

NIH Grants Conference PreCon Event, Human Subjects Research: Policies, Clinical Trials, & Inclusion

Day 2, December 7, 2022

Clinical Trial Session

Lyndi Lahl: So, hello, and welcome to day two of the Human Subjects Research PreCon event. Thank you for taking the time out of your busy schedule to join us today. This NIH PreCon event is part of the larger 2022 and 2023 NIH Grants Conference presentation series. We have a fantastic team of experts from NIH and OHRP with us today, but before we begin, I would like to go through a few logistics. Now, today's overall event will run about 4 hours, and it'll include several breaks. The event begins at 12 o'clock and ends at 4 o'clock p.m. Eastern Standard Time. At the end of the event, we request your feedback. A short survey will pop up directly in Zoom. Now, please consider taking a moment to complete the survey, which the planning team will use to improve the quality and content of future virtual events. Now, during this live event, we invite you to be part of the discussion. For Q&A, all questions that you want to pose to the presenters should be submitted through the Q&A box. We will try to respond to as many questions as we can, but as there are hundreds of you and limited time, we may not be able to get to everyone's question. So to help us identify the most relevant questions for our audience, we invite you to use the thumbs-up feature in the Q&A to upvote a question. Now, the chat feature will also be open throughout the presentations. Please note that the chat should be used to share comments and answer questions that the presenters may pose to the audience, but do not chat to pose questions to the presenters. You need to do that through the Q&A. Some people find the chat to be distracting. Now, if you fall into this category, I recommend that you click the little arrow next to the chat tab in the navigation and turn off those notifications. Now, you can find all of the PowerPoint presentations in the NIH Grants Conference Center once you're logged in. You need to look for the Human Subjects PreCon Event page and in the Agenda Planning section of the lobby. Now, outside the conference center, you can find the PowerPoints on the Grants Conference website, and we're going to be putting the page with the listing in the chat, as well. Now, the current versions that are posted do not include case study Q&A, but we will be uploading those versions by the end of the week. I want to address a frequent question that we've been receiving. Will there be a recording? So the answer to that is yes. The recordings will be posted in 7 to 10 business days in the same locations within the conference site. So today, our day will consist of three different presentations that are focused on NIH policies: an Overview of the NIH Policies on Clinical Trials; Including Diverse Populations in NIH Clinical Research; and Using the eRA Human Subjects System. And at 3:15 p.m. Eastern Time today, we will be continuing the conversation with Q&A and include a panel of all of our OHRP and NIH experts who have presented during this two-day event, so don't miss out on a valuable opportunity to get your other questions

answered that we haven't been able to get to previously. And, finally, I would like to remind you that this is a live event, so we ask all attendees to be respectful of one another in the chat. Please don't enter specific names of people or complaints in the chat. Instead, please direct any issues or concerns that you have via e-mail to our team at nihgrantsevents@nih.gov. Now, as we begin day two of our event, we would like to find out a little bit more about who has joined us today, so let's take a moment for a few polling questions to solicit this information, and here we go. So the two questions that we would like you to respond to are, "What is your primary role at your institution?" and, "What is your experience level?" So if you can take just a moment to address these two questions, that will be very helpful. And the poll is closed, and let's see who we have in the audience today. We have almost 1,000 folks. It looks like the majority of you are administrative and then scientific programmatic and other. Okay, and that's, I think, about the same as yesterday. So in terms of your experience level, most of you have at least 5 years' experience, and then almost 30 percent have between 1 and 5 years' experience, and then there's a smattering of other experiences. So thank you very much for providing that information to us. Okay, so thank you. We know that you're eager to get started on our first presentation, so let's go. So thank you for joining this presentation, which is on an Overview of NIH Policies on Clinical Trials. This presentation is 1 hour and 15 minutes long, and it will include not only valuable information on NIH policies related to clinical trials but also provide an opportunity for you to engage in some case studies and Q&A. My name is Lyndi Lahl, and I'm serving as the moderator for the first presentation. I'm the Human Subjects Officer in the Division of Human Subjects Research located within the NIH Office of Extramural Research. I am pleased to introduce to you your expert for this presentation, Dr. Pamela Kearney, who is the Director of the Division of Human Subjects Research in the Office of Extramural Research at NIH. Dr. Kearney is an otolaryngologist by training and has served as an IRB Chair of the combined neuroscience IRBs in NIH's intramural program for almost 10 years. Pam, I'm going to let you take it away. Thank you.

Dr. Pamela Kearney: Well, welcome, everybody. I'm really excited that you could come back for day two. This presentation, the very first one of the afternoon, we are going to talk about NIH policies on clinical trials. Let me see if I can ... All right. It's not going to work. All right. Before we get started, a couple of housekeeping things, you'll notice that this particular presentation wasn't uploaded yet on the resources pages. It will be almost immediately after this. At the end, we have some interactive cases, and all the answers are there in the presentation, and we didn't want all the answers to be there when you were going through this. For this presentation, you'll notice that there's a fair amount of text on the slides, and I did that on purpose because I want you guys to be able to utilize this presentation as a resource later, and I don't want you having to guess what was said on the slide. We'll still try to make it very interesting for you. And also, if I repeat a few things, I've done that on purpose throughout here. Pay attention to that because you may need that later on when we do our cases at the end. So let's get started. So our goals for today is, we are going to review NIH clinical trial policies. We're going to review how to go about determining if you are doing a clinical trial, and

