

Presidential Commission *for the* Study of Bioethical Issues

TRANSCRIPT

Roundtable Discussion

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DR. GUTMANN: We have a tradition now after hearing from each of you individually, we find it's really helpful to have a roundtable so we can discuss among ourselves and hear from each of you advice that you would have for us on the report that we will do.

The tradition is to ask each of you, we will go down the line starting with Robert.

If there is one specific issue that we address or one specific recommendation or finding that you would advise us to include in our report, what would that be?

I know that's a question that requires you to set one priority, but it has proven to be very helpful to our deliberations. Let's start with Dr. Green.

DR. GREEN: I'll come back perhaps with other comments. I'll keep this short.

I think one point you could make is sound a clear call for or against or somehow better characterize the return of findings in research.

When we started our ACMG recommendations, in part it was driven because of my experience with Susan Wolf's panel and think tank on incidental findings in research.

My thoughts were, you know what, we don't have a standard for clinical return of incidental findings to look to the way we do in radiology.

I thought in order to make sense of this, we have to have a standard in clinical, and it evolved from there.

I worry that the ethical drive to return incidental findings in research, however good some of the outcomes may be, obviously, turns the research enterprise into a proxy clinical enterprise. I am concerned about that.

I guess the one thing I would say is see if you can take a nuanced stand on return of incidental findings in research such that you don't burden the researcher with this clinical proxy.

DR. GUTMANN: Good. Thank you. Dr. Cho?

DR. CHO: I agree with that. I also think any kind of recommendations about incidental findings should be informed by data about the potential risks from the inaccuracy of the findings. I realize that is in flux. I think it is something that should be included, both for research and clinical.

I think this comment that Peter made about being clinical grade versus research grade, I think at this point for all the new technologies, there is not much difference.

DR. GUTMANN: Thank you. Dr. London?

DR. LONDON: Actually, I agree with the last point Dr. Cho made about emphasizing, that for many of these -- there are going to be clear cases of things that jump out at you and the difficult cases are going to be ones where there is pretty substantial uncertainty, and I think our practices have to be informed by how should we make those decisions under uncertainty in a way that is respectful to participants.

In that sense, I think I would caution you not to view incidental findings as a potential ancillary benefit of participating in research. I think that is a misguided way of thinking about them, and I think of it more as how is it that we ensure that when people participate in research that we take their interests seriously, where the other side of that is poor quality information can also cause harms to people.

DR. GUTMANN: Thank you. Dr. Bandettini?

DR. BANDETTINI: From this discussion, it occurred to me it seems like

there is a natural division of detection versus follow up as well.

I think the big area of uncertainty in neural imaging is detection, what is reasonable in terms of what are you going to do to detect, what kind of expert and whatever.

That is what I kind of meant, there is a slippery slope potentially, you can always do a little bit more to try to detect, and where do you draw the line.

In terms of follow up, the open questions are do you pay for the follow up or do you have a mechanism for paying for the follow up. At least there has to be a clear mechanism.

DR. GUTMANN: Thank you. Dr. Hilgenberg?

DR. HILGENBERG: I think I would just say I view my main role here as reminding you that despite being research subjects, we are humans. We are people. We have context. Not to forget to pay attention to that human side.

DR. GUTMANN: Thank you. Dr. Cowan?

DR. COWAN: Thank you. Two things that I find really interesting to pursue, in this morning's conversation, one was the notion that we should stop thinking so much about benefitting individuals and start thinking about what benefits families.

The other was the notion of considering research subjects as partners rather than as subjects.

I wanted to make one suggestion that combines my notion of the socio-technical system with some of the remarks that were made, particularly just recently, about research findings that turned into proxy clinical findings.

Surely we can find a way, a structural way, to include clinicians as clinicians, not as researchers, but clinicians as clinicians in research projects.

Maybe even find a way in the case of research that uses MRI to have clinically adequate MRI imaging required, access to it required in the research proposal.

NSF has found all kinds of ways to require potential PIs to do things that they didn't get trained to do, like figure out what the social significance of their research is. Why can't we require researchers to begin adding people to their teams or roles to their teams that research didn't previously involve?

DR. GUTMANN: What I would like to do is open up -- I know there are questions from this morning that we didn't get to -- I'm going to give Dan the right of first questioning because he was on the queue and got left off. The last shall be first.

