FOOD AND DRUG ADMINISTRATION (FDA)

CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)

MEETING ON HIV PATIENT-FOCUSED DRUG DEVELOPMENT AND HIV CURE RESEARCH

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Food and Drug Administration

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P R O C E E D I N G S

DR. EGGERS: Since we got silence, then we can go ahead and get started. My name is Sara Eggers, and I am in CDER's Office of Strategic Programs, and I will be facilitating the discussion later on today, but before we get into the discussion, we want to set a bit of the context for today's discussion, and so maybe I'll go over the agenda. Can we do the next slide?

So we're going to set the context, and I'll have some of my colleagues come up and do that, and then we'll get into our discussion topic, our first topic of the day, which is Patients' Perspectives on Current HIV Treatments and Most Significant Symptoms. And then after the lunch break we'll come back in the afternoon, again we'll set some context on HIV cure research, and then we'll have a discussion on that, particularly getting at patients' perspectives on participating in cure research studies and on the need for good communication through informed consent.

We will have an open public comment period after, at the end of the day. This is all in your

agendas, the times are in there. And if you would like to make any comment, anyone is welcome, patient representative or anyone else, to sign up to make a public comment on a topic that might not be as relevant to the discussion topics in the morning and afternoon, we encourage you to do so at the registration desk and we will take those registrations until the last break in the afternoon.

There are restrooms located in about as far away as you can be in the back, if you go behind the little cafeteria and down the hallway. And with that, I will turn it over to Dr. Edward Cox, who will give some welcoming comments. Welcome

DR. COX: Thanks, Sara. And good morning, everybody. And I want to start out by welcoming everybody to today's Public Meeting on Patient-Focused Drug Development for HIV and HIV Cure Research. And I want to thank everybody that's taken the time to come and join us here today and those that are joining us via the webcast. For those that traveled in, we're glad to see you here safe and sound after a rather eventful series of storms yesterday afternoon. So

welcome, all.

Today's meeting really is an important chance for us to hear from patients and patient advocates. And today's meeting is our second in a series of meetings conducted as part of the FDA's Patient-Focused Drug Development Initiative. So this initiative involves obtaining a better understanding of patients' perspectives on a particular disease and treatments. And Theresa Mullin will speak to this a little bit more in just a minute.

As part of this initiative, this meeting provides us a chance to hear directly from patients and patient advocates about living with HIV today, including the benefits and downsides of currently available treatments. And as we work through the day, Kim Struble will provide us a brief background discussion about the current status of treatment for HIV.

The advances in therapies to manage HIV have really been truly remarkable over the last few decades, and when I joined the FDA, it's been a little bit over a decade ago now, and reflect back upon my

time prior to coming to the FDA, I was an infectious disease fellow at NIAID over at NIH, also in my time as an ID practitioner, I never really would have imagined that the advances that we've seen in the development of antiretroviral therapies would have happened at the rate that they've happened.

So today HIV infection is often viewed as a manageable chronic infection. However, we also need to keep in mind that HIV still is a serious and life-threatening condition that can have a significant impact on people's lives. And the New York Times had an article a couple of weeks ago that described this very point, went through a series of discussions of patients and what they were experiencing with their HIV infection, so I think that really helps to illustrate the points of the challenges of living with HIV today.

So we're hear today recognizing that there is still more progress to be made and more work to be done to further advance the treatment and management of HIV. The meeting will also give us a chance this afternoon to explore important issues as we look

forward to research and development in the area of cure research for HIV. And for the purposes of our meeting today, when we are talking about cure research, we're using the term to refer to any investigation that evaluates a possible therapy intended to control or eliminate HIV infection so that no further medications are needed to maintain health.

HIV cure research is in early stages in testing in patients, but the products and approaches being evaluated may represent important foundational work for advances in treating HIV.

As in many areas of research, clinical trials studying HIV cure interventions may not provide direct benefit to a participant but may provide scientific information that could guide future research and drug development. Today's meeting is an important opportunity to hear from and gain an understanding of patients' perspectives on potential benefits and risks of participating in HIV cure research. What we learn today will help us as we evaluate sponsors' study protocols and informed consent procedures for trials exploring HIV cure

research. Ilan Irony, from the FDA Center for Biologics Evaluation and Research, and Sara Goldkind will give us a presentation this afternoon and provide background for the discussion on the questions that we'll be discussing as part of the HIV cure research discussion this afternoon.

Today's meeting focuses on having conversations with patients and advocates, and Sara Eggers will guide us through that and give us a little more information on the ground rules as we course through the day. And you will also notice that my FDA colleagues are sitting to my left here, and they will be here listening carefully to the discussions and occasionally asking clarifying questions as we go through the course of the day. And I thought also at this point what we would do is we would ask folks at the table to introduce themselves, and I'll start with Sara, and then we'll work our way down the table.

DR. EGGERS: Again, my name is Sara Eggers, from the Office of Strategic Programs in the Center of Drug Evaluation and Research.

DR. MULLIN: Good morning. I'm Theresa

Mullin. I direct the Office of Strategic Programs in the Center for Drugs, and I am leading this Patient-Focused Drug Development effort for CDER.

DR. BIRNKRANT: My name is Debbie Birnkrant. I'm Director of the Division of Antiviral Products, and I'm happy to say that I've been with the agency in the same division in different positions however, since 1989.

DR. WITTEN: Celia Witten. I'm the Office Director of the Office of Cell, Tissue, and Gene Therapy in the Center for Biologics. And our oversight includes products such as gene therapy and cell therapy products.

DR. IRONY: Ilan Irony. I am Chief of the General Medicine Branch in the Office where Celia is our Director, Dr. Witten. And we go over the cell gene therapies for a variety of indications including HIV, which is a major component of the work we do.

DR. SHERWAT: Hi. I'm Adam Sherwat, from the Division of Antiviral Products, Medical Officer.

DR. COX: Great. Thank you. And as Sara

has mentioned, at the end of the afternoon we'll have an open comment period, and for folks that are interested, at the registration table out by the doors where you came in is a signup sheet, so we do ask that you sign up if you would like to make comments at the end of the day, particularly in areas if there are comments that have not been covered over the course of the day's discussions.

We're happy to see so many folks here, and we know that a number of folks are joining us via the web for today's meeting. And we're excited to see the level of interest by patients, patient advocates, researchers, drug developers, government agencies, and other stakeholders that have joined us here today.

The disease HIV has served to unite us in a common goal of the continual search for safe and effective therapies to help millions of people that are affected with the disease. And FDA has an important part in drug development, but we also have to recognize, too, that FDA's role is only a part. FDA's key role is to ensure the safety of clinical trials and also the safety and effectiveness of

products that are approved. Critically important to the overall process and development of new medications is the collective work and participation of researchers, drug developers, patient communities, and patients all coming together to advance the field and the study of new agents for HIV care.

So with that, I want to thank all for joining us and we look forward to a productive day and discussion and opportunity to listen and to learn from the comments that we hear. And I will now turn it over to Theresa Mullin, who will talk to us a little bit more about the Patient-Focused Drug Development activities.

Thank you all. Overview of FDA's Patient-Focused Drug Development Initiative

DR. MULLIN: Thank you, Ed. And thank you to the people who just pulled my slides up.

So good morning. I'm Theresa Mullin, you know that already, but I am going to talk about this Patient-Focused Drug Development Initiative overall, and this meeting is the second that we're having under this initiative that we're beginning under PDUFA V,

and I'll say a little bit more about that, and we plan to continue this effort. We're in sort of a learning mode generally about this process that we're using to get input as well as learning in this case today about the questions that we're asking in particular for patient input related to HIV drug development and cure research.

So just to go on a bit here, this Patient-Focused Drug Development Initiative is connected very closely to an effort at FDA and CDER to develop a more formalized framing for benefit-risk assessment for new drugs, and, of course, FDA, in any decision making related to marketing of drugs, weighs the benefits against the risks to determine whether or not the drug can be approved and put on the market. And that benefit-risk assessment framework includes the severity of the condition, the degree of unmet need -- and we just consider those two components, severity of condition and degree of unmet need -- to really constitute the clinical context, and we recognize that patients have a unique and pretty critical perspective on FDA's understanding of that clinical context.

Patients are the ones who take the medicines, will get any benefit that can be gotten from it, will also suffer all the risks, so we really need a better understanding.

We have some ways to obtain that kind of input today through an advisory committee, but that's usually on a particular drug, and through our patient representative program, and again those are very valuable venues, but they are limited. So we are undertaking this Patient-Focused Drug Development effort to have a chance to talk to patients about questions that the review divisions are sort of grappling with or would really like to get greater input related to them to give them greater insight about how patients feel about the disease that they are living with and the therapies that they may or may not have to help us with both informing drug development efforts and the review of an application that comes in after we have this kind of input to really have that extra insight that we may not have prior to hearing from you. So that's why we focused this meeting on hearing from patients. When we get to

the public input part at the end, others can speak, but before that, everybody else is in listening mode.

And so as part of PDUFA V, which was reauthorized last year, we agreed to have at least 20 of these kinds of meetings in different disease areas over the next 5 years. Our review division staff are here to hear what you have to tell us, or they're listening in through our webcast, but that's one of the key listening groups. We hope that patients, patient advocates, health care providers, in the disease area, drug developers, are also able to listen to what we hear and what we learn in these meetings.

So how did this process start? Well, I would say that we waited until the ink dried on the reauthorization, but we didn't actually wait until the ink dried. We started last summer, and when we expected to get reauthorization, to try to talk to the review divisions and others in the FDA, and also we're listening to patients who have been talking to us throughout the reauthorization process and giving us their input along with the negotiations of PDUFA to sort of look at what kinds of criteria should we use

to pick the diseases because one thing we did hear from patient groups is concern that we are doing so few.

I mean, there are so many diseases and 20 doesn't sound like a big number when you think about how many diseases there are for which drugs are developed, but we try to develop criteria. I'll tell you in a minute what criteria we used. And we went to the review divisions to ask, what disease areas would you nominate for public comment? We developed a list. We published that list in September of last year. We had a public meeting in October to get input initially and talk about the list and our thinking. We got about 4,500 comments into the docket on this. There were about 90 disease areas identified through that public docket process, and we went back and analyzed what we got from the public docket and from the input in the meeting, talked again to the review divisions to sort of identify what diseases will we try to cover in the next 3 years.

And so we didn't want to speak for the whole 5 years, we went with the first 3, and it was based on

a combination of questions that are before the review divisions now or that they see coming where they had a sort of more urgent need to hear in certain disease areas. There were other diseases we were covering in other venues. So a variety of factors were taken into consideration, including what we heard in the docket and what patients identified as most critical, and that's how we developed this list, which we published on April 11th, and it's available on the internet. You can see the list that we have for this first 3 years, and in 2015, we'll come back again and finish it and say what other diseases we're going to cover in those last 2 years of this PDUFA reauthorization.

And so here we have the disease criteria that we had developed. And so we were looking for diseases that were largely chronic and symptomatic and that would affect the functioning or the quality of daily life of the patients, and thus a really critical aspect is hearing firsthand from patients how it feels to live with the disease, diseases for which we really are not capturing those considerations very well in our clinical trials today and the endpoints we have

today, and diseases where there are currently no good therapies or very few therapies available. We wanted to capture a range of diseases where there was a range of severity and maybe there are subpopulations that experience different severity, perhaps the elderly or pediatric population, and also, as a set, we wanted to cover a wide range of disease areas and affected populations in this set of 20, so that went into our thinking in what disease areas we chose.

Now, there is a very diverse set there, and so each of these meetings will be designed slightly differently. We have some standard questions that we had patients help us develop. We periodically have convened patient groups who will meet with us to help us think through process considerations related to all these meetings. We got a lot of great input from those sessions that we've had so far, and to make the questions, that are basic questions, as relevant and kind of meaningfully worded as possible going in to talk to patients, but we heard from patients in those meetings that we have to make sure we modify the questions to fit the special considerations of the

disease that they are experiencing and also the questions that reviewers in particular wanted to cover. We've modified the questions today along those lines for this HIV drug development and research.

We're also, as we go through this, experimenting with different methods because we're really learning how to do this. And one of the things we're trying to balance here is folks that are able to make it here and those who can't. And a lot of patients, for various reasons, whether it's the cost of getting here or just the inconvenience or the lack of mobility they may experience, we want to make sure we have good methods for remote participation.

And so this is our second meeting. The first one we had was on chronic fatigue syndrome, and that was held in April. And so we're trying some new technologies today. We have a webcast that's interactive today, and so that will be a new thing. And we're going to try using the clicker technology for some questions that are asked later to try to get a sense of patients' responses and how you feel about those questions. And we'll see how that goes.

This is a little bit of a work in progress; we're trying to see what's the best way to get the kind of input we're trying to achieve in these meetings. We'll be successful if we get input on how people feel about it, very frank, candid input. We hope and plan to faithfully capture that, capture the words, capture the way that it's described to us, provide that back to review divisions, and we're going to be developing meeting reports that we will also post on our website from what we capture in our meetings.

And just a little bit more about the format. We'll try to format each of these meetings to really capture the best way to get input, and it's a little bit based on the questions that we have, and perhaps the patient population that we're trying to work with.

So with that, I will turn it over to our next speaker. And we're really looking forward to hearing your perspective today. It will be very helpful to us going forward in this area.

Thank you.

Background on Current HIV Treatment

DR. STRUBLE: Thank you. My name is Kim Struble, and I am going to be giving you a background on current HIV treatment, a very brief background, to put into context the discussions that will occur later this morning.

As we all know, HIV was identified in 1983, and after 30 years, there is still no vaccine or cure, although a lot of research is ongoing, and that's going to be the focus of our discussions for this afternoon.

More than 1.1 million people in the United States are living with HIV, and despite all of the prevention efforts, that's about 50,000 new infections per year in the United States, and that's been fairly consistent over the last several years. We, at FDA, recognize that HIV/AIDS is a serious and life-threatening disease, and each antiretroviral therapy has its own benefits and unique toxicities or risks. And your input today is very important to us and for drug development process in general.

So FDA works with many groups, such industry, academia, and patient groups to foster

improvements to existing therapy approaches. There is also continued development of novel therapy approaches, and this is really the focus of today's meeting, because your input and perspectives really help us and hopefully industry and academia to move the drug development process forward.

As we all know, antiretroviral therapy has benefits, and today's treatments are highly successful. And the recommended treatment is three or more antiretroviral regimens, and the benefits of this treatment is that people are living near normal lifespans and it's being treated as a chronic disease today. And there have been significant improvements in the last several years for these treatment regimens. And the picture on the left shows a handful of antiretrovirals, it's what patients used to have to take, and, today, the picture on the right shows the simplified dosing regimen. So many patients have available to them one pill that's a complete regimen that they can take once a day.

But we all know that antiretroviral therapy comes with many side effects; they can be both short-

term and long-term side effects. The short-term effects can be some GI toxicity such as diarrhea and nausea, it can be headaches, sleep disturbances, skin changes. And there are also the long-term effects, such as body changes, kidney or liver or heart or bone effects. And antiretroviral therapy can affect the quality of life, and these side effects of this therapy can worsen over time.

We know that there are downsides to taking therapy because we recognize it takes a lot of energy and commitment to adhere to a lifelong treatment. And we know that people get fatigued, they get fatigued from having to take medications every day. They also get fatigued from having to live with a lifelong and long-term condition. And the natural response is people may not want to take treatment anymore. But we do know from recent studies that show that taking pill holidays or stopping and restarting your medications can result in serious health risks. Therefore, it's important for all of us to find ways to take medications daily because we all know that suboptimal adherence could lead to loss of virologic response and

resistance. So input and perspectives that we hear today will also help foster, hopefully, additional drug development to deal with some of these issues.

So we do want your perspectives. And the topic for this morning's discussions are going to center around current HIV treatments and your most significant symptoms. We are definitely interested in your input on, what are you currently doing to help manage your HIV symptoms? How well does your current treatment treat your significant symptoms? What are the most significant downsides to your treatments, and how do they affect your daily life? And what specific things do you look for in an ideal treatment to manage your condition?

And with that, I am going to turn it back over to Sara Eggers, who is going to give us an overview of the discussion format, and we are very much looking forward to your input today.

Thank you. Overview of Discussion Format

DR. EGGERS: Okay. Now the work begins. I want to thank my colleagues for setting the context. And now we're going to look for the patients and

patient representatives to provide the real input. And when I say "patients," when we all say "patients," we're using that as a shorthand to be people living with HIV; and "patient representatives," we're using that as a shorthand to be caretakers, loved ones, advocates who speak on behalf of patients and who can really kind of directly represent the points of view of people living with HIV.

So the discussion will be rather different from the types of government-sponsored public meetings that you may have participated in. And as Dr. Mullin described, today's questions and discussion format were developed based on a standard structure for the Patient-Focused Drug Development meetings.

This morning, we will focus on the current landscape of HIV and its treatment, and we're going to break this morning's discussion into two parts. We'll first focus on HIV treatments before the break, and we're going to include discussion on what are the good things about today's treatments and what are the downsides. And then after the break we'll focus on the most significant symptoms that HIV patients

experience because of their HIV infection or because of the treatments that they take to control the infection.

So I'm going to spend a few minutes just to go over the discussion format and some important ground rules to ensure an effective and fair dialogue.

And at this point, I'm going to ask the folks who are serving on the panel discussion for the morning to work their way up to the front and take a seat. And I'm also going to ask for the clickers to be handed out to anyone who is a patient or patient representative who identifies themselves as such, including up here, please.

So we are first going to hear from a panel of patients and patient representatives, and the purpose here is to really set a good foundation for our discussion. There are four panel discussants this morning, I'll introduce them in a bit, and they represent a range of experience with HIV and HIV advocacy. They have each prepared some minutes of comments in response to the questions. And after we hear from them, as long as time permits, we will have

follow-up questions for the panel, and my FDA colleagues can help ask those questions.

After the panel discussion, we will broaden the dialogue to include other patients and representatives in the audience, and I hope that if you identify as a patient or patient representative, you are sitting in the first four rows here on my right. The purpose here is to really build on the experiences shared by the panel and get a sense for what's generally similar and what may be different in your experiences from what you heard. So I'll be asking a number of follow-up questions and inviting participants to raise their hand to speak. And we're going to have FDA staff around with microphones to come to you so you don't have to go to a microphone, and if I can see name tags, especially if you're sitting as close as possible to the front, I can call on you by name. I'll be working to try to give priority to people who haven't spoken, as long as everyone who is comfortable speaking, we hope that you get to speak as much as you want to today.

And we are trying something new today. This

is an experiment. We will be periodically inviting those of you in person and those of you on the web to respond to specific polling questions. The purpose here is really to aid the discussion to see how many participants share a particular perspective. So the in-person participants will use the clickers, and we'll practice that in a minute, and those participating by the live webcast can add comments through the polling questions that will be up on your screen at the appropriate time.

We do have a lot of people participating on the web, and this meeting is your meeting as well. Those participating can add comments through the webcast comment box, and again we would ask for the comments to come primarily from people who identify themselves as patients or patient representatives.

This meeting is being transcribed, and we have many people on our team taking detailed notes, so we are listening to what you are saying.

There are a few ground rules that we'll ensure that this meeting adds the most value to FDA and to the patients and patient representatives and to

all the others listening here today.

We are first and foremost here to learn about the perspective of people who have this condition, who live with HIV, so I'm going to ask all the patients and patient representatives to contribute.

We are very happy to see participants here who represent industry, research, and government agencies and a number of other stakeholders, and we believe that this input is as important to you as it is to us. We just ask that you stay in listening mode and do not contribute to the discussion. Again, there is an open public comment period that we would welcome your participation in.

So the purpose of the opening panel is really to give the discussion a good foundation, but the opening panelists, their comments have no greater weight than anyone on the web or in the audience. And we will be taking all the comments and listening carefully and incorporating all of those into our final report.

So this meeting is a bit different in that

we hope to have the discussion flow building off on what people say. So since you don't have to come and stand in line at the microphones, we really hope that when you have a thought and it comes to mind, that you can say it as the discussion is flowing and we'll have a really good flowing discussion today.

If we don't get everyone's full thoughts on a topic, we strongly encourage you to elaborate on your comments in the public docket, and our meeting web page has that information on how you can contribute, and we really encourage everyone, even if you're here today, to follow up and to elaborate on what you share today through the public comment so that we can review those comments as well.

Our discussion today will focus on the common ground regarding the symptoms, impacts, treatment, and research regarding HIV. We understand there are other important issues to ensuring that people with HIV get the health care treatment and support that they need, and those are very important issues. For our facilitated discussion today, we want to focus on the questions that are being asked, the

topic that FDA needs the most input on today.

Our discussion may touch upon specific treatments; however, the discussion of any specific treatment should be done in a way that helps to understand the broader issues, such as what symptoms various treatments address or what general downsides treatments have. Therefore, as part of my job today, I will keep asking questions that keep us on this common ground and keep us from getting too narrowly focused. And, again, there is a docket for which you can elaborate.

So the FDA staff is here to listen and there is some time for FDA to sort of comment and provide some remarks at the end of the facilitated discussion.

Now, I'm going to give a personal disclaimer. I am not an expert in HIV or its treatment, and I, in particular, have a really hard time pronouncing drug names, so if I can do it, I won't say any today, so I'll stay more general, but that is why we have our FDA colleagues, my colleagues, up here who are the real experts in this, and they are helping me with some detailed follow-up questions, so

I thank them for contributing their time.

We do want your feedback on this meeting. Participant feedback is very important. And we have evaluation forms that I believe are at the front table, and if they're not up there now, then they will be during the breaks or at lunch, and we really encourage you to grab one of those evaluation forms, completely voluntary, and submit them to the front desk and provide your feedback.

Above all, courtesy and respect is paramount and so critical to a discussion like this. Our goal today is really to enable a fair and open discussion, so please wait to be acknowledged before speaking, speak into the microphone, and if you feel comfortable, we ask that you also just state your first and last name so that our transcriptionist can capture that, and we can put that into our transcription.

Of course, avoid negative and derogatory language. I don't have to say that here. And keep all side conversations to a minimum, and if you have to take a phone call, please do so out in the hallway.

If at any point you need to get up, feel free. I said the restrooms are located behind the cafeteria down a pretty long hallway. And we'll be taking a break at some point in the middle of our discussion.

That was a lot of talking on my part. I am excited to turn it over, but before we do, we want to practice the clickers and the web polling. So, Chad, if we could have questions 1 through 5.

We're going to ask a few demographic questions because we would like to get a sense of who is in the room and who is participating via the webcast, and we'll see how this goes. These are no longer draft, these are in real time, we are moving ahead with these questions.

So the first question is an easy one. Do you live within the Washington, D.C. metropolitan area or outside of the Washington, D.C. metropolitan area? And in-person, click the corresponding number on your keypad. Okay. And I think once everyone has done that, then the results will come up. I'm not sure how much time we get.

(Answering question.)
DR. EGGERS: Okay. Great. And this is Chad up here, and he is instrumental into making this work today, so I thank him. Okay. 50 percent. Great. That was easy. So okay. So questions? We all know how to work the clickers?
(No audible response.)
DR. EGGERS: All right.
Let's go on to, what is your age? Younger than 25, 25 to 34, 35 to 44, 45 to 54, 55 to 64, or 65 and greater?
(Answering question.)
DR. EGGERS: Okay, great. It's nice to see that we have our distinguished guests here today.
All right. Can we move on to the next question? Are you male, female, transgender, or prefer not to answer?
(Answering question.)
DR. EGGERS: Okay, good. A pretty balanced split there, with 60 percent male.
Okay, moving on to the next question, have you been diagnosed as having HIV infection?

(Answering question.)
DR. EGGERS: Okay. Great. So about half of you are here living with, half of the patients and patient representatives in person are living with the condition, and have of you are speaking on behalf of those who do. And I'm going to give my personal thanks to those living with the condition. It can take a lot of courage, and we really do thank you.
Can I ask on the web, can we get the sense of how people are living with HIV?
MS. FURIA-HELMS: About 92 percent.
DR. EGGERS: Okay. Great. So we really --
MS. FURIA-HELMS: Oh, I'm sorry. It's the opposite. I'm looking at the wrong one. Six percent or 7 percent.
DR. EGGERS: Six percent. Okay. Okay. So we are listening to you as well, even if your comments aren't summarized today and in their entirety or at all, depending on how the discussion flows, but we are listening to your comments, we will be reviewing them. Okay. Discussion 1: Patients' Perspectives on Current Approaches to Managing HIV and on Symptoms Experienced

Because of HIV or Its Treatment Panel #1 Comments on Questions 1 - 3
DR. EGGERS: So with that, let's start with the first panel discussion to give a few remarks. And I'm going to introduce them.
We have David Brakebill. Did I pronounce that right, David?
MR. BRAKEBILL: Close enough.
DR. EGGERS: Okay. I'm a little bit better with last names than I am with drug names, but still not perfect.
We have Melanie Reese.
We have Joseph Jefferson, from the -- oh, Joseph, can you -- I forgot my notes up here.
MR. JEFFERSON: I'm Director of Advocacy and Alliance Development with Health HIV, and I'm also a patient.
DR. EGGERS: Okay. And we have Catherine Connor, from the Elizabeth Glaser Pediatric AIDS Foundation.
So we're going to start with David, and if you could just give a few remarks that answer -- let

me get to the questions. Again, we're focusing this first part on treatments to manage HIV. So what you're currently doing to help manage your HIV, what you see as the greatest benefits of those treatments, and the most significant downsides to those treatments.
MR. BRAKEBILL: Well, besides the usual HIV treatments, because of advanced age and other comorbidities, I also take a daily dose of Lipitor. I'm on lisinopril for high blood pressure, and I do as much as possible with diet and exercise to try to control symptoms as well.
Probably the biggest challenge that I think a lot of people have is access to alternative therapies. You know, depending on where you live in the country, sometimes you have access to those and sometimes you don't. So I think that's something that's been proven to work in a lot of instances, but it's not always available to folks.
Go into A and B as well?
DR. EGGERS: You can keep going. Do you have any --

MR. BRAKEBILL: So the specific symptoms that my treatments address, obviously, the high blood pressure, the high triglycerides. One of the things that I recently found out that I'm sort of waiting to see if some of the symptoms I've been experiencing, about 3 years ago my physician changed by regimen. When he changed my regimen, he didn't change my Lipitor, which was contraindicated with Prezista, and so about 3 weeks ago I go to the pharmacy to get my prescription, and I noticed it's a smaller pill. And so even 3 years after being on a contraindicated regimen, it took a pharmacist to say, "Whoa, you shouldn't be taking this."

