industry, inside an economy, maybe even on a global level to set up rules, but these are always bound by more fundamental rules. My colleague and I call them hyper norms. You could call them fundamental moral principles. A good example would be human right.

It's interesting, though, when we start to hem the corporation in with something like a human right, even there we have to recognize the different character of the for profit organization. I mean these corporations are taller and richer than most of us, but they have exceedingly narrow personalities. They don't cry at funerals. One English barrister once remarked: "You know -- no soul to damn nor pants to kick." They are chartered for a very special reason. They are efficient, and for that reason we're something like a human right.

We've tended to assign -- it's almost a grand, micro social contract that's tended to assign only two or three major classes of duties to those organizations to not deprive somebody of the object of a right directly, to in some instances protect the right from deprivation, but not to restore the object of the right. Clothing the naked, feeding the hungry -- this is not usually an obligation assigned to a corporation; to us, and certainly to governments, but not to corporations, except -- except -- and it's generally agreed, in rescue situations things can change. And that is implications for incidental findings.

If I run Merck and my company has only intellectual property that's capable of curing river blindness, I may have a special obligation; and, that obligation

may extend beyond my obligation to enrich my shareholders. It may even mean that the firm has to sacrifice profits; and, that is generally accepted in most of the literature.

The social contract theory underscores the importance of evolving microsocial norms, and that's what we have with incidental findings. We have a lot of new technology. We have a lot of new routines. The direct to the consumer example is an example of not only novel technology, but of novel ways of marketing made possible now by the Internet. And we should be reminded that as microsocial norms evolve, being challenged by innovation, things get very messy.

Very important for those norms to evolve; think, for example, of what very simple technology now, the kind of technology that extended life over the last century, simple stuff: feeding tubes, oxygen. End of life situations became much more difficult, and in the beginning when we threw the Hippocratic Oath at it, it wasn't very helpful. Now we're living wills, codes, committees and so on. We've started to develop some microsocial norms that can deal better with some of those end of life situations that innovation created. And my suggestion is that the same is true in managing incidental findings. And this will sound odd, because I'm not an opponent of regulation; but, one of the things we have seen in the context of innovation that pushes the need for microsocial norms are the limits of regulation.

Now, we already know regulation can do some bad things. It can suffocate innovation, and in some instances it can protect established interests. I mean regulatory capture is not an unknown phenomena. It can be very expensive, but I'm really focusing more on two other limits that are especially relevant to the present context. One, innovation tends to race ahead of the capacity of regulators to manage the process.

Asbestos is probably the classic example. Chemists inside of the asbestos industry knew long before regulation could catch up about the dangers of asbestos. Now, they had obligations. They weren't legal obligations at the time, but they had obligations anyway. In the financial crisis, regulators couldn't understand as much as the person who was actually structuring one of these highly leveraged, collateralized derivative products. Inside the industry they knew more. BP -- Think of the oil flowing off the bottom of the ocean floor. You notice for the first month we had to listen to the BP scientists, because the regulators didn't quite understand what was going on.

The other is that regulation and the government works well, typically, in the jurisdiction from which it emanates, but less well abroad. And we live in a global world. I mean this direct to consumer stuff; it can come from anywhere, right, around the world. And in the absence of a global, legal mechanism, and we don't have that now, we have special challenges.

My final recommendation in effect is that in addition to regulations with respect to direct consumer entities, companies can be let off the hook. And, in some instances, that means they have to work together. Competitive disadvantages can be created, if I have to pay a cost, a safety cost a competitor does. So in an industry without collusion or antitrust, some of these things can be anticipated as they can be better off in the industry by the outside. Things can be created that regulation can't handle.

Do we have examples of that? Securities industries with FINRA; out of the industry Canadian Chemical Manufacturers Association with a responsible care initiative would be another example. And, here, by the way, the law can actually be an enemy. Some antitrust initiatives and court law can make it almost impossible for

people in industries to have the kinds of open conversations that they need about dangers that confront society.

DR. GUTMANN: Thank you very much. Our next speaker is Gail Javitt. Gail Javitt is counsel at the law firm Sidley Austin in their Food and Drug regulatory practice where she focuses on FDA regulation of medical devices, biological products and pharmaceuticals. She also advises on regulation of clinical laboratories, under the Clinical Laboratory Improvement Amendments, CLEA, and several regulations of clinical trials.

