



Presidential Commission
for the Study of Bioethical Issues

TRANSCRIPT
Community Engagement -- Needs, Models and U.S. Actions

Carletta Tilousi

Member, Havasupai Tribal Council
Havasupai Tribe

Mitchell Warren

Executive Director, AVAC: Global Advocacy for HIV Prevention

Roger I. Glass, M.D., Ph.D.

Director, Fogarty International Center, Associate Director for International
Research, National Institutes of Health

Meeting 6, Session 5
August 30, 2011
Washington, DC

DR. GUTMANN: If I could ask everybody to please take a seat, we are going to reconvene.

It is my pleasure now to introduce our panel on community engagement. I will introduce all the speakers at the beginning, and then ask each to speak, and then we will open it up for questions and comments.

And I want to thank everybody who has given us comments earlier this morning for really excellent comments.

Our first speaker will be Carletta Tilousi. She is a member of the Havasupai Tribe. If I pronounce that -- would you pronounce it for me?

MS. TILOUSI: Havasupai Tribe.

DR. GUTMANN: Havasupai Tribe. And a member of the tribal council. She has been a member of the tribal council for the last eight years. She was the lead plaintiff in the Havasupai versus Arizona State University case, which we touched on this morning. She holds a bachelor of science degree in justice studies from Arizona State University, and she was born and raised in the Grand Canyon.

Welcome, Carletta.

Mitchell Warren, who will be our second speaker, is the executive director of AVAC, which is an

international non-governmental organization that uses education, policy analysis, and advocacy, and a network of global collaborations to accelerate the ethical development and global delivery of AIDS vaccine, male circumcision, microbicides, prep, and other emerging HIV prevention options as part of a comprehensive response to the pandemic. Before joining AVAC he was senior director for vaccine preparedness at the International AIDS Vaccine Initiative, where he directed efforts to increase community understanding and national involvement in AIDS vaccine clinical trials.

Welcome, Mitchell.

Mr. Warren is also a member of the global HIV prevention working group convened by the Bill and Melinda Gates Foundation and the Kaiser Family Foundation.

Dr. Roger Glass, our third speaker, is the director of the Fogarty International Center, and associate director for international research at the National Institutes of Health. Prior to his appointment at the Fogarty International Center, Dr. Glass was the chief of the viral gastroenteritis unit

at the National Center for Infectious Disease at the
CDC. His research interests are in the prevention of
gastroenteritis from rotoviruses and noroviruses.
through the application of novel scientific research.
He has maintained field studies in India, Bangladesh,

Brazil, Mexico, Israel, Russia, Vietnam, China, and elsewhere. His research has been targeted toward epidemiological studies to anticipate the introduction of rotovirus vaccines.

Welcome, Dr. Glass. We are delighted to have you all here.

And, Carletta, may I ask you to begin?

MS. TILOUSI: Good morning. My name is Carletta Tilousi. Thank you for inviting me here to testify on behalf of my community. I have put together a small slide show, so that you can have a visual idea of where we are from.

This is the Grand Canyon. We are located in northern Arizona. Our population of my people is approximately 500-plus members that live in the bottom of the Grand Canyon. We have over about 120 families living in Supai Village.

This is an aerial shot of Supai Village. It's a remote canyon in the side of the Grand Canyon. Everything is flown down here through helicopter, mule, or hiking down is the only access to the village. We have a high rate of high-school drop-out rate.

We -- jobs are very limited. We have government jobs down there. Some of them are for social services, health services, and such that is -- provide the community.

We also have approximately five college graduates, and I am the third person that has ever graduated from college in the history of Havasupai. Farming is our main economic source. We just finished our harvest down in the village. This was our main way of surviving down in Supai Canyon.

A little bit of history. Our reservation was not formed as a formal reservation until 1975, which prohibited us from consuming our natural foods, which led us to the severe epidemic of diabetes. The reason why I'm here today is to explain a little bit about why my people have been plagued with diabetes, due to our people being removed from our original lands. We were forced to eat non-familiar foods that caused us to have high rates of diabetes in our youth, in our elders.

Our main economic base is tourism that come into Supai Canyon.

As you see here, a lot of the rock formations

in the village talk about the history of -- or Havasupai-- one of the studies that Arizona State University did was challenge our existence in Havasupai, which was claiming that we were from the Bering Straits theory, which contradicted our own cultural and religious beliefs.

Here is the Havasu Waterfalls, which we are named after. Havasu Baaja is the way you say it in our language. In English, lots of people say it, "Havasupai People."

These are other photos of my ancestors who have roamed in the Grand Canyon for many years. This type of existence of our indigenous people attracted professional scholars from Arizona State University to come into our community and seek blood samples. One of the samples that they used was to see where we did come from, how we lived for so long in these rugged terrains. And there were many, many publications that were published by Arizona State University.