DR. SULMASY: Thanks. Actually, giving Dr. Cowan a chance to talk to us a little bit more about something you emphasized in your presentation but didn't come up at all in the discussion, and that is the law of unintended consequences.

I think you are very right to point it out to us. I think you are also very right that the innovators are never the people who have the expertise to do so.

I was wondering if you could perhaps help us and say who could be helpful in predicting the possibility, anticipating possible consequences. Is it just always absolutely anything can go?

It seems to me quite often a lot of these allegedly unanticipated consequences seem very obvious, at least retrospectively, and I wondered whether a bioethics commission, for instance, isn't an important place to begin to really look very seriously at those kinds of questions, and I wonder if there are techniques or people, inclusiveness in terms of who we talk to that might help us in looking at unintended consequences, both for this or other technologies that we take up.

DR. COWAN: It's very difficult to do. There have been many attempts to

do it. There once was a Congressional Office of Technology Assessment, which contracted with sociologists, political scientists, specialists in whatever the field was that the technology was being assessed, and it turned out to be not very good.

Social systems are so complicated that it's very difficult to make predictions about them even when you know a lot about them.

I began my presentation by suggesting that historians have something to add. They can at least look at other past examples of unexpected outcomes and where they arose from or how they arose.

Many social scientists have enough training in what we now call science and technology studies to do the same thing.

Can we be predictive 100 percent of the time? Probably not. But we could try to make a stab at it.

DR. GUTMANN: Jim?

DR. WAGNER: Dr. Cowan, your comment in the opening of this round where you were talking about how it might be possible, even required, to have physicians on standby or possibly even be required in the case of neural imaging to have clinical quality imaging.

A principle seems to emerge, and I'm not sure I'm comfortable with it, that if clinical benefit is possible, steps ought to be taken even in research to make certain that it's assured. Is that what you are suggesting?

DR. COWAN: It was an idea that popped into my head about five minutes ago. Actually, that's not true. I've been talking with consumers, let's call them, generally, about incidental findings for a number of years in the context of chairing the Community Advisory Board on Long Island.

What comes up constantly from consumers of health care is the question of why can't a CLIA approved lab be affiliated well enough to look at the research findings and report them to me.

To ordinary people, it seems inconceivable that this can't be done.

DR. WAGNER: I was looking for if it should be done.

DR. COWAN: On that, I'm not sure. Actually, I am. I think it should be done.

DR. GUTMANN: Mildred?

DR. CHO: Sort of on that point, I have a story of an incidental finding from a research laboratory at Stanford that came to us at the Center for Biomedical Ethics with a request for a research ethics consult.

Actually, about half of our consultations have been about incidental findings. It is on the mind of researchers quite a bit.

In this particular case, I think it illustrates sort of what Christine and Anita had brought up earlier, which is this issue of follow up and how far the obligation might go for researchers.

In this situation, there was a study that was being done where the researchers thought they had an incidental finding that needed to be reported because it could be life threatening immediately, having to do with high blood pressure.

They tried repeatedly to contact the research subject, repeatedly being five times by phone and by letter, and was unable to get a response.

The person died, it turned out. That was partly why they didn't respond to some of the later letters. He had a good excuse.

Of course, the researchers were distraught because it did fall into that

category of we felt we had to do something. We tried to do something. We failed. What could we have done better.

I think the issue this illustrates is I don't think this person would have been turned down, turned away, had they come to the hospital for care, if there was something that could have been done. There was something that could have been done cheaply, so that wasn't an issue.

The person didn't have health insurance. The person didn't have a doctor. It never occurred to them to even come to ask for help.

I think this issue of people wanting to get information, there is a number of people there, as you said, maybe don't have friends or don't think they have friends. They won't even avail themselves of services.

DR. GREEN: Your comment where clinical benefit is possible, ought we to assure it, reminds me of in the 1980s doing clinical trials at Emory. I got troubled by the notion that we were receiving laboratory studies and they showed things, and some of the subjects didn't want us to contact their physicians. We felt caught in the middle.

I actually started on my own requiring that in order to be in our studies, you had to give us the name and address of your physician and permit us to contact them with any information we might find.

That actually took us out of the middle of this. I have suggested this to Susan Wolf on a lot of occasions, and all the ethicists hate it because it means you have to have a doctor, you have to share information you might want to keep private and so forth, but on the other hand, if you did this in some way as a requirement for certain kinds of research, it takes you out of that uncomfortable position and flips the information to the clinician where it actually arguably belongs.