So even though I consider myself pretty savvy about the treatments that are available, that was one that got past me. So I'm kind of sort of waiting to see if some of the muscle aches and those kinds of things that are indicated as side effects of statins will subside as the treatment sort of adjusts itself.

As far as how long I've been on treatment, I started in 1999. My first regimen was AZT/3TC before

they were Combivir, and Viracept, which if anybody was around Viracept, not one of the ones we use much anymore at all. And then I switched to Crixivan and Combivir, Norvir -- the first 400/400, and then 800/100, those of you who prescribe know what I'm talking about -- and 100, of course, boosted Norvir. Never failed a regimen and simply changed regimens to downplay side effects and to go to safer.

The last change I made was about 3 years ago to Truvada, Prezista, and, of course, boosted Norvir again, and probably the best results I've seen in terms of T cell, but even on the early regimen with Viracept and the AZT/3TC, my viral load was suppressed fairly quickly. I was diagnosed with full-blown AIDS -- well, we don't use "full-blown" because AIDS is what it is -- with seven T cells, and within about 6 to 8 months was able to get my viral load suppressed. So I think probably because I'm a good patient and I take all my pills most of the time I'm probably one of the poster childs for success stories of ART.

DR. EGGERS: That's great. Thank you.

Next, we'll move on to Melanie Reese, who

will share her experiences.

MS. REESE: Yes. And you asked him to identify who he was?

DR. EGGERS: Yes.

MS. REESE: Okay. I'm a consumer. I live with HIV, but I'm also a patient advocate, a patient educator, community health planner. I'm a caretaker, a lobbyist. I wear many hats. Okay? And I was diagnosed in 1999, and I began taking antiretrovirals in 2004. I asked to get on it because according to the CDC guidelines at that time, 350 T cells or less, they recommended. But that was before name-based reporting. I didn't want my name to get on the books, just my unique identifier, so I asked to get on medications because I had been on medications all my life, and I've had chronic illnesses since birth, so what's another pill or two or three or whatever to keep living?

So I've been on medication for 9 years. I'm on the same regimen; however, starting in 2004, it was three pills, and then it wasn't even 3 years later, it went to two, Truvada and Sustiva, and then now I'm on

the one pill a day, Atripla, but it's the same regimen. And my viral load never got higher than 6,500. And so the next visit, I was suppressed and I've been suppressed ever since.

Because I have a multitude of other chronic illnesses, my HIV is not something that my doctors are concerned with; it's everything else, and some of the treatments that would be the best for those conditions I can't have because of my antiretrovirals. They don't want that to be compromised in any way.

So I have chronic fatigue, fibromyalgia, chronic bronchial asthma, I have seizure syndrome, I have degenerative disk disease of my spine, I have arthritis, osteopenia, which is the precursor to osteoporosis, I have arthritis, bursitis, tendonitis. The list goes on. And I have irritable bowel. It's been going on long enough it's chronic, and they don't know if it's the disease or the syndrome, but because the immune system is primarily in the gut, when you already have gut issues, even if it's a slight chance to have gastro discomfort, it's magnified, so I have to take MiraLAX, Metamucil, Imodium Extra Strength,

it's a combination plus.
I take dicyclomine for my stomach issues and pain. I have GERD. If anybody doesn't know, that's gastroesophageal reflux disease, and so I have to take omeprazole. I take Lipitor, I take QVAR, I take ProAir, I take -- I'm bipolar, so I take Zoloft, and I used to take Depakote for mood, but since I have a concussion, had a seizure, brain surgery and all, they had to take Depakote away and give me Keppra. It's a long name because it's -- I don't know if it's generic or what, but "Keppra" I can pronounce.
So I have chronic pain, I cannot take anything for pain other than if it gets too severe, I can take Tylenol, but I have stomach issues where my lining gets very thin, and just so that it won't rupture, I can only take that periodically. So I just have to grin and bear it.
DR. EGGERS: Well, we will have a lot of follow-up questions, I think, after the break on how you manage all of that, but thank you so much for sharing that. Did you have anything else you wanted to add, or should we move on to Joseph?

MS. REESE: Go ahead and move on because --
DR. EGGERS: We'll move to Joseph.
MR. JEFFERSON: Well, I just have to start by saying when I read the questions that were disseminated, I sort of had to ask myself if I was the appropriate candidate to speak. That's perhaps because my status yields a somewhat boring analysis. I have been positive for 25 years, asymptomatic for 25 years, virally suppressed for 25 years. In the early years, there were a number of meds that came and went. I've been on a fairly consistent regimen for the last 8 years. I get sick less often than virtually everybody I know. So I'm sort of this outlier perhaps, but I thought, after giving it a little reflection, that folks in this room need to hear from those of us that are actually faring well, and I can't really go any further on a personal level without acknowledging the folks that stood on the steps of this building or nearby buildings 20 years ago fighting to get in and here we are on the inside.
DR. EGGERS: Yes.
MR. JEFFERSON: So I thank them. I thank

all of the folks at FDA that responded. I definitely want to tip my hat to the brilliant research community and to industry for really stepping up, and I likely would not be here were it not for the efforts of those groups.
So that's my story. I suppose I wanted to also come and give a voice also to those of us that are now I'm well situated in and many others are about to enter the new sort of emerging demographic of interest, which is, of course, the over 50 population with HIV, and, of course, most everybody in this room knows that in 2 years more than half of all folks living with HIV will be over the age of 50, and I think that presents a whole wide variety of challenges both in the clinical trial setting as well as in adherence issues, which is a big concern of mine that I'll get more into in the facilitated discussion later because I think that there are some things that we need to press forward on as it relates to tailoring, treatment methodologies, and adherence interventions for those of us that are going to be soon likely managing multi-comorbidities that are typically

associated with folks 10 and 20 years older than we are.
So there is a lot of work to do, and I am happy to participate in the discussion. Thank you for having me.
DR. EGGERS: Thank you.
And then I'll move on to Catherine Connor, who will provide -- we have asked her to sit up here and provide the pediatric point of view to make sure that very important population is represented today.
Thank you, Catherine.
MS. CONNOR: Thank you. And I have the unenviable position of trying to describe what the pediatric population is now. You know, it used to be very easy to say, especially when you look at the legacy of Elizabeth's Foundation of what the fight looked like, and now you have to remember that pediatric covers a wide range, and when you talk about managing symptoms and the drug regimens when you go from a neonate to the youth and teen years, even into college now, it's really a diverse population, and the needs of that population are really diverse, and then

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sometimes you forget that especially with the younger children, you have somebody else who is involved in this, which is the caregiver, and the caregiver actually has a lot, and they have differing opinions than the patient as to how to manage the symptoms and what needs to be done. And so I think that it's important with this group in particular to think about how the drugs are administered, how tough the adherence is for the different age groups in particular.

When it comes to the impact of the side effects, you actually don't see necessarily more side effects in children than in adults when it comes to using these drugs, but the impact of the side effects on young people and in children can be very dramatic. Before this meeting, we actually worked with AIDS allies to talk to some of the beneficiaries and the families that we work with, and it was interesting, when you talk to both the children and the young people and their parents, some of the ones that came to the top were some of the night terrors and insomnia. You know, if you're a 6-year-old or 7-year-

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old living with HIV having night terrors, the impact of that on you is different than an adult, who knows how to deal with it. The same thing with some of the gastrointestinal issues that come with medicine. As an adult, you kind of know how to deal with it. As a child who is in school or a child who doesn't even really know their status because of disclosure decisions made by the adult, how they handle those side effects can be very different as well.

Something that also came up in our conversations was an acknowledgement of some of the longer term impacts, and we have folks on the panel who have been addressing their status for a number of years. With children, obviously, one of my colleagues like to say it's not always the immediate side effects, you have to think about the bones, the body, and the brain, because all those things are developing at a time they're taking toxic drugs to deal with a chronic illness, and so you do see the longer term things that are still being studied, the developmental issues that a lot of people growing up with HIV or infected as youth with HIV have, impact on their

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organs. We have a number of families that we work with that now, being a 20-year-old who has had HIV since they were either perinatally infected or infected as a youth or a young child, really are getting more and more of the type of things where they have to worry about the impact of a lifetime on ARVs, what it's done to their bodies, and how they continue to live, and again acknowledging sort of the different side effects as these kids grow up.

When you talk to these families and these young people, they actually switch regimens quite often because puberty affects them differently, and anyone who knows pharmacokinetics, you know, you really do start to have to shift and change a lot and more frequently as a child on HIV medicine or as a young adult on HIV medicine, and so they may have -- actually their bodies are a little bit more worn down and the side effects change as they use these drugs in different age groups.

And one last -- well, two last points I kind of wanted to make on this topic is when you talk about managing HIV, we work with a practitioner here in D.C.

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who often remarks on how she has young people in their teens that are already on salvage therapy, and this is because of the very specific population who have gone through first-line, second-line, you know, there just aren't a lot of options for them, and I think that's something that's really important on the research agenda, that these kids do end up on some really harsh drugs at a very young age, and we have to keep that in mind as we start to look for better formulations with the least amount of side effects with the most effectiveness. That needs to be kept in mind.

Also -- and I thought about holding this off for the adherence conversation, but I think it's also important to mark for this patient population -- is sort of how the use of drugs impacts when they transition to adult care because a lot of times the adult HIV treatment community is a little bit more lockstep, you know, "Oh, you're infected. Here is our first line. Here we go." These are folks who have complicated medical histories, they've been on a number of treatments. They know their side effects.

They probably know more about HIV than all of us, having grown up with it, but sometimes when they transition to adult care, that isn't recognized or understood, and so a lot of times that can impact adherence, but it also impacts how these treatments affect them because there isn't this recognition as a young person or a child who has lived with this for a long time when they get to that new part of the health system.

DR. EGGERS: Great. Thank you very much, Catherine.

Do any of my FDA colleagues have a real question that they want to ask to one of the panel members before we move out to the large discussion? We'll be able to engage you guys as well. Thank you.

(No audible response.) Large-Group Facilitated Discussion on Questions 1- 3

DR. EGGERS: Okay. Then we're going to move to the facilitated discussion. I'm going to make my way out to the front, as it was called in our first meeting, "talk show style," so we'll see how that goes. And if we can get the next question up.

I can't squeeze through.

Is this on? Okay. I'm going to do my best to talk into the microphone, but sometimes I get a little lazy at that, so please let me know if you can't hear me. So we'll ask this question before we get into the discussion. So how long ago was your diagnosis, for those living with HIV, in person and on the web?

(Answering question.)

DR. EGGERS: Okay. So it looks like everyone here is 10 years ago or more, although we do have the pediatric population represented here. Do we have those numbers on the web?

MS. FURIA-HELMS: Can you hear me?

DR. EGGERS: Yes.

MS. FURIA-HELMS: Yes, more than 20 years ago, and it's 100 percent, but only four people have responded.

DR. EGGERS: Okay. All right. So we will frame this as having lots of wisdom in the room and on the web.

There is another question. Okay. So we

would like to get a sense of, how many different types of ART regimens have you taken? Have you never taken any, currently on your first, have taken two to three different regimens, more regimens, or if you're not sure?

(Answering question.)

DR. EGGERS: Okay. So again lots of wisdom in the room, lots of experience with many different things. Everyone has taken at least two or more regimens. Okay. Great.

So we heard a lot of great things from the panel's discussion up in front, and I'm going to follow up on a few of those things and get more feedback, and again I encourage my FDA colleagues to follow up.

We heard a lot about the benefits, being able to lead life with a chronic condition and living it for a long time, so I would like to follow up on that a bit more, and I would like to follow up on a few of the issues regarding decision making about how you choose a regimen and how you choose to change a regimen, and then look at some of the downsides of the

regimens that we heard about, particularly the complexity of that treatment that Melanie was talking about, and also, David, you alluded to that as well with the contraindications and the effects on the other conditions that you have.

So with that, let's start with the benefits of the current medications out there. We heard from the panelists up here, but I would like to see if anyone, any of you in the audience, wants to sort of echo or follow up on what you heard about the benefits that were mentioned up here.

Does anyone? Yes.

MR. SHARP: Hi, everybody. I'm Matt Sharp. I'm a long-term survivor and obviously have had a lot of benefits with treatments. I wanted to bring up one thing that I have had to experience, and that's immunologic non-response to the therapies. I've been pretty tolerant of almost every medication I've been on except, say, for Fuzeon. That's supposed to be a joke.

MR. SHARP: But I never was able to really respond immunologically. So I just wanted to bring

that up as an important issue with the state of therapy today.

DR. EGGERS: Okay. Would anyone else like to comment on what they see as the real benefits of today's treatments?

Yes, David.

MR. BRAKEBILL: Well, I think the benefit in terms of particularly people who are newly diagnosed, you can start on a once-a-day single pill regimen. You know, for me, even changing regimens when I was undetectable was a tough decision because, you know, if ain't broke, why fix it? So my doctor even tried to convince me that, "You need to move to these safer regimens," was something I struggled with, but if I change and it doesn't work, then am I using up one of those pools of meds that I have access to?

But I think the thing that sort of concerns me at the same time is even though we have simpler therapies, those of you who are familiar with the treatment cascade, we're not really seeing any improvement in viral suppression. So there is something about how we're approaching taking medicine

with suppression of the virus. You know, I don't know whether it's because we're asking people to start treatment before they're ready, where there is not the correct amount of counseling and advice around that, but that sort of disturbs me, that even though we have simpler regimens, we're not really seeing an increase in the number of people who have suppressed viral loads.

DR. EGGERS: Would any of my colleagues like to ask a follow-up question to that?

Yes, Catherine.

MS. CONNOR: This is just a comment, but I just wanted to comment on actually the phrasing of the question again for my population. "The rest of your life" is a very deep thing for young people, and again I'm 37, the rest of my life feels like next weekend, but for them it is a very daunting idea, and especially when you have an asymptomatic young person who is looking at having these pills, and, again, as we have moved to one-a-day pills, this has lessened a little bit, but it is very, very daunting to tell an 8-year- old or a 12-year-old or even a 15-year-old

that, "You're going to have to do this the rest of your life," and I think that's why you do -- again, I know this is more an adherence issue, but it's a different discussion with that population, and I think that's why you see such erratic adherence issues with that population, because that question in its own right is sort of heart-stopping for that population in a way I don't think it is necessarily for newly infected adult patients.

MS. REESE: I have a comment.

DR. EGGERS: Yes. Go ahead, Melanie.

MS. REESE: I appreciate your comment for the pediatric, but that applies across the age spectrum because people don't want to take anything if they're feeling okay, and they'll take it and then somebody will tell you, "Oh, you're UD, undetectable." "Why do I have to take this now?" It's hard to wrap people -- I started off my life with medications, so I know you take it regardless so you don't die. But most of the population, that does not compute.

DR. EGGERS: Thank you, Melanie and Catherine, from the pediatric perspective. Can we get

a little bit more into what you hear, the reasons that they give, for not wanting to be on those medications? Do they, for example, say, "Well, I'll go back on them when I need to," or do they have other reasons? And feel free, anyone can answer that.

MS. REESE: There are lots of reasons. Some, if they are trying to get in a relationship or are in a relationship and have not yet disclosed, they don't want anybody seeing them taking their medications, so they'll avoid taking medications if their companion, friend, are around. Some, it's even their family. If their family knew that they were infected with HIV, they would be rejected, wouldn't be allowed to eat at the big table or with regular utensils, everything has to be plastic, to be thrown away. So it runs the gamut, the reasons why people don't want to take it.

DR. EGGERS: Catherine?

MS. CONNOR: And sort of, as I mentioned in my opening comments talking about a wide range of people here, we see a lot of folks who just again growing up with HIV population, it's a little bit of

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exhaustion. I don't think it's unique to them, but they've been on this medication for years, they've probably been on their third, some of them would just sort of rather not -- you know, we have a couple of families, I mean, the Elizabeth Glaser Pediatric AIDS Foundation has been around for 25 years, and some of these families we've worked with a long time, you do see patients who just sort of throw in the towel, they're just a little exhausted from, again, the side effects of it, the memory lapses, inability to have people understand what they're going through, they would just rather not take treatment. You know, with other folks again, more the youth infected, again it is the cavalierness of, "I don't have any symptoms, I'm taking this medication. I don't feel like I have to." And, you know, part of this is attributable to just being young people. I mean, you know, you can only ask so much maturity from a certain age demographic, but I do think you see that.

And I do have one, again, a lot of the work that we do also is with the provider community, and I do think that where people get their care and

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information dramatically impacts whether you answer this question one way or another. And, again, in a lot of the pediatric care settings, you have some really dedicated professionals who are very good at explaining to parents and children why they need to take this and supporting them even in decisions to switch medications and discussing side effects. Other parts of the provider community are not as good at that. And so I think it really does matter, not just the medication itself but how the medication is explained and the support they get while taking medication.

DR. EGGERS: Great. Thank you.

Before I take one more, let's actually ask this question that's up here on the screen, so if you have your clickers, please feel free to answer, and on the web. For those that are living with HIV, which of the following statements best reflects your overall perspective on having to take multiple HIV medications every day for the rest of your life? Maybe you take multiple or maybe you just take one, but thinking about having to take multiple, overall it does not or

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would not have a significant impact on my daily life? Overall it does or would have a significant impact on my daily life, but I feel that I am able or would be able to take my medicines as prescribed by my doctor. Overall it does or would have a significant impact on my daily life, and I am worried that I might not be able to take my medications every day as prescribed by my doctor. Or if you are not sure which of those statements reflects your perspective.

(Answering question.)

DR. EGGERS: I've give you a few more seconds. Okay, we can put those up. So really a wide range. So, yes, it's a big burden for a lot of folks in the room. On the web?

MS. FURIA-HELMS: About 80 percent said it does or would have a significant impact. The total N is 5.

DR. EGGERS: Okay. But that they would be able to or they would not be able to? So the middle choice?

MS. FURIA-HELMS: The second choice: it does/would have a significant impact.

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DR. EGGERS: Okay. So it sounds like it does or would have a significant on life, though it, for many of you, would be manageable. Does anyone want to follow up on that? And I think Randy had someone? And could you state your name, please?

MR. SCRUGGS: Good morning. My name is Nathaniel Scruggs. I was listening and I thinking about my own journey getting to this seat where I'm at today, and I was listening to the panel. I think in dealing with AIDS/HIV -- and I heard you all mention that this is the second of this type of event or coming together -- but when I first found out, I didn't want nobody to know, I just didn't. I didn't want nobody to know, and that was because of my ignorance. That was because of my ignorance and it was because the way society viewed and the information that was presented about people living with HIV and AIDS. I was fortunate to be ignorant enough to go seek out help through alternative groups and was blessed to get a provider who could tolerate my ignorance and disrespectful behavior based off of the fear of what was projected to me through the

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community.
So I didn't know, and I was listening, you know, how I think one of the key things that is misgiving in the treatment of HIV and AIDS is that you can't lump everybody in the same basket, and which I know the government has what it's supposed to do and policies set, but they just talked about it. You can't take a child that was born with AIDS or HIV through their mother and subject them to what you expect a hardcore drug addict, sexual promiscuous, heterosexual male to deal with in taking medicine.
So I think what's happening here is vital to what's the next step going on in the treatment of HIV and AIDS because this is what needs to take place. You need to have everybody sitting in a room and discussing their perspective or their point of view around how they feel and what do they think the best outcome would be for that particular group of people.
And I was looking at the regimens. I've been on about four regimens, but what they didn't tell me until later on that I found out through my own, each regimen that I've been on affected me in some

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type of way and it's irreversible affectedness of this medication: cholesterol, high blood pressure, kidney problems. So it's vital to what we have to do.
And I was listening to Melanie, and Melanie was talking about the lesser of the two evils, that's what that really was, the lesser of the two evils. Do I bite the bullet to continue tolerating these other conditions so that I can manage my HIV? You know, I was in that situation at one time, I was taking medicine that was affecting my kidneys and my liver, but through medicine, pharmaceutical companies, they became more patient conscious, they're still making the money, but they became more patient conscious to realize that what they're doing to help us people that's living with HIV, they're hurting us in the same way. So we've got to do something with these formularies.
DR. EGGERS: Thank you very much, Nathaniel.
I think we had Matt?
MR. SHARP: So I just wanted -- there is no question that the medications have become more tolerable and easier to take, but the problem I have

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with the question is, it says, "Take my medications every day as prescribed by my doctor for the rest of your life." I find that just, you know, impossible for most people. You're going to miss a dose here and there. I do know people that are amazingly adherent every single day at the same time, a few, but I just wanted to point out that, remember, we need really to focus on long-acting formulations so that this is sort of the next hurdle, I believe, that we need to get over so that we can complete sort of the antiretroviral picture and make it 100 percent.
DR. EGGERS: Okay. Well, Matt, I hope that you bring up the long-acting formulas when we ask our last question before lunch, which will be: What are you looking for in an ideal treatment? So we'll come back to that.
Does anyone else want to follow up on what they've heard?
Yes, Wanda.
MS. COMMANDER: I have been infected for over 26 years now, and I'm symptomatic. I've had a lot of OIs, opportune infections. And I want to say

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that the medicines today are really doing some spectacular work in my life because even though I'm undetectable, I still have a very low CD4 count, and the medicines are keeping me going.
DR. EGGERS: Thank you very much, Wanda.
Does anyone else want to follow up on that?
Yes, Joe.
MR. JEFFERSON: Well, again, I think it's important to acknowledge that these questions are phrased in sort of an isolationist manner. It's to assume that HIV is your one and only or your sort of top-line condition that you're working with your provider hopefully to manage. And, again, for those in the room and others who are battling multiple conditions, I think it's hard to really bring a sophisticated analysis to these questions without considering the co-occurring challenges, if you will, of managing multiple conditions, and so I think as we get into the discussions before lunch about the future of pharmacology, there is a rich discussion to have around that.
DR. EGGERS: Yes, Ed.

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DR. COX: Can I just follow up on that? I guess I'm wondering, and we heard in some of the comments earlier, the issue of drug interactions that seems to be an ever-present challenge both with antiretrovirals and other meds. I'm curious if the panelists might be able to comment more about drug interactions. It sounds like I think it was David's comments where something sort of popped up a little bit and he didn't recognize the potential for interaction initially. And given the complexity in interactions, are pharmacists pointing them out to you? Are physicians pointing them out to you? Are patients? How are those things surfacing in the real world? And any comments that you might have on that would be appreciated.

MR. BRAKEBILL: Well, I think in my case, you know, I mean, most doctors that are practicing HIV or infectious disease or anything are seeing more patients than they can handle, so part of it is capacity in the system. The other piece of that is that this is a relatively new pharmacist. I've been using the same pharmacy for 11 years. The doctor

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probably, when he changed regimens, forgot that -- didn't look that I was on Lipitor, I mean, he's an HIV specialist, he's certified, the whole thing, just it never happened, and like I said, 2 weeks ago this relatively new pharmacist working at the pharmacy flagged it, and I'm immediately going, "What? What? What? What? What?"

And so I was as surprised by it as the system, but I think that's just a systematic thing. I mean, maybe with e-prescribing and some of these things that are coming up, that are coming online, those things will be flagged automatically, that when you're filling a prescription, and it just so happened that this pharmacist called the doctor and the doctor said, "Let's reduce the dose." You know, when I go back to see my follow-up visit in August, I'll say, "Okay, let's talk about this and see what we can work around."

But I think that happens, you know, in this case it -- I think for a number of reasons. As I mentioned, I think HIV docs, clinicians, people that are working just it's -- you know, and medical care in

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general is, "Get them in, get them out," unless you're in, you know, some specialized clinic in some big city that treats the whole person. That's the other thing. You know, you have for HIV patients you're sending them here for this, there for that, you know. If you have the luxury of being in a metropolitan area where you have holistic treatment available to people where four or five different people are looking at your medical records, probably the chances of that are slimmer, but I think in particularly small rural areas where access to care in general is an issue, that you're lucky to see a doctor, that those things are sort of not looked at as closely. That's my opinion.

DR. EGGERS: So I think both Melanie and Joe, and we'll see if anyone else wants to comment and then we'll go take a break after that.

So how about Joe first?

MR. JEFFERSON: I just want to amplify a couple of things David referred to. So at Health HIV, we do a lot of workforce development work with providers and health departments across the country, and we also do an HIV primary care survey every year,

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we just concluded our third annual survey, and what we're finding is that 40 percent of primary care providers are seeing HIV populations experiencing multiple conditions that they're having to manage, but as we all know, through many of the reforms that are forthcoming via the ACA, we've been doing a lot of work in these health centers and other facilities to really ramp up the capacity of the primary care provider to provide primary care to HIV-infected populations, and there is a huge shortage in the number of primary care docs that know what to do when somebody walks into their office with HIV or is diagnosed with HIV in their setting, and so one of the things that I think we need to really scale up is some really very stringent CME requirements around this.

We're also doing some mentorship initiatives where we're pairing HIV-experienced providers with HIV- naive providers to be able to provide that additional daily support so that when someone is in an exam room with somebody that's managing four or five conditions and they have no idea how to proceed, they can literally pick up the phone and call the more

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seasoned provider to get some guidance. So I think there is a lot of rich opportunity in the whole workforce arena as well.

DR. EGGERS: Thanks, Joe.

Melanie?

MS. REESE: To piggyback on what he said about primary care providers not understanding the complexity of managing multiple conditions, I guess my neurosurgeon just fired me because he said I have too many things going on, he throws his hands up because every time he tries to prescribe something to ease something that's going on in my head or my seizures, it doesn't work with what I'm already taking for all my other stuff. So he said, "Go to your primary care and see what they can do to manage it."

MS. REESE: So at one time when I was in the hospital with my brain surgery, I was overmedicated because they didn't realize that what they were giving me for my seizures and relieving brain pressure and all that stuff was counterproductive to my HIV meds and they were putting me in a critical situation, and I didn't know that was happening to me, and when I

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went back to refill what I got from the hospital, the pharmacist said, "How long have you been taking all this stuff together?" and I said, "Oh, 6 weeks," and he goes, "We have to call all these doctors and figure out something." So that's a scary thing.

And with ACA coming and people with an insurance card who are used to just going to emergency departments when they're on they think their death bed, they're not going to know what to do, they're not going to know what questions to ask, and doctors don't know how to speak to people who have more than one thing going on with them.

DR. EGGERS: Okay. Someone out here?

MR. TIETZ: Hi. I'm Dan Tietz, from Kryon in New York. I just want to add a little bit to what Joe said and then some to what Dr. Cox asked. As you know, for pivotal drug trials, pretty much they top out in terms of age at 58, 60.