we're going to do some practice cases, and I want you to be able to understand where you can find clinical trial resources after you leave this presentation today. All right. Let's get started on NIH-defined clinical trials. So first of all, what is a clinical trial? And at one point or another, I feel sure that all of you have seen any number of these terms associated with clinical trials. Now, the NIH definition, which was released in a guide notice back in 2014, and people still refer to it sometimes as the new definition of a clinical trial. It's really not so new anymore because we're pushing almost a decade. And the definition covers a wide variety of types of clinical trials. And the definition, in short, is, number one, a research study in which one or more human subjects, number two, are prospectively assigned to one or more interventions. Number three, the study is designed to evaluate the effects of those interventions, and then, number four, the effects being measured are health-related biomedical or behavioral outcomes. And you can see from this little graphic that it's not just your classic applied drug study that a lot of people think of when they think of clinical trial. An NIH-defined clinical trial can be a mechanistic trial. It can be a pilot study. It doesn't even have to be powered. It can be a pilot clinical trial, and it can be even basic science, and we'll talk about that a little bit as we go. All right. So when you are filling out your application to get a grant at NIH, you're going to run across these four questions, and these four questions are going to look very familiar because they are literally pulled right out of that definition. And these four clinical trial questions, number one, does the study involve human participants? Are the participants prospectively assigned to an intervention? Is the study designed to evaluate the effect of that intervention on the participants? And, number four, is the effect that will be evaluated health-related biomedical or behavioral outcome? If you answer yes to all four of those questions, then NIH considers that you are doing an NIH-defined clinical trial. And what will happen in the application is, it will then direct you to fill in more information. You'll have trial-specific information that you'll be required to give NIH in order for it to be properly reviewed as a clinical trial. All right. So why do we even care? Well, number one, NIH has clinical-trial-specific FOAs, and we're going to talk about that. And then there are specific clinical trial requirements. Again, we're going to talk about each of these, the registration, results-reporting requirement, the GCP training requirement. There are monitoring requirements for certain clinical trials, and also importantly, if you misclassify your study, and you submit a misclassified clinical trial, it might even be withdrawn prior to it even being reviewed. So this is actually quite important. So the very first policy we're going to talk about, you are getting ready to apply to NIH. And the first one you're going to run into is the clinical trial funding opportunity announcement policy. We call it the FOA policy for short. It was announced in this guide notice, and you'll notice throughout my presentation I have a number of links to guide notices and web pages and that sort of thing. And what I've done is, at the very end of this presentation, there are about four slides where I pulled all of those links, and I've put them all in one place. So if you're utilizing this presentation as a resource, you don't have to guess and try to go through 70 different slides trying to find the link that you're looking for. So that will be there at the end. So the FOA policy at base says that applications that are involving clinical trials have to be submitted to clinical-trial-specific FOAs. Now, the purposes of this policy is really to allow NIH to better

identify and track proposed clinical trials, and it ensures that key pieces of trial-specific information are submitted with your application, and it allows NIH to uniformly apply those trial-specific criteria during the review process. So the FOA policy requires that all applications after January 25 of 2018, so basically all of the ones that you are proposing now, all of the new ones, that are proposing one or more clinical trials have to be submitted to a clinical-trial-specific FOA. And applications that are submitted to an incorrect FOA are supposed to be administratively withdrawn without even being reviewed. So these are the different types of FOAs you may run into. There are actually more than this, but these are the basic ones. You might see a clinical trial not allowed FOA. You might see a clinical trial optional FOA, and you might see clinical trial required. There's also a special type of FOA that we'll talk about a little bit later on, which is a basic experimental studies with humans, or BESH, FOA, and those FOAs accept only applications that are proposing clinical trials that are also basic science. So what does the FOA policy mean for you? Well, what you're going to need to do is, you need to very carefully consider the work that you're proposing and make sure whether or not it is an NIH-defined clinical trial. And be sure because, as we mentioned earlier, NIH-defined clinical trials are much more than just that classic drug study that people may think of when they think of clinical trial. And you must choose a concordant FOA that matches your study. All right. Now, you've been funded. Congratulations, so now you need to actually do your study. So what's one of the first things that you need to do when you are putting your clinical trial together? Well, one of the first things you need to do is, you need to be compliant with the policy on Good Clinical Practice training for NIH awardees involved in NIH-funded clinical trials. We call it the GCP policy for short. It's outlined in this particular guide notice for your reference. There's also a web page if you want to do a little bit of a deeper dive after this and read more about that. I provide that link for you. The bottom line is, this policy was effective back in January of 2017, and it outlines GCP training requirements. Now, the purposes of the study is to make sure that everybody that's involved in the clinical trial has fundamental knowledge of the quality standards for doing a clinical trial, for designing and conducting it and recording, reporting, et cetera. And also, if everybody is trained in the fundamental knowledge of doing a clinical trial, it will help assure the safety of the participants in the clinical trials and make sure that the quality of the clinical trial is high. So the GCP training policy requires, number one, basically anybody that is involved in your clinical trial has to be trained, so this is the policy reads "staff involved in the design conduct oversight or management." So basically anybody who breathes on this clinical trial needs to be trained in Good Clinical Practice. The training is supposed to be consistent with the International Conference for Harmonisation. It's ICH. Harmonisation is spelled correctly there. It is for the document. The document link is here if you want to go in that document and see what those principles are. And the training needs to be refreshed every 3 years for those that take it. And when you do do this with your clinical trial, you need to make sure that you retain documentation of the training of the folks in your study. Now, there's no specific course or program that is outlined as required. So the GCP training can be achieved through any number of ways. You can have a class, a course. You can do an academic training program. You can do a certification from a recognized professional organization. The only thing

that matters is that all of the principles of that ICH are included in the training. So NIH actually offers some free-of-charge GCP training. NIAID offers one. The link is here. Again, all of these links will be at the end of the presentation, as well, so you don't have to search through it to find it. The Drug Abuse Institute, NIDA, offers one. If you're doing social-behavioral research, you might want to consider looking at OBSSR's training. They have one, as well. Keep in mind, though, GCP training doesn't have to be done through NIH to meet the NIH requirement. Your own institution can have your own GCP training tailored to your own investigators and the work that you do, and that is completely appropriate and completely fine. So there are no specifications as to which training has to be done. Now, what does it mean for you? We've basically gone over all of this. You need to identify the relevant staff on your study that are subject to the requirement, and you need to arrange for them to get adequate initial GCP training, and then make sure you retain the documentation. Whichever way that you do this, whatever administrative way that you keep up with these sort of things, make sure that the person charged with this, which ultimately is the PI, but whoever on your study is charged with this, make sure that they keep the documentation because when 3 years rolls around, these people have to do the training again, and you'll need to retain documentation that they got the refresher trainings, as well. So now, you are moving on in your study. You've got everybody trained, and your study is underway. You have to be also compliant with the NIH Policy for Data and Safety Monitoring. Now, there are two guide notices here. You can see that they are from a while ago. One is from '98. The other one is from 2000. And we also have a web link, a web page, here that you can read. But the bottom line for this requirement is that every clinical trial has to have provision for data and safety monitoring. Now, this policy is required for all NIH-defined clinical trials, and keep in mind this is a misunderstanding that I hear frequently. Data and safety monitoring is distinct from IRB review, okay? The IRB is going to approve your data and safety monitoring plan, right? But the IRB is not your data and safety monitor, so keep that in mind. The IRB review is different. And the data and safety monitoring is the method that you put in your protocol to monitor the safety of the participants in your study and to make sure that you have integrity of your data. And the type of monitoring that you choose needs to be commensurate with the risk of your study. Now, there are a number of different types of monitoring that you can choose. If you have a very low-risk study, the principal investigator may be the one who is the named monitor. If it's a little bit more risky, you might have an independent monitor, someone who isn't involved with the study, but there's only one person, and they're doing the monitoring of your study. It could be even stepping it up a little bit more. You could have an independent monitoring committee of several independent people who work together as a committee to monitor your study. And then the highest level of monitoring is a Data Safety Monitoring Board or Data Safety Monitoring Committee. The word is dependent on your institution, which one they use: DSMB, DSMC. And this particular type of monitoring committee, the FDA has some guidance, and the link is here. And that guidance outlines requirements for the DSMB, its requirements such as, what is the makeup? What is the note-taking requirements for the committee? It's a little bit more formal. And those are generally reserved for higher-risk studies. Now, the Data Safety Monitoring plans have to be