DR. GUTMANN: It's definitely worth our considering. I have Barbara and Raju.

DR. LONDON: I would like to say something, I think when you think about a researcher's obligations, it is important to distinguish what are their obligations prior to disclosure, so when they see something that might be worrisome, what is responsible treatment of that, vetting it to get a more reliable read on it or whatever. That is one area.

The other area is what do you do after disclosure and how much of it is the responsibility of the researcher and how much of it is the responsibility of linkage to care.

The research system is part of a larger social division of labor, and I think one thing that is part of the research system that needs to be reformed is making sure people have insurance for research related harms that they might incur.

I don't think incidental findings are research related harms, but if you don't have general health insurance, then a research related finding could have momentous consequences.

We want people to participate in research to contribute to generalizable knowledge, but we want to do that in a way that doesn't overly burden them.

I think linkage to care is probably a sound compromise between derailing the researcher to then provide clinical care, which some researchers won't be able to do, and sort of dumping it onto the patient and saying well, we hope that you find some way to take care of this.

DR. GUTMANN: Thank you. Barbara?

DR. ATKINSON: I wanted to go back to the public health issue. I think a

lot of us are intrigued by that whole concept. I hadn't really thought of it.

I have two parts. You said there were some states that do maybe seven tests and one that may do 50 tests. Is there something that determines -- who is deciding on what basis how many is the right number?

It is going to be our struggle with the whole incidental findings, what is important enough, and we have talked about that. Whether you lose sleep about it doesn't seem to be enough of importance. It seems either there is something you could do about it or there is something you should know about it ahead of time.

That is one half of it. I'm not sure if I heard you correctly, but were you implying that if you did the tests on the newborn, you would know something about the family and then you could actually infer that the parents may have some genes you should be looking at? Are those things actually happening?

Are there really research databases with these huge numbers of babies that have been tested that may have some information that may be applicable to the families in general, and should we be actually thinking about recommendations relative to all of this in our report?

DR. CHO: About the first question, the average number of tests done in states now for newborn screening is about 50. It's not a few, it's many more than that.

How the decision gets made, it is state by state. There have been a lot of attempts to try to harmonize that because does that make sense to have every state be different, make it dependent on what state you get born in to determine what you get tests for, and people agree it doesn't seem like it makes a lot of sense, but there has not really been any success at trying to harmonize all of the states.

I know in California they are interested in starting to think about using

whole genome sequencing or some kind of scaled up sequencing for both newborn screening and for prenatal testing in the State Health Department programs.

Why and to what extent, I'm not really sure, but I'm going to find out in the next month or two because I am going to go meet with some of the folks in the California Department of Public Health.

Your second question?

DR. ATKINSON: It's about whether you would use the information on the families. Would you then extrapolate that the parents might be getting Alzheimer's because you can test it in the child.

DR. CHO: Yes.

DR. ATKINSON: Would they be following those children for 80 years to find out if they got Alzheimer's if they decided they knew it when they were born, those kinds of things? Are people using this information for something and should they be if they are?

DR. CHO: If you do a genetic test, it depends on what kind of genetic finding you're looking at, but you could have the potential to find out genetic predispositions of the parents.

In fact, in some of the prenatal tests and in the newborn screening tests, they do ask for parental samples in order to interpret the sample that is done.

Yes, you will find out information. The significance of it varies depending on what particular analysis you are doing and of what. Yes, that is one of the issues that I think needs to be considered, specifically for the genetic findings.

DR. GUTMANN: Raju?

DR. KUCHERLAPATI: I have a question for Ruth Cowan. In your

comments this morning, you talked about the test and the fact that it was initially discovered for the purpose of trying to find a cure, and eventually it turned out to be for a different use.

As you know today, that test is used extensively for prevention. I wanted to ask you whether you have a value judgment on the utilization of that test for prevention, and whatever that value judgment is, why do you feel one way or the other about that?

DR. COWAN: Yes, I have a value judgment, and it is what I referred to at the beginning of my talk. I was puzzled by my own participation in this on ethical grounds when I first had amniocentesis. The conclusion of my research, which took a long time, not the research, but thinking through the ethical issues that I wanted the research to clarify for me, I came to the conclusion that it was a good thing.

In fact, my book on the subject is called "Heredity and Hope: The Case for Genetic Screening."

It was a good thing because it respected the autonomy of a woman to make decisions about who she was going to spend her life caring for as a mother.