DR. EGGERS: Yes.

MR. TIETZ: And most folks in ARV drug trials are otherwise, generally speaking, healthy, say, for their HIV disease, yet the people who are

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going to take those drugs once approved are almost to a person have other challenges or are on other medications, and yet there is little post-approval/post-marketing follow-up that's really compelled by the FDA from manufacturers to sort of go back and study and report in some really active way what's happening with people who are taking their meds in real life who have got other conditions, because, of course, in the original clinical trials on the way to approval, those folks weren't participants. So I think it would be really useful if that happened, and I think you could hear more than from folks who are in -- you know, if only in a trial that's sort of looked at, just their real life experience in reporting would be really useful.

DR. EGGERS: I see the follow-ups. If they're short, we'll take them now, otherwise, we can have a broadness discussion and have it after.

MR. BRAKEBILL: And I think to what Dan just said, you add women, you can add transgender folks. There are a whole lot of people that are being missed in the research end that really need to be -- I mean,

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why are women less adherent? I mean, we found that again and again in some of these big prep studies that women just for whatever reason don't seem -- you know, it's the mother thing or whatever, just aren't adherent to drugs as well as men are. So I think there is a lot on the research end that needs to be looked at in terms of if we're going to talk about more effective drugs, we need to talk about targeting populations in those studies as well.

DR. EGGERS: Okay. Then I'm going to propose that we ask, when we come back, we'll revisit this topic thinking about not just what an ideal treatment would be but maybe what an ideal treatment study will be, which I think will be a great prelude for the afternoon discussion when we think about HIV cure research.

So I want to thank you all. We'll come back after a 15-minute break, so at 11:15, and we'll resume the discussion just like we're having. Okay?

(Whereupon, a brief recess was taken.) Panel #1 Comments on Question 4 - 5 Large-Group Facilitated Discussion on Questions 4 - 5

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DR. EGGERS: Okay, if we can again work our way up, we'll get started. And you can feel free to if you, of course, need to leave or head out of the room at any time, this is, as you can see, a very open discussion and very free flowing.

So we want to continue on what we talked about before the break, there were some very good points, and my FDA colleagues have given me some really good follow-up questions to probe a bit more into particularly managing the complex decisions that you have to make when managing your multiple conditions, including HIV. And so we'll probe into that in a little bit.

But, first, we did have a series of questions that we wanted to get from our panel discussions to set a foundation for moving into a discussion as well in this before lunch period that really talks about any conditions or any symptoms that are the most significant or conditions that you believe are associated with HIV infection that really have the most significant impact on your life. And we heard earlier the range of things, you know, the range

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of conditions, but maybe just now focusing on, what's life like trying to manage all these conditions, and how does that impact life?

So I think I'm going to put the panel members back on the spot, and if you have any comments that you want to present to start the discussion, we, of course, will revisit them. Then we'll do that. Should we start again with David, or would you -- okay. Why don't we start and we'll talk about the pediatric point of view with Catherine, and then we'll move our way this way.

MS. CONNOR: Thanks. You know, looking at the questions again, I feel like I'm making an excuse, but it's sort of difficult because of the wide range of the age population I'm talking about, but a lot of it has to do again with managing or the significance of the symptoms, you know, age, disease state really matter?

I think, you know, across the board when we talk to our families and our kids and, again, remember the population we're talking about, I think nausea really is a factor. And, again, I keep putting this

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qualification on there, but these are kids who don't have a lot of control over their lives, and so the caregivers are very much in control, but when you have a school age child, they can't schedule around, "I know I'm going to be nauseous 40 minutes after taking this, so maybe I'll have to miss 15 minutes of math class." I mean, it's a real scenario for some of these kids.

We have a lot of discussion with some of our older age groups about they've told us they schedule college classes around when they take their medications and sort of the immediate side effects afterwards, so there is a real sort of impact there that I think makes more of a mark when we talk to them than some of the other ones.

And then, of course, with the significance, I think the long-term stuff is very important to my population, some of the bone density things that have happened with some of our longer term patients as well as obviously the fat distribution issues. Again, the younger population is a little more vain, I don't think that's quite true, but, you know, again, there

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is a little bit more of a stigmatizing group that can affect them that way as well.

But I think, you know, again looking at the last one, the ideal treatment, I'm going to give a moment to the younger patient population, even though the patient population in the U.S. that's perinatally infected is small, anything we do in this form actually translates globally, and I thinking finding -- you know, I wrote it down specifically, you know, a new medicine that's easy to administer with the fewest side effects and the maximum effectiveness. I mean, that's sort of the Holy Grail if we're not going to find a cure, is, again, administration with the younger populations is very difficult.

We have an ambassador we work with who is now in her teens, but she tells the story about how her grandmother made a book about taking pills just for her, and it's because she didn't understand why she had to take handfuls and handfuls of pills at a young age, so she would sit down with her grandmother, and her grandmother would read this book about Janice takes her pills, and that was how they kind of got her

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to kind of get used to it and to take them regularly. But, again, so it's sort of interesting that you have to kind of think about the easy administration when you work with the younger population.

DR. EGGERS: Can I ask a follow-up question? You mentioned earlier about the night terrors. And can you expand upon that a little bit and maybe what degree that's felt, that's experienced, in the population that you're familiar with and how it affects?

MS. CONNOR: I hesitate to only because the stories are very personal and they're also told by people who could tell it better than I can. But, no, I think it is something that happens frequently. And one of our ambassadors, it started when he was young and they continue to this day, and he's almost 30 now. But there are the sort of -- and they just wake up -- I mean, I can't describe a night terror any better than anybody else, but, no, it shakes them, and it's hard for them to understand it's part of their condition and part of the medicine they're taking. It's a bad dream, and it's a very bad dream, and if

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you had that regularly, there are some of our patients that we've worked with who it could be a deciding factor on going off of medication because it is so traumatic for that age group. But as far as the specificity, I probably can't speak to that very well.

DR. EGGERS: Okay. Well, that was very helpful. Thanks.

MS. REESE: Can I say something about that?

DR. EGGERS: Sure.

MS. REESE: Night terrors and bad dreams, Sustiva, anything with Sustiva in it, it goes across the age spectrum because people refuse -- it's 4-D, 5-D, you know the impact of 3-D, the vividness and the strangeness of how things -- you're -- Atripla has Sustiva in it, and they said, well, after a while it would diminish. It doesn't. I have them. But I've also been programmed from birth to take medicines regardless because you want to live and experience life. So that wouldn't be an excuse for me, but I know a lot of people who had to stop that or stopped it and didn't tell their provider, especially when it was a separate pill. They would take two of their

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components of a cocktail and not the third. But night terrors.

And my worst thing is even after -- I'm postmenopausal, and so I had the hot flashes and night sweats, but several of my conditions have those, so it's compounded, so at any moment I can feel like I'm going to just burst into flames and disintegrate, and then not long after be so cold to the bone that there isn't enough heat or blankets or clothes that I can put on to be warm, and there is no rhyme or reason to that. And so that's the worst thing for me. And then, you know, add my seizure syndrome and brain surgery and all that, I can't drive, so that's one element of mobility. And then I have balance issues because with the trauma to my head, I have ringing in the ears, whooshing and pulsating and whatnot, and I have vertigo.

MS. REESE: So those things are the worst things for me.

DR. EGGERS: Okay. Joe, would you like to follow up?

MR. JEFFERSON: As I said at the outset, I'm

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so boring, I don't have a lot of these problems, and so I don't take it for granted, and I recognize the challenges.

UNIDENTIFIED MALE SPEAKER: That's great.

MR. JEFFERSON: Yeah. And so certainly I'm aware of the science, I know what's coming, and I'm concerned about that. I suppose my public health orientation keeps pointing me to sort of the structural problems. I mean, we can sort of get at what's good about medicine applied optimally, but I think we have to think cross-departmentally in the bureaucracy about, what are FDA's specific responsibilities to address this whole adherence question? There are many other bureaus within HHS that have a foothold in this certainly, and we in the advocacy world as well, as well as those of us who want to sort of empower a more robust consumer accountability sort of philosophy, so there are a lot of moving parts here, but I think we have to sort of ask ourselves, what is it that's holding folks back even if the medication on their shelf is good and can work?

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You know, we just finished a survey of consumers, an HIV survey, and we found that though it's a bit skewed because we find that most of the respondents are fairly seasoned consumers who are relatively good at self-care, but even among that population, 95 percent of them say they're on treatment, and only 60 percent of them self-report as being adherent, and this is a very good sort of population in terms of self-care. So if it's 40 percent, almost half, of them are not adherent, you know, that speaks volumes about the larger population of folks that are -- and this is just HIV, we're not even talking about all the other meds. So I just think that the whole system has to work more collaboratively to really come up with some interventions to get people to pick up the bottles and take the pills.

DR. EGGERS: Thanks, Joe.

David, would you like to provide any comments?

MR. BRAKEBILL: Yeah, I think in terms of the side effects that probably most impact my daily

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living, probably number one on the list would be peripheral neuropathy. You know, when you're trimming your toenails and realize that you've cut your toe because you can't feel where the clippers are going, and there aren't really, in my experience, a lot of really good treatments on the market for that that are labeled for use in people with HIV, let's put it that way, and so I think the FDA probably could look at some of the treatments that are available for, say, people with diabetes that are approved for diabetes treatment for neuropathy but aren't necessarily approved for HIV. I know that in my experience there are doctors prescribing Lyrica for that condition, and it is working in some patients.

Probably secondarily to that, fatigue. Some days I get up and I can conquer the world and do 500 reps of 500 sets of exercises at the gym, and some days I just want to lay on the couch, and I never know when that's going to be. And, again, is it HIV? Is it the meds? I think the jury is still out on that.

Probably third, I think not a real common occurrence anymore, but I still get the occasional

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night sweats. You know, the primary driver -- and I think this goes back to a lot of the research that's come out in the past years -- is the whole situation of inflammation and, how do we control that constant revving of the immune system that seems to put people at risk? We know inflammation is the number one cause of heart disease, which we see presenting more and more in older folks with HIV at earlier ages.

So probably -- and the other sort of fatigue thing is only being able to sleep 4 or 5 hours at night and then having to take a 2- or 3-hour nap in the afternoon, so that my clock is sort of constantly in flux.

So those are the kinds of things that sort of keep folks who -- you know, I'm sort of one of those people who has been on disability for a long time because at the time that -- that was what happened. You know, people were diagnosed with AIDS, you went on disability, so there is sort of that dynamic plays out in the HIV community as well about those disability people and, "Why do I still have to work?" sort of mentality.

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So I often think that I would like to be productive again, but then when I have one of those days where I can't make it quite through the day, I go, "How can I hold an 8-hour job?"

And I think the other dynamic that has to be continued to look at in research and in terms of medications, too, is we know that depending on your nadir in terms of your T cell count and/or your viral load, you know, how high your viral load once was or how low your T cells went, that outcomes are different for people. So success in viral suppression and things like that are a lot dependent on where you started treatment. So that also needs to be considered in terms of, can we find more effective treatments for people who have an AIDS diagnosis versus people who simply are HIV-positive? Because we tend to have better outcomes with people who have never experienced an AIDS diagnosis, and I think that while there has been some study, I think there probably are some, at least on the genetic side, maybe as to why more people are more predisposed to developing AIDS and the more long-term progressives.

So I think those are sort of the things that were probably in terms of -- are you ready to move forward with the next question in terms of the complete cure?

DR. EGGERS: Well, let's wait on that ideal question, and first let me see if my colleagues want to follow up on any of the symptoms that they've heard.

Yes, Ilan.

DR. IRONY: Yeah. I wanted to follow up on something that David just touched upon, but Matt and Wanda also alluded to, which is the immunologic non-responders, people that have virologic suppression or undetectable viral load but have no rebound of CD4 counts. And since the topic here is about symptoms or concerns related to a particular lab finding, I wanted to know what kind of impact this has either as type of symptoms, of not having an immunological rebound, or concerns about this.

DR. EGGERS: Okay. So the impact of the viral load? Is that essentially what the --

DR. IRONY: The immunologic non-response.

DR. EGGERS: The immunological non-response. Can you tell? In other words, can you tell or does that have any impact on your life as you experience it?

David, do you want to go -- oh.

MR. BRAKEBILL: I think anybody that --

DR. EGGERS: Let's give Wanda a chance because she hasn't had too much, so if we could bring a mic up to her, and then we'll come to David.

Oop, I don't think it's on yet.

UNIDENTIFIED MALE SPEAKER: Here you go. Try this one.

MS. COMMANDER: Okay. I wanted to say something about the CD4 count, about it being so low. Physically, I feel as though I have to pace myself all the time now. I'm vulnerable because with a low CD4 count and me not being able to take certain medications for preventative measures, I had hep C real bad, so a lot of things went on with me that cause me to take it one day at a time now. It allows me to be grateful for whatever rest I get now. I'm thankful for the medicines that I do take because

there was a long time before I could get to UD, it wasn't until about 5 years ago after taking all the different medications and having all the different side effects.

I developed some type of resistance to many medicines over the years. I'm on a salvage regimen, and I'm not doing as well as I want to do as far as physically, but mentally it can cause you to feel depressed a lot, and some people have to go to see a psychiatrist, who take medications for that, so I, in turn, decided to do that, and that's allowing me to feel a lot better knowing that my CD4 count is so low and that I'm still undetectable. I know that it seems like it should have rose with the different medicines over the years, but it has never, it's gone as high as 3 something, but it always drops below 200 and stays that way.

I probably could go on and on and on, but right now it's an emotional time for me right now. I'm feeling it because I know that I push myself every day to do things that a lot of people would take that chronic illness and just lay down and not do anything.

I get involved in a lot of groups, I go to a lot of organizational functions, and even here, I live in Baltimore and I'm here in D.C. today, but that's only through the grace of God that I'm able to do what I do, do. I'm thankful and I'm grateful.

DR. EGGERS: Thank you, Wanda.

We're going to come back to the question, the issue, of HIV as a chronic condition, so, Wanda, we will be revisiting that topic. But I do want to follow up on Ilan's question and let David, did you or anyone at the panel have anything to respond to, to Ilan's question?

MR. BRAKEBILL: Well, I just want to be clear exactly what it is that you were asking. I think what you were saying is how quickly your immune system responds has better outcomes? In other words, if you can get your viral load suppressed more quickly, yes, I believe that's true. I still don't think they've figured out why some people haven't progressed that are -- because they remain asymptomatic for 20, 25, 30 years. I mean, we think it's genetic, but, you know, we're not sure. There

have been studies that indicate that.
But I think really this goes back to the whole epidemic and it's a lot of stuff that's outside of the purview of just the FDA, but in terms of, you know, we continue to see 50,000 new infections a year, we continue to see younger people infected, we continue to see all these things that, you know, it's just frustrating as a person living with the disease. You know, vaccine studies, you know, takes us 30, 60, 90 years sometimes to develop a vaccine. You know, it's just frustrating that science doesn't move as quickly as we want it to, and I'm sure that happens to you guys all the time.
But I think a lot of it in terms of how people get over -- you know, it's really about the individual and how they deal with their diagnosis. A lot of it is psychosocial support. You know, in a lot of the comments today I continue to hear, although I haven't heard the word "stigma" around taking medications, around disclosure, around everything. So I think that still -- I don't know -- I mean, we've been talking about stigma for 32, 30 years now into

the epidemic, and we're still talking about it. So I think that's a lot of the frustration for people living with HIV, is, you know, it's been 30 years, you know, but we've been studying cancer for hundreds of years probably now, those kinds of things.
So I think that certainly there are advantages to people, depending on where you're diagnosed in the disease progression, and I think it's been proven that outcomes are better for people who have never fallen below 200 T cells, for example, or haven't had viral loads above a million. And I don't know what the answer is to stop all of that or improve all that except that, you know, trying to get people and engage them in care. Hopefully in states -- unfortunately, mine is not one of them -- that have chosen to expand their Medicaid programs and we'll see more people have access to care and get into care and probably try to solve some of this.
DR. EGGERS: Thank you, David.
So Debra asked me a question at the break, and I'm going to ask it as a follow-up question here, and it ties to what Wanda said, it's tied to what

you've all said up here at the panel, which is Kimberly gave in her opening presentation, and we've made remarks otherwise, that HIV being this manageable chronic condition, and the question is, do you view that, especially if you have other chronic conditions, do you view HIV infection as a chronic condition like you view the other types of conditions that are considered chronic as well?
If anyone would like to comment. Maybe we'll start with Melanie and then if anyone in the room wants to comment.
MS. REESE: Okay, because I am someone who has a multitude of chronic conditions, I would never, even though I'm well managed, and that's not the object of concern for all my medical providers, is HIV, it just irks me when they lump it into a manageable chronic disease because there are so many factors that aren't just medical that come with HIV: fear of rejection, toying between, "Do I disclose? When do I disclose? Who do I disclose to?" It's not talked about enough in community intelligently, too many people are still ignorant, people still think,

"It's never going to happen to me."
CDC since 2006, it's supposed to be a routine test. So there is still lots of fear about taking tests. And risk, people have judgment and stuff about what the risk. If you are alive and breathing and engaging in sex and you're not doing and using safer sex practices, you are at risk, and until that mindset can incorporate this world, we're still going to be in trouble, we're never going to get to zero.
DR. EGGERS: Would anyone else like to comment on their view of HIV as a chronic condition?
Nathaniel.
MR. SCRUGGS: I listened to Melanie, and I take a different set. I don't personalize it because today it's manageable for me, but I had to get to that place. And I think what happens -- and like I said earlier, in the whole of our society, our society and the way we advertise has a big impact on how children, on our cigarette smoking, on sodas, on our sex lives, and I think what happened for me, a lot of the medical conditions I got now I didn't have, at least I didn't

know I had them, because I wasn't going to the doctor, but I'm able to manage my HIV very well.

And I was listening, I don't know how many people that I know, and I don't do it, some days I do miss my medicine, that's just me, but as far as it being manageable, yes, my HIV is manageable, to the place that when I go see my primary and we discuss some of my other conditions, my HIV is not at the forefront of our conversation. When I go see my infectious disease doctor, my HIV is not the primary conversation. So I take that that it's manageable.

My T cells are superb from when they were single digits in 1996. I'm like over 1,000 now, but I understand why, because all my T cells are not valid. My viral load is not fully undetectable. It's low, but HIV is not physically affecting me as much as it does some days mentally being concerned about, will I continue to keep insurance? If I happen to lose my job, will I be able to manage my lifestyle? Will any of the opportunistic infections reoccur if I don't take my medicine?

So it's other things that play into, and you

can't look at HIV from just a physical standpoint. Melanie just spoke to that. You've got to address HIV in the realm of a person's mental capacity, what the emotional and spiritual support they have, and how physical they are. I heard David talk about how he can go to the gym. I don't trick myself. I ain't going to the gym. I do a lot of walking. That's my exercise. And I commend people that can go to the gym and do all that, but I had to learn how to fit my life where it best suit me for the information I have at that time.

Melanie just talked about how, you know, the stigma -- David just talked about how the stigma is still happening, it is, but why is it happening? Why aren't people listening to the facts? If you're having unprotected sex, you use protection and you won't have it. I tell people all the time, guys, women, if you're going to have unprotected sex, the quickest way to let somebody put on a condom is tell them, "I like you, I want to have sex with you, but I don't want no babies."

DR. EGGERS: That's a good point.

MR. SCRUGGS: Yeah, but my -- different people it's manageable with.

Different people, they do manage their HIV, and it comes not just from a physical point. And it has to be looked at in threefold.

DR. EGGERS: Thank you, Nathaniel.

We have another comment. Matt Sharp?

MR. SHARP: Just what about chronic inflammation? That's been brought up already. You know, this may be considered a chronic manageable disease, but what I worry about and what many people are worried about as we grow older is the inflammation that has not been controlled by antiretroviral medications. Certainly, we know that it's controlled to a point, but there is still that low level inflammation and consideration of what may happen in terms of heart disease, bones.

And then the second thing I wanted to bring up is like cumulative effect of medications, that toxicities cumulatively, what is the long-term effect? We haven't really talked a lot about that today. And I don't think we know, and we won't know until we get

further into the epidemic, but what's the cumulative effect on organs? is one of the big things that is being focused on today.

DR. EGGERS: Okay. Go ahead, Joe.

MR. JEFFERSON: I just wanted to also point at two things. I think it's important to distinguish are we distinguishing between a manageable disease and a clinical -- under a clinical sort of rigor in terms of lifestyle and sort of other comorbidities? Because I think if one has their HIV in check and yet the HIV is the precursor to all of these other conditions, is HIV actually a manageable condition? I don't know.

I'm also concerned about the impact that the whole messaging of a manageable chronic disease sort of portends for the prevention efforts that we're all engaged in because we, I think, know that for those who are infected, they might hear that and think that, again, "I'll deal with it when it's a problem, I don't have to take meds until that time," or for those who are not infected, of course, it diminishes a sense of urgency around practicing safe sex. I think from a research standpoint also it may sort of turn the dial

down on the sort of volume of urgency because now we can move to another disease state that maybe isn't manageable because we've now got HIV in -- we can check that box and move on. So I'm concerned about us locating too much emphasis on this notion of manageable disease.

DR. EGGERS: Thank you very much.

I want to make sure that we get to the ideal, not cure, the ideal treatment question, and I'm going to broaden, like I said before the break. Actually, can we go back to the presentation slides and not the question slide anymore? Yeah, thank you. Because we'll close before we let my FDA colleagues speak, really getting your final thoughts on what major improvements could be made for future treatments to help manage your condition, and we'll include in that if you want to comment on the research studies to help foster to those treatments.

Theresa, do you want to follow up?

DR. MULLIN: Yes. Maybe before we go on, I would like to just follow up with something that David

said in the beginning. And you were mentioning that a big challenge was access to alternative therapies, and I wonder if you could say more about what you had in mind with alternative therapies.

MR. BRAKEBILL: Well, let me qualify this by saying that in many cases, particularly if you live in a larger metropolitan area, I'm speaking particularly of the coasts on either side, because of the large amount of money that tends to flow to the bigger cities in the epidemic, there is much more money available for those sort of auxiliary things like massage therapy and acupuncture and acupressure and seeing an herbalist and those non-traditional medicine sorts of things. If you're living in the rural South, you're lucky if you don't have to drive 200 miles to see a doctor to have your HIV treated.

So the health disparities that continue to -- I live in Florida, I live in Key West, it was the epicenter of the epidemic. Fortunately, it's the kind of community that sort of rallied around and we own and operate 98 units of housing for people living with HIV, we have three great HIV specialists there that

have been there for years, but if you live in Marathon, 50 miles up the road or up the Keys, your doctor comes and sees you once a month. If you live in Sebring, which is smack-dab in the middle of the state, there is a nice health department that offers lots of HIV care, but specialty care? You know, unless they find something therapeutic in gator hunting, there is probably not much to be offered there.

So I think that as the model moves, I think there is going to be less and less available in terms of even in the larger metropolitan areas. I know they're already feeling the pinch of reduction in Ryan White funding, but it's just not something that's available, widely available. Personally, I believe in it, I think it helps a lot. We actually have written a small grant for massage therapy. You get a prescription from the doctor, we have a volunteer massage therapist that comes in and gives you a 30-minute massage once a month or whatever. So there are ways to work it, but it's just not something that's available, widely available, to people, and it's just

not accessible. And again, this goes to our whole system of care and how it works and whether you live in a big city or whether you live in rural America, if you live in the Northeast or you live in the South. So until we sort of fix a lot of things that are broken about how health care is administered and delivered in this country, I think we will continue to see health disparities, you know, across disease states depending on where you live. You know, it's economics, it's everything.

DR. EGGERS: Thanks, David.

Yes, Ilan has a question?

DR. IRONY: I just want to follow up with what David was saying, that the same kind of health disparities we see in medical care we also see in clinical trials. We always want, in particular, for Phase III trials when it gets to the end of the preapproval development of a product to have participation of as many people as possible to reflect the real world use of that particular product, but sometimes access is a problem, access to clinical trial sites. If you live in rural Florida, for

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example, it's difficult, so it's not going to reflect older people or female because of different schedule obligations to have participation in clinical trials that sometimes are demanding in terms of travel or cost, et cetera. So we see that reflected in what the studies show even though we try to extrapolate as much as possible to the real use population.

DR. EGGERS: Thank you. Well, that's a great segue. Let me ask if anyone wants to follow up on what they said this morning about clinical trials and other improvements that you have.

Yeah.

MR. TIETZ: Yeah, I think one of the other things that comes up increasingly, and not necessarily with folks who are older with HIV, although I think mostly, and it's the folks who are highly treatment experience, and the real challenge I think is the narrowing of the antiretroviral drug pipeline. There are in the last few years been a few drugs that have been pulled from development by the companies that were developing them I think mostly because they thought that they were too much of a look-alike or me-

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too drug and they wouldn't capture enough market share or they wouldn't make enough money on it, and so end of development.

But, you know, there is probably, you know, what, 10 percent? It's hard to know exactly, no one tracks the folks who are resistant to four, five, and six classes of drugs that are currently available, and for them, the absence of many drugs in the pipeline is frankly scary, they're running out of options. They're never nondetectable anymore. Clinicians across the country who have been at this practice for a long time, have these highly experienced folks, and it's that each of them are sort of waiting for that day when their viral load spikes and there is nothing more to be done, and so I think that's a real worry.

And I realize that the FDA isn't exactly in the position of developing drugs, they're in the position of approving drugs developed by others, but I think in some instances you may need to look at ways of taking some of those drugs that pharma has declined to finish development on and finish it.

DR. EGGERS: Any other comments?

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MR. BRAKEBILL: And to see the progress that we made in HCV. I mean, virtually now HCV is curable with drugs that have been developed just within the past few years. So I think that there is stuff out there, and I think part of the incentive for the pharmaceutical industry is to follow whatever disease they see the most money in.

DR. EGGERS: Melanie, did you have something to add? Oh, put your mic on.

MS. REESE: You know, osteoporosis and some other diseases, they have like either a once-a-month or twice-a-year dosing to control. Why can't we get to that with HIV since it's a disease that can easily be transmitted if you are careless?

And another thing I wanted to say is we do a lot of work with prevention and we're really going to have to pay attention to the cascade to develop new prevention techniques, but there are people who don't realize that just because that person has HIV and this person has HIV, oh, wow, throw all the stuff away. They can get a different strain of HIV. Prevention among positives, did it go out the window? I don't

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know. But that's an area that still needs work.