submitted for all NIH-defined clinical trials, and you have to submit a DSMP, and I highlighted the P because people get confused with DSMC, committee, DSMB, board. The DSMP, or the Data Safety Monitoring Plan, has to be submitted in your NIH application. And that plan has to address the overall framework of your monitoring that you are going to do. You have to identify the monitor that you have chosen, your IRB has approved, and it needs to describe the procedures for adverse event reporting to your IRB, to the FDA and to NIH. Now, each IC has different requirements for adverse event reporting. Some ICs require that all adverse events need to be reported to NIH, and others only require a summary report, so make sure that you know the requirements of the IC that has funded your study. Now, DSMB or DSMCs, NIH actually has some requirements for clinical trials that have to have this highest level of monitoring. And in general, all NIH-defined Phase III clinical trials have to have the DSMB, and all multisite clinical trials, regardless of risk, have to have a DSMC, and again, here is that same link to the FDA guidance. Now, there is one exception that I will say about the all multisite clinical trials. If you are doing a clinical trial that is Exemption 3, and, yes, it is possible for a clinical trial to be exempt, largely exemption, you'll see it in Exemption 3, which is the Benign Behavioral Interventions. If you are doing a study that is multisite that's an Exemption 3 study, NIH says you do not have to have a DSMB. You can use a type of monitoring that is more commensurate with that lower-risk type of study. All right. So what does the data and safety monitoring policy mean for you? Of course, you're going to choose the appropriate monitoring based on your study, the complexity, the size and the risk. Use the DSMB or DSMC if it's required. Submit the appropriate DSMP, your plan, with your application. Monitor the study, per that plan, and report the AEs as required. Remember, you have to monitor your study per your plan because that plan becomes part of the terms and conditions of your award, and if you don't monitor your study per your plan, you are in violation of your terms and conditions of your award. So make sure that you submit the plan, and you follow the plan. Right now, you're almost done with your study. You've conducted your study. You're getting close to the end, and now you need to be compliant with the dissemination of NIH-funded clinical trial information policy. Now, this policy, we generally refer to as the registration and results reporting policy. The guide notice is here, and it is complementary to a couple of other regulations. There's a section in FDA, and there's 42 CFR part 11. Again, it's beyond the scope of this talk to go into the details, but the links are here if you want to take a look. The bottom line is, all NIH-defined clinical trials have to register and report results in clinicaltrials.gov. And this is regardless of the study phase. It's regardless of the type of intervention. It can be a drug study. It can be a benign behavioral intervention. It can be basic science. It's subject, and it's regardless of whether or not you're subject to the regulation to register and report. And here is the website if you want to do a deeper dive on looking through that if you've got a lot of time to read. Now, the clinical trial registration and results reporting policy requires that you submit a plan on how you're going to be compliant with this with your application. And, again, like the DSMP, this becomes part of your terms and conditions of your award, so you have to follow your plan. You also have to include a statement in your clinical trial consent form that notifies the participants that summary results are going to be posted on clinicaltrials.gov. You have to register your clinical

trial in clinicaltrials.gov no later than 21 days after you enroll that first participant, so pretty quickly, so once you enroll someone, you've got to get your study registered. And you've got to report summary results in clinicaltrials.gov no later than 1 year after your primary completion date, and these are very important. Now, there are some potential consequences of noncompliance. Registration and reporting are going to be verified by NIH before any remaining funds or funds for a future grant are given, so if you are looking to get funds later in the study, we can't release those funds if we see that the registration reporting hasn't been done the way it's supposed to. And you're not going to be able to submit your RPPR if your registration and results reporting are overdue. And if you are doing an applicable clinical trial, there are some actions and federal regulations that might kick into play. Right now, let's talk about a particular type of clinical trial because there are some temporary flexibilities for this type of clinical trial, and these are your basic experimental studies with humans. These studies are both a clinical trial for the NIH definition, and they also meet the definition for basic research. We have some great resources. There is a BESH website on the OER website that is really nice. It was put together by some program officials that handle these type of studies, and it's a really nice resource even for people who aren't doing basic science studies to take a look. There's also a podcast that you might want to take a listen to if you're interested or you do that type of study. Now, basic research, here's the definition. This is basically a systematic study that's looking for knowledge or understanding of fundamental aspects of phenomenon or observable facts. And there isn't a specific application towards processes or products in mind, and if it is both basic science and clinical trial, then it is a BESH, and this is important because some BESH have some temporary flexibilities for registration and reporting, okay? Here's the latest guide notice on that, and if the BESH is submitted to a designated BESH FOA, and remember in the beginning of the presentation, we talked about the different types of FOAs, clinical trial required, optional, and these designated BESH FOAs. If a BESH comes in through a designated BESH FOA, they can register and report in platforms other than clinicaltrials.gov through September of 2024. But it's only for those that come in through the designated BESH FOA. So what does the registration reporting policy mean for you? It means you have to submit the plan in your application. You have to register no later than 21 days after you enroll that first participant. You have to report your results no later than 1 year after the primary completion date, and you need to include a statement in your clinical trial consent that the summary results are going to be reported in clinical trials that go. All right. Now, there is one more requirement that we need to talk about, and this one, I'm always surprised that this is one that people aren't as familiar with. There's a requirement that you need to post a consent form if you are doing a clinical trial. This is a consent form that was used at some point during your trial. The requirements are here. It's actually in the revised common rule, and NIH put out a guide notice regarding our implementation of this, and I'm going to talk about here NIH's implementation of this. And the bottom line is, all clinical trials have to post a copy of the consent form used on a federal website. And for NIH studies, if you had an English-language consent form, you have a choice of posting it on clinicaltrials.gov, and the instructions on how to do that, I've also linked to that here. Again, all of these links will be at the bottom of this presentation, so you can find them