DR. GUTMANN: I have a question from a member of the audience, Les Biesecker. Regarding the question of whether incidental findings should be sought or only returned if stumbled upon, the latter approach that is only returned if stumbled upon seems to be arbitrary and capricious. Is the latter approach ethically defensible?

In other words, this question opens either way, which is if you feel that it should be returned if stumbled upon, why not seek it, or if you don't require seeking it, why return it if stumbled upon. There are two horns here.

DR. BANDETTINI: I think at least in the context of neural imaging, it's

very practical. If you sought every single possible thing that could be wrong with somebody, you would be scanning for a day at least, to try to see everything. I think it's practical that is not possible.

On the other hand, a lot of researchers would argue that they are doing research and not at all responsible for clinical -- to even do anything that would help them screen the obvious things.

I think the answer is somewhere in between. It is sort of a little bit of just practical, what can be done, and there is a point at which you could probably collect a little bit higher resolution image during the scan and then look at it and say, is this reasonable or not, and if you see something unreasonable, bump it up to a physician.

That's not really stumbled upon because you are doing something reasonable. You are not completely having blinders on.

DR. GUTMANN: Nelson, I have you on the list.

DR. MICHAEL: You're always very sensitive to that. I wanted to delve a little bit more into the issue of potentially using linkage of care as sort of the way to get around the conundrum of not taking the research enterprise and turning it into a clinical enterprise.

I'll give you one anecdote from my own experience in my program in Nigeria, and then ask a question that isn't so theoretical. It's happening very historically in my institute.

We do work in Nigeria. We do a number of scientific studies there. We are also heavily engaged in the American bilateral program for HIV/AIDS assistance called PEPFAR.

As a consequence of that latter work, we went to an area very close to the

capital city, about ten kilometers outside there, for reasons that were unclear, just to sort of escape the net of doing incidence studies or prevalence studies. No one really knew what the rate of HIV was going to be in that community.

We were looking for relatively high incidence populations that might be prepared away for vaccine studies there one day. We did an initial prevalence study and we were stunned to see the prevalence was in the 15 to 20 percent range across this population.

That immediately triggered, since our research team also sits on the PEPFAR Working Group in the Embassy, it nearly triggered a public health response by the program in that country to make sure there would be linkage to care.

From an ethical standpoint, we wanted to ask that question anyhow, so for us, it wasn't an incidental finding. We were seeking that answer. It provided a very quick resolution.

That is sort of the background. The more difficult conundrum that has come up from time to time, in areas of the world where we work where there is a very high prevalence of malaria infection, there is also a finite prevalence of HIV infection.

What is the ethical basis for a malaria researcher to say, well, maybe the incidence of HIV in this population is going to be relatively low, the prevalence will be relatively low, I'm going to do a pharmacodynamic study looking a new malaria drug, I'm going to choose not to screen for HIV infection, it's not the purpose of my research, but understanding this might be the best way for the public health community in that particular country to identify an actual result.

This isn't as straightforward as it seems. You identify someone with HIV infection in this part of the world, especially a woman, you develop a significant set of

criteria that aren't always so positive like stigma and social harms, but also there is a barrier to the malaria researcher to do her or his work.

Is it reasonable for researchers to in fact choose not to ask certain questions because they don't want to deal with the incidental findings that will come up, even though there is a public health benefit? How do you choose a middle ground?

DR. GREEN: I'm sure there are plenty of opinions on this, but briefly, I think it is reasonable for a researcher to choose this. I think the researcher's primary mission is generalizable knowledge, and unless that is explicitly part of some hybrid mission, which it could be, I don't think the researcher of necessity is requested, required, empowered, or funded to take on public health issues.

If I may just reach back to Barbara's question because I differed from my colleague here, your question: do child results impact parental risk. I would say unambiguously yes.

If you find that a child has adult cancer producing syndrome, our recommendation suggests you want to give that information back to the family's physician because one of those parents has it, and far more frightening than that child having to be exposed to that information is losing their parent.

DR. GUTMANN: Dan?

DR. SULMASY: Thanks. I was going to take us back to our definition of "incidental" again, the earlier discussion. The way we framed it is it's finding information that is not the intended aim.

In fact, that works for an old paradigm in which I would test for creatinine and find the calcium was elevated, or I had to do a scan of a liver and find there was a nodule in the kidney. That seems incidental.