Here are pictures of two of the professors, John Martin and Dr. Theresa Marco. These are members of the Havasupai Tribe who have -- did at this point

travel to Arizona State University to participate in a diabetes study. Here are our people who have worked in the field of food and health. Some of these ladies are clinical health representatives, or working in the cafeteria, providing food for the children.

And one of the collaborative efforts that ASU tried to do back then was to provide education of diabetes. This was one of the only things that they did that we found documentation on. I also want to note that half of these women in these pictures have passed away, due to diabetes complications.

These are also victims of research. These are the people that found out about how the blood samples were transferred from institution across state boundaries, and were used for other research, such as schizophrenia, the Bering Strait theory, as I mentioned earlier, inbreeding amongst the Havasupai. These are very -- studies that were very embarrassing to my people, and also to myself.

I also sit before you as the victim of a scientific research. I also gave blood. I provided blood, and I did not provide any written consent.

These are our tribal council leaders who also stood up against the State of Arizona, and the institution and said, "This is not going to happen any more to any of -- other indigenous people around the world," and took this step forward to bring this issue to light.

One of the main goals of the Arizona State University blood case was to bring the blood samples back. We were not going to just fight for monetary funds. We felt that it was very important to bring our blood samples back -- of our ancestors back. Due to our religious beliefs, when an individual passes away, everything that he or she owns goes with them during their burial. So this really went against our religion.

Here you see in this photo some of the blood samples that we retained back. We only got about 98 -- approximately 98 samples back. This is their grandfather's blood sample back that they are properly reburying back into this person's cemetery.

Again, this is the -- my ancestors. The one on the right is my great-great-great grandfather. His

name is Burro. That name was given to him because he was found roaming around in the Grand Canyon.

There are many implications that came out of this blood case. I would like to let you know some of them. The reason why I'm here today was a lot of our blood samples were misused. The people's trust in the institution was shattered. Right now, the tribe had to -- the tribal council had to no longer allow Arizona State University people to come on to the Havasupai Reservation.

One of the main things that we learned now is the lack of IRB rules were not being enforced, the lack of IRB processes were not being followed. The lack of legal enforcement was also being overlooked. The only thing that happened to these institutions that we found out in the end was their funding will be revoked. And the professors currently have not been disciplined. They still hold different professorship positions in other institutions.

And it continues. We are very upset about the lack of informed consent that was not even translated into my language. English is my second language. I

speaking Havasupai 100 percent of the time. Some of the terms that you use here when you're talking in your meetings need to be translated to me, you know, so that I can properly answer.

When these folks approached my community, they just verbally told these people that were willing to find solutions to diabetes -- of course, everybody wanted to find some solution to this health epidemic that is killing my people. We just finished burying one of my elders who had a stroke, who had been fighting diabetes for many years. We just buried her three weeks ago. So this is something that we face every day.

And if these IRB boards are there to review such subjects and such kind of work that is being done by these institutions, they need to be enforced, and in a way that we understand. For instance, when the blood samples were taken from the Havasupai Reservation, they were taken across boundaries. They were taken to state jurisdictions.

And when we decided to take this case into court, the state court said, "We don't have

jurisdiction." The federal court said they didn't have jurisdiction. It was just getting tossed around, back and forth. And it was such a high-profile issue, no law firm also did not want to take this case, because a lot of people worked for Arizona State University, or knew people within the institution.

And then, the other thing is I would also like to recommend that our -- when these studies are being taken within tribal governments, they need to be enforced within tribal court systems. So, due to these other implications, Indian tribes are now reluctant to participate -- we, as Havasupai, are reluctant to participate -- in any further human subject research until we further understand what is the process, until we further understand the translation and implications of what needs to be done.

How do we handle internal review board regulations when they are being violated? Are they going to be fined? Where are they going to be enforced? What happens to these professors when they go in and promise solutions to certain epidemics?

So, those are some of the things that we have

here.

We found that there was no written consent by any of these professors that were obtained.

Translation for people.

And also recognizing the fact that lack of education, economy, all those factors need to be considered when professors are coming into third world conditions. I come from a community that, any time, the water can go out. Any time the lights can go out. Flooding can happen. Those types of things that we face every day.

We are not against research. We feel that research is needed. But it needs to be done in a proper way.

So, I thank you for my comments, and I hope that we can seek a solution together.

DR. GUTMANN: Thank you very much. Mitchell?

MR. WARREN: Thank you. Let me -- thank you very much. First and foremost, let me thank the commission for inviting me. And, perhaps more importantly, thank you for grappling with some of the most important and, I would argue, some of the most

interesting issues of our time.

We at AVAC, a small policy and advocacy organization, have followed your work for some time, provided comments back in April, in fact, related to, hopefully, the reinstatement at the FDA of focusing on the Helsinki Declaration and the highest protection provisions. So we have watched and followed, but that is not the purpose of my remarks this morning.