easily. Or, you can submit them to a docket on regulations.gov, and that docket is also linked here. Now, if you have a non-English-language consent form, you have to post it on regulations.gov because clinicaltrials.gov is not equipped to take the non-English-language consent forms. All right. Now, here is a caveat for this. It sounds very easy, about posting your consent form, but there is a really tight window of time that will make you compliant. You can't post this until after enrollment closes, and then you can't post it any later than 60 days after that last study visit by any participant. So if you are doing your study, and you think you're going to get ahead of the game, and you just go ahead and post one of the consent forms, but your enrollment hasn't closed, your not in compliance. So you need to make sure that you wait until enrollment closes. So, again, whichever admin person is taking care of your timeline, again, it's the PI's responsibility, but make sure that you have this marked on your clinical trial timeline that when enrollment closes that you post this clinical trial consent form. And if you post it before enrollment, it doesn't count. All right. Now you're experts in the clinical trial policy, so now it's important to find out, am I actually doing the clinical trial? So let's take a look at clinical trial determinations. All right. We looked at these before. I'm not going to read them again because what we're going to do is, we're going to go through each one of these questions, and we're going to talk about some rules and pitfalls of each of these questions. Remember, if you answer yes to all four of these, you are doing an NIH-defined clinical trial. And a reminder, the devil is always in the details. I've had people come to me, an investigator added an aim four. They weren't doing a clinical trial, and then they added an aim four, which added this kind of pilot type of efficacy clinical trial, and it kicked them into clinical trial territory, so be careful that you don't have a paragraph or two in there that has kicked you into clinical trial territory when you didn't think you were doing one. And remember, if any one part of the application is a clinical trial, the application is a clinical trial, so even if it's aim 10 or it's one part of one of your studies kicks you into clinical trial territory, the whole project has to be classified as a clinical trial. And remember, NIH-defined clinical trials are so much more than those classic drug studies. So, people, if you're not thinking about, what exactly is an intervention, that it can be a probe, it doesn't have to be a drug, you might get tripped up. So keep this in mind. So let's take a look at question number one. Does the study involve human participants? I'm not going to spend a lot of time on this Lyndi Lahl did a very nice presentation yesterday, and OHRP actually did some presentations on engagement of research and human subjects participants. But the bottom line is, a human subject is a living individual about whom an investigator gets information or biospecimens through intervention or interaction and then uses studies, analyzes that information or biospecimen, or they obtain, use, study, analyze or generate identifiable private information or identifiable biospecimens, and that will make it human subjects. All right? Now, remember, exempt human subjects research is still human subjects research, and it is possible for certain exempt human subjects research to be clinical trials, and I'm thinking specifically of Exemption 3, the one with benign behavioral interventions, okay? So don't think just because it's exempt that it can't be a clinical trial, because it can. All right? And we've got some resources here. You can go to our human subjects website, and then I've got a couple of links to the Revised Common Rule if you want to take a

look at those. Now, let's move to the second question. Now, the second question actually has two parts: the prospectively assigned and the intervention. So let's talk about prospectively assigned first. Now, prospectively assigned is just that predefined process that you have specified on how you're going to assign your research participants to one or more arms. In other words, you have decided in advance that this is the way it will be done, prospectively assigned, okay? So it doesn't matter if they're randomized. It doesn't matter how many groups. You can have one group. You can prospectively assign people to have an intervention in one group, and it doesn't matter how that group assignment is made. You can decide in advance that the participants are going to pick their own group. You can decide in advance that the physician is going to assign somebody based on their medical need. You can decide the investigators are going to put people in one of two or three groups. So it doesn't matter about how it's assigned. It only matters that you decided in advance that this is how it's going to be. All right. Again, I'm repeating this for a purpose. Randomization doesn't matter. It is the most common reason people come back to me and say, "I can't be doing a clinical trial. It's not randomized." Yes. Yes, you can, because randomization doesn't matter. All right. So, now, the second part of this is, are the participants prospectively assigned to an intervention? Now, an intervention is a manipulation or a probe of the participant or their environment for the purposes of modifying one or more health-related biomedical or behavioral processes or endpoints, okay? And remember that this is a probe. It doesn't have to be a drug. It doesn't have to be a big, risky procedure, okay? This can be health-related education training programs. It can be a computer application you're asking them to do. It can be a task that you're going to ask them to do in an MRI scanner. You can show them emotional faces. That is a task. It's a manipulation. It's a probe, and you're looking for the effect of that on something. Now, the one thing you need to remember is the intervention has to be done as part of the study. All right? So if you are just taking advantage of a program that somebody else is doing, a health department, an HR department or something like that, and you just say, "Hey, I'd like to know what the effect of that is going to be," but you are not doing the intervention, it's being done by somebody else and will happen regardless of whether you do your study. It's not a research intervention, okay? So that is not an intervention that you would count. All right. The pearls and pitfalls, question number two, again, randomization, number of groups, how the group assignments are made, types of manipulations or folks do not matter. I'm repeating this for a purpose. It's helpful to think of the intervention as the independent variable, and I think if you start thinking that way, you might be able to start identifying these. And don't mistake the intervention for a measurement. This is very, very common. Just because you're doing an fMRI doesn't mean that this is a measurement, per se, okay? The BESH website actually has a really nice little paragraph on determining intervention versus measurement, and I would encourage you to take a look at that. I think the folks that put that together did a nice job. All right. Now, let's take a look at question number three. Is the study designed to evaluate the effect of that intervention, which you just identified in the previous question, on the participants? What I generally do when I'm looking at these is that I go through a proposal, and I look at all of the effects that an investigator is proposing to measure. And these are anything including changes