Ms. Javitt is also a research scholar at the Berman Institute of bioethics at Johns Hopkins University and has served as adjunct professor of law at the Georgetown University Law Center, University of Maryland School of Law, and American University's College of Law. She received her JD at Harvard Law School and her MPH at Johns Hopkins. She has written extensively on the intersection of law, science and policy, direct-to-consumer marketing of genetic testing, and FDA regulation of biotechnology.

Welcome.

MS. JAVITT: Thank you. Good afternoon, everyone, and I appreciate you inviting me here to talk to you this afternoon.

(Slide.)

MS. JAVITT: So in my 10 minutes, I'd like to very briefly cover these three bullets that you see on the slide, "Defining Direct-To-Consumer Genetic Testing," so we're all working from the same hymnbook, as it were, giving you really a thumbnail sketch of the regulatory landscape, and then trying to think through what does an incidental finding mean in the context of direct-to-consumer genetic testing. So, the

first; and, as a lawyer, I always try to start with the definitions.

Direct-to-Consumer: Certainly, what I think we're talking about is a testing paradigm in which the consumer decides whether to order a genetic test, what test to order, requests the test, performs the procedure necessary to have the testing done, which is either saliva test or blood spot, and gets the results directly. There may or not be a physician involved to order the test, depending on state laws, and I'll talk about those in a few minutes. But, it's not the traditional paradigm where you go to your doctor and they say, "We recommend you do the following test." It's something very different. There may or may not be counseling involved.

When we talk about a genetic test -- moving to the next word in the phrase -- it could be a single gene test, several genes, SNPs, or sequencing of a large part of the gene; or, more, even the whole gene, while that's not yet affordable for most mortals. And, then testing. Well, testing means the same thing it means in the non-DTC context. It's a laboratory analysis of a sample.

So as I said just a few minutes ago, it's a method of marketing genetic testing services. So, any test, in theory, if you can perform it on a saliva sample or a blood spot, could be provided DTC. And, last I checked Genetests.org, there were several thousand diseases for which genetic tests were available. So it's potentially very broad. And in the interest of time, I'll go here. So although it's potentially very broad -- let's get these all out there -- in practice there's been a more limited subset of tests that we have seen over the past decade or so that have been offered direct to consumer.

(Slide.)

MS. JAVITT: Now, I can't tell you which one of these are still out there

today. It's a very fluid marketplace. As of about five years ago there were several dozen tests -- not several dozen companies. Well, actually, yes; several dozen companies offering more than several dozen tests. There has been a contraction in the direct consumer marketplace as a result of some regulatory issues that I will get to in a minute; but, it's very fluid, as I said. And why is that?

So there's a couple of different things that have come together to make this sort of a perfect storm: the regulatory environment or lack of a regulatory environment, or lack of clarity of regulatory environment; the tsunami of data that we have gotten from the human genome project. So we are learning so much more about the meaning of different genetic variations, and the decreased cost of doing the testing itself, that makes it something that consumers may want to order makes it affordable.

(Slide.)

MS. JAVITT: So let me switch now to regulation. Well, so what do we mean by oversight of regulation. Regulation of what, by whom, and for what purpose? And when I look at the slide, I realize I am in Washington, D.C. Outside Washington, D.C., sorry. You see an alphabet soup, and unless this gives the impression that there's a lot of regulation, I want to distinguish between agencies that could exercise some level of oversight in different parts of the enterprise and those that do. And then the third category, those that may not have the authority, but think they do. All of the above.

Let me draw down on that for a moment. So there is regulation of the laboratory activity itself, the analysis necessary to provide the results. That's under CMS, the CLIA statute, and that is basically a laboratory quality statute. It doesn't look at whether the results tell you something meaningful, just looks at whether the performance is meeting a certain level, certain standard.

Then, moving to FDA, as you may already know, FDA regulates medical devices, and that includes in vitro diagnostic devices, kits that are used to perform laboratory tests. Most genetic tests are not used. You do not use kits. They are what we call laboratory developed tests, developed in-house, using proprietary methodologies; and, there is a long, tortured and evolving history involving FDA's oversight of laboratory developed tests, generally, and direct-to-consumer genetic tests, specifically.