I am going to talk about the good participatory practice guidelines that you heard a bit about from Colonel Michael. I am hopefully going to provide some flavor, in a sense of where they came from, and, more importantly, where they are going. It is remarkable, what a difference a few years makes.

Only five or six years ago, when one talked about research, looking at what in HIV prevention is called pre-exposure prophylaxis, was almost a euphemism for unethical research, or at least claims of unethical research. And now we sit four months since results have been released that tell us that, in fact, these research results provided some of the most ground-breaking and important findings in HIV

prevention research.

So, how did we traverse those five years from research called unethical to research called ground-breaking, game-changing, and perhaps epidemic ending? I certainly don't want to pretend that good participatory practice was the way in which that research transitioned. But I do want to highlight the fact that when those trials first erupted in controversy five years ago, a number of us, including leadership at UN AIDS led at the time by Peter Piot, who I know was part of your international panel and we at AVAC, looked at these controversies as an important opportunity to reflect on the way research was happening.

Many of the claims that were taking place in communities that were engaged in this research, both in Asia and in West Africa, as well as communities who claimed a right to be engaged in the research discourse -- mainly in Europe, and advocates like myself sitting in the United States -- were looking at the research endeavor taking place and commented on several lapses that were perceived to be taking place

in those trials. And some of you mentioned those in the last session.

People were concerned about the informed consent process, people concerned about the issue of language that was used with trial participants, the lack of clarity about post-trial access, should these interventions prove successful. And, perhaps most challenging, what would happen to someone in one of these trials, should they become HIV-infected? Huge issues.

And we at AVAC wrote a report back in 2005 that did not seek to blame, did not seek to say this research was ethical or not, but sought to really understand what was at the heart of the problem. And what we really came to find was that many of the claims made were not entirely true, but they were never fully answered by research sponsors, research implementers, and the trialists. And I won't try to judge cause and effect, but it was very clear that the lack of communications between the different stakeholders was really at the heart of key problems.

Coming out of that in 2007, UN AIDS and AVAC

convened an international panel of researchers, ethicists, community activities, to really look at how could we do better. And one of the main recommendations coming out of those early discussions was that we were missing something critical in the research process. Every clinical trial had good clinical practice guidelines that were being followed and monitored. Every product being tested would be through a good manufacturing process -- again, a process well known, well documented, well monitored. Similarly, laboratories under good laboratory practice.

But in terms of community engagement, in terms of participation of multiple stakeholders, there was no guideline. There were lots of idealized visions of what community engagement should be. Sometimes it was done very, very well. Sometimes it was done very, very badly. And most of the time, none of us would know the difference. Not unlike the Supreme Court and pornography, we seem to know good community engagement when we saw it, but we couldn't actually measure or monitor it. And that put everybody involved in the research endeavor, frankly, at risk.

So, the initial guidelines published finally in late 2007 went through the research process, and really started at the one area of community engagement best known to people, the community advisory board, and really articulated a desire that while community advisory boards were important, they were not sufficient to say that was indeed community engagement. And again, if you go back to good clinical practice guidelines, the CAB is help up as the way in which communities are engaged.

And instead, the panel that put together the initial GPP guidelines went through the research process and tried to identify different aspects of the research time line where communities could or should be engaged. And you can see in this graphic from the latest guidelines that, really, community engagement, stakeholder engagement, should take place throughout the entire life cycle of the research process. Recruitment is recruitment. Stakeholder engagement, community engagement, is not. And that is often missing, I think, in the dialogue.

So, in beginning the GPP guideline

development, it was an attempt to try to understand the research process, and recognizing that language matters. Even just earlier in this session this morning, the discussion of communities -- and it is a term that is like Jello in one's hands, it can mean many different things to many different people -- and you will notice that we transition from good community practice ideas to good participatory practice, and we transitioned in this second version from talking about community engagement to stakeholder engagement, recognizing that many different types of stakeholders are engaged throughout the research life cycle, and we need to ensure that they have mechanisms to engage throughout. And this is just one diagram that shows you the many different layers.

And who gets to decide? In some of the early controversies around the prep research, activists outside of the geography of the trials claimed a voice, and really were allowed to subvert the research process and close clinical trials down for reasons that, frankly, boarded on the unethical on the closing them down, rather than in the defense of ethical conduct.

So, different layers of this onion, so to speak, really have different voices, different views, and different ways to engage.

Just to differentiate, GCP talks a great deal about connecting research teams to trial participants through the informed consent process. In GPP, we tried to find a bidirectional approach between a range of different stakeholders, and the research teams, not only the clinical trialists, but the funders and sponsors, as well.

GPP is divided into three sections. The first identifies the importance of good participatory practice. The second looks at key principles that underlie these guidelines. And the third, then, takes a view at each of the clinical trial process points and looks at what might be seen as minimal standards, minimal ways to really measure and monitor good practice.