The new paradigm seems to be let's do a bunch of tests and see what we find. That is whole genome sequencing is in some ways, the aim is sort of can we find anything, and we know even in scanning, you can do this. There are people that do screening tests of whole body imaging.

Can we consider that anything that comes up in those sorts of tests to actually be incidental, if that is the definition, and then at least from a clinical point of view or an ethical point of view, even from the viewpoint of screening, do you think that kind of testing is actually defensible?

DR. GUTMANN: Any takers?

DR. SULMASY: How about context by context, clinical versus research? My point there is if you take it out of the genome and say start with the clinical.

DR. WAGNER: We will have the clinical information this afternoon.

DR. COWAN: I don't have an answer to your question but I want to add another context which I think is crucial, which is the commercial direct to consumer.

DR. GUTMANN: Let me take a question from our audience before I ask other Commission members.

Philip Colina. Thank you for this question. It has been suggested that participants in clinical studies be required to give contact information for their physicians. Excluding participants because they do not have physicians or will not share their contact information has the potential to introduce new biases in the resulting sample.

Good observation. I see a lot of nod's of agreement here.

DR. GREEN: Agreed, but volunteer populations for research clinical trials never were and never will be representative, so it doesn't matter.

DR. GUTMANN: John, you wanted to say something earlier, I didn't notice. Do you want to come back on it?

DR. LONDON: I just was going to say in response to Dr. Michael's comment that I think there are differences when you are working in a low resource setting. You know there are going to be significant unmet health needs in the populations in which you are working, and you want to make sure that when you conduct research there, it is expanding the capacity of health systems in those countries to meet local needs.

It may be the case that when you do testing in that population, you can link to care in that population, that has a public health benefit for the country.

Whether you could go there and do a test on A, without screening for something else, there are often such vast unmet health needs, the question is what is a reasonable contribution that we can make with the resources we have available in cooperation with the host community.

I'm not sure that's really incidental finding, because you know a priori that you are going to have huge unmet health burdens. I would say there I don't think the researcher can just say I know I'm going into a high burdened population, but I'm just here to gather data.

I think that is a kind of exceptionalism that would say my role-related obligations free me from doing something meaningful in this population to help the public health system. I don't think that is justifiable.

DR. GUTMANN: Nita?

DR. FARAHANY: Thank you. I'm struggling a little bit with some different perspectives that I'm hoping you can weigh in on.

I've heard a few different people say with direct to consumer testing, it's different because it's a contract-based relationship and the contract doesn't require, or shouldn't necessarily require, the return of incidental findings.

But researchers should have a duty to just investigate what it is they have set out to investigate and look for or report incidental findings.

I'm trying to understand why. Is it not possible to define the relationship between researcher and subject, and physician and patients, in a way that a consumer company could define the relationship between the company and the consumer.

What is it that's unique about those relationships that say you can't define it and say the only thing I'm researching is X, and I will not be running a panel on anything other than X, but if you would like me to, we could provide that service to you, but otherwise, we will not searching for it.

What is it that makes us say in these other contexts you can't do that, you can't have a contract-based relationship that's limited?

DR. LONDON: I guess this does sort of get back to the question about if you stumble, what's the difference between stumbling upon something and actively looking for it.

I don't know how to speak precisely about the direct to consumer side of this, but it seems reasonable to think there is a continuum with the strong fiduciary duty on the one hand and then an arm's length contractual relationship on the other, where you may be governed by does your product meet safety standards, does it do what it says.

In the middle, I think is the researcher/subject relationship, where you are saying look, I have an important question. I want to answer it. To do that, I need your

participation. Your participation means we are going to draw blood or we are going to put you in this machine, we are going to do other things.

It's a limited relationship, right? Your relationship with your clinician is we are going to address my health needs.

Here you are going to participate with me to answer this specific question, and then if along the line, something unintended comes up, then there are questions about what is your duty to assist that person, what does it mean to take their interests seriously.

You have a relationship with that person where that person is helping you do something. They are contributing the data that you need in order to answer your question.

I don't know if the direct to consumer side has that sort of relationship, but I guess that would be a question for the panel later.

DR. FARAHANY: Your view is what's different about the relationship is you actually have something that you view as a special arrangement because the person has agreed to help further your interests.

You could say that about a consumer as well, they are furthering the interests of the company, but maybe there is something more there.

DR. COWAN: The boundaries between researcher, clinician and commercial entrepreneur are fading. For example, there are commercial enterprises that are doing research. There are clinicians who are doing research on their patients, with the patient's consent but nonetheless, it's happening in the doctor's office.