And the biomedical interventions for people at risk. Well, you might as well put it in the water like fluoride because the people who could be at risk don't think they're at risk. You're just going to have to put it in there and have them take it so that transmissions will get to zero.

DR. EGGERS: Thank you, Melanie.

Anyone else?

Joe, were you going to say something about ideal treatment?

MR. JEFFERSON: Well, I would just echo what I think others have commented on, you know, long-acting meds, of course. I actually wonder sort of what barriers might exist in the laboratory to developing, say, compounds that treat multiple conditions. And so when we talk about combining four or five HIV meds into a pill, is it possible to treat high blood pressure or hypertension or any other cardiovascular condition, for example, alongside of HIV in a single dosage? There may be some barriers. I don't know what they are. I would be interested to

hear about that, but I think to the extent that we can start to narrow the quantity of pills folks take that are dealing with multiple conditions and reduce the frequency, I think we start to address the adherence question.

DR. EGGERS: Catherine, would you like to give any final words from the pediatric perspective?

MS. CONNOR: I really sort of made the comment before. I mean, administration is always something that we really worry about because our populations are younger ones, you know, you have to use the liquid syrups, or sprinkles are a big thing, in the developing world.

But also I would just be remiss if I didn't mention sort of the research lag time for pediatric drugs. A lot of the reasons it happens is very justifiable, but there is still a very long lag time between when adult ARVs are available for the younger populations, particularly the neonatal populations, which, again, may not be as much an issue in the United States but globally is a big issue. So I always sort of encourage folks in FDA to sort of

remember that there is this lag time for our population with the banded age group studies.

DR. EGGERS: Great. Any final comments?

Matt?

MR. SHARP: Hello. So we're going to talk about this, this afternoon, obviously, but even before we get to talking about a cure, there is a step before that called a functional cure, which is using the host response to treat HIV basically without medication. So I think we'll talk about that this afternoon, I'm sure.

But then the other thing I wanted to bring up is, you know, I am passionate about the salvage population because I was a salvage patient for so many years, and I know that that population has certainly decreased because of the effect of great antiretroviral drugs, but there are still people out there who fall into that category that we need to remember.

DR. EGGERS: All right.

Yes, Deb.

DR. BIRNKRANT: I want to thank everyone for

their comments on this most recent topic that we've been discussing. We do recognize that the pipeline for HIV drugs is not as great as it used to be, and that's why we're happy to have not only our participants here today to state the obvious, but also industry here so they can hear that there is still a need to develop drugs for HIV, new drugs, and drugs for salvage populations as well. So we appreciate all of your comments. Thank you.

DR. EGGERS: Thank you.

And with that, that is a great way, I think, to end the morning discussion. We're going to save some time for the FDA to give comments and questions.

Did you want to say something?

DR. BIRNKRANT: Now?

DR. EGGERS: Let me just say one thing, because there are a few things that we didn't get to cover today, and so you have homework. Those of you in person and those of you listening to the webcast, we didn't get to talk about as much the decisions about how you change medications and why you change medications and how you choose to go to a combination

therapy and why you choose to go to a one pill once a day, or if you decided not to, why that, too? And so I really encourage you to go to the docket and follow up with what you've said here and address that topic and address more the symptoms that you experience and the other conditions that you attribute to your HIV infection and explain more about those. So you heard David and Melanie, for example, talk about -- oh, help me out with the --

MS. REESE: Peripheral neuropathy?

DR. EGGERS: Yes -- and the night terrors and the night sweats and the fatigue, follow up on those and provide your experiences to that.

Discusion with FDA Panel

With that, I will turn it over for a few minutes. We are going to lunch in about 10 minutes, but I want to see if any of my FDA colleagues want to follow up on anything else that they've heard and if -- well, we'll see how long we go with that, if you want to follow up. Maybe we might have time for a question from the patients.

Go ahead, Deb.

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DR. BIRNKRANT: Thank you. I wanted to follow up on something David had said earlier about fear of switching regimens if you're controlled with your viral load. I was wondering what other panel members thought and if David could elaborate a little more on that topic. So, in other words, if you're well-controlled on a regimen that may be a little more complex, how willing are you to switch just because a regimen may be somewhat easier? So do you still have concerns about switching even though perhaps it may be a little easier to adhere going from a few pills a day to one pill a day? Is that something that would be attractive to you and would make your lives more manageable?

MR. JEFFERSON: I'll jump in. I've given that some thought. I take three pills at night. I think there are four or five compounds in those treatments, and, of course, it would be great to take a pill, but this regimen is working, it has been working for 7, 8 years. No, I wouldn't make the switch to a single dosage, a single pill dosage, if it meant changing the regimen. I would prefer instead

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for there to be -- and this gets back to drug development -- some means by which whatever combination one happens to be taking that's working for them -- this is a little pipe dream, pipe dream for the pipeline -- is how about a more tailored sort of capacity to put together the meds I am taking into one pill at some point in the future?

MS. REESE: Well, for me, since I have so many other conditions, opportunity to change would have to go through all the other medications I take to see if those would be impacted versus -- I'm only taking one pill for HIV, which is a cocktail, but I take 20 others for everything else I have, so, you know, it's really like for me I would not change unless it was a once-a- year.

MR. BRAKEBILL: Well, I think for me, I mean, the most recent change in my regimen was Prezista going from 600 milligrams, two 600s to one 800 milligram, so it's one less pill, but for me, you know, the whole thing about even switching from Crixivan and Combivir, Crixivan, which is notorious for buffalo humps and kidney problems, what finally

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sort of convinced me was my blood sugar was starting elevate, so we did a fasting glucose and the doctor says, you know, really this is better.

But I think, you know, the whole point is to get your virus suppressed, get it undetectable, so as a person living with it, you've met that goal, and so fear of change I think for everybody regardless whether it's a disease state or just fear of change in general, people, by their nature, are sort of resistant to that.

Would I go to a once-a-day pill? I don't know. You know, 80 percent of our regimens have Truvada in them now, which makes me nervous about using Truvada for prep, that's just a personal thing. It concerns me a little bit. But I have to say that for me, I'm a creature of habit, so taking three or four pills at a time, you know, my partner looks at me and says, "How can you take all those pills at once?" and he says, "I can barely get one down at a time." I said, you know, when you're taking 12, you know, you learn. And so for me, at some point in time maybe. For me right now where I am, it's sort of like the

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question about, would taking all these pills the rest of your life -- you know, I don't know whether I'm going to be 85 or 90 years old sitting in assisted living having somebody force-feed me and giving me my HIV meds. You know, at that point in time, I might say forget it.

MR. BRAKEBILL: But for me, it's not something for right now I would do. I think it's easier for physicians to prescribe now, particularly newly infected, you know, it's only one pill once a day. On the other hand, we still have the ads in the magazines that show the guys climbing mountains, which, you know, some of us who have been around a while sort of push back on that when that happened, that, oh, you can cure all of this by taking one pill.

So the message is still that -- you know, this goes back to the chronic disease, you don't get diabetes from having unprotected sex with someone, you don't get fibromyalgia, you don't get lupus from having unprotected sex with someone, you do HIV. So I think the fact that it's still communicable makes it a little different than other chronic diseases for me.

DR. EGGERS: Any of my other colleagues?
(No audible response.)
DR. EGGERS: We would probably have time if there was one question or two questions for you to answer on this topic. Is there any?
DR. CALDWELL: Hi. Thank you. My name is Dr. Robert Caldwell, and about 15 years ago I was involved in an HIV vaccine study. Well, it was a collaboration between the NIH, Vanderbilt, and Chiron Pharmaceuticals. And, sure enough, I got the experimental. So when I get tested for HIV, like I did last week, the ELISA comes back positive, the Western blot and the PCR come back negative, and that's been 15 years ago.
So my question is, if you look at breast cancer and HER2 as antibody-based therapy and Provenge as a prostate cancer-based therapy, why aren't there currently any second-line drugs for HIV therapy? Is there a higher standard or a higher bar set for therapeutic HIV vaccines as a current treatment option?
DR. WITTEN: I'm not sure exactly how to

answer that. Your question is, why aren't there therapeutic HIV vaccines? Is that the question?
DR. CALDWELL: Yes, ma'am. Why aren't there more vaccines or perhaps pro-vaccine options in the pipeline? Therapeutic vaccines, not preventative; I'm speaking specifically to therapeutic.
DR. WITTEN: Okay, specifically to therapeutic. I just think it's a very complex area, and even the Provenge, which you are citing, was the one vaccine that's been approved for a cancer indication following several decades of efforts of development in that cancer immunotherapy area. So I think it's really just a matter of it being a complicated effort. We certainly meet with sponsors or researchers who are interested in developing products, and we would like to see this area move along, but I think it's just a matter of the science and the technical issues involved.
Did you have a more specific question?
(No audible response.)
DR. WITTEN: I know that's not a very satisfying answer, but that's probably the best answer

we can give.
DR. EGGERS: Okay. So we have one question here?
ROBERT: My first name is Robert. And I have a question about hepatitis C and co-infection with HIV, and I'm wondering why the FDA, and I think it's about politics, why the FDA rushed when Anthony Fauci was being pressured by AIDS activists to approve drugs for HIV, and yet they're sorting of dragging their feet, it seems to me, on hepatitis C infection. There is a new drug coming available sometime in the winter of 2013 that, you know, it's amazing, and I don't remember the name of it, but there is not the political pressure on the FDA, and you all don't seem to be responding the way you did when Anthony Fauci was being pressured by AIDS activists. So I'm wondering if you could address that as well because I do have cirrhosis of my liver, and I would like to get it treated before it turns into liver cancer on the hepatitis C.
DR. BIRNKRANT: Thank you for your comment. We know that that patient population, the population

who are co-infected, is a very seriously ill population. We also understand how difficult sometimes it is to do trials in that population because we first have to learn in the beginning whether or not a drug is active, and then to allow a population who is taking other medications, we have to do drug-drug interaction studies, so that takes a bit of time compared to a mono infected or a population who only has HCV.
I will say that the urge and the enthusiasm that the division had back in the '90s with the protease inhibitors is there today as well for the new hepatitis C treatments. One example of that is we recently modified the endpoint in clinical trials to shorten it by approximately 3 months to enable us to get the therapies to patients even sooner, so we're quite excited about that.
In addition, I will share with you, unlike the HIV pipeline, the HCV pipeline is quite full, and we have dedicated teams working on a multitude of products, not only alone, that is, single products but multiple products together in fixed dose combinations

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to be able again to take perhaps one pill once a day.
So I think you can be assured that we have drugs in the pipeline and we have a team of scientists and experts ready to do the review work that we've done all along and will show you in the next few years that there will be more drugs on the market for hepatitis C.
Thank you very much for your question and comment.
DR. EGGERS: Okay. Well, so one more, and then it's time for lunch.
MR. TIETZ: I would just second that on the HCV. In fact, you can see some drug companies have moved almost their entire virology divisions to work on HCV from HIV, but it raises the thing I mentioned earlier, which is that it's all about the money, they want to be first out the gate with some product, and so it's narrowed the -- I mean, we're pleased with what the FDA is doing and what industry is doing with regard to HCV, but there has been some tradeoff there as well.
I will also just note that I don't know if

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this can be fixed in the current regulatory scheme, it may actually require action from Congress, but there actually are a few drugs that are in development that are long-acting. So, for example, Timed (ph) has a monoclonal antibody that is in trials, injectable, maybe every 2 weeks, maybe every month, that's still being worked on, but they have a challenge in terms of financing for finishing their clinical trials, and so in the scheme that we have, that's their problem, not your problem, and yet, you know, this goes on and on and people wait and wait.
DR. EGGERS: Okay. So I think we are going to stop to break for lunch. I do want to thank sincerely the panelists who have been up here and have shared their stories, and, as sincerely, thank those of you in the audience.
On the web, I am going to suggest that if you want to get some comments, if you have any comments that you would like to put in through the webcast in the next 15 minutes or so when we open up in the afternoon discussion, we can see if there are some things that we haven't heard yet in the morning

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and just summarize those as part of our afternoon opening remarks.
With that, we will come back at 1:30 and we will get started with our afternoon discussion then. Thanks a lot.
(Whereupon, a lunch recess was taken.)
DR. EGGERS: Well, welcome back to the afternoon session of the Public Meeting on HIV Patient- Focused Drug Development and HIV Cure Research. We had a great morning discussion, and we look forward to a great afternoon discussion. For those of you who are just joining us, my name is Sara Eggers, and I am from CDER's Office of Strategic Programs, and I will be facilitating much of the discussion today.
Before we get to the discussion, we will have a few welcome remarks, and then we'll set the context for our discussion and some of my FDA colleagues will present some background information. And then we'll get into the discussion. I'll go over a bit about the discussion format after that before we do.

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And with that, I would like to turn it over to Dr. Janet Woodcock, who is the Center Director, for a few comments.
Thank you, Dr. Woodcock. Afternoon Opening Comments
DR. WOODCOCK: Thank you, Sara. And good afternoon, everyone. It's great to see the folks who have turned out for this meeting, and I hear there are a lot of people on the web. That's fantastic. I especially want to thank the HIV patients and patient advocates for sharing your experiences and your perspectives on this disease and on the therapies.
Today's meeting is part of an initiative that we are running that is called Patient-Focused Drug Development. We are quite excited about this. Theresa Mullin gave an overview this morning, but I would like to reiterate some of her points especially since some of the folks were not actually able to be here this morning.
As Theresa mentioned, Patient-Focused Drug Development was an important aspect of the package for the fifth authorization of the Prescription Drug User

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Fee Act, or PDUFA V, and it's an enhancement of our current mechanism for getting patient input on important issues regarding their diseases, which have tended to generally focus on specific drug products, and we want to focus more broadly on the disease entity.

Patient-Focused Drug Development, therefore, is a broader, more systematic method of obtaining patients' perspectives on the severity of the condition and its impact on daily life as well as their perspective on the range of available treatment options and the impacts for good and for ill of those various treatment options. And we recognize that even within a disease -- and in some diseases this is more true than others -- there is a range of severity that people are experiencing often from being relatively well and functioning to suffering severe effects from the disease or from the treatment in fact, and we want to hear about that, we want to hear about the burden of disease and the burden of therapy.

It's valuable for our drug review because it helps provide the clinical context in which we

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evaluate new treatments because we don't do that in a vacuum. We say they're safe and effective but really mean the benefits of a new treatment outweigh the risks, and therefore you have to understand the disease, its risks, and the effect of the current treatments and really do that I think partly from the patients' point of view as well as from the medical point of view.

Patient input can help drug development's efforts more broadly also by highlighting where new types of outcome measures are needed to help make sure that new therapies treat the symptoms that most matter to patients or they avoid side effects that are most important to patients. And often we don't put all of these outcome measures in the trials, so we may not know about certain important impacts on patients. For example, for many diseases, we have never learned anything about impact on sexual function of some of the treatments for various diseases, and some therapies have very profound impact on sexual function, and if you don't ask about that and record it, then you never learn, and people simply have to

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experience that.

But more broadly, we would like to have outcome measures that we devise for benefit as well that are really relevant to patients and patients feel are the right outcome measures for that disease and the burden of disease that they experience.

So this is an ambitious undertaking, I think, and part of our commitment under PDUFA that we made to Congress, we will convene at least 20 public meetings over the next 5 years with each being focused on a different and specific disease area. And today is our second meeting within this initiative.

Our first meeting was on April 25th, and it focused on chronic fatigue syndrome and myalgic encephalomyelitis. It was, from our point of view, very valuable, and that's a disease that really doesn't have any approved treatments at all and has a very profound effect on the most severely afflicted people. We received a lot of positive feedback from participants in the patient community who attended that meeting, they felt it was very helpful, and in that disease we're really seeking to attract drug

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development and understand what outcome measures would be most appropriate in that disorder.

This morning's discussion here focused on the most significant symptoms associated with HIV infection or its treatment and what impact it has on daily life. We also heard your perspective on the currently available therapies to treat HIV. This afternoon's discussion is a bit different, and I think each meeting we have will have different flavor. It will focus on some important issues with respect to cure research studies.

In the past, HIV cure did not seem possible, but today researchers are looking at new ways to either clear HIV from the body or control the virus without the need for antiretroviral therapies. One of my colleagues is going to provide more background on what we mean by "cure research," but understanding the patient's perspective on the potential benefits and risks of participating in HIV cure research studies will help FDA evaluate drug sponsors' protocols for clinical trials and their informed consent procedures.

So this is very exciting I think for HIV and

shows that in this disorder we're in a more advanced state of treatment, say, than we are with, say, chronic fatigue syndrome, where we really don't even understand the etiology and we have no available treatments.

So thank you again for your valuable time and input on HIV symptoms, currently available therapies, and I wish you luck this afternoon. I hope we have a very good discussion on both the ethics and the feasibility and desirability of HIV cure research.

Thank you very much.

Summary of Morning Discussion

MR. KLEIN: Thank you, Janet. And good afternoon, everyone. My name is Richard Klein. I am the Director of the Patient Liaison Program at FDA in the Office of Health and Constituent Affairs, formerly known as Office of Special Health Issues. And I just wanted to do a brief overview of the main thoughts, at least that I heard this morning, and try to summarize what we heard.

To me, one of the main issues that came up and kept coming up was comorbidities, people dealing

not only with HIV but with HIV's concomitant problems and other diseases. So it had a lot of ramifications that kept coming up through the morning, managing hepatitis, managing hypertension, managing new drugs and drug interactions. And drug interactions was I think the second most common thought that kept arising for me this morning, people dealing with multiple drugs for multiple conditions and how to work those drugs together and deal with the drug-drug interactions and finding the right drug combinations.

I think e-prescribing was raised as one potential way to address those kind of problems. Could people have electronic records that would help guide and prevent the use of drugs that shouldn't be used together that are contraindicated or that had drug-drug interactions?

Adherence and ease of dosing was another issue that came up this morning, and that led to another question about challenges of changing meds. Were people comfortable with simply changing meds when you had a workable, successful therapy? Would people be able to switch to something else for ease of use

and better adherence? And people were a little reluctant to do that if they were successful; it's kind of if it's not broke, don't fix it.

Unanticipated consequences, I think people were talking about hesitancy of changing drug regimens also because of the fear of switching regimens and then using up something that would have been a future option for you to use, and so people didn't really feel comfortable with the idea of burning through different classes of drugs. So changing regimens is a difficult decision that people were dealing with, and that question about using up scarce options for future.

Whether HIV is a manageable condition was a question that came up and that differed from person to person depending on whether or not you thought that the problems that you were having related to your therapy and to your HIV were part of the question. So if you could manage HIV but still had all these adverse events from the drugs, was that a manageable disease?

I think we were pretty well reminded that

stigma is still a problem, that people are worried about diagnosis, talking about their HIV diagnosis, talking about even being on therapy, and that stigma remains a problem.

And, finally, reminded about the fact of transmissibility of HIV and whether or not being a chronic but manageable disease could affect whether or not people were going to be -- whether or not prevention could be impacted by the ease or the alleged ease of treating the disease and the question about whether or not that could possibly undermine prevention efforts.

And I think those were the top issues that had occurred to me this morning. I don't know if other people had other points, but, if not, then we want to shift gears for the afternoon and talk about the future, about cure research and where that is, where it's going. And for background on cure research, I want to introduce the Chief of the General Medicine Branch, Division of Clinical Evaluation and Pharmacology/Toxicology at the Center for Biologics, and his name is Ilan Irony. And with that, I'll turn

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it over. Background on HIV Cure Research
DR. IRONY: Hi. Good afternoon. Again, my name is Ilan Irony. Thank you very much for the introduction. And I am from CBER, the Center for Biologics Evaluation and Research. And so this is an outline of my brief introduction to the subject of HIV cure research and this is the background. And so I'm basically going to describe the FDA organization and our particular place in the FDA organization, our center and our office, talk about the strategies for research that aim towards a cure of HIV infection. I will talk a little bit about gene therapies as they pertain to HIV cure research, which is part of what we do in our office and our center, and then wrap up with combination strategies, and the ideas and the controversies in combination strategies in also HIV cure research.
So first a word about the general FDA organization. We are all under the Office of the Commissioner of the FDA, and the list here contains a list of the centers, each center is particularly responsible for an area of human health or animal

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health, but I wanted to emphasize the last three centers here that pertain also to HIV, human health related to HIV. So the Center for Devices and Radiological Health, Center for Drug Evaluation and Research, which you heard from representatives this morning and from Dr. Woodcock. And in red here, the last, the Center for Biologics Evaluation and Research, where Dr. Witten and I here on the panel work.
And within the CBER organization, there are multiple offices that support the operations of the center, but I also want to emphasize three offices that pertain particular to HIV treatment and HIV research, one of them being the Office of Blood Research and Review, which regulates the blood supply of the nation and tests for HIV, in vitro tests for HIV; Office of Vaccines Research and Review, which regulates the development of preventive vaccines for HIV to prevent transmission of HIV. As we heard in the morning, there was some discussion about the unmet need in terms of having a vaccine, successful vaccine, for HIV prevention. And finally in red here, in the

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last bullet, the Office of Cellular, Tissue and Gene Therapies, which is our review of what we regulate and what we approve in products that are primarily for gene therapies and cellular therapies.
So why cure research? We heard a lot this morning about HIV infection being transformed in the last 30 years from a lethal condition into a manageable chronic condition, and that's debatable how manageable it is. We heard a lot about the comorbidities and the symptoms that remain. So the fact that it's not lethal doesn't mean that there is no unmet need for patients and caregivers and for society in general, but we have to recognize that it's been a big progress over the last 30 years in terms of transforming a lethal disease that quickly progressed to AIDS and opportunistic infections into something that people can live through medications.
But still there are some drawbacks to this. There is a lifelong requirement for antiretroviral therapies with both long- and short-term side effects of those therapies, of those drugs, and we heard a lot about them, about the effects on comorbidities,

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effects on other medications that people need to take because of complications of those antiretroviral therapies. So there is a need that FDA perceives and the community perceives of cure research.
And even with very low viral loads, when you have very low or even undetectable viral loads, we know that there is some degree of viral replication that persists and some latent viral reservoir that spreads, and then it's debatable where the complete knowledge of this viral reservoir is, but we think that the gut, the brain, bone marrow, are places where HIV hides, and as soon as there is lack of drug, HIV can flare, can result in reinfection and manifestations.
But recently in the last few years, we had some isolated examples that point against towards a possibility of a cure, so we have Timothy Brown, known as the "Berlin Patient," or the Visconti cohort or more recently the Mississippi baby that point to the possibility that some patients can be cured from HIV infection. And as Dr. Cox alluded to early in the morning, our definition, our working definition, here

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of cure is either elimination or control of HIV infection without further medical intervention to maintain health.

So what are the research strategies that we have seen in development? One approach is in the first bullet, is the shock and kill. Shock we define as activation of the virus from reservoir from this where it's latent, where the virus is sleeping, to be awakened, to be manifested, and then followed by kill. So clear the viruses from the body using both boosters of the immune system plus an antiretroviral regimen that's effective to clear the virus.

Another approach would be the induction of resistance to HIV infection, and that, in theory, can be accomplished by transplantation of immune cells, CD4 cells or precursors of CD4 cells, from donors that are resistant to HIV, known to be resistant to HIV, or through gene therapies that modify some cells to make them resistant to HIV and then transfuse them to a patient with HIV.

And a third possible approach is some experimental drugs or vaccines, therapeutic vaccines,

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vaccines aimed to treat rather than prevent, to stimulate the patient's immune system to recognize and eliminate HIV.

So that's the realities that there are lots of challenges in cure research. One of them is for FDA, we need to look at each development step about the protection of subjects in human research. So safety is paramount for that. And making sure that there is a good balance of risk and benefits. So the risks for the patient versus the benefits for patients and benefits for society in general for that research to be accomplished and to yield some results.

In the balance of recent benefits of research interventions, they change over the course of each product development, so as a product moves along the development from Phase I first in human study all the way to Phase III, there is a change in the notion of how much we accrue in terms of knowledge about the product and what the risk-benefit balance is. And as we learn more about parallel development of other therapies or new approved therapies, for example, how does that impact the risk-benefit for that particular

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patient in that particular research study?

And there is a challenge also in defining what is sterilizing cure, that means no detectable virus, because, as you know, the assays for what's detectable virus and what's the limit of quantification of that has changed in whether we consider a fragment of the virus a detectable virus or not. Those are debatable issues in terms of sterilizing cure.

Equally, there is some debate about functional cure. So functional cure we define as no evidence of disease and no ability to transmit HIV infection, but it's very hard to validate those measures, so the endpoints, as we refer to in clinical trials, for each type of cure to make this a valid endpoint for research and for clinical trials.

So let me talk a little bit about gene therapies as they pertain again to HIV cure research. So first there are some challenges with manufacturing. The production is usually relatively slow compared to manufacturing of a small drug and identification of the gene subtype and the general manufacturing issues

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are more challenging than for a small drug. The use of retroviruses or lentiviruses, gene carriers, those are the buses that carry the gene of interest that you want to insert in humans, they allow for prolonged gene activity. So it's not like you can turn off the effect by stopping a pill, for example, it's another challenge.

Usually, the product activity, if present, is from a gene-modified cell that needs to survive and function in the patient, and the goal here is to raise resistance to HIV infection, but for that cell to survive, that gene-modified cell to survive, you need to some Busophren (ph) or chemotherapy or some other drugs that are risky to try to make room for these cells and improve the odds that more and more of those cells survive and function and provide resistance to infection.

And then there is also the issue of the long presence or long duration of activity, perhaps a lifetime, for those retrovirus or lentivirus gene vectors that carry the gene of interest to the human being. So there is an inability to withdraw or

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discontinue the product when adverse events occur. And they have also concerns about late onset risks such as cancer, malignancy.

And I'm going to talk also about the combination of strategies. People in academia and industry recognize that it's likely that if there is a chance of success for curing HIV, it will come from a combination of multiple different approaches. And to attack the different mechanisms of HIV persistence, for example, the low level replication or the reservoirs of HIV, it recognize that combinations with these different approaches may be needed. But there are some scientific issues that are associated with this approach of combination therapies particularly when we include investigational therapies in the combination. So if it's two approved products and we are combining them, it's a little less challenging because we know a lot about those products, but when it's one product is new or new in humans and investigation, it creates some challenges in looking at the combination therapy. One of them is how much information we need about the safety and the

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effectiveness of each of components alone in the course of this development. And the recognition that if combination therapy is needed, each component alone may not work to cure HIV, so patients may be at risk of this drug, but they are unlikely to benefit from research from each component alone, so that raises some informed consent issues, and Dr. Goldkind is going to be talking more about this.