in behaviors, changes in knowledge, intent to change behavior. Have you changed their intent to do something? So, vaccine study, you've got a program to increase vaccines, and you're going to measure whether or not folks had changed their intent to get the vaccine. That counts. It's often helpful for me to isolate how the effect is being measured so that I can kind of better identify the effects. If I can find the questionnaire and look at the questions, that kind of tells me what they're evaluating, and I find that a helpful step and that you might be able to use that, as well. All right. So, pearls and pitfalls, remember. Effect does not necessarily mean effectiveness. You don't have to be looking at the effectiveness of something, a drug or something. You're just looking at, did it affect it? Was there an effect of your manipulation, of your probe? Now, are these effects on the participants or an institution? Because if it's just on the institution, it's not a clinical trial. But be careful. Be careful, because if you're looking at institutional effects, sometimes, remember, devil in the details. Sometimes what happens is that investigators measure effects on participants, as well. Even though the main purpose is the institution, they've kicked themselves into clinical trial territory because they're also measuring things on the participants and the effects on the participants. So be careful. Any one part is a clinical trial, the whole project is a clinical trial. And it's helpful to think of the effects as the dependent variables, which are tested and measured. And remember, the words, designed to, simply means that you plan to do it, not that it's the main purpose of the study. I once had an investigator who was very upset that his study was classified as a clinical trial because the clinical trial part was in aim three, and he said, "That's not the design of my study. That's not what I'm intending to do. That's not what my study is designed to do." Well, it wasn't the main effect. It wasn't the main purpose. But you did design your study to measure it. It's an aim three. It's only a minor aim, but it is. So designed to doesn't mean main purpose. It just means that you're planning on doing it. Okay, so now, let's look at the last question, number four. Is the effect that you're going to evaluate a health-related biomedical or behavioral outcome? If the questions one through three are yes, in my experience, question four is almost inevitably yes, as well. I had one of my colleagues from OBSSR once joke to me that if you're applying to NIH for money, do you really want to say that you're not looking at biomedical behavioral outcomes? It was a joke, but it rang rather true. While this is not always the case, I find that it usually is. So once you've answered yes to one, two, three, look at question four very, very carefully, okay? And remember that these can include health-related knowledge and learning and intents to change behavior. Okay, now you've gone through all of that, and you're still unsure. Okay, that's good. We've got some resources for you. I would refer you to the NIH clinical trials website. On that website, there is a clinical trial decision tool. It's very basic. It walks you through the processes that we just talked about, but it's a helpful exercise if you're really having trouble sorting out the details. You can look at our BESH website, which I find to really help you kind of think about the issues. And then I would urge you to seek help from your program official. If you don't have a program official there's a nice tool that NIH has called NIH Matchmaker, and you can find this off of NIH Reporter. When you go to that website, I found it was a little bit hard to find, so I wanted to point it out to you. You kind of have to scroll down just a tick, and it's on the right-hand side near the bottom, and this arrow is pointing to it. If you

click on that link, you're going to get this field and this text field here. You can type in your abstract. You can type in some text. What it will do is match you up with program officials and ICs who manage similar types of work as yours to help you identify folks that have expertise in your field. All right. Now, all right. So let's do some examples. Let's do some exercises, and for this I'm going to have you guys answer the questions here. So when I get to certain questions, I'll say, "Put your answer in the chat." And I actually am able - they've set it up here so that I can actually see the chat. There are so many of you. Don't worry about getting things wrong. I'm not going to be able to - I can see names, but there's so many I'm not going to be focusing on names. I'm just going to be focusing on the answers. So let's go through these examples and test our knowledge. All right. This example, FYI, is theoretical. It's completely fictional. Please don't do a critical dive into the science here, okay, because this example was put together just to demonstrate some points. All right. So let's look at it. We have a study that's going to design and implement a workplace mindfulness program. They're going to enroll employees of a company. They're going to randomize them to experience this mindfulness program versus not, and at baseline and then in 1 month, they're going to measure the participants' blood pressure, their cortisol levels, and they're going to administer a survey about stress levels. So is this an NIH-defined clinical trial? I'm already seeing some answers here, and I'm loving what I'm seeing. So this one is pretty straightforward on purpose, but we're going to go through each one of these questions, and we're going to talk about it a little bit. So does the study involve human participants? It does, so, yes, yes, yes, I am loving this. You guys are awesome, amazing, amazing. Okay, yeah, yes, the employees of the company. All right. What about, are the participants prospectively assigned to an intervention? And I'm seeing tons of yeses. I've yet to see a no. It's going so fast, some of them. Somebody wrote in some text that I couldn't read, and it flashed by so fast. The answer is yes. Participants are prospectively assigned to participate in a workfulness, mindfulness program. Somebody says, "Mindfulness is an intervention." Yes, indeed, it is. The mindfulness program is the intervention, and they've decided in advance that people will be doing this. All right. Number three, is the study designed to evaluate the effect of the intervention on the participants? All right. I'm seeing a lot of yeses. Excellent, excellent, and the answer is yes. They're going to measure the effect of the mindfulness program on blood pressure, cortisol levels and stress levels. All right. All of those are effects that they're measuring. All right. And then the last one, is the effect a health-related biomedical behavioral outcome? Yes, pre and post. I'm seeing a lot of yeses. All right. And the answer, indeed, is yes. So blood pressure, cortisol level and stress levels are health-related biomedical and behavioral outcomes. I did see one comment that flashed back really super fast, what they're measuring, the effects pre and post. Now, keep in mind you wouldn't necessarily - To meet the definition, it may not be good science, but you don't have to do the pre. As long as you are measuring an effect, you are measuring the effect, okay? So if you're measuring the effect, it doesn't have to be before and after. All right. Now, here is the summary slide. We've answered yes to all four questions, so, yes, you guys got this right. This is an NIH-defined clinical trial. All right. Now, let's go back here. I think I jumped. All right. So now, what we're going to do with this is, we're going to shake it up. We're going to use this example, and we're having