It may be that we need to re-think that, because in the social reality, they are not so distinctive any more.

DR. GUTMANN: I began commenting on Dr. Hilgenberg's take on the basic respect that any human being, no matter what relationship you are in with them, you owe to somebody else because it's just so obvious.

Now let me make a comment on the other side, which is based on Nita's very helpful question.

We have public health people. We have direct to consumer people. We have researchers. We have clinicians. It's not as if these come with a platonic ideal attached to them of exactly what their obligations are and are not, as Ruth points out. These evolve over time, and they evolve in part due to policies that people make, due to cultural understandings they have.

Here's my question. It's not meant to skirt our need to actually draw some lines, but is there something to be said for having more certainty rather than less certainty here, even if there aren't platonic ideal lines to be drawn?

Are we in an area now where there is so much uncertainty about whose obligations are what, that it would be helpful if we could do nothing else, to make sure that people know what to expect?

DR. GREEN: That's a softball pitch, in a good way, to the ACMG recommendations, because that is exactly the thinking that led us to say look, we're ignorant of a lot of the evidence, but there is so much uncertainty and confusion, we're going to -- I agree with Ruth, the boundaries are fading between researcher/subject, physician/patient and company/customer.

I do think there is still a primary duty in each domain that is different. The primary duty of the researcher is to discover new knowledge. The primary duty of the company is to survive for its shareholders, and the primary duty of the physician is to

take care of their patients.

That does not mean that each domain does not genuinely and authentically share other duties as well or priorities. Those can be negotiated by sort of contracts.

The DTC company has goods and services and then also has a consent form that enrolls people in research. The researcher/subject has consent language and it can clearly say you will not get anything back, and if that's clearly communicated, then the subject is clearly informed.

DR. LONDON: I agree with Henry Richardson and as a moral matter, a contract is nice. It's a way that we can try to define what we owe to each other, transfer rights and obligations, and things like that.

I am one of the people who thinks there are limits to the degree we can hide ourselves off from our fellow people, and that we can create contracts that say I can interact with you to do this project and then I can be completely indifferent to your autonomy or your welfare.

It may be an ambition that private corporations or researchers would like to be able to be indifferent towards people outside of the narrow realm in which they are interacting, I just think from the moral perspective, it can't be done. Claims of assistance or aid, they escape the bounds of a contract.

The other thing I would say there is yes, it may be true, clinicians are performing research in their clinics and corporations are performing research. Insofar as you are doing those things, to me what matters less is the category, the name, the role. The question is are you entering a relationship with a person where you are saying join me in this enterprise where we can do X, Y and Z, and when you do that, you incur some added responsibility to that person, that if you find something out about them

that's of momentous import for their interest, that you may have a duty to disclose it. I say "may" with all the caveats that we have talked about.

DR. GUTMANN: Of momentous import as well, which is a qualifier. We are actually out of time. We will have one last question by Raju and one last response, not by everybody, a few if you feel so moved.

DR. KUCHERLAPATI: It's not so much a question but a comment. I wanted to follow up with Dan Sulmasy's comment, which is fundamental maybe to our discussion.

That is the way the technology is proceeding, it may be cheaper to be able to do whole genome sequencing than doing one test or two tests at a time.

When all of those results are obtained, those results, if it's a clinical test, it will become part of the medical record, and the medical records are owned by the patient.

It is not possible to actually try to withhold any information. I think there is a very important case to be made here, that in those circumstances, there may be no incidental findings.

I would like to hear the panel's views about that.

DR. WAGNER: Robert, you talked about testing for 24, it's certainly not incidental once you tell everyone.

DR. GREEN: I think Raju is right, if you look into a little bit farther future, in the immediate future, it still takes work to interpret the variants and you have to choose which ones to interpret. I totally agree that is where we are heading.

DR. GUTMANN: I think it is a really astute observation that we are heading in the direction where less and less becomes incidental. We are not there yet.

If we were there, it would be easier terrain to navigate.

I am going to conclude this session by saying what I believe is true, which is nothing that you have offered us today is an incidental finding for us.

[Laughter.]

DR. GUTMANN: It is all something that we will take directly and use as best we can for making as good a report as we are capable of doing.

I want to thank you all for extremely helpful comments. Thank you.

[Applause.]

[Whereupon, at 12:41 p.m., a luncheon recess was taken.]