This just gives you a little bit more detail of what is within each section, really not an attempt to test your eyesight or to have you read it, but to give you a sense of the depth of these guidelines.

Again, I do want to focus a bit on the different types of advisory mechanisms, because so often, if there is a functioning CAB, and if it has minutes and notes from its meetings, it is perceived to be enough. And what we've tried to articulate here is a range of different types of ways to engage.

And similarly, here you can see that there are many different types of mechanisms, both informal and formal. And they need to be seen in the context in which the research is taking place. This work that I am describing took place entirely in the context of HIV prevention research, and more particularly, biomedical HIV prevention research.

Can these guidelines be extrapolated to other research? I believe they can. I think it's the task of this commission and many other groups to really judge that on its merits. Can these guidelines be distilled to a point where they provide the basics of implementation and monitoring?

And finally, we have gone over the last four years from the principles that underlie these guidelines, to the guidelines themselves. And now the

issue really is how do we implement them, how do we monitor them, and how do we evaluate them. And much of this is going to come down to the trial sponsors, much as any trial must follow the GCP guidelines.

I would argue that trial sponsors need to take these guidelines just as seriously, if we truly want to see communities engaged. Why does this matter? Well, it matters not just for the conduct of a single trial. It matters for the way trials can take place in a long-term process with communities over many different types of research endeavors. It really comes down to how do we create the trust and respect for the research process that researchers and clinicians have, but communities often don't, for lack of their input and engagement throughout that process.

So, I would argue that while there are costs involved in doing this, as in anything, it is one of the best investments we can make in ensuring that the research process goes smoothly, and that the answers from research can be well implemented into our policies and programs, going forward. Thank you very much.

DR. GUTMANN: Thank you very much. Roger,

you're on.

DR. GLASS: Thanks very much. And I must say I am honored to be here before the commission to speak on behalf of our programs at NIH and at Fogarty. I wear two hats at NIH: I am the director of the Fogarty International Center, and I'm also the associated director for global health research, which means I interact with all of the 27 institutes and centers on campus.

And where our focus at Fogarty has been on research and training for global health, our strategic plan includes both infectious and non-communicable diseases, and we work with all of the institutes and centers. We have an emphasis on implementation, which brings us directly into the community involvement that Mitch just spoke about.

Training is a key for our -- training for research is key to our mission, and we really have made an effort to build partnerships between U.S. and foreign academic centers to build up their researchers and their academic activities. And we have over 400 separate grants, mostly in low and middle income

countries.

I want to just start by saying that we see at NIH a tremendous growth in clinical trials being conducted abroad. It's a growth industry. And I work in India, where they're anticipating over the next decade over \$10 billion of clinical research that's being taken overseas. Why is this so, and how do we address it?

Part of the reason for the shift is the harsh bureaucratic and regulatory environment in the U.S., and the cost of doing business here, so that many companies are subverting these hardships by going overseas, which raises a major question of how do we deal and provide ethical oversight and training for these activities, and the quote here from the New England Journal was that we must ensure the ethical and scientific integrity of this clinical research globally, as you can see.

Well, where do we go from here? I wanted to bring up Zeke's presentation this morning, because -- this is from 2004. Before this, there was a review of ethical principles for research in the United

States. And when this moved from the United States to the developing countries, this collaborative partnership, this community participation, was a key change that occurred. And that is the sphere in which we at Fogarty are involved.

Our mission, then, has been that for the past decade, over a decade, we have invested in bioethics research. And much of the research that is conducted and support and training in bioethics internationally is conducted and supported by the Fogarty International Center. Many of the institutes and centers participate in these activities with us, and co-fund.

But our goal is to build the research ethics capacity in low and middle-income countries to strengthen local input and participation in questions of ethics, to address ethical controversies locally, and to promote clinical global health research at NIH. We feel it's absolutely imperative that we have a framework in place for the protection of human subjects. That's key.

Well, we do this through our international research ethics training programs. And these have

developed on creating curricula that are widely used, case studies -- and there are two books there that have been published by researchers Jim Lowry and Richard Cash that are used and are available online -- running IRBs and training an IRB in research review, and writing guidelines for research.

Our programs, the yellow dots, are scattered throughout the developing world. And over the past decade, we have trained over 500 -- 560 -- master's level bioethics trainees through these programs. We have just set up line listings of where these people are and what they're doing. And I amplified a few of them, just to see the types of activities that these people have become -- these graduates, trainees, have become engaged in working on their national ethics committees, training and academics and the like. So, these are really key and influential people in their own settings.

Our grantees are from many countries. And you can see Latin America, Africa, Asia. There are so many countries that are not represented, and so this really reflects where we have the greatest investment in

research, but not all the places where research is being conducted.

South Africa and India are on the top of the list, and I wanted to just give you a few vignettes of what these people are doing. I would also say that these graduates are involved in teaching or administration and policy and research, all of these. And I think many of you around the table are familiar with or have worked with some of these grantees.