questions in the Q and A, but I do see somebody that says, "Poll questions." There are no poll questions. We're just putting answers in the chat, okay? So we're just doing this because there are so many of these questions, the polls would have taken too long. So now what we're going to do is, we're going to shake this example up, and we're going to play what if, okay? So are the participants prospectively assigned to an intervention? So, now, what if there was no randomization? Is the answer to question two still yes? Put your answers in the chat. Is it still yes? Oh, you guys are great. I love this. I haven't seen a single no. Yes, that is correct. It is still yes, and it is still a clinical trial. What if there was only one group? You don't have that not-group. Everybody is going to get the intervention. Is the answer to number two still yes? Yes, lots of yeses, yes. All right. Correct, it is still yes. It is still a clinical trial because the number of groups doesn't matter. All right? Now, what if participants chose their own group? You didn't randomize them. You came in, and they were able to just pick which one they wanted. They didn't really want to do the mindfulness program, but they wanted to be in it, thought it might be a fun exercise. Yes, you guys are great. Yes, it is still yes. All right. Now, number four, the mindfulness program is being conducted by the HR department, and it's going to happen regardless of whether or not the study happens. Is this answer still yes? I'm seeing a fair number of nos, a few yeses, a maybe, a lot of nos, yes because they're measuring effect. All right. So, no, this is not a study intervention, okay? So the HR department is going to do this regardless of whether the investigators come in and do measurements on it. They are not doing this. It's not a research intervention. It's just something the HR department is doing. The investigators are just taking advantage of said thing, and they're observing what's going on. This is an observational study. It is not a clinical trial. So the answer to this would be no. This is not a study intervention if the researchers aren't doing the intervention. This going to happen regardless of whether the research happens or not. All right. Very good. Most of you got that right. All right. Now, let's go to question number three and do some what-ifs. So we're looking at evaluating the effect. What if the investigators are only measuring feasibility or usability of the mindfulness program only to see if it's possible to set it up? But we have more mixed answers. All right, a fair number of nos. Okay. So, no, it would not be. If they are truly only measuring the feasibility or usability of implementing a mindfulness program at this office, and they're not measuring any effect on the participants, they're just seeing, "Can it be done?" they're not measuring any effect on participants. So the answer to number three would be no, and therefore it would not be a clinical trial, because all four questions wouldn't be no. No. They're testing the usability and feasibility, and their surveys include questions about stress level. Is the answer to number three still yes? I'm just watching the scrolling, a lot of yeses, a few nos, a couple more nos. All right. The answer to this is yes. It is still yes because what they've done, and this is why you have to be so very careful with these feasibility studies, whenever somebody gives you one of these to review, you have to be careful about what they're actually measuring. If they are only measuring feasibility and usability, it is not a clinical trial. But if they go into this pilot effectiveness stuff, and it just seems like you investigators just can't help themselves, they've got to find out, could it possibly be working? Is it worth a bigger study? And they throw in some of these effectiveness studies, and if they start asking questions

about stress levels to see whether or not that was something going on there, then you've now moved into clinical trial territory. And I see this somewhat frequently with investigators who go in, but it's a feasibility study, but, yes, you did a pilot effectiveness study on it, so it's still a clinical. That part is a clinical trial. If any one part is a clinical trial, the whole project is a clinical trial. So when you're designing these, or if your administrative and your investigators are designing these, make sure you point out because it would be very easy for them to do that in another study or something like that. But be careful you don't bump yourself unintentionally. Now, if you intend to do it, great, but if you're not intending to do that, don't unintentionally bump yourself into clinical trial territory. So now, what if they're testing the effectiveness of the mindfulness program, and there is a tiny, minor aim? We're still in an otherwise very large study that's not a clinical trial. So this particular study is aim six, and would the project still be designed to measure the effectiveness of the mindfulness program? And you guys are nailing this one. You're hitting it out of the park. Yeah. Yes, the answer to this is still yes, and it would still be a clinical trial. So now, let's do some what-ifs on question number four. What if they were only measuring the employees' learning and knowledge of the potential health benefits of mindfulness activities? They're not going to do the blood pressure. They're not going to do blood draws. They're not going to measure stress levels. They're just going to measure before and after their knowledge about the health benefits. You guys are great. I'm so encouraged. This is so amazing. Yeah. You guys are really hitting this out of the park. Exactly, the answer to this is still yes, okay? All right. Now, what if they were measuring the intent to go forth and engage in healthy activities? Is the answer to four still yes? Awesome. Awesome. I'm seeing an awful lot of yeses, and you guys are 100 percent right. It is still yes, therefore it's still a clinical trial. All right. All right. Now, that was great, guys. I'm really pleased. You guys did an amazing job. Now, what we're going to do is we're going to go into an example that is a little less obviously straightforward, okay? So this one also is a fictional study. It's adapted from our case study number 42 off of the clinical trial website. In this study, you've got a group of young, healthy adults that are going to perform a go, no-go task while undergoing MRI. The purpose of the study is to characterize the pattern of neural activation in the frontal cortex during response inhibition. So we're going to look at, is this one an NIH-defined clinical trial? All right. I'm seeing some mixed answers, so let's take a look. Let's go, again, question by question. Does the study involve human participants? This one is easy. I won't spend a lot of time. Yes, they're looking at young, healthy adults. All right. Let's look at question number two. Are the participants prospectively assigned to an intervention? All right. Is every some yeses, one or two nos, a few nos. All right. All right. More yeses, but a few scattered nos. All right. So the answer to this is yes. The intervention here is the go, no-go task. Okay, and it's decided in advance that these people will undergo the go, no-go task. The go, no-go task is a probe. It's a manipulation, okay? They are probing. All right? So this is an intervention. This is an NIH-defined intervention, the go, no-go task in this particular study. All right? All right. No, this is definitely an intervention, the go, no-go task in this study. They are probing something to get an answer here. All right? So is the study designed to evaluate the effect of the intervention on these participants? Right, this one, yeah. We're getting a lot of yeses. I won't wait any longer on

that yes. They're going to measure the effect of the response inhibition on neural activation in the frontal cortex, so they're looking at the effect of neural activation of that response inhibition. All right. So lastly, is the effect that will be evaluated a health-related biomedical or behavioral outcome? And the answer is, yes. A pattern of neural activation in the frontal cortex is a health-related biomedical outcome. So with this example of the go, no-go task in the MRI scanner, they're probing the participants, and they're exploring a phenomenon. They're looking at the pattern in neural activation. Is this an NIH-defined clinical trial? And the answer is, yes. This would be an NIH-defined clinical trial. All right. As I can see, I expected the answers to be a little bit less definitive on this one because this one is not as classic. The other one was more classic. This one is an example of a BESH. It's a clinical trial that is also basic science, so this is an example of BESH that we've talked about. These are both NIH-defined clinical trials and basic research, and they're exploring understanding of fundamental aspects without any process or product in mind. And just to go back, and I would refer you also to the BESH web page that we have where we talk about measurement versus intervention, and they have a really nice little paragraph there. But now that we've established that this is a BESH, what type of FOAs can this BESH be responsive to? Now, it can respond to a designated BESH FOA. All right? It is a clinical trial, so it could respond to a clinical-trial-required FOA as long as that FOA allowed for it. Now, there are some FOAs that will specify that they won't take basic science or have some other reason why it wouldn't be able to come in. But theoretically it is a clinical trial, and it could respond to a clinical-trial-required FOA that will allow it in. Again, same difference, it can go into a clinical-trial-optional FOA as long as that FOA did not say that BESH could not. All right? So, all right. I'm not sure why my answers are showing up on that next slide. My animations got ... All right. All right. So this is unfortunate. My slide ... The animations got taken away. But what we'll do is, we'll talk about it anyway. So the answer is, will this study be required to register and report results? And the bottom line is, yes, it is a clinical trial, so it has to register and report results. Okay. So does it have to register and report in clinicaltrials.gov? And the answer would pop up, and I was going to ask you guys, would it have to? And the bottom line, that's a trick question because it depends, okay? It depends on what FOA it was responsive to. If it's responsive to a clinical-trial-required or optional FOA, and it's not a designated BESH FOA, if it's clinical-trial-required, then, yes, it will have to register and report in clinicaltrials.gov. There's no flexibility for BESH that come into those type of FOAs. Now, if it goes into a designated BESH FOA, these studies, these BESH, can use a platform other than clinicaltrials.gov through September of 2024, and I hope the rest of my animations are okay. No. All right. Well, it's okay. So the bottom line here, kind of spoiler alert, the answers are all up here. But talking about all of the rest of the clinical trial requirements, will the investigators on this BESH need GCP training? Yes. It's a clinical trial. They have to follow all of the clinical trial requirements, okay? The flexibilities are only for the registration and results reporting, and they still have to do that, but they can do it on different platforms through 2024. They have to submit and follow a data safety and monitoring plan because they are a clinical trial. You see the theme going on here. Will they have to upload the consent form in clinicaltrials.gov or regulations.gov? And the answer is, yes. They are a clinical trial, so they have to upload the consent like all of the other