And so for Topic 2 for the afternoon, those are the basic questions, and we are going to hear them again and discuss them individually during the course of the afternoon, so I am not going to go over them in detail now, but basically what we want is to know what you perceive as being the benefits of participating in research or the factors you want to consider when you decide to participate in research for HIV cure or not and what kind of risks you would accept or not accept to take into your decision to participate in HIV cure research studies. Or if you are required to stop your antiretroviral therapy which makes you stable and relatively healthy and manage your chronic condition, how would that affect your decision to participate?

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And, finally, what else do you want FDA to know about HIV cure research?

So this is my contact information. I just want to emphasize that in the last point here is that Learn webinar series from our office, Office of Cellular, Tissue and Gene Therapies, which is available in the FDA external website and provides a little bit of our thinking about general product development and issues in pediatric research or some of the challenges we face in clinical trials with our products. And this is also some of the websites of public access to the Center for Biologics and Evaluation Research.

Thank you very much.

DR. IRONY: With that, Dr. Goldkind.

Informed Consent Issues in HIV Cure Research

DR. GOLDKIND: Good afternoon. So I am Dr. Sara Goldkind. I am the senior bioethicist here at the FDA, and I would like to talk to you today about issues related to informed consent and provide some background for our future discussions because we would really like to get your input on a number of different

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issues that are impactful on being able to accomplish an informed consent process in a way that's most useful to patients who would be enrolled in clinical trials, which I'll call "participants" in this presentation.

And before I get started on my presentation, just by a show of hands, I would like to see how many of you have been enrolled in a clinical trial before, a clinical trial of any sort, and have gone through an informed consent process.

(Show of hands.)

DR. GOLDKIND: Well, that will be great. I am really very, very interested in hearing the input from those of you who have experienced an informed consent and those of you who are naive to one of those processes.

So just by way, I am going to very briefly summarize the informed consent process for you today and then I am going to discuss out of the 15 or so elements of informed consent that are required under FDA regulations, I am going to discuss three of them in specific, and then I want to talk about a

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particular issue called therapeutic misconception, which I'll define for you during my talk, and then finally outline a number of the questions that we would like to have your input on during our discussion session.

So first of all, what is an informed consent process? Ideally, what it should be is an ongoing educational process between the investigator or another qualified individual that the investigator appoints, and the potential or the current participant in the trial. And a summary of the process and what it should really accomplish is that there would be adequate disclosure of information to allow for an informed decision about participation in the research. There should be adequate comprehension of the information that's presented and adequate opportunity to consider whether or not to participate, it shouldn't be done in such a hurried manner that you really don't feel like you had ample time to consider the clinical trial and its ramifications, to talk to trusted family or friends, and then, finally, a voluntary agreement to participate.

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But the informed consent process doesn't end there, it's more than just signing the informed consent document. It should really be a continued disclosure of information as the clinical trial progresses. There may be new information that arises during the course of the trial that you, as a participant, will want to know about, perhaps new risks, or you may have some particular questions that are pertinent to you and you would want to go back and have continued discussion with the investigator.

So as I mentioned earlier, FDA has quite a lot of requirements for the informed consent process. I like to say that these are not just simply regulatory requirements, but they are requirements that were developed by the National Commission, which was a presidentially appointed what I would call almost an ethics think tank, if you will, that was appointed after there were a series of egregious clinical trials that were exposed, and in the early 1970s, the National Commission came up with a set of recommendations for the federal agencies about what informed consent should look like, how it should

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ethically be accomplished, and we have actually incorporated those recommendations into FDA's regulations. And I am going to present to you three of them today for our discussion, the three that we feel are the most challenging in relation to HIV cure research, but certainly our discussion can go beyond these if you feel that you want to raise other issues.

And the first one is the description of any reasonably foreseeable risks or discomforts to the participant; a description of any benefits to the participant, either direct benefit or to others who may reasonably be expected to benefit from the research; and then a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant. So, in other words, if you're not in the clinical trial, what would you be getting as a form of treatment or what would be happening with you?

So I want to drill down. In the next few slides, what I want to do is take each of those three elements that I just pointed out and look at them a little bit more in detail. And the first, the

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description of reasonably foreseeable risks or discomforts FDA advises should describe the risks or discomforts of tests, interventions, and procedures required by the protocol, especially those that carry significant risk of morbidity or mortality; the possible risks or discomforts due to changes to a participant's medical care -- that is, what's going to happen differently in the clinical trial than would have happened if you were receiving your care in the clinical setting? -- what are the risks of the drug itself? and what are the common and serious risks of the drug and what might be done to lessen these risks or discomforts?

And so, of course, we don't feel that the informed consent should in any way understate the likelihood, severity, or duration of these reasonably foreseeable risks and discomforts. And it may actually need to include information on foreseeable risks to others, such as to a fetus or to someone because of an infectious -- possibility of infection to others or radiation exposure to others.

And then the description of benefits we feel

should be clear, balanced, and not overly optimistic or overstated. We don't want to encourage people to be part of clinical trials by promoting the clinical trial, we want it to be a very balanced approach to the description of risk in the informed consent document.

And, again, it should describe the benefits not only to the participants in the research, but to others, if there are any. And if there aren't any benefits that are direct, that should be stated clearly as well.

And here I want to pause and describe what the therapeutic misconception is. This was a term that was adopted, proposed, in the early 1980s, and it was proposed by Dr. Paul Appelbaum and others, Dr. Appelbaum is eminent psychiatrist, and what he noticed is that people were confusing the intent of clinical research, and they were thinking that clinical research was really being designed to provide medical care.

And in some circumstances, that certainly can be true, but there are very notable differences

between clinical research and clinical care, and that is that clinical research is ultimately designed to answer a series of specific scientific questions or to meet a series of specific goals or objectives, and the care that a person will obtain in that clinical research protocol is dictated by the protocol itself; whereas the medical care that a person receives in the clinical setting delivered by his or her own physician is tailored to what would be the best medical care for a given patient.

And so we tend to use the term "therapeutic misconception" when people believe that they are coming into a clinical trial to get the best medical care they can for themselves rather than they may get the best medical care they could get as part of that clinical trial, but the overall objective of that activity is to increase scientific knowledge and the objectives of the trial.

So, finally, the last element of informed consent that I wanted to describe for you today in more detail is the description of alternatives. Participants should be made aware of what the

alternatives are to their entering research, if any, that might be advantageous to them. It should include, if any, current medically recognized standard of care, approved therapies, or other forms of therapy, for example, surgical care or supportive care, and it should describe if participation in one clinical trial prohibits participation in another clinical trial, in other words, being enrolled dually in two clinical trials simultaneously.

So today, in particular, we would really like to have your perspectives on -- and this is all within the context of HIV cure research -- how should the informed consent clearly communicate to you the purpose of the research, the potential benefits, particularly if there are no direct health benefits for the participants, and the potential risks, particularly if there is very limited understanding about those potential risks? As Dr. Irony said, as the product moves down the trajectory of development, our understanding about its risks as well as its benefits may change, and so when you're in the very early phase where you've only introduced the product

in animals, we don't know always what the risks are for human beings, so we want to understand how that can be best communicated to potential subjects, potential participants. And then, finally, is there any other information that you think we would find helpful?

I have included my contact information and the contact information of my office. We receive queries to this particular website, if you have any. And I have also included a public access to our web page, which I think you would find very interesting because it has lots of information that's helpful to clinical research participants as well as investigators and sponsors.

Thank you.

DR. EGGERS: Thank you, Dr. Goldkind.

We're about ready to get started on our discussion, but I'm going to do two things first. The first is there were some comments on the web this morning that pertain to the morning, and so I just want to make sure that those get summarized a bit. But while we're doing that, I'm also going to ask my

colleagues at the table to reintroduce themselves because there are some new faces up here and we also have some new faces out there, so it would be helpful if we could just go down the line.

You already introduced yourself, so maybe --

DR. DEMING: Damon Deming. I'm a virologist with the Division of Antiviral Products.

DR. MURRAY: Jeff Murray, Deputy for Antiviral Products.

DR. STRUBLE: Kim Struble, Medical Team Leader, Antiviral Products.

DR. BIRNKRANT: Debbie Birnkrant, Division Director, Antiviral Products.

DR. WITTEN: Celia Witten, Office Director of the Office of Cell, Tissue and Gene Therapies at the Center for Biologics at FDA.

DR. IRONY: Ilan Irony. I'm the Branch Chief of the General Medicine Branch in the Office of Cellular, Tissue, and Gene Therapies at CBER.

DR. SHERWAT: Adam Sherwat, Medical Officer, Antiviral Products.

DR. COX: Ed Cox, Director of the Office of

Antimicrobial Products within CDER, FDA.

DR. EGGERS: And while Andrea is summarizing these, if I can ask the panel members for this afternoon to come up. And we are getting one more chair for you because I guess I don't count very well. It looked like there were more chairs up there than there were.

MS. TAN: Hi. So I'll just briefly summarize the webcast comments we received from this morning. We have a few folks who commented about the side effects from HIV and taking HIV meds. So someone commented that taking HIV meds when dealing with nausea from chemotherapy is incredible horrible.

We have someone else who said that their dreams for HIV treatment would be no food restrictions and long-term dosing. And the most debilitating side effect for that patient would be intractable neuropathy.

We also have someone who mentioned that the biggest issue is lipodystrophy in the form of facial wasting, and he provided some more details about that, about the treatments using facial fillers and that

they're prohibitively expensive and out of reach for most, and that this issue is still huge in terms of stigma, self-esteem, depression, and isolation. So I think that's something new that we didn't touch on yet.

And then just two other comments about developing long-acting injectable treatments and monthly visits that would be required. So this person was interested, maybe we can work this into the discussion or if patients have comments on this, they could submit it to the docket, but this person was wondering how best they could support patients for monthly injections and if patients would be willing to receive monthly injections versus daily pills and the impact on their lives.

And then, finally, we had a general comment about the context of this meeting and its relevance, and this commenter said that it's important to understand the importance of these issues in a global context and not just the U.S. And this person provided more details about the conclusions about today's meeting will have wide influence

internationally, that this is a start, but it's important to also reach out to others.

DR. EGGERS: Thank you, Andrea. Overview of Discussion Format

DR. EGGERS: Well, I'm not going to spend too much time going over the discussion format, but again we have some new folks in the room, so I do want to make a few points about our discussion. Our discussion format will be very similar to this morning. We will first hear from a panel of patients and patient representatives. And, again, when we say "patients," we are talking about people living with HIV; and when we say "representatives," we mean caretakers, loved ones, and advocates who speak on behalf of patients and who can provide comments that fit the patient's perspective. Again, we're really focusing on getting the patient's perspective on the issues that we're discussing today.

So we're first going to hear from the patients and patient representatives. I'll introduce them in a minute. And again the purpose is just to set a good foundation for our discussion to give us

something that we can react to and discuss further. And then we will be moving out into the audience and opening it up like we did this morning, which is much more of a free discussion.

So we're going to try our experiment again. Periodically we will invite in-person and web participants to respond to some specific questions. Again, this is just a discussion aid, it just helps us understand the perspectives in the room and see how many participants share a particular perspective without needing a raise of hands or anything in the room.

In person, we use the response clickers, and if you haven't gotten a response clicker and you are identified as a patient or patient representative, could you please raise your hand?

(Show of hands.)

DR. EGGERS: All right, so Andrea will take care of that.

And the web participants can respond through the poll through the webcast, and we got feedback that we went really quickly through those, so we will try

to give you some more time. And regarding the webcast, if you're just joining us on the webcast for this afternoon, we have about 180 to 200 people on the webcast -- no, we have more than 100 people on the webcast, I can't give an exact number -- and you are very important to this meeting as well, and we are talking to you and we are listening to you. Even if we can't summarize all your comments in real time, we are taking them. Use the comment box and share your experiences as well.

And for all of you, for those in the room, on the web, and others, we encourage you to provide your comments to the docket that is available on our meeting web page. You can add on to what was talked about today, you can react to what you heard. We will be taking all of these comments and reviewing them, and they will ultimately get into our final product, which is a report on what we heard today.

So a few ground rules. We really, again, want to hear from patients and patient representatives. There are a number of other stakeholders here from industry, other government

agencies, et cetera. And as I said this morning, we hope that you find this as useful as my colleagues up here, but for today, you are in a listening mode and asking not to contribute to the discussion. There is an open public comment, and we will take until the next break, if you want to make a comment in the open public comment, please see the registration desk.

Our discussion today will focus on understanding the common ground on important issues, and we fully recognize that there are a number of important issues regarding HIV care and the support of patients, people who live with HIV. We will be trying to stay to the questions that we are trying to discuss today, the participation in cure research and the informed consent and how to clearly communicate about that. Again, there is a public comment if there is something else that you want to comment on.

And if you haven't gotten a feedback form, we encourage you to grab an evaluation form and provide your feedback. This is completely voluntary, but we appreciate the feedback we get on how to make these meetings in the future as effective for

everyone, for us, for the patient communities, and for other stakeholders.

So thank you.

Okay, so with that, we're going to test the clickers again and we're going to ask the same demographic type questions that we asked this morning because we do have new folks here, and I guess practicing the clickers never hurts.

So if we could have the clicker questions come up. While we do that, can we have the front panel members introduce themselves? I'll let you introduce yourselves.

MR. SHARP: Good afternoon, everybody. I am Matt Sharp. I am San Francisco. I'm a long-term HIV treatment activist. I have worked with several AIDS service organizations. I've been on many, many advisory boards for pharmaceutical companies and also for research institutions. I am currently doing independent consulting work. And I am no longer in San Francisco, I'm in Alameda. I had to say that.

MR. PENNER: Good afternoon. My name is Murray Penner. I am the Deputy Executive Director of

the National Alliance of State and Territorial AIDS Directors, or NASTAD. We are a membership organization that represents state health departments and their staff in HIV/AIDS programming as well as viral hepatitis programs all the way from prevention through access to care and treatment primarily through the AIDS drug assistance programs.

I'm a person living with HIV and AIDS since 1986, and I have been in this field since '96, but it's only recently that I've become much more involved in sort of the advocacy community. Up until that point, I was doing a lot of on-the-ground work at a local health department.

MR. TAYLOR: My name is Jeff Taylor, and I have been living with HIV for over 30 years. I first got involved in the first AZT trials back in the '80s and have been involved in clinical research ever since. I was on the AIDS Clinical Trials Group, Community Constituency Group, and currently I work with a group called the AIDS Treatment Activists Coalition, serve on the newly formed CARE Collaboratory Community Advisory Board, and I'm on the

Antiretroviral Guidelines Panel. And I live in Palm Springs, California.

MR. EVANS: Hi. My name is David Evans. I'm a patient representative here from Project Inform in San Francisco. And where I come at this is that back in 1989 some eventful things happened. First I came out, then I got a boyfriend, and he told me a week later that he was positive. Shortly thereafter, two of my closest friends died, and then by cousin came out as both gay and positive and had 30 T cells and pneumocystis pneumonia. And as a result of that, I joined ACT UP, which was a direct action group that still fortunately exists in some places, and shortly thereafter joined Project Inform's treatment hotline where we answered thousands of calls from all over the country for people who were desperate for information about treatment.

And one thing I just want to say about that activist background and doing this so long is in one way or another we've been talking about a cure for a long time, but we didn't use the "C" word, we called it pathogenesis, we called it other things, and I just

think it's important to note that we've been doing this for a long time, but it's great that we can actually get to the point where we can use the "C" word.

MS. DEE: The "C" word. Okay.

Hi, I'm Linda Dee, and I'm from AIDS Action Baltimore. Let me see, I'm all these little hats. I think that I've probably worked with most of the groups that everybody has talked about, AIDS Treatment Activists Coalition, the Community Constituency Group of the ACTG, the CARE Collaboratory. I've worked with the FDA on a number of things, including their advisory panels, industry, advisory boards, you know, Hopkins Advisory Board for a very long time. You know, just invested.

My organization was formed in 1986, '87 it was actually incorporated, and my husband died as a result of AIDS in 1987, and so many friends that probably as many people as are in this audience. So I'm sick of this, and I want this to go away, and I know that the only way that it will happen is if we find a cure for this. And I have worked with all of

these people for many years, a lot of the people that are in the audience for many years, and it's very heartening that we're getting to even think about the "cure" word, let alone say it and working in that regard, and I really would like to applaud the agency for getting to these questions and these points from not only a patient perspective but in a timely way so that we can really have more of a chance to prepare for this than we did the first time around. So we're not knocking the doors now, we're working on this together.

DR. EGGERS: Okay. Thank you very much.

So let's ask those demographic questions that we asked this morning. The first one is an easy one. Do you live within the Washington, D.C. metropolitan area or outside of the Washington, D.C. metro area? If you can figure out the clickers, it's 1 or 2.

(Answering question.)

DR. EGGERS: Okay. Can we have the -- all right. We are 50-50 this morning, so it's nice to see so many people travel from outside, and we really

thank you because this is quite an effort to do so. So our appreciation always for those living in town, too, but our special thanks to those who have traveled here.

Okay, let's go on to the next one. What is your age? Younger than 25, 25 to 34, 35 to 44, 45 to 54, 55 to 64, or 65 and better.

(Answering question.)

DR. EGGERS: Okay. Again we have a distinguished crowd here today, so it's great to see all this wisdom in the room.

Okay. Can we go on to the next one? Are you male, female, transgender, or prefer not to answer?

(Answering question.)

DR. EGGERS: Okay. Just like this morning, we have about the same split. Okay. Was it 50-50 this morning?

UNIDENTIFIED MALE SPEAKER: 60-40.

DR. EGGERS: Okay. Thank you for correcting me. You guys keep me honest.

Okay. Have you been diagnosed as having HIV

infection?

(Answering question.)

DR. EGGERS: Okay. Great. So two-thirds of patient and patient representatives here today who have answered the question.

Can I ask Andrea, are the numbers available for the web?

MS. FURIA-HELMS: Yes. About 70 percent answered no out of 20 responses.

DR. EGGERS: Okay. Well, I would have to do math for that, but we've got representation on the web as well. So, again, we encourage those on the web to keep your comments coming in.

Do we have one more? Yes. For persons living with HIV, how long ago was your diagnosis? Less than 2 years ago, 2 years ago to 10 years ago, 10 to 20 years ago, more than 20, I don't know, or prefer not to answer.

(Answering question.)

DR. EGGERS: Okay. Again a lot of wisdom in the room. Okay. And then I think there is one more demographic. Let's see. Yes.

For persons living with HIV, how many different types of antiretroviral treatment, ART, regimens have you taken? And please include your current ART regimen if you're on one in your count. You've never taken any ART regimens, you're currently on your first, you've taken two to three different regimens, more than three different regimens, or if you're not sure.

(Answering question.)

DR. EGGERS: Okay. Lots of experience, too, with different treatments and different regimens. Okay. Good. Thank you.

This really helps us set sort of the understanding of who is in the room and what kind of perspectives we're getting today, so I thank you for answering those questions. We're going to have more questions throughout the afternoon, but enough of my talking. I'm going to ask the panel members to go down, and I might start with David. I understand that you have some data, some to share, so we'll start with David, and then we'll work and go throughout.

Now, agendas are what they are, we're a

little bit behind the agenda, so if you could stick to your comments to 2 to 3 minutes, and then we'll go and you'll have plenty of time after that.

So, David, thank you.

MR. EVANS: Sure. So one of the reasons that I wanted to be here today is that a really fantastic activist named Nelson Vergel and I conducted a survey of people living with HIV about a year ago about cure research, and one of the things that I want to say about the survey is that we did so based on the belief that people really would want to show up for these trials even though they might not get any benefit out of them. And we fielded the survey between December of 2011 and early 2012. Within 6 weeks, we got 2,100 people to answer the survey, which for an online survey that we did for free and begged and borrowed and stole any kind of advertising that we could get, that's a pretty high response. The design of the survey was such that we made people have to answer every single question, so we got 100 percent completion on the survey response.

You know, I don't have time to describe all

the demographics. I can say that despite really extensive outreach on our part to groups that are serving women, people of color, and people who are more recently diagnosed, our demographic looks a lot like the people who are here today, and that it tended to be a little bit more male, white, older, and having lived with HIV for a very long time.

We also asked people before they answered the questions to read a primer that I would call it medium length. It wasn't short, but it wasn't really long, and it described a lot of the risks of the kind of cure research that we are engaged in right now or soon will be. We couldn't be sure that people actually read it, though, before they answered the questions, so we can't say for certain how much they really understood the risks when they answered questions that we did.

But when we asked people to state how motivated they were to participate in a study that would benefit others but might carry risks for themselves, 88 percent reported being at least somewhat motivated, and 24 percent reported being very

motivated to participate. Granted, there is a tremendous risk for what they call social desirability bias -- of course, everybody wants to help somebody else -- and so that could be affecting the results a bit, but we still felt that was a pretty profound response.

We also asked the question in a different way, and received a very similar response. We asked people what their willingness to participate in a study would be if it definitely would not benefit them but it might advance cure research in general, so a little bit more diffuse, not will it help people, but it will advance the scientific field, and there we still had 81 percent reported being at least somewhat motivated, and 16 percent reported being very willing to motivate to participate.

But I think that there are other benefits to participation in a study beyond altruism, and there are things that I think we have to really be careful and keep in mind, and we'll be talking about some of those things. But one little piece of data that we did when we did a deeper dive that I haven't talked

about before is that when we looked at people who were very motivated to participate to benefit others, they were also very, very motivated to benefit themselves in a study, and so I think that if we're depending on people's altruism, we also have to be very careful not to in any way play on any misperceptions they may have that they are going to benefit from a study when they actually won't, so we'll talk more about that.

DR. EGGERS: Thank you, David.

Discussion 2: Patients' Perspectives on HIV Cure Research Panel #2 Comments on Question 1 - 4

DR. EGGERS: And then we'll start here with Matt and address the rest. And I didn't remind us, because the panel will come back later after a break later this afternoon, so right now we're just focusing on the participation in cure research, what you believe are the benefits, what would motivate you to participate or not in an HIV cure research study, what risks you would find acceptable and why, and in particular if you are asked to stop any HIV medications that you are currently taking, how that would affect your decision to participate.

So, Matt.

MR. SHARP: So I have some prepared statements if you don't mind. So I've been a participant in dozens of clinical trials over the years. I was actually first in every first-in-class trial of almost every antiretroviral drug class except for nucleoside analogs, and I survived, obviously, but unfortunately developed resistance due to sequential monotherapy.

I was always most interested in host targeted approaches to HIV, but, as you all know, you all know what ended up taking precedence. So I needed other options to buy more time, as my immune system was not up to snuff, and I am in that older HIV population at risk for inflammatory-related comorbidities that we talked about this morning.

I participated in invasive trials such as Dick Hong's thymus transplantation trial. I was in the first injectable Fuzeon TORO trials. I was in the first placebo-controlled human growth hormone trial. I was in the placebo arm at first of that trial. And most recently, I entered a Sangamo zinc finger

nuclease gene therapy trial.
So mostly I really had no choice to be in all of the studies, and despite my highly resistant virus, I've been undetectable for over 5 years now, and my T cells have doubled, remaining that way 2 years after the zinc finger trial. So I believe I'm really here as a result of being in clinical trials and aggressive approach to fighting HIV from the very beginning.
But the motivation for entering these cure-related trials is different today than what it was in the early days of the epidemic, as you all know. People needed treatment to buy time to live and survive. We have to do better today. There is much room for improvement in the care and treatment of people with HIV. This is something that we may have already discovered through Sangamo's first gene therapy trials where a functional cure may not be likely but additional immune recovery certainly has been shown in a few patients in the first cohort.
So there are a lot of people out there like myself who want to take these risks and where there is

no benefit because we want to live to see a cure, we want a cure ourselves, or we want at least a functional cure. And then, as David said, many people enroll for altruistic reasons.
And at least I know in the gay community, it's known that people want to give back in the form of clinical research to help their own. When I go out and talk about a cure in the community, I always ask how many people would want to be involved in a cure-related trial and almost every hand goes up in the room. But there are risks. And I'm a very different patient; I've been willing to risk a lot to be in these clinical trials. In the thymus transplantation study, I risked an invasive surgery in transplant rejection drugs. In the gene therapy trial, I obviously took a lot of risks with the manipulation of my own CD4 cells. Everyone is individual, though, and the risks they take might be more or less than others. Everyone needs to weigh their own informed decisions against the risk and benefit obviously. And as the treatment guidelines state, everyone is individual.
I feel that since there is going to be much

variety in cure-related research, setting a standard of what is too risky or, on the other hand, not in depth enough to get a clinical outcome won't really move the field forward. It's for this reason that the scientific and community collaboration is critical so that each risk and benefit is weighed carefully as we go in a step-by-step manner and everyone learns and eventually we're all going to win.
And I guess I'll stop there.
DR. EGGERS: Thank you very much.
MR. PENNER: So much like Matt, I've been infected since 1986, and in the very early days of the epidemic, as you all know, there were few treatment options, and so I was fortunate enough myself as well to participate in several clinical trials. And at the time, I was really looking at it from a very personal and a very selfish motivation because I wanted access to what I knew was very promising in terms of options for therapy. Obviously, we are in a very different place now, and then I think that even at the time I felt like there were probably a lot of risks that I didn't know the answers to, but I was willing to take

those risks based on not having other options.
We are at a very different place today, and so I think the whole motivation -- and David's statistics were very interesting to me and actually not terribly surprising because I think a lot of people do believe that there is really a good thing to be had by participating in these, but that therapeutic misconception that we heard about earlier is something that I think is in the minds of patients that are considering getting into these things now.
One of the things I would like to see if I were going into a clinical trial now was that there would be some kind of benefit for me and I would get maybe more monitoring than I would and more deeper dive into what's functioning inside my body than I would get if I just go to my HIV doc. So I think that it's a very different environment now in terms of what we look at with giving informed consent and having participants in cure research.
For myself, I would really want to know the benefits, the scientific benefits, and the risks that we believe are in place very clearly without having to

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go through a 5-hour process with 9,000 different pages of something I didn't necessarily understand.

From risks that I would find unacceptable, I think I'm very used to sort of the nausea, the fatigue, and the diarrhea. Of course, some of that could be that I'm getting older, so you never which is caused by what, but nonetheless, some of the more immediate risks are symptoms that you might experience or ones that I would be concerned about to try to minimize, whereas some of the longer term risks, I probably wouldn't be quite as concerned about, even though I know there could be a risk for cancer or others kinds of longer term events, blood clots, seizures, et cetera. I think I would be less worried about that than I would be about the day-to-day kind of interactions that medications have on me.