Moving to the Federal Trade Commission, it's there for completeness, but not necessarily because of activity. Like any product that's sold on the marketplace, the Federal Trade Commission is there to make sure that claims made about it in advertising are truthful, not misleading. DTC genetic testing has not been an active area for the Federal Trade Commission.

And, finally, the states: For the most part, this has been in the realm of the Federal Government with a few exceptions. States do regulate medical practice, and that includes laboratory practice. Some states don't permit direct-to-consumer genetic testing. Enforcement may be more challenging, but companies that are seeking to abide with the law, don't sell, for example, to consumers in New York State. And some of that is because of the control over the laboratories themselves. If you need a doctor's order or have to return only to doctors, that's a limitation on DTC.

(Slide.)

MS. JAVITT: So, not to frighten you too much with this slide, really, the take-home message is that FDA has been thinking about laboratory developed tests, and whether how, to what extent it should regulate laboratory developed tests; but, as of 2013, we still are in a bit of an ambiguous situation. With the exception that FDA has

raised significant concern about direct-to-consumer genetic tests, and has signaled that it will regulate, there are substantial concerns about its procedures that we'll use, and whether those would be appropriate and about its underlying jurisdiction to do so. But, there have been hearings, as Joanna well knows, and statements that have been made by FDA officials. It's still a revolving story.

So in the remaining time, I think we all know what people's concerns are, what the potential impact of consumers is, so I'm going to skip over that and just try to get a handle around what is an incidental finding in the meaning in the context of DTC. And there's our friend Kermit. So, when I started thinking about what is an incidental finding when it's DTC, you may have no idea what you're going to get, and just say, tell me something. Tell me everything. Well, then, nothing's incidental.

Narrowing it down a bit more, if a company is saying we are offering the following types of tests, at least maybe you have a ballpark, but you still may be surprised. So, even the esteemed Dr. Collins was quite surprised when he had a direct-to-consumer genetic test, because he had no history of diabetes, but yet he was told he was at risk. And in response, he made some health-related changes, including getting off his motorcycle.

So that's certainly a finding he did not expect, and it led to an action. There's another sense in which we can think about incidental findings in the context of direct-to-consumer genetic testing. What if you didn't ask, but they tell you anyway? So you want to know if you're going to be like your grandfather. And, you know, male have involvements and lose your hair early. So you sent in your sample. Lo and behold, the company has also performed tests for cancer risk, and they tell you something you really didn't want to know, sort of like the last panel was talking about.

Is there a legal violation involved? Is there an ethical violation? You certainly didn't get what you thought you were going to get.

And then there's a final sense, and maybe this is, if not unique, more likely in the direct-to-consumer context. When you would have thought you were getting certain information that means less than you might think it was, and sorry for my tortured English. Let me unpack that a bit. A company tells you you are not at increased risk for a particular disease, but they don't tell you the limitations of that finding.

So, for example, Tay-Sachs disease. There are many mutations, 23andMe, just to pick one company, tests for the most common, but that does not mean you are at zero risk for Tay-Sachs. It means you don't have the most common mutations; and, particularly, if you're not of Ashkenazi Jewish ancestry, you may still be at greater risk. Now, 23andMe does tell you that "We test for the most common mutations."

There's also a component of enzyme testing, which is the standard of care that is not offered when you get a Tay-Sachs genetic test. So, again, you may still be a carrier. So your finding to you, the consumer, may mean I'm not at risk. And you may go to your OB-GYN, and if they are doing their job right and ask you your background, and offer you the test, you may say, "I've been tested already." Now, is your physician going to say what were you tested for, how many mutations, did you have the enzyme? It's unclear.

So I think that's a third dimension of DTC that we need to think about.

Thank you.

DR. GUTMANN: Thank you very much.

Filling out our panel is Dr. Joanna Mountain. Dr. Mountain is senior

director of research at 23andMe, a DTC genetic testing company where she leads research projects and takes primary responsibility for the protection of the rights of those customers who participate in the company's research program. She joined 23andMe from Stanford, where as a faculty member within the anthropological sciences and genetics department, she specialized in human evolutionary genetics.