This is Clement Adebamowo, who is from Nigeria. He has been training extensively in Nigeria, 21 master's university students at Ibadan University. But most important, and highlighted with a red arrow, he has drafted the Nigerian national code for research ethics. He has been an absolute mover in that country for both training and research. And we could not do much of what we do in Nigeria if it hadn't been with the help of Clement and his staff and his graduates.

Another graduate is Nandini Kumar from India. She is -- she trained through a Fogarty program in bioethics at Toronto. She set up a bioethics training in her own country. She moved on to the Indian Council

of Medical Research as deputy director for ethics, so she's done the whole range. And I would say that training is a little bit like your retirement fund. It's not worth much a year after you've finished your training. But at 10 and 20 years, it really accumulates and grows. And I think that it's growing not only her, but all the graduates and the long-term trainees in India.

So, there we have three countries where we've been involved. And last, South Africa -- three countries -- Jerome Singh, an absolute academic in bioethics. He's at Capriva in Durban, University of KwaZulu-Natal, where the microbicide trials, the circumcision trials, some of the most testy and thorny issues of biomedical ethics, and here we have a grantee who is trained and is able to address these needs.

So, how do we go forward with this program? These have been terribly effective programs, but they've been effective on a small scale. We haven't begun to address the needs that we see with -- if I can call it an epidemic of clinical research that will be going on in the next decade overseas, and the growing

trend in that direction.

We project this huge increase in clinical research overseas. We cannot foresee this happening without proper attention to protection of human subjects and substantial increases in both the infrastructure for bioethics and the capacity-building and training that's required. And this is an area where Fogarty, with the other institutes and centers at NIH, has played a key role. And Joe Millum, in the audience back here, is our ethicist at Fogarty who works closely with Christine Grady's group. So we collaborate even on campus.

Well, I want to leave you with three challenges. One is that ethics starts at home. And if we go back to that Guatemalan case from yesterday, it was really an American investigator who had an American chain of command that was all responsible. We feel that protection of human subjects has to begin with the training of American medical students and future bio researchers here, so that ethics and understanding of the protection of human subjects, of community engagement, of equivalent protections, of publication

of results, of standards of care, those basics, are infused in graduates from the very early days, so that at least they have a starting point.

And this -- I hope will be music to your ears -- would require more investment in the training of biomedical scientists at home in our own institutions and academic institutions. Many of you are here because your institutions have strong ethics programs. Those who aren't here are the ones who we might well be speaking to, and who could benefit from this.

The second is that we have gone and, over this past 60 or 70 years from this case in Guatemala, we've gone from parachute research to partnerships. I think the parachute researcher was the person who dropped in with his own ethics values, and left with a bunch of specimens, exactly what Carletta was talking about. And I would say that global health research and local research are not extremes, in contrast, but are part of a continuum. And what we do overseas we should be doing in our own backyard and our own inner cities.

So, global health, it's not parachutes, it's

partnerships. And to -- and the challenge for you, then, is how do we build independent, local bioethics capacities, IRBs, and training programs that will be a match for what we are doing at home, because we feel this is terribly critical, and this is exactly the space where Fogarty has been working for the past decade or more.

And finally, sustainability. What we haven't mentioned is training and funding for ethics. We think this is critical, because unless we have a way to support the ethics training and the participation of ethics into the research agendas into the future, we are going to have continuing programs and under-funded programs, and we will be liable for the same problems from the past.

So, just to end, this is a picture of our recent graduate just last year from Agakhan in ethics. And these people will go out with -- to ensure that the ethics and the clinical research done in Pakistan meets the certain international standards that we all accept and would like to see.

Thank you very much for giving me this

opportunity to address you with these challenges.

DR. GUTMANN: Thank you, Carletta, Mitchell, and Roger, for three excellent presentations. And we will have some discussion.

Before I ask commission members, there is a question held over from the last session which is appropriate here, and it comes actually from Joe Millum. And, Roger, I think you're -- you may be the perfect person to answer this question, and you will see why the smile is appropriate.

What evidence is there that training investigators in ethics will improve the conduct of research? Exactly what are the outcomes that could be different?

DR. GLASS: I would have to throw that back to Joe Millum, who is our ethicist, and Christine Grady.

(Laughter.)

DR. GUTMANN: No, no, no --

DR. GLASS: I think that certainly -- and in my own experience -- the ethical issues -- and I go back to Caprisa and the trial -- the ethical issues around bringing those trials of microbicides and

circumcision to the fore had been absolutely mind-boggling, because the ethics of how you -- and the prep trial.

I mean these are sophisticated, complicated ethical issues that could not have been bridged without having a strong ethics program at the University of KwaZulu-Natal. We have been training there extensively for over a decade. And the ethics -- participation of the ethicist in those trials has really been critical, both to having the trial be conducted properly, and to ensure that the funding was consistent, was there.