And then, lastly, I think being asked to give up my treatment regimen that I've worked very hard to get something that works, number one, and, two, doesn't interrupt my daily flow is a real barrier in terms of participating in cure research. For myself, I'm not sure I would do it, giving that up and

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having the risk of further complications as a result of not staying on medications. I've taught myself over many, many years how to stay adherent, and to change that whole regimen up might be difficult for me to make that leap.

I'll stop there.

DR. EGGERS: Thank you, Murray.

MR. TAYLOR: Well, like Matt and Murray, I started early on basically for the same reasons, to get access to drugs to stay alive. And I think it's very different now, but back in those days, I mean, most of the trials were placebo-controlled -- you got the drug, you didn't -- and then they waited to see who lived or died, which is a kind of grim way of measuring efficacy, and fortunately we moved beyond that, but I think as we move into this arena, we're going to be back in those situations where there is no benefit in the control arm, or even in the treatment arm for that matter.

And I would like to share an anecdote about a couple of trials I was in where I didn't receive benefit and actually had some harm and kind of how I

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got to that place and how it shaped my perceptions.

One of the early ACTG-PCP prophylaxis trials was comparing Bactrim, Mepron, and aerosolized pentamidine to see which was most effective at preventing PCP. And I started on Bactrim, got the horrible rash, the same thing with Mepron, so I was finally put on aerosolized pentamidine, and as the study progressed, it was becoming more and more evident that that was not the optimal arm to be on. And my private physician came to me and said, "You know, you're on all these different antibiotics for all these things, I could desensitize you back to Bactrim, I've done it with other patients, I'm sure I could do it with you, you take fewer pills, and it would be better at preventing your PCP as well."

And so I was presented with a real dilemma. I went to the study nurses and I said, "My doctor has told me this," and they said, "You know, you're right, this is an option for you, and we're not going to tell you what to do, all we can tell you is that on our site nobody has broken through with aerosolized pentamidine, they've done fine, you've got 6 more

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months on the study, and the decision is yours." So being the altruistic individual that I was, I said, what the heck, what's another 6 months after 2-plus years of being in this trial?

Well, sure enough, with 2 T cells, I developed PCP, both my lungs collapsed, and then I nearly died. But I pulled through and it was a valuable lesson learned. And would I do it again? Maybe not. I think I might have placed my own health as a priority because I still have lasting lung damage as a result of that.

More recently, I was in a vaccine trial that had a structured treatment interruption, and I did the interruption. It was unfortunate enough to be during flu season and I got the flu the same week I stopped my meds. So I think I really skewed their study results. And when I had to go back on the regimen, I restarted my original regimen, and for some reason it didn't work. We couldn't find any evidence of resistance fortunately, but they had to throw more pills on top to make me undetectable again. So I think again it's a personal example of where something

where it didn't work, and I didn't get a benefit, and I would probably not be eligible to do a structured treatment interruption again.

But even given that, I mean, in other circumstances, I think it's well worth it. I'm very committed to research. And we're asked these questions, and there are no answers, it's just a lot of situations where it's highly individualized, each person has to look at their own situation, sit down with their personal physician as well as the study doctors and staff, and figure out what's going to work for them, what their options are if it doesn't work, you know, examine all the scenarios one-by-one, and decide what's best for them.

That's all I'm going to say.

DR. EGGERS: Thank you very much.

And, Lynda?

MS. DEE: So, you know, I'm struck by something that on the CARE CAB, the doc, the PI of the study came to us and gave us a letter from somebody from the North Carolina area who was a heterosexual who I think he may have said that he had all these

religious issues, and I think felt very guilty that he was HIV-positive and that he might have infected his wife, and all of that sort of thing. So he was begging to be put on one of these clinical trials because of his situation. Now, here was a person that had no idea that these trials couldn't help him really, that he would really have no benefit.

So I guess the point that I'm trying to make is that we really need to be sure that people know what they're getting into. I mean, not everybody has been through what the panelists have, you know, through years of the epidemic, so people hear "cure." You know, in the United States we're like, you know, little blurbs of cure, so, "Okay, well, where can I get some of that?"

So we really have to be careful, and I think it's the community's role as much as the agency's role to make sure that people know what they're getting into, and we'll talk about that more in the informed consent stuff.

And what would motivate you to participate? You know, being involved with the Hopkins CAB and the

CARE Collaboratory, I have helped them get study participants for their leukapheresis cell trial, and I was wondering because everybody that I thought of -- because you have to sit there for 3 hours -- was on disability and could really use that $50 that they got, you know. So those are the kind of people that I got in touch with and a lot of them signed up. And I talked to a number of the other docs there, and they have found exactly what David's study has found, that there are a lot of people that are really interested in being in trials just for altruistic reasons, and most of those people are not on disability, you know, at least in that little Hopkins group. So I guess people have different reasons for participating.

And what would be an acceptable risk? I just finished a clinical trial in HCV, and you get these pages and pages of stuff that say, well, this could happen, that could happen, and I really often wonder again if people really understand what some of this stuff means, they either want to do it or they don't, or that they pay attention to what's even included in the informed consent. But with HIV cure

trials, it's going to be so important that people understand that this could really affect where you are now. So it's I think important to look at people in different groups.

Now, you know, a year ago I would have said, well, maybe if I was newly diagnosed, I might be a better candidate for this, there might not be as big a chance for me to get off my treatment or I wouldn't have a regimen like Murray described that has taken him years to get right, but now then you have this new data that says, well, you know, if you can get treated early enough and stay on for just enough amount of time, that you might be essentially able to go off treatment. So maybe that patient population is not the right patient population to start. I'm trying to think about this as how I would think about it.

So maybe the patients in the middle are the best ones. I don't know. But somehow all of this information has to be communicated to people to be sure that they understand what the risk really is. You could get cancer. Well, what does that mean? When? How much? I mean, you see people that smoke,

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still smoke, well, "Oh, I won't get cancer." You know, you've heard people say that, I'm sure.

So if we could somehow do a better job of actually defining what risks we're talking about and if it's risk of a disease, if we could get a little bit more clear instead of this -- and I'm sure we'll talk about this more when we get to informed consents, but a lot of those documents are really not anymore, I think, not to protect patients, but they're to protect the IRBs and the institutions. So I think we need to really, really drill down on what they should say, and I think we'll talk about that later, as I said.

About stopping medications, I mean, that's really a tough one. I mean, it's really hard to have somebody that has really been sick for so long and say, okay, you're all right now, but the way to prove this drug is for you to stop taking your medications to see, or procedure, that it's really worked. So, I mean, I think that it's going to be so important to be sure that people know what it is they're getting themselves into.

DR. EGGERS: Thank you, Lynda.

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Do any of my colleagues want to have a sort of clarifying question?

Kim? Yeah.

DR. STRUBLE: I have a follow-up question for Murray. I guess I was kind of struck by your comment because I thought the other way, that you thought that unacceptable risk, the long-term toxicity like having cancer, wasn't immediate for you, it was more the day- to-day types of toxicities, and the known toxicities versus the theoretical toxicities. And I was wondering if others shared that same perspective or could elaborate more on what they found was the immediate versus long term, hypothetical versus known, unacceptable risk for cure research.

MR. PENNER: Well, I just want to make sure that I'm clear. It's not that I wouldn't care about that. I think that's far less in my mind than would be what I have to deal with every day. You know, I feel like we've all sort of experienced, "Oh, you could die." I mean, I was told when I was diagnosed that I had 6 months to live, and here it is nearly 30 years later fortunately, but I think it's sort of the

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down the road kinds of things I'm willing to take some risks on more so than I am my quality of life now.

MR. EVANS: I can add to that a little bit just based on the survey that we did. First of all, it was interesting that people who had been positive the least long who had the highest CD4 count were the least likely to take part in these kinds of studies.

The other thing we found that I thought was interesting, though, that runs a little counter to what Murray said, was that people felt very positive about their current antiretroviral therapy, and almost everybody was on it. Ninety-two percent said they felt positive or very positive, so very few people didn't like their therapy. And 75 percent reported only having mild or moderate side effects. And when we tried to analyze it and see how people felt about therapy affected their choice to participate in a clinical trial, what we found is that it didn't, whether they felt great about their therapy or didn't like it, it didn't seem to matter. Granted, the people who didn't like it, there was a smaller number of people.

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What was I going to say? Yeah, that's it.

DR. EGGERS: Anyone else from FDA?

Okay. I'm sorry, Matt.

MR. SHARP: Yeah, just quick another anecdote. In San Francisco, Quest Laboratories is performing some of the gene therapy trials that you may be aware of, and they performed my cohort, and in the protocol they came back and asked us if we would like -- after the initial infusion of the product, asked us if we wanted to stop therapy, and there were eight participants in that cohort, and only person said that they would, so that's just that example.

And then there is a second study, a follow-up study, that Sangamo is doing that they are actually looking at a treatment interruption, and surprisingly, Jay, Dr. Jay, is finding enough people to enter and enroll in that study.

DR. EGGERS: Celia?

DR. WITTEN: Yeah, we had some comments about stopping a treatment, about the treatment interruption, and a comment to stop to see if the treatment really worked, but in a lot of cases, the

treatment interruption would really be more to stop to measure something, to see how well it's worked and not really with the expectation that it's worked. So I'm wondering if that would change any of your comments.

And other question I have is about risk and the comments made, "Well, we would like to know better what the risk is." But at least for our products what we have is just a level of uncertainty regarding what the risks really are because truly the animal models are not good enough to even delineate them, and the kinds of things that Dr. Irony talked about, like the risk of cancer, what vectors to integrate, those are risks, but those kinds of things can come up without really being understood from the animal models.

So I'm just wondering how the additional layer of uncertainty as it relates to risk would factor into your answer to Number 3. So it's a question about your answer to Number 4 and Number 3.

MR. TAYLOR: Well, I think to piggyback on the discussion, I'm unlike Murray in that I would be willing to tough out some short-term discomfort and inconvenience if I thought it was going to benefit

science, but if I thought I might get cancer later, that might give me more pause. So I think people are very different and you can't generalize in this, that it's going to be very different across the board, and you really can't make assumptions, but I think if you ask enough people, you're going to find people to step forward for whatever reasons as long as you ascertain that they're genuine and they really understand the risks.

MR. PENNER: Yeah, I think Lynda mentioned earlier that it is very individualized, and I would certainly concur with that. And I think that your question about potentially stopping for a period of time to determine the effectiveness and then have the particular options again, that might change my mind. I think some of the comments that I have made have been very broad and not specific to a situation. So I think that's certainly an important part of this as well as the situation in which you're asked to do things.

You know, for me, I went through a period of time when I was determining regimens that worked for

me where I had a lot of diarrhea, where I had a lot of nausea, and I had a lot of vomiting, and those were terrible days, and that's why I think I'm motivated to say it the way I say it, that those things for me are really something that I don't want to repeat again, whereas the longer term ones, yes, important, are less in my mind as those initial symptoms might be.

MS. DEE: You know, I may have said that badly about to see if it works per se, to see if what you're measuring is really happening the way you would like for it to be coming out, but, you know, I guess what I was trying to get at is that maybe there are some populations for which that's less of a risk than others.

And, you know, for some of this stuff, we don't know what the risk is going to be, and if you asked five people the same question, you might get five different answers about that. So when I was looking at these questions, I went around in circles a number of times, and I thought, well, we're going to be a lot of help, you'll have more questions than answers by the time we get done.

But I think if you think about it really, if you think about the way we have developed drugs before, you know, try and look at the populations where you can do the least harm, try and make sure that people know what it is you're talking about, try to define the risks as best you can, be sure that you delineate or that the person understands that there is no benefit here for you, you know, that sort of thing, are the concrete things that I could think of that were good take-home messages.

DR. EGGERS: I'm going to interrupt this because I want to make sure that we allow the folks in the audience to also participate and contribute and build on what we're hearing. And before we do that, just to set the context, we have a couple of questions for your clickers and for the folks on the web. This just lets us understand the experience with clinical research.

So have you ever participated in any type of clinical study related to HIV? Yes, no, or I'm not sure.

(Answering question.)

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DR. EGGERS: Okay. So the majority of you have participated in some form of clinical research related to HIV.

Do we have the experiences on the web?

MS. FURIA-HELMS: About 66 percent have not, 33 percent have.

DR. EGGERS: Okay. Okay. And then another question is, have you ever participated in any type of clinical studies specifically related to HIV cure research? Yes, no, or you're not sure.

(Answering question.)

DR. EGGERS: Okay. So more experience with the clinical research just in general related to HIV and less with cure research, which is not surprising, but it does help us understand where the perspectives are in the room.

Did we get the numbers for the web?

MS. FURIA-HELMS: Yep. The majority have not, 93 percent.

DR. EGGERS: Okay. Great. Thank you.

Large-Group Facilitated Discussion on Question 1 - 4

DR. EGGERS: So I know that my colleagues

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have more questions to ask, but what I want to ask first is if anyone here in the audience found anything said by the panel members really surprising, like it doesn't necessarily relate with your experience or you would have thought something different or just surprising in general. Oh, and if you could state your name before you speak.

MR. GARNER: Hi. My name is Alex Garner. And I guess I was more surprised by what wasn't said in the sense that as we had those demographic questions earlier before the discussion, I was struck by who wasn't represented and who isn't here and who historically isn't represented in studies. And as we talk about the sort of vast experience that all of us in this room have, it's troubling to think of the future of the epidemic which looks like it's black and brown young gay men, and they're not here.

So part of me wants to encourage all of us to sort of remember that because it's critical to the work that we're doing especially when communities of color have such a troubling history with federal agencies and studies and stuff like that. And when we

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talk about how people will feel inclined to participate in this study, how they're impacted by all these other elements of their life -- class, race, sexuality, gender, et cetera -- have an impact on that, and it's not just whether or not they're going to be feeling altruistic or not, it's all these other elements.

So that's it.

DR. EGGERS: Great. Thank you.

Does anyone else have any first reactions that were surprising?

Yes, Melanie.

MS. REESE: Not surprising, based on the fact that a lot of these are long-term survivors in the beginning -- being infected in the beginning of the epidemic, and their desire to continue to live, to grab onto hope, that it would transform from just staying alive to eventually being able to help somebody get a cure and not have to live long term with having to take meds, I wasn't surprised about that.

But, for instance, in my particular case

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with all my other conditions, I would not be willing to risk getting off the medication that I have been on because I don't know if pulling the plug on that would cause something horrendous to happen to all my other conditions. So that's my perspective, although altruistically, idealistically I would be happy to be in a trial. But being a woman, there haven't been that many.

However, I was able to be in one because I was on Depakote, and somewhere in Australia Depakote was shown to deplete the reservoir of the virus, you know, when you were suppressed, and so I was able to be in that one, but most of the other ones I was not.

DR. EGGERS: Okay. So let's -- oh, go ahead. Was there another hand up?

(No audible response.)

DR. EGGERS: Let's just make sure that we have fully discussed the idea of the benefit. And we heard the altruism.

Can I ask, David, did people have open-ended responses, the 80 percent who would participate, did they --

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MR. EVANS: No. It was on a Likert scale, so it was "Very willing," "Willing."
DR. EGGERS: So does anyone want to follow up and build upon what we heard about any of the benefits or the perceived benefits of participating in a trial, understanding that there is perception of benefits and then there is actual, you know, real benefits, so if we could focus on what you believe are the benefits of the trial. If anyone wants to comment on that?
And the panel you can expand upon -- Matt.
MR. SHARP: So something I brought up this morning was getting to the cure, there are going to be a lot of steps along the way that we discover, and one of those might be improvement in immunology and immunologic response. So that's one thing that could be a benefit.
DR. EGGERS: Any question from FDA to follow up on that?
(No audible response.)
DR. EGGERS: No? Okay.
Any other benefits?

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MR. EVANS: There are a couple things that people might perceive as a benefit that we sometimes don't like to think about, and one of the things that I can tell you is that when I was a broke student living on part-time money, I participated in research because it paid money. And another experience I've had as a clinical trial participant was going in even though I knew I didn't want the therapy, but it would give me access to diagnostic procedures that weren't standard medical care that I had read would be beneficial to me. So just things that people think about.
MS. DEE: You know, and a lot of the people that we have referred to Hopkins, a lot of them are African American MSM and a lot of them are on disability, and a lot of them were interested in the money that they got because they needed it. Now, I think we have to be really careful about the inducement there and whether we're getting people into things that are harmful or that they don't know what really the score is about.
But I think that we really should -- well,

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let me just put it this way. When I talked to one of the doctors at Hopkins, I also asked about biopsies, and does that dissuade people when he talks to them about what's actually required in a trial? And he was saying, well, no, you know, that they're required to do anal biopsies in some of the prep trials, and people don't seem to mind, but that they really need to be compensated for what they're going through, and there is nothing wrong with that. I mean, I think that people are putting themselves on the line and some people need the money, some people don't, but it ought to at least be offered to people if we're sure they know what they're getting into and we're not using them in any sort of illegal way. But I think that's a real important thing in the beginning of this.
DR. EGGERS: Anyone in the audience?
Yes, go ahead. And if you could state your name, please.
MR. FISHER: My name is Kevin Fisher. One of the questions about benefit or one of the things where sort of altruism overlaps with benefit, is that

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there was a study that was very similar to the study that David referred to that was done in Holland with HVM where they asked HIV-positive individuals what they thought about a cure and why they might be interested in a cure, and interesting, one of the things, as David said, a lot of people weren't necessarily concerned about their medications or toxicities necessarily, but one of the biggest concerns was about the future, like what will things happen in 20 years and basically how will my life end and how will this disease affect me in ways that I don't quite understand? And one of the benefits of going to cure research was actually maybe to get a step towards that way.
So this would be a case where you might join a trial even though it wouldn't necessarily benefit you, but you would actually in some sense push forward the general knowledge -- this actually kind of goes to Matt's point -- push forward the general knowledge so that maybe one day actually people will have an answer to that and they can maybe diminish some of that anxiety.

DR. EGGERS: Are you talking of helping your future self or something different than that?
MR. FISHER: Yes, a little bit. I mean, there is a general altruistic, but helping your future self in some sense, and so that's where altruism and personal benefit kind of overlap in a way.
DR. EGGERS: Okay.
MS. DEE: You know, I think some people think, too, and they did in the old days of the epidemic, that, "Well, I'm going to get my foot in the door because if I get in here, maybe I'll be considered for the next one and the next one, and I'll be in line for something that really will be beneficial two steps down the line." Now, a lot of times, it disqualifies you from being in the next step and people should be informed of that, you know, but I do think people think that way.
DR. EGGERS: Okay.
MR. PENNER: Yeah, I was going to reiterate that a little bit. That's sort of the motivation that I had early on, Lynda, was really like I'm going to get in, it's going to lead to the next place, it's

going to lead to the next place. Of course, there weren't any options at the time, so it was like looking for that option that may be out there that ended up being there. But one of the things that I did find out, obviously, is that my T cells increased, my viral load decreased as a result of being in this, and so I was seeing personal benefits.
So the continuous feedback about consent about what's happening as a result of your participation in the study at least for me would keep me very motivated thinking that there were other options that would help me improve my own life moving forward.
DR. EGGERS: Do my panel members have any follow up questions on the idea of motivation for participating or benefit?
(No audible response.)
DR. EGGERS: If not, let's continue the discussion on the risks and the uncertainty about those risks. And we heard a lot mentioned up at the panel, and what I would like to ask is in the audience if you had any thoughts that came to mind as you

listened to the panelists about risks and your thinking about those risks and how you might consider those for a cure research study.
Nathaniel?
MR. SCRUGGS: Good evening. I was listening and looking at the panel, and I thank you all for doing what you all are doing so I could be here, but I was listening to Murray, and I had almost forgot the days of diarrhea and throwing up and headaches. And I'm somewhat appreciative of your honesty. You know what I mean? Because what happens today, medicine, scientists, come together and they say we're coming up with these clinical trials and we want this certain cohort of persons in the trial, and, Lydia (sic), you spoke to it. A lot of them don't even read all that information that's in there, and they don't even look at the long-term effects that might happen down the road. I know I was one that didn't, and I got in the trial for what David spoke about, for the money, at first, and then it dawned on me that I could get free health exams every 6 months, not for my HIV but for my high blood pressure, whatever else might be going on.

And I was thinking, would I sacrifice the quality of my life today to get in a clinical trial for the future of somebody else? No, I wouldn't, and the reason I say, no, I wouldn't, because the way the quality of my life is right now, can't no clinical trial help me to maintain not a high level of my quality of life but just a minimal level without me going back into throwing up, the aches, the pain, the sleepless nights, and that's just the physical aspects. I ain't talking about mentally thinking I'm on the island by myself.
So, no, no. Clinical trials have to give me more of a guarantee that I can still have some remnants of a mental and spiritual quality of life. Physically, I'll be able to deal with that if my mind and spirit is in tact. So a lot of times -- and I'm looking at you all and I want to say when you have people in your life that support you, your life is more healthier and enriched. When I was single, my life wasn't enriched because I felt like every time I threw up, it was going to the worst, not fully understanding what was happening.

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But what clinical trials are not looking at -- and Murray kept speaking to it, and it's so true -- once you get over a hurdle of physical discomfort and you realize that you are over that hurdle, you are not willing to subject yourself to that hurdle anymore for any particular reason without you getting a guarantee. You want a guarantee. And if anybody is involved, and they have enough courage and integrity to self-impose, they will say that. I don't care how much money is involved, Lydia (sic), but your quality of life is more than money.

DR. EGGERS: Thank you very much, Nathaniel.

We have a follow-up question, or comment I mean?

MR. SCHAICH: Not to that, but just to the risk versus the benefit?

DR. EGGERS: Sure. Yes.

MR. SCHAICH: My name is Fred Schaich. I'm with IFARA and ATAC. I am concerned. I don't discount in any way David and Nelson's attempt to really get a good chunk of information from the community, and they did. The one thing that I do care

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about is that when you take an arbitrary idea and you put it out there, it is that, but I think when you're talking about the reality of a trial, you have to really understand -- that's what we're really going to be talking about next, I guess, the consideration of, what is actually in that trial? What are the risks? What are the perceived risks? What are the discussed or potential risks that person could really evaluate fairly and honestly in themselves? And then the fact that you have a family or a job that may be interfered with in this protocol, those are all those considerations that may make a difference.

Altruism is a wonderful thing, and I tell you, most people have it, but it comes to a point where you have to take the reality in perspective, and that's the only thing I would like to throw out there.

DR. EGGERS: Thank you.

Anyone else want to comment on risk?

Yes.

MR. GARNER: Hi. This is Alex Garner again. As I'm thinking about the sort of risks and benefits associated with being in a trial, I am reminded of how

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we worked so hard to change the risks associated with getting credit. You know, you get very simple language, you understand what your risks are if you get a credit card, and we worked really hard to do that. I would suggest we do the same thing around clinical trials so that people fully understand what the risks are in very clear language. We're also sort of assuming that they're at a particular level of health literacy, which isn't always the case.

So I think those sorts of things help people understand what the risks are better, and they're more likely to trust the institution who is going to potentially put them at risks and therefore more likely to want to participate and engage in that way.

DR. EGGERS: Can I build on one thing that you just said, which is trust in the institution? And we haven't talked about that at all today. Would anyone like to comment on that point? Does that matter?

MR. PENNER: I'll take a stab at that as I've been thinking after a couple of people have talked. One is that I think at least some of us up

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here have the benefit of a really informed treatment network and brilliant friends and really good doctors and a working relationship with the FDA and other agencies, et cetera, to the point where I think we probably do have a lot of trust, and I think that makes a big difference.

Many underserved populations, people living with HIV and AIDS, and it's been referenced here, don't have access to that, and I think it would be a lot more difficult to really have an honest dialogue with those individuals and have them involved in this, and we need those people involved in this type of research, and so that's one of the schisms I think that's out there that needs to be addressed to develop some trust such that individuals do feel as though there is a good support system as well as really clear informed risks, benefits, et cetera, rather than just what's on a piece of paper that you sign.

DR. EGGERS: Great. Thanks.

Anyone else want to build on that?

Yes.

UNIDENTIFIED MALE SPEAKER: I want to

basically say what Murray said in terms of like involvement in the process from the beginning, not just in the process after you have developed your informed consent, until you have your conversation. Like, I mean, I love all my comrades here from years, but here we don't represent the demographics of the epidemic, the experiences of all people with AIDS, so in the process, that would be a good way to start building that trust for the future, and more in cure research that is going to be even more complicated.

DR. EGGERS: I think when we come back after the break I think we should spend quite a bit of time following up on how to engage the folks that aren't like those here in the room, so we can follow up on that.

I want to ask my colleagues, though, before we -- there are two more polling questions, so we're going to get to those before the break, but before we do, are there any follow-up questions that you want to ask?

Sara, yes.

DR. GOLDKIND: I have a follow-up question,

but it might be something that we may have to revisit after the break. I've been hearing a lot of repeated comments, it's become a theme. There are two themes that I wanted to flush out a little bit more. One is that it's an individual decision whether someone participates in research or not, and it's a very different decision from one person to the next how risks and benefits are weighed.

And so my question that I would have is, how do we help participants make that individual decision? Is the onus on the investigator or the person who is doing the informed consent or on the participant or on their discussion together? So, in other words, we could communicate information to the potential participant, and is it then that person's job to take that informed consent document to his or her health care provider or family members or community and figure out the risks and benefits? Or should there be a second meeting after the original consent discussion with the investigator again for there to be additional discussion about the contents of the informed consent document?

So I would like to understand better what you think would be an ideal informed consent process in a sense.

And the second thing that I've been hearing is that people don't read these very long, complicated informed consent documents, and so how can we communicate the information that's really salient in the informed consent documents to participants in a way that they will understand the information?

DR. EGGERS: I have a feeling we won't -- we're going to be taking a break in a few minutes, and that's a huge discussion, so if we don't get to it now, we'll revisit that.

But maybe one thing that I think could be asked that's more directly related to the questions that will lead into after the break is that role of the personal physician, your own personal physician. I'm curious on how they shape your thinking and your motivation to participate in a trial, and I think that would feed into -- we can revisit the question about informed consent then after the break.

We heard a couple of folks up here. Would

anyone else like to comment on that?

Melanie?

MS. REESE: Yes. My name is Melanie Reese. I get my treatment at Johns Hopkins University, and they are a teaching research medical facility, and they push, push, push you getting into clinical trials. I don't know if they get a kickback if they get so many of their patients in or not, but they don't really -- they leave that informed consent to the investigator, and whether or not you get through the -- what's that called when you get screened? You go for the screening and then see if you could go to the next step, to the next step. But they push it.