Dr. Mountain has published numerous scientific papers on a broad range of topics, including consumer reactions to BRCA test results. Dr. Mountain's areas of expertise include the interactions among genotype, environmental culture and disease, and other areas of human diversity, the extent to which genetic data revealed details of human history, ethical issues regarding human genetics, biology genetics and concepts or race and ethnicity, and the development of statistical tools for interpreting human genetic data. Welcome, Dr. Mountain.

DR. MOUNTAIN: Thank you very much. I am very happy to be here. It's been a very stimulating day, so far. So my title up there is "Incidental Findings: A 23andMe Perspective." I am here with the full support of my colleagues at the company, but my perspective is possibly somewhat unique. I have an academic background, and I have over 25 years of experience exploring and studying human genetic variations.

So, that's my passion; is understanding the nature of that variation and what it means for people. So incidental findings is really right there in terms of the genomic realm. Well, like many of my colleagues, I am also a customer of a DTC genetics company. I own I haven't tried too many of the others yet, so that gives a slightly different perspective as well, though many of my colleagues are as well.

(Slide.)

DR. MOUNTAIN: I am speaking today about the direct-to-consumer context, but I'm hoping and expecting that the perspective we have at the company may have some relevance to the realms of research and the clinic as well. Not promising, but hoping that it goes beyond this particular context. And my overall plan here is to just describe how we present an evolving set of interpretations of a single, genetic test.

So, for a particular customer, we get a saliva sample and give them some genetic results; but, over time, we provide an initial report. But over time we provide additional reports to add to that interpretation of their genetic information. And I'll talk about the fact that we actually enable people to look at their raw data -- their raw, genetic data -- and the implications of that in this context.

Finally, I'll talk a little bit about the research program of 23andMe. I think there might be some insights there.

(Slide.)

DR. MOUNTAIN: Going to the next slide, it's a little tricky to read there, but I felt a point to start out with the mission of 23andMe, certainly, there's something about shareholders and that kind of thing. But, what drives the employees of 23andMe is this mission. We look to provide a service to give consumers access to their own genetic information, plus the features and tools to make that information useful and interesting.

In turn, we have a flip side of that mission. We look to perform genetics research and support genetics research, because we believe there's so much more to be learned. And, if we want to give our customers full value, we need to contribute to the research and enhance the value of their genetic information. So, let's see. We have heard a little bit about this question of contract in the commercial context.

I would say that contract with the customer is spelled out. It's spelled out by having a website, but specifically we have statements on the website, such as "23andMe is a DNA analysis service providing information and tools for individuals to learn about and explore their DNA," a very broad description of what the service is. And because of that broad description, we tend not to use the term "incidental findings." Basically, anything we can tell you on the basis of your DNA is part of the package, but things might at some point get beyond what we might have expected. And there's a difference between what is spelled out as a broad set of information you might receive and what you might have expected, as we just heard. And I'll come back to the terms of service.

I am the principal investigator for some of our human subjects protocols, and so I think on a regular basis about what people care about, and they care about what they learn about themselves, what other people might learn about them, and even what other people learn about, say, their relatives by them getting tested. But the focus today is on what I might learn about myself if I sign up for 23andMe. Incidental findings is most centrally about this. And so it's just part of our overall evaluation of where people might find risk.

(Slide.)

DR. MOUNTAIN: So here is the -- let's see. We're still not getting the full picture. We're missing a lot of the text in here, but that's okay.

Basically, when someone signs up for 23andMe, they send in a saliva sample, and that's to our partner lab. That lab extracts DNA and then sends the resulting genetic information to 23andMe. We then post it to the web, and the customer gets to login and start exploring their features. And so here's the front page of when I log in

and it gives me some features that are recommended. It says if you want to go to the health overview, you can do that.

(Slide.)

DR. MOUNTAIN: And here's the health overview that I receive when I go to that section of the website. So, immediately, you'll see 20 different lines there with complicated health labels. It can be quite overwhelming, but that is a key part of it. This is many, many health reports for each customer, and every customer gets to see the summary, if they choose, and see an overall sense of where their risks might lie from a genetic perspective. And I won't go into too much detail here, but I will give you an example.