clinical trial requirements. So for more information, this is the BESH web page that I told you about. This is a screenshot of it. It's really nice in that it goes through each of the clinical trial questions, one through four, from a basic scientist's eye, from a basic scientist's point of view, and kind of explains it. I actually find it very helpful just in regular clinical trial determinations. And now, just going through some of the resources, we've put together a seminar resource document, which will be with all of the rest of the resources from this presentation, and that will have a fair number of the links on it. But the next four slides here, I just kind of did it by policy. This one has the definitions and the policy and the web pages and the podcast and that sort of thing. The next one has the FOA policies and GCP links on it. The next one talks about the data and safety monitoring requirements and the registration and results reporting links that we had. And then the last one has some links to the common rule and some instructions for posting the consent in clinicaltrials.gov and that regulations.gov docket. And then the last one are some of the Human Subjects ones, as well, and the link to the matchmaker on reporter. So now, you have become an expert in clinical trial policies at NIH. You have reviewed and practiced how to make a clinical trial determination, and you have reviewed some clinical trial resources. So I hope this was helpful for you, and at this point, we will be able to take a few questions.

Lyndi Lahl: Hey, Pam. There have been a lot of questions. NIH staff have been responding to a few of them, but we still have a lot more left. So there were a number of questions on DSMBs. One of those questions is, would a DSMB be required for a phase I multisite clinical trial?

Dr. Pamela Kearney: Yes.

Lyndi Lahl: Okay. That was ...

Dr. Pamela Kearney: Yes, because it's multisite. It's a multisite NIH study. It is, yes ...

Lyndi Lahl: Okay.

Dr. Pamela Kearney: ... because of the multisite part.

Lyndi Lahl: Okay, very good. Can you give an example of the difference between an intervention and a measurement? I think this came in a little while ago. I think it was when you were talking about BESH.

Dr. Pamela Kearney: Right. Yes, this actually ... Interventions in measurements are pretty easy to determine if you're doing a classic applied clinical study, a drug study. The measurements are your X-rays and your hemoglobins and your glucoses and that sort of thing. And the intervention is going to be the drug that you give. Now, it gets a little bit more nuanced when you start crossing into basic science. I like to think of a measurement in order for an intervention to be a measurement. Now, let me give you a good example of where you have kind of this intervention that is an actual measurement, a known measurement. Think of a glucose tolerance test. A glucose tolerance test is a recognized way to help diagnose diabetes. A patient, not a participant, a patient, is given a bolus of glucose, and then they measure the glucose levels over time over 4 hours. And then they do that. But that is characterized. It's in

the literature. It is a true measurement even though if you're kind of overthinking it, you could say, "Wait a second. The glucose is an intervention." Okay, but that is a well-characterized, well-studied measurement. Now, it is possible that you could have some research measurements that are so well-characterized in the literature that you would have to be using it to literally measure something. So I'm going to get myself in trouble here trying to do the science because this is not my area of science, but I'll try. So if you're doing a study in a flashing checkerboard, I understand that the effects of a flashing checkerboard in MRI is very well-known, and it's very well-characterized. So if you're going to use that, and you've got another intervention, so you're going to do something, and I'm just going to pick something out of the air, that you've got an agent that you're going to give the folks, and you're trying to explore some basic science things, and then you're going to put people on the scanner, use the flashing checkerboard, and you're going to measure with the flashing checkerboard and the MRI scanner the effect of that other agent, the other agent is the intervention. The flashing checkerboard fMRI is the measurement. Now, those, I understand, are quite extremely rare. Most of the time, the researchers are using the task as a probe. And if you're using that task as a probe, and you're using the MRI to measure the effect of that probe, then the probe is an intervention, not a measurement. So unfortunately this is not my area of science, so I hope I got that right. I'm channeling some of the BESH POs that I worked with on that. But in order for it to be a measurement, it would have to be very well-characterized as a measurement, and you're using it to measure the effect of something else. If you are using it, and you are just using it as a probe, if it's a probe, then it's the intervention. I hope that didn't make it clear as mud there.

Lyndi Lahl: No, that's great. Thank you. So someone asked the question, can you provide some more examples of what constitutes an intervention? Because it sounds very broad, meaning any manipulation of the person or the environment, regardless of the duration of that intervention, or is it invasiveness that makes it an intervention?

Dr. Pamela Kearney: No, you're absolutely right. It is broad. And, no, it does not have to be invasive. You can do the Zen effects of gardening. You can put them through a gardening intervention and measure the Zen effects. That's the clinical trial. It can be anything. It can be using a computer application. It can be any sort of probe. You can show people emotional faces, and you're looking at a particular response in a particular part of the brain. You're exploring that. That can be an intervention. So, no, it does not have to be invasive. It can be very, very benign. Like we mentioned earlier, you can even have interventions that are so benign that they're exempt from IRB review. Think of Exemption 3, those benign behavioral interventions. It is possible for those to be a clinical trial, which, by the way, is the only exception to that multisite DSMB requirement. So if you're doing an Exemption 3 study, and it's multisite, you don't have to have a DSMB. You can have a more appropriate, lesser monitoring. But, yes, interventions can be quite benign. It just has to be a probe or a manipulation of the participant or their environment.