DR. GUTMANN: Yes.

DR. GLASS: So I think we could -- but I think it's a good question I think we should go back and evaluate. But I can say that we could not be doing much of the research in those key countries if we didn't have IRBs in place, if we didn't have competent, ethically-trained people to speak out and speak locally for the local institutions in ethics.

DR. GUTMANN: Let me say something on this, because it definitely cross-cuts everything this commission has been doing in this session and in

previous sessions.

When we found moral culpability on the part of researchers in Guatemala -- Raju said this, and Nita said it, and a number of other people on the commission said it -- we were judging, in retrospect, and we wanted to be very careful about our judgments about culpability of individuals.

If we don't have ethics education, we cannot expect individuals to live up to the ethical standards that we impose. So, we may not know -- and we don't have controlled experiments; it would be very hard to do them, not impossible -- but we don't know for sure what the results of ethics education are.

What we do know for sure is if we -- and when I say "we" here, it's government agencies who are responsible for sponsoring research -- if we, if the government agencies don't ensure ethical training, then they don't have the moral responsibility -- they don't have the moral authority to expect people to live up to the standards that ethics requires. And so, I think there is something very fundamental here about ethics training.

That leaves open the question of what the most effective ethics training is. Let me just say, then, you mentioned several individuals here, and we should just say that Nandini Kumar was on the international panel, representing an area of -- a very important area of the world. And she, as her fellow colleagues, did a fabulous job. So we thank Fogarty for its ongoing contribution to ethics education.

I am going to open it up for other --

DR. GLASS: Let me respond to that.

DR. GUTMANN: Go ahead, yes.

DR. GLASS: I think also, if you think about Nandini and India, much of the growth in trials in the next decade will not be NIH-sponsored trials, or just Gates-sponsored trials, it will be trials by pharma. And if we create an ethical framework for India through these, it should permeate or could help permeate, and make sure that all trials are conducted with the proper --

DR. GUTMANN: Yeah.

DR. GLASS: -- ethical approval, not just those that are government or donor, NGO-sponsored.

DR. GUTMANN: And one other part of what you -- and I think one of the intents of Joe's question, as well, if I may read into it -- is that it's not enough just to train individual investigators in ethics. It's also important to train people who are going to be responsible for setting up institutions and research projects to understand what are the institutional requirements for having a good scientific and ethical study conducted.

So, I am going to let other people -- John and Nita and Dan, and I will keep the list. So let's start with John.

DR. ARRAS: Okay. This is a question addressed to Ms. Tilousi. Earlier this morning we had an interesting exchange with Zeke Emanuel about the Havasupai experience. I was puzzling over this notion of a kind of blanket consent for tissue -- you know, research on human tissue. Zeke's response was, well, that really will give people the power to decide whether they want to participate or not.

But I am still puzzling over this. I am still puzzling over his position. Because it seems to me

that that sort of view puts a lot of pressure on local communities, in terms of foresight of, you know, what could be done with their samples in the future. I would imagine that most people not trained in medicine don't have the foggiest idea what their tissues might be used for in the future.

So I just wanted to ask you whether you were listening to that conversation and, if so, what is your response to his proposed rule of a kind of open-ended blanket consent for tissue acquisition and research?

MS. TILOUSI: As I mentioned earlier in the presentation, some of us got our blood samples back. I was one that didn't get my blood samples back. So I always question on where it went, what it's been doing. You know, there's been several of us that haven't received it back. I would like to know where it went, what it's being used for. If it's for anything good, I would like to know.

I don't think that there should just be a blanket full release, you can do whatever you want. I think if it's going to be used for something good, I would like to feel good that my body had contributed

something, something positive to someone's life, or some solution to some research. But I don't -- to me, I always still wonder where it went, if it's at the University of Southern California, or if it's in the University of Arizona, if it still exists, if it's damaged. What is it being used for? I don't know.

So that is the question I am going to have to live with. But I don't like the blanket idea.

DR. GUTMANN: Nita?

DR. FARAHANY: Thank you for all three of these presentations, which gives us a lot to think about.

I want to focus on the linkage between training and bioethics and community engagement. And as I understand, Roger, the way that you have presented it, you know, there is training the leaders in a community so that we can set up the institutions and the frameworks for ethical research.

There is the training of the scientists, and helping them not just in understanding the rationale, but having it be an integral part of the education, so it's not just another check-box, but actually part of

education from day one. But I wonder if the missing link that we have been struggling with and discussing is really community engagement, in that for many researchers they undergo ethics training already, at least domestically somewhat abroad, as well as these programs start to become more widespread.

But understanding the importance and the rationale of it, perhaps community engagements and being required, encouraged and, from the get-go, understanding that participating with and the dialogue with the stakeholders would really make the ethics requirement real. Right? It gives a real face to the issues, whether it's at the research population level or the broader community.