Some of the information, if someone drills down, if they click on one of the reports, this is the kind of thing they will get. They'll get a description of a condition such as venous thromboembolism, which is related to the formation of blood clots. They'll get some images. They'll get links to the scientific publications that support this report. They will get a comparison of their particular risk for the condition versus the average risk. And so this is the kind of thing that they will get, and an explanation of how genes and environment play roles in giving someone risk for this particular condition. So these have changed over time.

That's the key thing I want to mention here. We've added reports. We started with 13. Now we have over 240. So if you got tested in 2007, you would have an increasing number of reports based on that. So that's part of the model.

We have a lot of text in our terms of service here. We note that you should not assume that any information we may be able to provide you, whether now or as genetic research advances, will be welcome or positive. So we've been blunt from

the beginning. You may discover things about yourself that trouble you and that you may not have the ability to control or change.

You see that your father is not genetically your father; surprising facts related to your ancestry, or that someone with your genotype may have a higher than average chance of developing a certain condition or disease. So I've just highlighted a few of the things that our customers learn. About 8% of them learned about this blood-clotting propensity. 25% of our customers learned that they carry one copy of a genetic variant that gives them maybe double the average risk of Alzheimer's disease and so on.

These are the kinds of things people are learning when they sign up; however, the key thing, we have four reports that are locked, meaning you have to opt-in to see them, so that you're not going to be looking for your hair loss report and come across something like a BRCA report. And, roughly, three-quarters of people do choose to open at least one of these. And before they open them, they are given some background information, that it's explained to you this is what you will be seeing.

What are the implications for your family? And then you have to actively click, "Please show me my results for this particular report." So we have one of, I guess, here today, who also came in as a guest expert to help us with a video to provide support and background information for our customers as they make this decision whether to get tested. So we have that for four different reports, as I said, including the BRCA report. And I'll skip that, a little bit.

People make discoveries about their ancestry. They may find Native American ancestry or Ashkenazi Jewish ancestry, African ancestry, European ancestry, things that they did not expect there. Family relationships, probably the most common,

where we have a customer I quote here said: "I'm the family genealogist; spent all my time looking up old records. And I'm at this reunion of my dad's family recording information thinking, I'm not even related to any of these people." Right -- because he did genetic testing of himself and his aunt, discovered that his father was not genetically his father.

So on the other hand we have people who find relatives through this genetic testing, so we have the opposite happening. These are half siblings who discovered each other. One was adopted and they connected through the DNA. So things are going both ways. You could call this an incidental finding. It certainly was for the sister who didn't know she had a brother who had been adopted away.

So I'll say a little bit about research here. We note what we've shown you previously may be incomplete or inaccurate, and there may be more for you. So I think just to wrap up, we allow people to download their own information. They can actually take that information for about a million different positions in the genome, and they can download it, take it to third-party services that will then interpret that information. So the customers have a lot of leeway, and they could find things there they wouldn't have anticipated.

So, I think the last thing to note is that we also publish research and we give that information back in terms of new reports when we make discoveries. So if we discover something in using someone's sample, we can give them that information back. So, it's not incidental, it's something they expect from the research.

DR. GUTMANN: Thank you very much.

DR. MOUNTAIN: You're welcome.

DR. GUTMANN: We're open for questions and comments. John?

DR. ARRAS: Yeah. First a comment. Thank you all very much, but the comment goes to Dr. Mountain. So one of the big questions for us is when our health professionals or testers are obligated to inform people of incidental findings? Is it another way of telling us what you're saying, is that 23andMe just doesn't have this problem? Because you put all the information out there, you make it up to the patient or the customer to make the decision about whether they want to see it or not.

DR. MOUNTAIN: I think that that's the model; however, I think we also have to take into account by having these four opt-in reports, we are acknowledging that someone might not have fully appreciated the breadth of the information that they could get through this testing. So it is backing away, a little bit. It's about what people expected to get and us making sure they understand the breadth of that information.

However, there can be other information. For instance, we probably have in our imaging data we receive from the lab information; and, sometimes, we've seen this about chromosomal abnormalities, but we don't report on those unless it comes up where we can actually validate it. We have the issue. We have to validate the things that we report.