Lyndi Lahl: Okay, great. So can you explain? How do you know if it is an effect?

Dr. Pamela Kearney: I ...

Lyndi Lahl: Yeah, that's all that they said. I think it was when you were going through the four clinical trial questions. How do you know if there's an effect?

Dr. Pamela Kearney: Well, the effect is what you're measuring. The effect is what you're measuring, so when you're thinking about the study, you do an intervention, and you're looking for the outcome. So the outcome really is the effect that you're measuring. So the effect, it can be just about anything. You could have a program that you're putting forth in the community to increase vaccine uptake for a particular illness, and you have this community program, so you are manipulating the environment of people. And then you're going to measure folks' change in their intent to get a vaccine. Does seeing these billboards, did that change your intent to get the vaccine? Are you more likely or less likely to get it? That would be the intent, would be the effect, of that campaign. So the effects can be quite broad. I hope that answered sufficiently.

Lyndi Lahl: Yeah, I think that there was a little bit of confusion if you don't have a pre and post test or a pre-lab and a post-lab that you're looking at baseline versus what happens afterwards. How can you say there is an effect?

Dr. Pamela Kearney: Well, I didn't say it would be good science. But again, for example, let's go back to that vaccine, the vaccine campaign where you've put out billboard and signs and radio ads and TV ads and that sort of thing around a particular event in a community. And you're going to enroll people who stop by the booth and ask them about the effect of that campaign that they had. You will not have a before. You're just going to be asking them. There was no way you could have asked them, what is your intent now? You can only ask them, before you saw it, what did you see? What did you think? And now that you saw it, what do you think and that sort of thing so that you would be measuring the effect there, and there would be no pre? So, yes, you don't have to have a pre-post. And, again, make sure that whatever you're doing, that the science is sound because you won't get funded if it's not. But, yes, it is possible to not have the pre-set and still be measuring an effect.

Lyndi Lahl: Okay, yeah. Thank you. I think that that is helpful to our audience. That seems to be what they were asking about.

Dr. Pamela Kearney: Mm-hmm.

Lyndi Lahl: So somebody asked a question. Does NIH awards dictate if the research study with human subjects is a clinical trial?

Dr. Pamela Kearney: Say that again. I'm sorry.

Lyndi Lahl: Does the NIH award dictate if the research study with human subjects is a clinical trial?

Dr. Pamela Kearney: Well, when you apply, when you submit your application, you have to indicate whether or not you're doing the clinical trial. And so that is what's going to determine it unless someone at NIH sees that you've misclassified it. So you can't really say, I guess, that it

depends on the definition of NIH saying it, but if you are going to put it in your application, and then when it comes to NIH, they'll determine if it was misclassified or not.

Lyndi Lahl: Okay, thank you. So there's a question. If we do a trial to test whether navigation increases clinical trial participation, they're assigning people to be navigated or not. Are there any ethical problems in not offering navigation to a group?

Dr. Pamela Kearney: All right. I don't know what you mean by navigation.

Lyndi Lahl: Well, they didn't really explain that.

Dr. Pamela Kearney: Mm-hmm.

Lyndi Lahl: Yeah, I'm assuming that there are people in the community that are helping to get people into different services, and possibly a clinical trial is one of them, and ...

Dr. Pamela Kearney: So, well, I guess rather than looking at the specifics of it, your clinical trials all have to be IRB-approved, so you need to make sure that whatever you're proposing, that it is ethical and that the IRB agrees that it is.

Lyndi Lahl: Okay, excellent. Thank you. So there were a few questions as you were going through the scenarios. So in the scenario, or we can just say a scenario, that only one aim of the proposed research is a clinical trial and that the only aim required to meet clinical trial requirements including registration and reporting ... Wait. Wait a minute. In the scenario that only one aim of the proposal is a clinical trial, that is the only aim required to meet clinical trial requirements including registration and reporting. Is that correct?

Dr. Pamela Kearney: Correct, and I can have Dawn jump in here, too. But what will happen is, that application, the project code will be clinical trial, so the whole project is going to be flagged as clinical trial. But when you actually start ... I'm sorry. The study level codes will be different, so, Dawn, can you jump in with the coding, with the whole ... The whole project has to be clinical trial, but then each of the studies will be coded differently.

Dawn Corbett: Right.

Dr. Pamela Kearney: And only the study will have to meet the registration reporting and that sort of thing.

Dawn Corbett: That's right, and so depending on the kind of grant, application that you're submitting, you may have one or more studies in that grant. Some of them may be trials, and some of them won't. So your entire project will include in the notice of award terms and conditions, which indicate whether or not a trial is included, and you'll need to meet those terms and conditions. But in terms of registration and reporting, it would only be for those studies that were designated as clinical trials.

Dr. Pamela Kearney: Oh, and, Lyndi, just jumping back to the question that we had previously about the effect, something that I forgot to mention is that if you're trying to figure out what

your effect is, it's helpful to think of the effects as the dependent variables that are going to be tested and measured. So I'll just kind of throw that out there, as well.

Lyndi Lahl: Okay, thank you. So I just want to mention we have 5 minutes left in this session. Oh, actually, 1:25 p.m., are we supposed to be done right now, Cynthia?

Cynthia: I think we're out of time.

Lyndi Lahl: Yeah, I was thinking that it was 1:30, but I have a note to myself saying it was 1:25. We are done. I am so sorry. I missed the 5-minute warning.

Cynthia: We could go on all afternoon. Let's keep going, so .. .

Lyndi Lahl: Okay. Well, because we are done, we're going to stop the Q and A for now. Remember, at 3:15 we are going to have another opportunity to be answering your questions. So thank you, Pam, for sharing your expertise on clinical trials, Dawn, for jumping in on that last question, and to everyone who joined us for today. Now, remember, the PowerPoint and related resources are located in two locations, one on the NIH Grants Conference website and the second inside the virtual NIH Grants Conference Center. And Pam's slides are going to be uploaded later today, is my understanding. So look for the Human Subjects Research Pre-Con Event page, and you'll be able to find them there. So I'd like you to take a moment to stretch, refresh or even check out our exhibit hall resources. We'll be returning in about 5 minutes for our presentation on diverse populations in NIH clinical research. Thank you very much.