So, is community engagement the way in which you take the check box of ethical research and make it a real experienced issue, such that it's integral, or, you know, is that not enough? And that's directed to, really, any of you.

DR. GUTMANN: Mitchell, why don't you begin?

MR. WARREN: Sure. It's a fantastic question, and I really think it hits to the heart of how research

gets conducted. And, you know, because we have created the tic box system, and the CAB is really -- and I'm exaggerating to make the point, certainly, but CABs are often "If I have it, I therefore have done good community practice, I have been ethical in my conduct, I have engaged community."

But very often we fail to recognize the enormous power imbalance that takes place between trial participants, the communities from which those participants may come, and the researchers and the sponsors. And while, again, no single document or guideline is going to address that power imbalance fundamentally, the GPP guidelines are certainly meant to provide a bridge to address those imbalances so that there is a discourse that can happen.

You know, if I had to distill the entire guideline down to one idea, it's to create a robust discussion between the researchers and the communities, writ large. Now, that's a challenge, because robust discussion is often not what many trial sponsors want. Many of them are quite risk-averse. And yet, we need to move to the point where we recognize it's not just

about the conduct of one trial. It's about the way in which trials take place over time, particularly as we look at the globalization that Roger is describing.

Many of these communities are engaging in dozens of trials at any given time. So it's not just about one trial, it's about how this process engages. And I think critical to it is the evidence to show how the inputs around the training, on the one hand both of ethicists and of researchers, and of community stakeholders to be engaged in the discourse is really at the heart of it.

DR. GUTMANN: Dan?

DR. SULMASY: Thanks. This will probably also be mostly for Mr. Mitchell, but -- or for Mr. Warren, but could be for others as well. It's the -- a question of who actually represents the community or the stakeholders, and whether you have advice within your guidelines for who to engage in these robust discussions with. Because people will still be helicoptering in, and often engaging new communities, and we don't know whether the government or the university, or whoever we're talking to, actually

represents the community. So, advice about making it broad, as well as robust in an engagement.

MR. WARREN: That is the trillion-dollar question. Who gets to represent whom? And very often the controversies have erupted when someone not fully allowed to or mandated to represent someone decides to be that representative.

What the guidelines do describe is at the very outset, before we get to protocol development, to informed consent processes, is the kind of formative research and community mapping -- and this is particularly important -- and again, remember, these guidelines came out of an HIV prevention research world, which is not working in every country and every community.

But certainly much of our research, HIV and otherwise, is happening through research centers. And it is not enough to decide in our protocol we want to recruit Population X, and therefore we will go to the community group that represents that population. It's really important to understand that broader community.

Who are the people who either validly speak

for others and with others, and who just might parachute in themselves to decide to be that voice? I think it's at our peril to try to define it too narrowly. Because if we do, inevitably we will start a trial and we will encounter problems if we don't understand that broader universe. And we may not like who is saying, "I represent X or Y," but if we don't understand those dynamics, we really are going to find ourselves with many more trials mired in controversy than in positive results.

DR. GUTMANN: Jim, do you want to --

DR. WAGNER: Just very quick. A question.

Carletta brings up something that we really haven't talked about as a commission, and I would be curious to know if all three of you agree that it would be worthwhile for the commission to spend some time thinking about a system of sanctions.

Carletta seems to express disappointment that, having set up the -- not "seems to," she does express disappointment that having set up good practices, even improving those practices and having education around those practices, we will still have violators, and the

sense that the public, who needs our confidence -- particularly as we imagine an increasing need for certain kinds of human subjects research -- doesn't feel as though we are holding ourselves accountable. Would you recommend that there be some conversation about appropriate sanctions?

DR. GLASS: Absolutely. And some trials have been closed down because of aberrations of ethical review. Perhaps not enough. We certainly spend more time at the beginning of a trial than in the continuity.

I know, in my own experience, trials we did in South Africa with rotovirus vaccine, when we interviewed the women who brought their children for a vaccination, they had been asked to give a thumbprint of their consent. When I spoke to them about the meaning of a thumbprint, the women said, "The only time I have ever given a thumbprint was 10 years ago, or 15 years ago, during apartheid, when that thumbprint, to an official, meant that I lost my property."

And so, for us to ask for a thumbprint for her was asking her, potentially, to do something adverse.

And I think that's one of the reasons why this local involvement is key.

And while training -- we can't train all the IRB people and all the medical students. But by training leaders in-country and building their departments to be linked to academic departments in the U.S. so we get that, we can really have an amplification that goes much beyond the small investments that we make.

DR. GUTMANN: Nelson?

DR. MICHAEL: Just very quickly, to comment on Roger's colleague's issues about the impact of training, when we started working in Nigeria in 2004 in a partnership with the Nigerian military medical activities, working on HIV/AIDS, we spent about 2 years developing initial capacity to roll out the PEPFAR program within that community, and then begin to segue to do research.