So for us, all those health reports are based on genetic positions that are validated through independent testing that we do. And if we come across something that looks a bit unusual in someone's genome, we don't know right away what it means. So we have had to deal with some of these, but we are in our terms of service and our other statements, we say we are not necessarily giving you everything. Things may be discovered in the future that we cannot present to you now.

So I think the way we do it is do our best to educate people about the changing nature of our understanding of their DNA, the changing nature of the research,

and basically getting people to understand that science isn't done yet.

DR. ARRAS: Okay. Thank you.

Could I ask a question as well? Dr. Prof. Donaldson, my ears were perking up as soon as you mentioned your attempt to get beyond the kind of narrow contractual understanding, because one of the questions that I keep coming back to today is whether it might be possible for us to develop what you might want to call a unified field theory of incidental findings. Right? You've got these three different areas: clinic, research, corporate; and, I'm wondering whether there is a kind of moral center -- you know -- common moral standard that animates providers in all three of those regions with regard to positive obligations.

And one final snarky comment about language, I'm not sure I follow the use of the word "micro" in microsocial, because it seems to me that what you're saying is that over and above these individual contracts that people make, there's a kind of social glue that holds us together. And the way that Adam Smith talked about there being morays that are more important than the invisible hand, even. Right?

So it seems to me that the use of the word micro was unfortunate, because it gives a picture of just timing social contracts. Right? Whereas, what we're talking about is the environment of social contracts and what animates the moral texture of those contracts.

PROF. DONALDSON: So, unified field theory, I'm not going to touch with a 10-foot pole, but --

DR. ARRAS: One can always hope.

PROF. DONALDSON: Yeah. No, in fact. I think, first of all, microsocial contracts -- I'll explain that term in just a second -- sort of reveals how

there's typically not one solution to especially problems that arise out of innovation and new products. And if you stop and think, we can drive on the right side of the road or we can drive on the left, but we need to determine which we're going to do.

Insider trading laws can be arranged in many different ways. It's not clear one is absolutely right, and I think the same is true here. And, for that reason, conversation among providers, and especially for profit companies are doing this kind of thing, I think is absolutely crucial to set these up. It could be a unified filter, perhaps. I mean there's certain norms, certain hyper norms, such as the right to privacy, that are going to flow through all of these. I mean I find that a fascinating challenge. Well, maybe I'll just stop. I'll stop there.

DR. GUTMANN: Nelson?

DR. MICHAEL: This is also for Dr. Mountain, to see if I can understand your logic completely. But if I was to subscribe to your service, I would understand upfront the range of how many morphemes you're going to look at. So as a consequence of the discovery of those polymorphisms, there is nothing incidental. Because, in a fashion, both parties understand exactly what information is being culled, and one learns that, and there is nothing that's incidental.

But, two years from now, is it possible that now you've strengthened the rigor of your bioinformatic processes, and now you understand that you can squeeze 10% more information out of the genetic information that you already have? Can I go back to that website and say, "What else have you learned?" Or, do I need to once again reengage with you to understand that there are now 10% more, to get around the issue that you may in fact have discovered something that you learned two years from now that you wouldn't have known today?

DR. MOUNTAIN: That's correct that a customer who signed up this year or received, say, 240 different reports, in another year there may be 10-20 more reports based on that same sample that you submitted this year, because we look at a million different positions and we are far from interpreting all of them. And that is part of the model, and customers get used to receiving an e-mail message saying there's an update to your reports.

And that, I think, helps people understand that it's not all known yet. And then that's a key educational concept we need to get across.

DR. GUTMANN: I have Anita and Raju, Anita first and then Raju.

DR. ALLEN: A couple of questions, one for Dr. Mountain. How much does 23andMe cost?

DR. MOUNTAIN: Right now it's \$99.

DR. ALLEN: Flat? You only ever pay \$99?

DR. MOUNTAIN: That's right.

DR. ALLEN: And so all the subsequent e-mails and more disclosures never cost more than \$99?

DR. MOUNTAIN: That's the current model.

DR. ALLEN: Okay. Is there any cost that I might not expect that I might discover if I became a customer of 23andMe?