DR. EGGERS: Anyone else have a different experience?

Yes?

UNIDENTIFIED MALE SPEAKER: The regular physician of the patient?

DR. EGGERS: Your regular physician.

UNIDENTIFIED MALE SPEAKER: Well, I mean, I have the same experience that everybody in terms of like having access to good doctors. But now you made

me think about the changing environment, like with expansion of Medicaid, the Affordable Care Act, Ryan White changing also in terms of how they provide the services, that when I think about the rest of the population that depend on that, and that probably they will go with primary care physicians that will have just 15, 10 minutes to see these people, where would we have that conversation? How we support the physician to bring up that conversation? I just bring that up.

DR. EGGERS: Great points. Okay.

I want to make sure we get to a couple polling questions, and then we'll have a 15-minute break because that's what my agenda is telling me.

So we've had a very rich conversation, and these are just two summary points, questions, to get at the perspectives in the room.

So if we could have the next question. Okay. Now, this is completely voluntary, and we're not going to hold you to these answers, but after hearing this discussion today, would you consider participating in an HIV cure research study if it was

unlikely that you would gain any direct health benefit from participating? Yes, you would consider; no, you would not consider participating in a study; or you're not sure.

(Answering question.)

MS. DEE: While people are answering that, can I say something about this question?

DR. EGGERS: Sure.

MS. DEE: You know, we've kind of lumped together trials here today, cure trials about whether you're going to get any benefit or whether it's going to really harm you and that you're going to have to stop your regimen, or you might put yourself in danger. I mean, there are a lot of trials in the beginning that aren't going to really be like that, they all don't require that you stop your medications, so there are some where you have to sit there for a couple hours and let somebody take some blood, you know, come back and that sort of thing. So, you know, and it's going to be a very stepwise sort of thing. Now, there are other trials that do require more or will require more, but it's not all, you know, "You're

going to get hurt," "You're not going to get hurt," it's not all that clear, I think.

DR. EGGERS: You make a very good point. Perhaps for this would be the more intensive kind of trials.

Okay. So a lot of folks would still consider participating in a study, although there are some folks who would not consider. Okay.

Andrea, do we happen to have on the web?

MS. FURIA-HELMS: 50-50.

DR. EGGERS: Okay. Okay. Good. So lots of good discussion. There is one other question that we want to put up, a similar question to the last one.

Would you consider participating in an HIV cure research study if it meant that you had to temporarily stop taking your current HIV medications? Yes, you would consider participating in a study; no, you would not consider participating in a study; or you're not sure.

(Answering question.)

DR. EGGERS: And I understand that these two questions are really tied together, you know, it's

very related to the last question. Okay. Okay.

Maybe it's not so related to the last question. This might be surprising to some of my colleagues. Thank you for your input. And on the web, so for those of you on the web, we had over half who said, no, you would not consider participating in a study, and about 20 percent of you in this, again, very small, small N, but are not sure about that.

On the web?

MS. FURIA-HELMS: 40 percent yes, 40 percent "I'm not sure," and 20 percent no.

DR. EGGERS: Okay. There are a lot of unanswered questions then.

Yes, go ahead.

UNIDENTIFIED MALE SPEAKER: Just a real comment on the risks before we go to break. I think it's really important that the FDA pay attention to exclusion criteria and what I call "eggs in the basket." So with a lot of the earlier trials, you know, there were all these things like you can't have taken this class of drug or you can't have done this or you can't have done that, so what I think there is

going to be a lot of concern on is, "If I do the HDAC inhibitor, will I be excluded from the PD-1?" and, "If I do disulfiram trial, will I be excluded from this?"

In other words, there needs to be a really good reason if you're going to exclude under those types of things, if you know what I'm saying. And I understand that early, small pilot proof-of-concept studies need to be really clean, you don't want to muddy it with anything, but I think in the more advanced trials, you really have to justify very well any reason you're excluding people.

DR. EGGERS: Okay. Good. Okay. So why don't we take a break. We can revisit these topics again. We will focus first on the informed consent issues, but that's related to what we've been talking about all afternoon. So we'll take 15 minutes, and that means 3:45. Am I correct on that? We'll be back at 3:45. Thanks.

(Whereupon, a brief recess was taken.)

DR. EGGERS: As we take our seats, I will say that I spent such a fascinating conversation before the break, and we look forward to carry that on

now for the remainder of our discussion. What I do want to say is on the web, it's been very clear we have a group of perspectives here in person that are shared, and those might not be shared by folks who are on the web, so I will encourage the folks on the web, if you have a brief comment about something that you've heard today or something that you think you experience or your perspective is much different than what you've heard expressed here by the folks in the room, then I encourage you to submit those comments and we will do our best to review those, and even if we don't review them, we will have them and we will read that and it will be included as part of the public record as well. Okay?

Panel #2 Comments on Questions 5 - 6

DR. EGGERS: So now we're going to turn to -- we have alluded to this and we've touched upon it some, but we want to now talk about informed consent, and I have a feeling that the questions and the discussion is going to be broader than just the questions that are up on the screen.

So the questions that we do have up are

really about, how should informed consent clearly communicate the purpose of a study, especially when it's not directly -- you know, it's in the early stages perhaps? How the informed consent should clearly communicate the potential benefits, and we talked about what we perceive those benefits to be, and how should it communicate the potential risks? And that includes the uncertainty about the risks, so in the cases where it's really unclear, it's uncertain, what those risks are. And other information that you would find helpful when deciding whether to enter an HIV cure research study.

And for those of you who have participated in a study, perhaps what we could do is focus on things, information, that you haven't yet seen in your experiences, what kind of new information would you get if you're already familiar with those consent procedures?

And I think we also want to ask a question -- and so maybe the panelists, if you have some thoughts as we go through, as we make our opening remarks -- about how we reach people and make sure

that the communications are reaching the range of folks who may be considering participating in a research trial, even if those perspectives may not be fully reflected here today. So you can comment on that.

And then I think Dr. Goldkind will probably also have some other follow-up questions to ask. She has been instrumental in helping us shape this portion of the day.

So with that, I'm done talking. We'll have the same format. We're probably, of course, a little bit behind schedule, but that's okay, we're going to have a full discussion, and we'll get you out of here on time. So I think maybe we'll start down the row and we'll start with Matt to address these questions, and we'll open it up for the full discussion.

MR. SHARP: Thank you. So I guess I want to start out by saying that we've been talking about informed consent and the informed consent process for so long and we've been trying to explain it and trying to make it easier involvement with the people that we train and teach and talk to, and so I don't think

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that's -- none of that's changed, it's the same issues. What's changed is the science and the technology, so those are differences there that we need to remember. This is not a new thing, we've been doing this a long time.

And one of the main things that I think is so important in informed consent is the word "process" and is the word "counseling." Why can't we make this a counseling effort that really goes in depth with these protocols? And I know there are issues with time and who is going to do it, but all of those things could be worked out later.

But I love the idea of especially with the new technology that exists out there. I know there are new startup companies using tablet technology for informed consents, other ways of implementing informed consent rather than just a paper document that often the words are too big and nobody wants to read. I mean, I honestly, after you get a fifth revision of a protocol, often I don't even read it. So there is a lot of new technology. More time needs to be taken.

And I was going to say, oh, testing, testing

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the individual after an informed consent is performed, and just a simple test to see if they really understood what they were reading.

Those are my ideas.

DR. EGGERS: Thanks, Matt.

MR. PENNER: So I have been thinking a lot about this, and I even have mentioned some of this, so I won't go into a lot of detail here, but I think informed consent is a very -- it's a large process, and it's more than just a form that you sign, and I think we really need to be thinking that that's really sort of the last thing that probably happens, that there should be a lot of other discussion. I think Matt's suggestion about a counselor or even if it's your provider, you know, I can't imagine any of our providers sitting down with us and going over an informed consent about all the risks and benefits about a potential trial for 30 minutes or 45 minutes. What provider is going to have the time to do that and take the time to do that? But the more resources that can be provided as part of that informed consent process, I think would help clearly communicate what

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the purpose is. And then also talking about the potential benefits as well as the potential risks.

You know, I think as much as possible to quantify things in terms of this is very likely or it's unknown completely, we have no idea, or there is a slight likelihood, or in rare instances, if it can be as descriptive as possible about what is known based on previous trials or previous studies that have been done, I think the better.

But I guess the last thing related to it is that we can't underestimate the power of working in the community through this process. And you asked the question at the very end, how do we get this outward? And I think we're not the representative folks, we're not the ones that need to be a part of any kind of these studies. I mean, we may need to be as well, but we really need to be thinking much broader, and that's a challenge, and I don't think any of us have the answer to how we outreach into the community because if we did, we wouldn't have 20 percent of our HIV infected population in this country that don't even know their status. So there are some real challenges

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with that, but it's a critical piece that we need to be focusing on as well.

DR. EGGERS: Thank you, Murray.

MR. TAYLOR: Yeah, I think Murray hit it on the head when he talked about outreach to community because we're fooling ourselves if we think that any document or any process, no matter how involved, is going to fully provide informed consent for something this complicated. The reason you can provide informed consent for the standard, you know, what's the next 3-in-1 combo pill is because people understand the process, the science, they know what they're getting into because they're familiar with it. This is completely unchartered territory for the patients and often for the researchers.

So I think we need to step back and look at the much bigger picture and realize we need to start educating the entire community. I think all stakeholders, regulatory, the Delaney Collaboratories, pharma, need to collaborate with community leaders to go out and educate the community about the research as it's happening so we're bringing people up to speed in

real time because this is going to be a lengthy process of years if we're really going to let people know what's going on and what they're getting into.

And so I think this could include the development of robust community advisory boards and the Delaney Collaboratories and the communities where the first studies will be taking place, public forums by those CABs, the Collaboratories, to educate their communities, well written, and the emphasis on well written and not sensationalized or hyped stories in the press about what's happening and what it means, webinars, and especially -- and I think Alex referred to this earlier -- targeting the education of the underserved communities, such as the African American community and women, in conjunction with groups like the Black AIDS Institute, that have done really good work in educating the communities and bringing up community leaders to ensure that study participation is open and understood by those communities to avoid the usual skewed demographics that we've been talking about today.

So this will take time and resources, but I

think we need to start now so we can ensure that the community is well educated and able to provide the consent so that when we do sit down with them, with a possibly long piece of paper and a counselor and a follow-up test, that they're going to have the background to actually comprehend it and provide that informed consent.

DR. EGGERS: Thank you, Jeff.

MR. EVANS: Yeah, I agree with everything that's been said so far, but first I think it's important to keep in mind that investigators have a rather perverse incentive when it comes to informed consent. You know, they are driven by cost and by resources and by time, and I know for a fact that there have been complaints in at least one of the research networks by the investigators for having to do testing of informed consents because it takes so much time and it takes so much personnel, and that's a short simple that they do. So I think, you know -- so that's important to keep in mind.

That said, I think that there are some things that we can do. I think in devising the

consent process, we can actually test the process before we test the people who are consented. You can have a provider go out to a local community-based organization, you can pay participants 20 bucks, 25 bucks to show up, you can have them do their spiel, you can do a sample consent form, and then you can test the participants to see how understandable it is before you ever field the process. And, you know, businesses do this kind of stuff all the time, so I think we can learn from them.

I think also video technology has gotten so much cheaper, and I think that sometimes people really learn better from watching a video, particularly when we're describing complex processes that are very difficult to imagine if you don't understand the underlying biology.

I think something else that's important to do that's a little bit different than I see sometimes in the consent forms that I'm asked to review is that when you're describing the potential benefit of some of these very early studies and you're talking about the research goal -- so, for instance, I'll give a

very specific example, when you're talking about HDAC inhibitors, and they might describe that an HDAC inhibitor we hope will wake up latent virus, therefore perhaps making it more susceptible to the body for destruction.

Now, that's the research goal that's described, but I think what often doesn't end up happening is the little bit further information that perhaps we think people are too dumb to understand, and that's to explain the fact that we don't even know how much you have to wake up the virus. So there is the sort of additional information that I hope we don't oversimplify because I think that's really important for people to know.

That's it.

DR. EGGERS: Thank you, David.

Lynda?

MS. DEE: So everybody has been great and said a lot of good things. You know, informed consent is like a legal term of art, and I think it has left the patients behind, you know. I think that when you look at an informed consent form, it's this long, and

it has nothing to do with protecting the patients anymore. I mean, I really believe that. I think it's about making sure that people don't get sued and that the IRBs are protected and that the institution is also protected, and the patients have gotten lost in this, I think. I think investigators are too busy. When is the last time -- I don't know of an investigator except some individual docs, but from an institution that sits down and talks to the patient and goes through the form. I mean, you're lucky if their phone number is on it, you know. That page is usually empty, you know. Anyway.

But, I mean, I really think it behooves us to get people educated and to learn about what things are happening and what things mean, and I think that, you know, how can you clearly communicate -- let's see, the purpose of the study.

Oh, there's one, benefit. How can you -- I'm sorry -- communicate potential benefit? Well, it should be the other way around. How can you be sure to communicate that there is no benefit there and that people get that? And we can educate everybody in the

world, but then there will be somebody that comes in that hasn't been to one of our things -- do you know what I mean? -- that isn't aware of any of this stuff. So you've got an investigator who really wants to get the study enrolled and get those bodies in there so he can get his study finished, and you've got some that have even more wrong motives than that, I guess.

So what is it that we do? It's funny, I just finished a trial at Hopkins, and I was interested to hear what my friend in the audience said about what her experience was. Now, I don't know, just because it was me, and they all know me there, that the nurse sat down with me until she got on my nerves, you know what I mean?

"Okay, this, this, this." But that's what you need to do with people, you need to sit there with them individually. Some people will need to take it home and discuss it with their family. Other people were like me, like, "Okay, I understand this. Where do I sign?"

But, you know, just like there are people that will do things and won't do things, there are

people that know what this stuff means and there are people that don't. So we have to be able to try and get things as much individualized as possible, and I think a good way to start that is to have a good study nurse that's going to take time with people to really know that they get it.

I mean, you know, I think the video technology that David talked about is really helpful. I think it's really helpful, too, to videotape the nurse to make sure she's asking the right questions of people. You know, I don't know how that would be for privacy concerns if people want to be on tape, you know, but, I mean, I think that really nobody is better to get this stuff done than the great research nurses that are out there that are used to taking time with patients that are ones that make sure that you come in and that you stay enrolled and that you're doing what you're supposed to. I mean, they're like -- you know, women run the world, right? Most of them are women. A lot of them are men, but, I mean, I think that -- that's a joke, I'm just joking here with that.

But, you know, I mean, I think somebody has got to take time with people individually to make sure that they get it, you know.

DR. EGGERS: Thank you very much.

Large- Group Facilitated Discussion on Questions 5-6

DR. EGGERS: I want to pick up before I ask my colleagues to see if they have any questions, and I think instead of doing that, I think we'll open it up for the whole discussion so that everyone can do that. But I was struck, David, you presented a really concrete thing about -- was it the length -- did someone mention the length of time that the study was going to be going? David, you presented something. It lost me. A concrete piece of information that you would want to see communicated in the informed consent. And I was wondering if you could each go through and talk about something concrete, description of something or -- oh, it was how much is needed to activate the -- okay, there I got it. I got it.

So if you could go through as I make my way to the front, and give an example of something that you would really concretely like to see included and

be clearly communicated in an informed consent. And I'll go to the front.

MR. SHARP: Well, you know adults learn in different ways, so you can go back to the adult learning model, you know, use of new technology, different technologies, drawings. I mean, it may sound silly, but some people can get a better idea of a concept through a drawing or a picture than through words.

DR. EGGERS: But is there a specific concept that you think should be communicated in the informed consent about cure research or about what we've been talking, about the science or about the risk or how to communicate the uncertainty, et cetera?

MS. DEE: You know, I really think -- and I was trying to read it when I was speaking before, but I really want to reiterate that you should say that there is no benefit here, you know, no immediate benefit, period, because people just don't think -- don't know that.

DR. EGGERS: And what words would you use?

MS. DEE: "There is no immediate benefit to

you as a result of participating in this study."

DR. EGGERS: Okay.

MR. SHARP: But there might be an unknown benefit --

MS. DEE: Right.

MR. SHARP: -- so you need to clarify that, you know, if that's going to be the case.

MS. DEE: "There is no known immediate --

DR. EGGERS: Oops. Can you turn on your mic? Yeah.

MS. DEE: "There is no known," put the word "known" in there. But, I mean, this is amorphous, "Well, this may not --," you know. I mean, people want to get cured, people want to do better, you know. I mean, I think that there is altruism and there is altruism, they want to do what's good for the group and themselves. So I think it's really got to be straightforward from Jump Street that, guess what, you ain't getting cured if you get in this protocol.

DR. EGGERS: Any other concrete things?

Oh, Deb, do you want to follow up on that?

DR. BIRNKRANT: I was wondering also, what

do you think about the whole title of this research, cure research? Should it be called something else, like Reservoir Elimination or something else? What do you think about that?

DR. EGGERS: And we'll let anyone address this as well. So we'll start with David.

MR. BRAKEBILL: I just think the word "cure," it opens up a whole thing. I mean, take Facebook or any social media network over the last couple of weeks, anybody that follows any of the listservs or anything, all these stories break and people are talking about stopping taking their meds, and it's like this is crazy.

So I agree with you, Debra, that perhaps we need to look at some other nomenclature in terms of -- because I think, although those of us who work in the field and live with the disease certainly hope for a cure, we know that realistically it's probably sometime away, and I get discouraged every time somebody uses the "C" word, as David used earlier, that it gives people false hope, and it's sort of like NSA secrets being let out or something, you know?

DR. EGGERS: Any follow-up?

Yes. In the front.

TIN: Just one point I wanted to make, and I was talking with David and Lynda about this earlier --

DR. EGGERS: Oh, can you state your name?

TIM: -- which is in the concept of cure, a lot of us, myself included, who actually participated in the pathogenesis study around 12 years ago, I think some of that data has actually contributed very much to where we are today. So that concept of cure research is something much, much larger than I think what we're talking about here. There doesn't necessarily need to be this treatment endpoint. So I think this is something that we've really been involved in for many, many years.

MR. SHARP: Can I just add that even the NIH has trouble with describing this, and there was a group of people that tried to assess how much funding was being put into the NIH for cure research. Well, the coding system for cure is specific to the word "cure," but there could be a lot of other things like pathogenesis, vaccine trials, and so forth, so it's

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been even hard for the scientists to come up with a good word.

DR. EGGERS: Murray?

MR. PENNER: I do agree that if I hear the word "cure," and I'm in the community and potential for me to go into a trial that is cure related, whether I'm told there is a benefit, you know, or not, and an informed consent process, I'm going to be hoping that there is a cure at the end of that for me, that that could result in that. So I think that is an important consideration and/or the way that's described.

DR. EGGERS: And, David, I'm also going to ask you to reflect on the survey that you did and maybe provide some of that perspective as well.

MR. EVANS: Sure. So the first thing I want to say is that for me I think it's a really hopeful sign of where we are socially in the epidemic, that the "C" word can even be used, but when I'm talking about research and what I think is appropriate for research, I don't think it should be used at all. And if there is a term -- I don't think any term is

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perfect because with some of the gene therapies, we may not reach eradication of the reservoir, but they may still very well control the virus, but maybe reservoir depletion would be -- because that is one of the goals regardless of what we're doing, so I think that's a term that I think is safe to use, it's a little obscure, but it's safer to use, I think.

And in terms of the studies, you know, our partner Nelson and I are hoping to get funding to do a second study, and we want to do it this time not on the cheap, and this time with some social scientists and some ethicists, trials experts, because we want to understand better how much the word motivates people and demotivates people and maybe misrepresents what's going on, and we also want to really better understand in a very specific way how they understand and perceive risk in a meaningful way, not just in an abstract way. So I don't have a lot of data on terminology yet from the study we did so far.

DR. EGGERS: Let's go with Jeff and then we'll go here.

MR. TAYLOR: Yeah, I mean, I think we

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shouldn't underestimate the amount of optimism that talking about the cure has provided the community, both the research community and then the people living with HIV. It's really too late to turn back the clock on that, I think that's unrealistic.

And I'm not really concerned about the individual trials because none of these trials are going to be called, "This is a cure trial," it's going to be, you know, eradication or latency or waking up the immune system, and it's not going to be described in those terms. So I don't really think there is a danger in that, and I think as long as the individual sites, when they're advertising these trials, are being ethical and not advertising it as cure research but saying we're doing a trial about the immune system or something like that, it's going to be fine, so I don't think we need to tie ourselves in knots about this.

DR. EGGERS: Okay. Go ahead.

MR. DOROSH: I was just going to say I don't like the "cure" word at all.

DR. EGGERS: Can you state your name?

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MR. DOROSH: Michael Dorosh, Treatment Education Network, Denver.

So I don't like the "cure" thing. And just a real quick little anecdote. When the ACTG reformed into the TSGs, and they always have the short names for everything, like in the old days, you know, TRAD (ph) and OpMan and OPART (ph) and all that. So they were coming up with a name for us, and the actual name of that, Cure TSG, it's not a Cure TSG, it's HIV reservoirs and viral eradication. So I suggested, why don't we call it RAVE, like this is the latest rave, Reservoirs and Viral Eradication? Joe Eron liked it. John Miller said, "Oh, that implies circuit parties and drugs, we can't call ourselves that." So now we're called the Cure TSG, and I think that's crazy.

MS. DEE: The cat's out of the bag with that cure business; I think there is no going back as far as trying to get the word out to the community. And like everything, it's a double-edged sword, it has good things and bad things. I mean, as I think Jeff says, if you do it like the Collaboratories, you know, therapy, gene therapy, eradication therapy, none of

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those -- you know, they all mean a lot of different things, too, but you can take the sensationalism out of it by using those kind of things, but I think people are interested in cure.

DR. EGGERS: Yes. Oh, and then we'll come back to the yellow shirt.

MR. BRAKEBILL: But I also think that if you went back and asked those poll questions and used, "Would you participate in a whatever study instead of a cure study?" that the responses might be different.

DR. EGGERS: Yes. Good point.

MS. MARTIN: Hello. My name is Mabel Martin, and I'm thinking something more along the likes of HIV virus advance target research so to not as like proclaim that there is going to be some kind of a cure but to kind of make it seem more like it's more advanced research than what's available now.

And also to piggyback on the informed consent, I think in creating an informed consent, it's important to allow the individual to understand that although they may not benefit directly from this

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research or participating in the research, that they will get satisfaction in knowing that them participating in the research will potentially help others.

DR. EGGERS: Okay. So Sara asked a question earlier that I'm going to revisit about who should be doing -- do you want to restate your question about should it be with the investigator and the person who should be -- well, you state it better than I did.

DR. GOLDKIND: So what I'm trying to drill down and understand better is, what would be an ideal consent process so that we could really feel comfortable that we've allowed the potential participant to analyze the risks and the benefits and alternatives for himself or herself, and they've had the opportunity to ask the questions that they need to ask to understand that calculus for themselves, and that the investigator or whoever is doing the consent process would have a sense that the participant understands what's being asked?

So you started to touch on it a little bit by saying you think that there needs to be more time

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given to that process and maybe it needs to be a multimodality process, but I'm wondering if you have more to say, and within as you think about what that process would look like, if there are any other specifics. We've already heard Lynda say that we should really be very cut and dry, very clear, that it should say you will not get benefit from this trial if there are no projected benefits, but if there are other examples that you have for us about how to explain the risks or benefits, we would like to hear those, too.

MS. DEE: You know, I wonder, Murray, and I think maybe Jeff, talked about this earlier, you know, I think human beings, you worry about what's happening to you now and what you're going through now and if you're suffering side effects now and maybe that will go away and you don't want that to happen again. You know, that's more of a reality than, okay, well, maybe you'll get cancer. Well, maybe I won't, you know. I mean, that's more far away and we'll worry about that later.

So I think if there is a way to -- and I

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know a lot of informed consents that I've seen list what the risks of these other things are, but, I mean, you know, if you could put into -- I mean, if you could put in there definite information about what the percentages of, how many people does this happen to and how many years from now? It may be that if I have a life- threatening disease, that I ain't going to worry about what's going to happen 20 years from now. You know? So if you could be more definite about not only the risk, but what the real risk of that happening to you is. Does that make sense?

DR. EGGERS: Can I follow up and say, how would you characterize uncertainty if you couldn't give those -- if you couldn't give as clear-cut numbers that you're looking for, that you, as the person deciding to participate, if those numbers don't exist, how would you communicate the uncertainty about that?

MS. DEE: I mean, you just have to say that. We've been doing Phase I trials for -- how many years have you guys been in existence? But there have been Phase I trials that do this all the time. So I really

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think it's important to say we're uncertain about -- you know, I like really short sentence, boom, boom, boom, boom, and I think that's easier for people to read than some long rolling sort of paragraph.

DR. EGGERS: Celia.

DR. WITTEN: And to add to that uncertainty about what the risks are and how to quantify them, we are interested in communicating for some of our treatments that the treatments have perhaps an indefinite residence in the body. In other words, unlike the therapies that have been so far under investigation or development, some of the ones in our office may last, so the risks may be lifetime risks, and that is a bit different, you know, it makes it a little less, well, it's something in the future, because sometimes I think people think, "Well, I'll withdraw the drug, and then after a certain period of time, that risk is not there," which I think is often true, if you didn't have the risk in the short term, you may not get it in the longer term.

DR. EGGERS: So there is a --

MR. PENNER: I think to the extent that that

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is potentially happening if you go off of a treatment and it's going to remain in your body as best you know, that has to be said so clearly up front even though you may not know what the risks of that happening are, that's got to be really -- those are the kinds of things that have to be explicitly stated, and then you can get into kind of the mumbo-jumbo that's necessary in order to achieve true informed consent, but it's almost like there is a fact sheet with bullets that are really short and to the point that sort of lay out what the document itself is trying to tell you.

You know, when you go to sign all the papers at your mortgage company when you're buying a house, you're signing all kinds of crap that you don't know what it is; right? So if there was a cheat sheet that said, "Okay, Form 1 is going to tell you about this," and just in very simple language, those kinds of things I think would be really helpful.

DR. EGGERS: Lynda, and then someone in the audience.

MS. DEE: I think it was David.

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DR. EGGERS: Oh, David. I'm sorry.