And we were able to do that fairly seamlessly because of Clement's West African bioethics activity that he had at the University of Abadan which then spawned the Nigerian research ethics committee. So

exactly at the time we began to segue into science activities, the research absorptive capacity had been built there by Fogarty, and it allowed that partnership to go forward, and was enormously helpful. That's an anecdote, but I think it's a pretty good one, and you've put a lot of investment.

My question really is to Carletta. Listening to what you said was very hard to hear. And I would wonder if 10 years ago, if you had known the gentleman sitting next to you, if that sort of thing would have happened. If you had known these two gentlemen, you knew about the process of good participatory practices, if you had struggled with the issue of other tribal community advisory boards or other liaisons to diabetes foundations, if you had representation to your state and federal congressional members, would this sort of thing have been prevented?

And so, the question really is to the three of you. What can be done that's cross-cutting across fields to ensure that people like Carletta know about the work that is being done by Fogarty or that's being done in an HIV prevention field, that it begins to

suffuse this process across multiple disciplines?

DR. GUTMANN: Let me ask Carletta to answer.

Would any of this or all of this have helped?

MS. TILOUSI: Yes, I think so. If I had a better understanding when they first took my blood and explained to me, "This is what it's going to be used for. We're going to come back to you in 30 days and tell you if you're going to have diabetes or not, and these are the prevention steps that you need to take," I would have been more agreeable.

At that moment in time, you know, you want to know the answer, whether you're going to be diabetic or not.

DR. GUTMANN: Right, right.

MS. TILOUSI: You know, so I think it would have been much easier for my community if we all met 10 years ago. But we can't go back in time, you know. We need to correct what has happened and move forward.

DR. GUTMANN: So, let me ask this question that comes from a participant who will actually later be a presenter. But it's a challenging question which needs to be asked. It's from Ruth Macklin, professor

of bioethics. We all know Ruth. Ruth just reminded me a few minutes ago of how many decades it was since we last met. But I have followed Ruth's work since then. And it is to you, Roger.

And Ruth writes as follows: "As a recipient of an award from Fogarty for the past 10 years in Latin America, I have encountered hostile public response from a few people, claiming that the Fogarty program is an instance of American ethical 'imperialism' on the part of the NIH. How can we counter this criticism?"

DR. GLASS: A good question, Ruth. And I think a part of what we have done at Fogarty is to build the partnerships and the training together, so we have really tried to avoid exactly that kind of criticism. And I hope we are doing that. And if we are not, I think we have to address that.

DR. GUTMANN: Let me ask Mitchell, because this is a broader question. Let me just -- I should say the international panel did recommend that the training be done not only by Americans, but that other countries develop the capacity as, you know -- and it was actually Fogarty, while not -- we not mention by

name -- was an example of what the international panel wanted to see more of in their own countries.

Mitchell?

MR. WARREN: Well, I think it's absolutely critical. I mean when I look at the future, it's when -- you know, with all due respect to Roger and everybody at Fogarty -- it's when Jerome, who I know in South Africa and have worked with, when it's Clement, when they're the ones sitting at this panel, when they're the ones leading the discourse in their countries and regionally and internationally, is when we will see the real shifts that we need to. And that's not just true of the ethicists at the table. It is going to be true of the researchers at the table. Hopefully some day soon a funder is at the table.

And I think the fourth kind of leg to that stool would then be the communities, too. We often do our work, I think, in these siloed approaches, where we have the ethicist getting this, and the researchers getting this, and the funders doing this. And communities are the nice to haves, but the first to be cut out of a budget, or the first issues to be left

behind. We will only be successful in that example that Ruth gave when communities in those countries are engaged and receptive to that work coming, whether it's coming from Ruth or from a local investigator.

So I think we really need to frame this much more broadly, and with many more seats at the table, and with many different types of representatives in those seats.

DR. GUTMANN: Factually, we should indicate -- because I and my colleagues have been involved in this now on the international engagement side -- that there are many, many countries in the world that have extremely well-developed ethics training and groups that are engaged in ethics of medical research. There are many that don't. But we are, as Americans, by no means alone in wanting this to move forward. And the dialogue is very robust between our commission and others.

Yes, Roger?

DR. GLASS: Yes, just a comment. I think we are interacting with the DCTP, the Nuffield Center, WHO on these. We are trying to build the partnerships. And my own work

in Bangladesh -- the ethics committee in Bangladesh was started by NIH 50 years ago to allow cholera vaccine trials to go on in that country. And now it's a very robust organization. So I think it's building those partnerships so that people can participate in this dialogue, or the international dialogue, and represent themselves, just like Carletta has done here for us today.

DR. GUTMANN: Thank you, Carletta, Mitchell, and Roger. Very interesting session.