DR. MOUNTAIN: We may have a new chip, a new technology that we roll out. Some day we may go to some sequencing. I'm sequencing not just a million positions. In which case, if you wanted the reports that were based on that new technology, you would have to sign up and pay again for the laboratory component.

DR. ALLEN: Okay. And I don't mean to sound unduly negative, but I

just have these questions for you. Some people are unhappy about the development of direct consumer genetic testing because they believe this kind of product, corporate product as it were, plays on anxieties about people's identities. I don't know who I am, because my ancestors were slaves, and I don't know exactly what my ethnic mix is. I'd like to know. I'm a little bit worried, so I turned to these products in order to find out my real self, which is in some ways client mythology. But I want you to comment on that.

And, also, people who are unduly anxious about their health might be the kinds of people who would freely, voluntarily contract to buy this service. So I just want to reflect on someone inside the company on this. There's concerns about people being easy targets for the product, because they have all these anxieties about their health or their identities. Then, I have one more question for the other panelist.

DR. MOUNTAIN: I'd love to discuss this with you at great length, because each of those is worthy of a full discussion. But in terms of the ancestry and identity, people are hungry to learn more about their ancestry. If we could tell many more people that we see DNA evidence of their Native American ancestry, we'd probably sell a lot more kits. And there may be some companies out there who are willing to do that.

That is a great concern to us; that we are very careful with the kind of sort of stories we tell people or the interpretations based on ancestry that we can stand behind them. And I think it's partly because we have a health product as well that we have a level for the whole product that maybe is not necessary for or as central for other companies thinking about ancestry.

On the health side, we have people signing up for all kinds of reasons. I'm

not sure the people were particularly anxious. I think we have many, many people state they are curious. So we have a broad range of reasons for people to sign up. I wouldn't say that it's particularly the people who are susceptible to health anxieties. I wouldn't say that that's a core piece.

Many people come in because they're interested in ancestry, and they fall in love with the information they've learned on the health side, and vice versa. So, because it's such a broad service, people are getting a lot of different information, and they find value where they might not have expected it, and that kind of thing.

DR. ALLEN: My other question is about how we're defining direct-to-consumer. I thought that we were including things like whole body scans as part of our discussion, and maybe even the kind of HIV testing that one does through the mail. Are we also interested in these other kinds of direct-to-consumer products?

DR. MOUNTAIN: Yes.

DR. ALLEN: So could I have some reflection on the whole body scan, or the HIV test by contrast to the 23andMe type genetic testing as to what sort of ethical issue we should be thinking about and how these kinds of companies might as corporate entities differ from the kind of entities that 23andMe represents.

It's nobody's expertise on this panel, but I think our mandate is to look broadly at direct-to-consumer. And it isn't just genetic testing that we have to think about. I got a letter in the mail a couple of days ago from a whole body scanning company, you know, just invited me to sign-up to come down to have my whole body scanned. You know.

MS. JAVITT: I think that some of the same gaps in oversight may exist with some of these other technologies. With the HIV testing, with which I'm more

familiar, at least the original, I believe subsequent home consumer-based kits for HIV were required to go through FDA and were put through the hoops in terms of how they were communicating results and validating them. So that is quite different from the DTC genetic testing context.

With the whole body, that's where you really get into this gray zone between practice of medicine, where a government entity may regulate the machine, but then state law to a greater or lesser extent regulates the use of that machine. Tanning beds are another example. But I agree with you that there are some similarities; the DTC genetic test is not sui generis.

DR. GUTMANN: Raju?

DR. KUCHERLAPATI: Thank you. They come back with this issue about incidental findings. I'm trying to understand what the issues are. Joanna said that as far as 23andMe is concerned, they clearly define what the tests are they're going to conduct. And they provide the results that are made from that test; and, therefore, there is no opportunity for any incidental findings.

If every company that is a direct-to-consumer company would identify what the test is, and they're sending out the results, where is the possibility for finding these incidental findings? Can you find examples that would illustrate how we might be able to get such incidental findings?

MS. JAVITT: So there are a few assumptions there, though, we might want to look at further. First is that everything is clearly laid out. So going back to the Tay-Sachs example, do you really know everything you are getting and what the limitations are? And I think you could say that about a lot of other that ask that question.