MR. EVANS: No, I just wanted to give a process suggestion, and that's that -- I mean, you, I'm sure, you know this better than I would know it, of course, be it you're a decision-making scientist, but I think that how we pose the opportunity for a decision to people is so critically important, and I think if you simply say, "Do you have any more questions?" you get one answer. I think even if you say, "Do you have any more questions? Would you like some time to think about it?" you get another answer. And I think if you say, "I would suggest that you take some time to think about this, and we can talk about it again later if you have any more questions," gets you yet another answer.

And so I know that the FDA can't mandate a process, but I think those kinds of processes could be really helpful to suggest to investigators.

DR. EGGERS: Okay. We'll go to Tim. Oh, I'm sorry. And then Tim.

MR. MUNK: Hi. I'm Bob Munk, from the AIDS InfoNet. And I have long been concerned about the

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patient consent process because there is no disinterested party or no third party involved. I've been to some investigator meetings that are like the most cheerleader kind of things that you could imagine, you know, "Yea, you've enrolled 34 at your site." Of course, your goal is 50. And there is a lot of pressure on these research nurses to produce. I don't know how it would be feasible, but I like the idea of, "Would you like some time to think about it? We won't sign you up today. Come back whenever." But I'm very concerned about that.

DR. EGGERS: Okay. And then Tim, and then we'll go back.

TIM: I just wanted to go back to a point that David raised earlier in this session, which is I think he talked about really the concept of taking advantage of different technologies for informed consent, one such being video. We don't do that, because there is a very famous literacy study that came out about 10 years ago that basically said that 10 percent of what is read is remembered versus around to 30 to 40 percent of what is watched and heard is

remembered. And we're not really just talking about providing an educated permission to participate in the study, we're also talking about getting people to remember why they participated, remember what the risks are, remember what the potential benefits are, and importantly, to remember what their rights are. So I think that we really have a very wide array of different technologies that we can take care of that were really not talked about here.

DR. EGGERS: Okay. So then --

MR. KAYTES: Andy Kaytes. I think health literacy plays a really, really big role in this because if informed consents are supposed to be written at the 8th grade level, is that 8th grade at an Ivy League prep school? 8th grade at an inner city school? 8th grade at a school on the border in El Paso, Texas?

And to Tim's point, I think that videos are something that can transcend all of those grade qualities, if not levels, and certainly you can't have a video of every aspect of informed consent, but if you can show a video of procedures and maybe have

interviews of people that have gone through those procedures that have had good results, bad results, that can be very helpful.

The other thing is one of the hurdles that I perceive is the community members or research participants you would be looking for aren't necessarily the ones that have gotten the most education regarding research. So those of us that have volunteered our time to learn, to understand, to be able to speak to our peers in lay terms, we're in some ways cut out of that informed consent process due to HIPAA and other things, we can't go out and actively recruit for trials, we can't sit in the lobby of a research site and talk to people before they go in and meet with a study nurse.

I'm not saying we shouldn't have privacy and confidentiality, but if the people that we're looking to get into research trials are those that are not necessarily in the know, they're newly infected, they're in acute infection, they're going through crazy thoughts in their head about their diagnosis, yet they're the ones that we would really like to be

able to study, you know, how do they get reached? It seems like we need to kind of start earlier in the communities as a whole, in schools, and start to educate people not just about HIV research, but research in general, and then have a mechanism that would allow those of us that are advocates to be able to reach them in a much more fruitful way.

DR. EGGERS: We'll go down the row.

MR. DOROSH: I'm going to tag again on what Tim was talking about in terms of a video. I don't know about where you all live, but where I live, when you get called for jury duty, you have to sit and watch this video, and it's very simple, it's very basic, it's aimed at anybody, and it tells you about the whole trial process and the defendant and all the rest of it, and you just sit there and you watch that and then you kind of know a little bit more.

And I don't know if you guys could do this, but I'm just wondering if the FDA could create, you know, a really good slick, quick, maybe 5 minutes or less, video just on cure research in general that's a

requirement of anybody who is considering entering a clinical trial before they even get to the informed consent process, something like that. I don't know if that's possible. I don't know if IRBs would freak out on that. That's one thing to consider. When you look at the word "informed consent," "consent" is easy, that's yes or no, you consent to let the guy in your lane when you're driving. "Informed" is information, it's informing, and really need that more and more and more in this whole arena.

At our pre-CROI community cure workshop this year we identified that educating and informing the community, our HIV community, about this whole field is crucial, and it's an unmet need right now, and we're currently trying to come up with ways to do that. There are national publications, videos, a number of other things, but I think it's really, really important and -- I just lost my train of thought. It needs to happen -- the informed consent process shouldn't start with the informed consent, I think it needs to start with that information dissemination.

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Oh, what I was going to say was a bunch of us put out all kinds of fires after those press releases, the daily telegraph, all that crap that was going on. I was getting e-mails. It was crazy what was going on. I mean, we all knew good Kate was pregnant before she was pregnant in this day and age.

DR. EGGERS: I hear a recurring theme about needing to start earlier than actual informed consent, and my colleagues can echo on this. I think it needs to be reiterated that drug development is -- the FDA has a part in that, and so I hope that there are other folks hearing what you're saying.

Discussion with FDA Panel

DR. EGGERS: Does anyone want to comment on the theme of sort of general education about research? Not to put any of you on the spot.

DR. SHERWAT: Actually, it's not that, but I'm wondering, do you think there is any utility in, say, a post-test process where you go through the informed consent process and then you have a very brief focused test that you take that covers the most salient points, covering the biggest risks that have

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to do with whatever this type of research is, and unless the person is able to pass that, say, on one or two attempts, you just feel like they're not getting these points and they're not going to be someone that really should be in that type of a trial?

DR. EGGERS: This is a great question. In fact, we have a polling question on it. It's our final polling question.

DR. SHERWAT: Never mind.

DR. EGGERS: No, let's ask it now, this is great. We just need to get it set up, but it's directly to this point. Okay.

Do you think it would be appropriate for HIV cure research study participants to take a post-test at the end of the informed consent process whether they understood important aspects of the study, its purpose, the potential benefits, and the potential risks? Did I get that right?

(Answering question.)

DR. EGGERS: Okay. Yeah, Matt.

MR. SHARP: So I want to just say with a caveat, I mean, I don't think you should call it a

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test, number one. Call it a survey or whatever. That freaks people out. But also don't disqualify people, but you have them have another opportunity to learn the information so that you might be able to use them in the study.

MS. DEE: You know, if this was a requirement, I bet the docs would find a way to get somebody in there to actually explain what they were supposed to be knowing. Right?

DR. EGGERS: Oh, we have someone. Okay.

MR. SCHAICH: Yeah. Three things. One is that certainly it would be far from me to say anything bad about video, I love it, but I think it's important to get the -- the nice thing about a video is you can custom make it for the culturally and ethnically specific and languages, et cetera, so it makes it really a buy-in for the people that it needs to address and work with.

The other one is I think it's really important to consider families who that person feels is important in their decision making process, and make sure that happens because I've heard I don't know

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how many meetings like this where people said they were pulled from the trial by their husband who were outraged that they were in this trial in the first place. So I think it's important to have that discussion as a part of the process before they get into the informed consent.

MR. EVANS: I just wanted to note really quickly that I think there are a couple of ways you can do that kind of an assessment, and I would call it an assessment and not a test, and I think that one of the ways you can do that is verbally, and you can ask people to explain in their own understanding what they know, what they think they heard about X, Y, or Z. So I think that's important.

DR. GOLDKIND: Also I just want to point out -- and maybe Richard Klein wants to speak to this a little bit more -- but FDA does have resources about clinical trial research and what it means to be in a clinical trial. So, I mean, it's a starting point, but I take your point, that maybe us or other groups can do something more specific to these issues, but we do have some sort of education system in place

already.
DR. EGGERS: Thanks for clarifying.
We'll go to David?
MR. BRAKEBILL: I'm just curious. You know, one of the models that's really worked well on the care side is the use of pure navigators and the possibility of using somebody to do the informed consent who has been through a trial before. I think you sort of alluded to it when you said using people that have been in the video, "I did this," and so and so forth, but I think that that may be one way, a better way, to engage people to get into trials but also keeping them in, that you also have some sort of peer support system that once they're in a trial, to keep them engaged in the trial. It's been very successful in the Ryan White CARE system for keeping people in CARE and engaged in CARE, and I think it's the same sort of principle with research.
DR. EGGERS: Murray?
MR. PENNER: I recently became or heard a presentation of a doctor in Denver that had done some tremendous work related to linkages to CARE and

keeping patients in CARE, and I think this could be applicable. They did on the initial arrival of the patient to the clinic had a kiosk where they were asked a series of questions related to substance use and homelessness and the kinds of things that a doctor might not either be comfortable talking with the patient about or have time to or whatever, but it was an anonymous kind of way of getting some input from that patient early in the process of an entire visit, and they showed some incredible outcomes as a result of that. So I'm wondering if there could be some things like that that could be built into an informed consent process either on a tablet where you answered some questions and then came back later and the conclusion was another set of questions, and that could be a pre- and post-test to really kind of see where you're going, but it's not called that, and you think you're interacting with the whole process that way.
DR. EGGERS: Could you include that in the docket? If you write to the docket, include that in there.

MR. PENNER: Sure.
DR. EGGERS: Okay. I'm going to do a time check. We are at 4:35, which is, according to the agenda, the end of the large-group facilitated discussion, but we don't have any public comment signed up. Am I correct in that?
(No audible response.)
DR. EGGERS: Okay. So we are shaving some time off. So I think that given that it's a Friday afternoon in June, and I'm thinking it's gorgeous outside, I think we can cut the meeting a little bit short and still make sure that we have gotten done with all the questions and all the points that we want to make. So my suggestion is that we can try to close out and see if FDA has any further questions. And then if you have any remarks that you want to make, we'll do that. And then we'll ask Theresa Mullin to come up. And between this and Theresa, we'll have if there are any web comments, we'll summarize those.
So if you're on the web, this is your sort of final chance. We can't promise that we'll review all of them, but if you have something that's really

different than what you've heard said here today, you can include that.
MS. DEE: Sara, before we leave this --
DR. EGGERS: Yeah.
MS. DEE: You know, I don't know, I feel like we really haven't done justice to this informed consent thing. I mean, I think it's broken the way it is now, and I think we've been around the rosie, but I wonder if there is anything else we could do to work with Sara directly to convene something to talk about this, just this one aspect, a little bit more to make some recommendations or something. I don't know. I'm not sure what you are allowed to do and what's within your purview as far as the informed consent processes, but I think of all the things that we've talked about today, this might be the most important, and I think we've probably given you the least concrete information.
MR. KLEIN: Hi. If I could make a quick comment. What we could do is put together a webinar through my office and continue a conversation that way if that works for you. So I can work with Lynda.

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DR. GOLDKIND: That would be great. And the other thing I was going to say is that FDA is developing a guidance on informed consent, and when it is published, it's going to be published in draft, and we would welcome comments to our public docket that can be as detailed as you would like, and they will all be carefully considered.

But before we close, I don't want to stand in between us and a beautiful day, but I did want to see if anyone had any more specific comments about how we could sort of chip away at this idea of the therapeutic misconception, whether there are any suggestions about how people can understand that they're enrolling in research that's not going to be designed to treat them specifically but that the care they get is going to be protocol driven.

MS. DEE: "There are no known benefits to you participating in this trial."

MR. SHARP: Just really quickly, I think one thing that we can do with these studies is to be abundantly clear that the therapies that are being prescribed or a treatment interruption that is being

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conducted is not consistent with the federal guidelines on treatment for people living with HIV, and I think that should be in every consent form, only because it's true. And recommended medical practice is one thing, and research is another, and I think making that very clear in a consent process is important. It might dissuade some people from participating, but you know what? That's great because if they understand that and they don't want to participate, it's good that we knew that, you know.

DR. EGGERS: Murray? Murray, do you have --

MR. PENNER: I'm thinking to some of the vaccine trials and some of the vaccine research that's going on, I know that there are portions of studies that don't really result in any benefit, and I'm just wondering if there are messages that can be borrowed from that process because I know they've done a lot of work on making sure that the messages are clear about we're not developing a -- "You're not getting vaccinated and this is not going to protect you from getting HIV."

DR. EGGERS: What about informing -- is

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there any concrete perspective that you have on how to inform about having to stop the medications and the risks that could be associated with it? I don't think we've talked about that at all yet on how to communicate that.

MR. PENNER: I think it's sort of what David just said, that, you know, this is not consistent with, you know, U.S. Public Health Service recommendations, you know. There could be risks that we don't know what these are. And it has to just be as clear and as simple as what Lynda and David were talking about.

UNIDENTIFIED MALE SPEAKER: "Kids, don't try this at home."

MR. PENNER: Yeah.

MR. EVANS: Well, and I think also it depends on the population that you're studying. I think if it's people who have CD4 counts in the 750 range and they happen to already be on therapy, that's one kind of consent in process. If someone had a CD4 nadir of 50 and they currently have a CD4 count of 350, so it's technically above the range of the SMART

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study, they need to really understand that SMART study and what the results of it were.

DR. EGGERS: Okay. We had Robert and then someone. Okay.

ROBERT: I want to thank all of you from the FDA that are here for all your hard work. I'm wondering if you could just comment generally about the sequester and what effects it's going to have on your funding and what your plans are, the constriction that might come for your research.

DR. BIRNKRANT: Don't quote me.

DR. BIRNKRANT: I mean, the impact we've felt to date has been basically that our travel has been limited, but we've still been allowed to hire new reviewers and we are fortunate that we are able to hire, not large numbers, but what we feel at this point are enough to get our jobs accomplished. And as far as we know, there won't be any furloughs of FDA employees.

And I will be honest with you, it has had an impact on morale overall in general, but I think we're all grateful that we're able to come to work, we have

a job, and we have a meaningful job. So I guess in the end it hasn't really directly affected us as it has perhaps some other agencies. But we're still continuing to do the work that we are asked to do by the public.

MS. DEE: Deb, and that travel can be a big thing, though. I mean, you don't get to go to research meetings, where they just presented, where you can interact with researchers and industry.

DR. BIRNKRANT: Well, that's true. Right.

MS. DEE: I mean, that's a really important thing.

DR. BIRNKRANT: You're right.

MS. DEE: It's not like you're going to Paris; right?

DR. BIRNKRANT: No. We haven't been to Paris in a long time.

But we do participate in webinars and we go to local AIDS and hepatitis meetings, and we give our talks on the phone to large groups. Kim just did one on long-acting therapies, and others have done similar presentations via phone. You're right, though; it's

not the same as being at the meeting, networking, et cetera.

DR. COX: And there may also be some new activities and some additional planned activities that either may be difficult to get to, may take more time to get to, or that we simply just have to wait before we tackle them, based on the current prioritization of activities. And that really just is in essence common sense with regards to when you're facing a situation where there are limitations on the resources or resources that you thought might be there aren't present.

ROBERT: I was just wondering if (inaudible).

DR. COX: So that's probably getting beyond the scope of what we can cover here today.

DR. EGGERS: I'll do the ground rule check that we are kind of focusing on the questions that we're being asked, but a fair question.

I'll go here.

MR. DOROSH: I'm tagging on I think what Dave was saying, that it really needs to be specific

to whatever in terms of the interruption in any informed consent. For example, if somebody is taking efavirenz, you know, there is a whole protocol for how you interrupt that therapy, you just don't stop it like all at once, and that needs to be conveyed, and again some people really get it and some people really don't, so that can be a very tough thing.

And then general education again. I know a young guy in his twenties just infected a couple of years ago, he acquired a resistant virus, and so they had to like adjust his regimen or whatever, so now he's on a specific regimen, he knows that, and he wants to do like the Sangamo zinc finger trial, heterologous still to 32, and he's like, "Oh, I can't interrupt because I have this resistant virus." Well, really, couldn't he interrupt if it works? You know? I mean, we don't know. We know and we don't know, you know, but that's part of this whole information thing that really has to happen before the informed consent and definitely be a part of that for that individual.

DR. EGGERS: Anything else from up here?

Adam?

DR. SHERWAT: Just a couple of questions that I had jotted down.

DR. EGGERS: Great.

DR. SHERWAT: From your perspective, is there -- oh, I'm sorry, can you hear?

(No audible response.)

DR. SHERWAT: Is there a threshold that you feel the FDA shouldn't allow a study to go forward based on the safety risks that may be inherent in the trial, or should it always be up to the patient via the informed consent process to make that determination? And if you do believe that there is a safety threshold, where do you think that exists? Where would you draw the line if you were on this side of the table if you think that that's a role?

MR. EVANS: I mean, personally, I get uncomfortable with treatment interruptions with anything below 500 as a CD4 count just personally. I would prefer that we don't allow people with high Framingham Risk Scores to enter these studies. I just think, why do that to people?

And I think also that, you know, we probably

are going to have to talk about treatment interruptions that are longer than 16 weeks at some point, and I think we need to start thinking about that just because there may be therapies where the stopping rule is that your CD4 count falls below 500 or your viral load climbs back up above 50, and if someone hasn't met that stopping rule, should they be allowed to continue on their treatment interruption, and what might that tell us scientifically? So I think those are the things that I think about when it comes to treatment interruptions.

DR. SHERWAT: Besides the population that you would be choosing as far as choosing the safest population, are there any particular risks inherent to the drugs that might be used or that the genetic manipulation that you think would be something that we shouldn't allow to go forward? Do you think that should also be up to the patient to make that decision?

MS. DEE: It depends on if it's been four people and three of them died. I mean, you know, it's kind of you have to be a little bit more -- give us a

little bit more information about -- do you see what I'm saying?

DR. SHERWAT: Yeah. I mean, a lot of times the problem is that the medications that are being used, of course, they weren't approved for that population, so it's hard to gauge some of the risks, even the risks that are known for the drugs let alone the theoretical risks. So that's always the difficulty. I was just curious from the patient's perspective, where you do kind of draw the line where you think this much risk is too much risk for us to even -- if you were on our side of the table, for us to even let it go forward as a study?

MS. DEE: I see.

MR. EVANS: I mean, I think you can always do more animal studies. I think that's always good to do because where it will give us information -- I know it won't always give us that information, and I know you can't always do that with gene therapies, but I think that's really important. I think, you know, like the vorinostat study is I think a perfect example where you had a drug that was Ames-positive, so there

is a theoretical risk of cancer, but you were only giving them a single dose, it was a small dose, and you didn't see risks of cancer in the -- you know, additional cancers in the cancer studies, so I think that was a reasonable go decision to make.

So I think it's hard to say it in the theoretical because it really depends on the therapy that you're looking at. I think it's important that, though -- but I think there are two other important things about studies. One is that I think it's not always just about the safety of the drug, it's about the trial design, and I think we have a real obligation if we're going to ask people to donate their bodies and lives to these things to make sure that the trial is designed, as best as it can, to get the answer that you're going for. And I think a perfect example of that -- and we were talking about it earlier today in a different meaning -- are the assays that you use to determine latency.

You know, the Siliciano study came out and said that there was absolutely no correlation between six different assays. And so what do you do about

that? Well, maybe you require that they have to do three, you know, three different ones, to prove that you've done something to the reservoir, I don't know, but I think that there are things you can do cleverly to manage and mitigate risk.

MS. DEE: I think David gave you a perfect example about vorinostat, and now we're in a position to, well, how many doses can we do now and to look at, 23, 25, and to do that safely. But, you know, I mean, the way things are, we don't know a lot of the answers, so doing it in a stepwise fashion like you've been doing I think is all you can do.

DR. EGGERS: Can I interrupt with a real process question? Can we collect the clickers so that we can let Chad go home?

And I think we should give Chad a round of applause for helping us with this.

Okay. Now we can continue.

MR. SHARP: So in regard to this question, I don't want to sound naive in saying this, but just in working on the DARE CAB with UCSF and some of the researchers in Australia, I know they are being

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extremely careful about moving forward in the trials that they're doing, and you don't want to completely rely on that obviously, but it's moving very slowly in terms of some of these riskier procedures and drugs being used so far, and that may be because of you guys.

But it's true, I think they're really being -- and actually some of the biotechs are, too; others aren't.

DR. EGGERS: Anything else?

Okay, yes, go ahead, Jeff.

MR. TAYLOR: Well, you know, and I think most of these processes have already been in place for a long time to ensure patient safety, and I think we need to rest assured that they are in place, and as everybody said, evaluate each therapy as it comes up, but on the other hand, I hate to see us become overly paternalistic to patients and not let them make decisions because these are their lives and they're allowed to make that decision. So there needs to be a balance.

DR. EGGERS: Okay, with that, I think we'll

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call the facilitated discussion closed, and my job is almost done, and the panel members' jobs are almost done. As Theresa is making her way up to the front, I'm going to ask Andrea just to see if there are any web remarks.

MS. TAN: There were actually quite a few comments on the webcast, and I apologize, I won't be able to summarize all of them, so just bear with me as I sift through them.

We have some comments based on our earlier discussion about clinical trials and the case of a trial that shows therapeutic benefit in an immunologic non-responder with a doubling of T cells. And the comment asked: How can the FDA help provide a clear pathway for further development of the therapy?

We also have a comment about incentivizing patients to take part in cure research in clinical trials. I think that's a new thought, that it might be a standard and often necessary practice, but would patients be willing to take more of a risk if they received an incentive or medical care during a cure trial?

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And then a few other comments about the informed consent process. One comment echoes what we heard about education, especially those on the front line, i.e., the research coordination staff because of the lack of time on the part of principal investigators. And also echoing the comments about videos with pre- and post-testing. And also a suggestion about study participants taking part in half-day or full-day training at a local ASO or health department.

Finally, we have a few comments. Someone commented it might be interesting to the community that there is a Generic Drug Regulatory Science Initiatives Public Meeting that the FDA is holding on June 21st about the public discussion of agency generic drug research priorities and an overview of current efforts.

And then, finally, we have someone else who commented that maybe an HIV 101 document would be helpful, a long legal 20-pager, and then a short 2-pager that is really for the patient. Those are just a few of our comments.

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DR. EGGERS: Great. All right. And with that, I will thank the panel members, and I will thank the folks in the audience and the folks on the web. I think this has been some great input. I have learned a lot today. I think Theresa is going to probably echo my comments. And with that, I will turn it over to Theresa, Theresa Mullin, to give the closing remarks, and then we'll be done.

Closing Remarks

DR. MULLIN: Okay. Well, I guess I really am the last thing between you and a beautiful weekend, so let me try to finish up. And I want to thank you so much also for coming here to this meeting and giving us the benefit of your very thoughtful perspectives, a lot of great ideas.

I'm not even a transcriptionist, and I took 21 pages of notes. So I'm going to spare you most of my notes, but on the other hand, I want to sort of say a little bit of what I took away from what we heard today.

And so on the patient perspectives on current approaches, just hearing about the critical

importance of paying attention to comorbidities and of including people in trials who really are like the real population that has HIV and also considering the drug- drug interactions for those drugs that you have to take to treat the comorbidities, the adherence to your regimen and changes in the regimen and the concerns about changing the regimen, trying to find ways to ease administration and concerns that no more drugs in the same class might be getting developed, and so there may be fewer options going forward for new therapies in those classes, the same in any class.

And the special challenges we heard earlier for many of the pediatric populations because there are various age segments and times when people become HIV- positive, the prospect of having the rest of your life on therapy and the earlier age at which you experience the side effects from those therapies, and things just like night terrors, which are also harder for young children probably or children to have to contend with.

And then in terms of perspectives on cure research, I mean, one thing I clearly heard is that

you're not making a participation decision from the same perspective that patients made it when the epidemic began, you're at a very different place, and available therapies that work, they work pretty well. You're looking at potential loss of what you have from that therapy, so you're at a very different place in terms of prospect and looking at the risks. And that just has to be understood, and it was also confirmed by the clicker input, that about half said they would not be interested in participating in this kind of research.

And we have to be much clearer about what the benefits are. In fact, the point was made by many of you that we have to be very clear, or the sponsor, the clinical investigator, needs to be very clear about what the specific risks and benefits the patient would be exposed to, and you need to really understand exactly what is entailed in the trial protocol. What are you going to experience? What specific benefits, if any? And the more clear and quantitative and simple we can be and that can be in being presented, simple but not simplistic, the better, to help really

achieve that.

And that there might be specific benefits that different folks mentioned. Money may be something that some will want to include in their calculus of whether or not they want to participate, high quality care, access to high quality care that they might not otherwise have, and, of course, clinical benefits if there are any.

And that you made the point I think repeatedly that this is a very individual decision and that the individual's perspective has to be reflected. And another observation that came after that I think was that there are critical subpopulations that are not here today, that the young and maybe minority populations are not here, women populations are not here, and that their perspectives are going to be critical to take into account.

So all of that about what people need to understand to see whether or not they even are willing to participate in this kind of cure research led us very I think nicely to the informed consent process discussion. And the point was made, at least that I

heard, that paper forms today, they're often long, they're not clear, they're not particularly quantified or helpful, that people don't necessarily even go through a careful reading let alone understanding of them.

And the process today may be a little bit motivated toward enrollment and the parties involved are disinterested, and that makes things more challenging for a good process. And it's not clear that people understand already, what does cure research mean? That might not even be a good name for it. We spent a while talking about maybe that name is misleading and how to talk about the benefits, and there may not be any to being in these trials.

You talked about the potential value of video and visual presentation and how that might be better understood. At least I think you're saying providing background on what this sort of research is about, maybe general information about this kind of research or trials to give people some understanding going into the informed consent process. And there was wide support here for some sort of assessment, 100

percent support for assessment, of subjects or prospective subjects' understanding of the trial that they're being asked to be enrolled in. And I think that you've given us a lot of great food for thought and ideas for where we could look at trying to make that process better and understand your perspective on cure research.

So I just want to thank you again for traveling here from wherever you've come, even traveling around the Beltway can be challenging in Washington, but many of you have come from the West Coast, so I hope you didn't travel during that storm yesterday. Maybe you were riding in right behind it or something. But thanks again for coming, and we'll look forward to any comments you have or information you want to send in on the docket.

We view these meetings as like the beginning in some ways or somewhere in the middle, but certainly not the end of our need to work on this. And so thanks again. And with that, I'll end. Thank you.

(Whereupon, at 4:46 p.m., the Meeting on HIV Patient-Focused Drug

Development and HIV Cure Research was adjourned.)

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I, NATALIA THOMAS, the Court Reporter before whom the foregoing proceeding was taken, do hereby certify that the proceeding was recorded by me; that the proceeding was thereafter reduced to typewriting under my direction; that said transcript is a true and accurate record of the proceeding; that I am neither related to nor employed by any of the parties to this proceeding; and, further, that I have no financial interest in this proceeding.

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