DR. KUCHERLAPATI: Yeah. But that's a different issue. That's sort of your scientific ability of the testing.

MS. JAVITT: No. No. It's that you --

DR. KUCHERLAPATI: Right.

MS. JAVITT: Well, it's different. I think you may think your test has more meaning than it does, because four mutations is different from a hundred mutations.

DR. KUCHERLAPATI: Would you call that incidental findings?

MS. JAVITT: So what I think I was trying to get at before was, is it about getting what you expect or having expectations that should be met as a minimum? So if somebody is going to say they offer carrier screening for a particular disease, is there a minimum? Are there a minimum number of mutations? Is there a minimum package they should offer? Now, in the clinical context, I think that there are guidelines on that, but that does not necessarily exist in the direct-to-consumer context.

DR. GUTMANN: Let me just read this question, because it's on the same topic from an anonymous member of the audience. 23andMe could easily detect gender mismatch or Klinefelter's. Do you, and if you do, do you disclose? Isn't that incidental?

DR. MOUNTAIN: Great question. So gender mismatch is something that we detect because it's part of our quality control system. In order to just have checks on making sure there's no sample mix-up, we ask people for their sex. And so it's really a sex mismatch rather than gender. And they will report to us their understanding of their sex, and sometimes they report gender. But, if it doesn't match with what the DNA says, we will contact them.

We will hold the data and contact them and ask them if that's what they reported. We want to make sure we give them their own data. A sex mismatch would indicate it's not. And, in some cases, it turns out that, for instance, they have most of the Y chromosome, but not the SOI gene, or something. Something about their Y chromosome means that they are physically a female, even though they have a Y chromosome or most of it. There are cases where -- I think there was a case where someone had surgery, and didn't know about it; was told they had ambiguous genitalia, and so they were given surgery.

They understood themselves to be, I believe it was, female, but they ended up having a Y chromosome. So in that case we had one of our staff members who's an M.D. clinical geneticist work with that person, explain what was going on at the genetic level. So we do have some cases like that, but we explore those on a case by case basis.

In terms of Klinefelter's, we have not validated our ability to detect whether someone has the XXY signature in their DNA, because it's possible. But, in order to tell someone, we need to actually do the testing. We need to test enough people to be sure that we can call that confidently. And we haven't done that work. It's one of several projects we would like to do, but each of these is a validation project, and on an ongoing basis validating our chip.

DR. GUTMANN: That isn't qualitatively different from a researcher who has a scan and decides what to and what not to pursue.

DR. MOUNTAIN: Absolutely. If I can just jump in, 23andMe has invested a tremendous amount of money in order to basically return genetic results and the interpretations, asking a researcher to do what we're doing in a thorough way and give people options as to what kind of information they want, it's hard for me to

imagine. I mean there are limited ways that a researcher can return things, but to do anything near as complete as we do -- and we're certainly not complete yet, as we continue to do the validation. So I think in some ways, even if 23andMe has the scope of incidental findings is possibly smaller or even non-existent, we are attempting to return genetic results to people, and that's maybe an example for the roots.

DR. GUTMANN: It is not non-existent, because you choose not to return some results that you don't have complete confidence in your ability, whether scientifically or cost-effectively, to analyze. You clearly have the material --

DR. MOUNTAIN: That's right.

DR. GUTMANN: -- to provide more results. It might not be the right thing to do, but you have the material that could provide more results than you provide.

DR. MOUNTAIN: So I will say we do allow people to download their own information. So they can take it and do analyses through a third party or themselves.

DR. GUTMANN: It's not the results.

DR. MOUNTAIN: Because they have the information we have.

DR. GUTMANN: Right. It's the raw data. Yeah.

DR. DONALDSON: If I could just add a point, there can be incidental findings, too, incidental to the contractual arrangement, an arrangement which allows people to opt out from finding certain kinds of information. So there may be very important kinds of information you're holding that's not part of the contract that they have to access; and, it may be -- perhaps not now, but in the future -- that some of that information we feel should be provided.

DR. GUTMANN: Thank you very much. We could go on, but we're

going to take a break and reconvene at 3:45, but not before we thank our wonderful presenters. Thank you.

(Recess.)