

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

Day 2, December 7, 2022

Inclusion Session

Dr. Rebecca Favor: Hello, everyone. Thank you for joining today's presentation focused on including diverse populations in NIH clinical research. During the next 45 minutes, our presenter will be highlighting some important information related to diversity and inclusion in your clinical research followed by the opportunity to get your questions answered during our Q and A portion. My name is Dr. Becca Favor, and I'll be the moderator for today's presentation. I serve as the NIH Human Subjects and Inclusion Policy Analyst in the NIH Office of Extramural Research. Now, let me introduce your NIH expert on the topic. Dawn Corbett is the NIH Inclusion Policy Officer within the Division of Human Subjects Research in the Office of Extramural Research here at NIH. Dawn, take it away.

Dawn Corbett: Thanks so much, Rebecca. So today, I want to talk to you about including diverse populations in NIH-funded clinical research. And to start out in our discussion, I first want to discuss NIH's longstanding commitment to ensuring the inclusion of diverse participants in our research. This commitment goes all the back to 1986, when NIH first established a policy encouraging the inclusion of women in clinical research studies, which was largely developed out of concern that women of child-bearing age were routinely excluded from clinical research studies. In 1994, it became a requirement that NIH include women and members of racial and ethnic minority groups in all clinical research studies, and this was based on the NIH Revitalization Act, which became law in 1993. In 1998, requirements for inclusion extended to children, and when we found there were similar concerns about the inclusion of children in clinical research studies, we made a small change in 2015 to change the definition of a child to an individual under 18. It had previously been an individual under the age of 21. And then in 2017, we had some new changes in response to the 21st-Century Cures Act, which was passed in 2016. We had new requirements for reporting of NIH-defined phase III clinical trials, which I'll talk about a bit later. And then in 2019, most recently, we started requiring inclusion of individuals of all ages in any research. So I'm going to talk about those requirements in depth in this presentation, but I do want to acknowledge that despite all of these efforts over the years, we are still not where we want to be, and this is where you all come in. So while we'll be talking about requirements and forms and things that you need to fill out, what we're really looking for here is a paradigm shift, and we need all of you for that paradigm shift. I think this was illustrated quite nicely in a recent report from the National Academies of Science, Engineering and Medicine. This was published earlier this year. There were a number of recommendations for NIH and others involved in inclusion, but among the insights was that without a paradigm

shift that looks beyond tactics and process-oriented changes, disparities in research access and inclusion will persist at the expense of minority population subgroups and the nation's public health. So I want to keep in mind that what we are trying to achieve is we're trying to achieve science that answers the question for all of those with a condition that's generalizable and that's asking the right questions when needed. So with that, let me go into talk a little bit about what our policies are. So NIH has two inclusion policies, and the first is the Policy on the Inclusion of Women and Members of Racial and Ethnic Groups. And this requires that women and members of racial and ethnic groups must be included in all NIH-funded clinical research studies unless there is a compelling rationale for their exclusion. So what does this mean? This means that women and members of ethnic and racial minority groups must be included unless there is a good reason for not including them. What is a compelling rationale? So usually this should be based on the science. So, for example, if you are doing a study on prostate cancer, and you are not including individuals whose sex at birth is female, that's probably okay because the condition does not occur in that group. However, if maybe you're doing a study, and you want to exclude women because it's too expensive to do pregnancy tests on everyone, this would not be acceptable. In fact, the law specifically says that cost is not an acceptable reason to exclude groups. I would extend that and say, to NIH, convenience is not an acceptable reason to exclude these groups in research. If you're doing a NIH-defined Phase III clinical trials which these are these broadly-based prospective studies that compare two or more interventions, and for FDA-regulated studies, these are often the last step before approval. If you're doing these, they have some additional requirements that you have to do analysis of the primary outcome by sex or gender, race and ethnicity, and the progress of these analyses needs to be stated in your progress report, and you also need to report the results of those analyses in your RPPR project outcomes which is a section of your progress report that is made public and is available on the NIH report site. If you're doing a NIH-defined Phase III clinical trial that also happens to be an applicable clinical trial which means, generally, it's a drug or device, an FDA-regulated drug or device study, you also need to report results of those analyses in clinicaltrials.gov. So in addition to you other study results, you need to report the results of the analyses of your primary outcome by sex or gender, race and ethnicity in clinicaltrials.gov, and that's due at the same time as all the rest of your results, within 1 year of the primary completion date.

So our next inclusion policy is our Inclusion Across the Lifespan policy, and this policy requires that individuals of all ages must be included in NIH human subjects research unless there are scientific or ethical reasons not to do so. So this was an expansion of our inclusion of children policy, and the requirement now has extended to older adults and to the entire population, but if you're going to exclude people based on age, you need to have a reason based on science or an ethical or safety concern for them not to be included in that study. Again, for example, if you're studying pediatric cancer, and you don't have older adults in the study, that's okay. The condition does not occur in that group. And I also want to emphasize that if there are specific groups that are at higher risk, there's a scientific reason to study a specific group, that's okay,

but you do need to justify it, and that justification needs to be based on the science or ethics. I have had an investigator say, "I don't work with children. I don't know anything about them, so I'm not going to include them in my study. Is that okay?" The answer is no. That sounds a lot to me like convenience, so I need something else to know that children should not be in your study. We would expect in that case that you would reach out perhaps to pediatricians or other groups and make sure that you have the study expertise to work with children, unless there was some other reason that children should not be in that study. There's some additional progress report requirements under the Inclusion Across the Lifespan policy. I should mention this applies to applications that were submitted for due dates January 25th, 2019 or later. So if you submitted an application, and it's been funded after that date, this applies to you, that in your progress report, you need to submit individual-level participant data on sex or gender, race, ethnicity and age at enrollment. So this is your Inclusion Enrollment Report that you will submit. I'll show you what it looks like a bit later.

But before we move on, I want to do a quick knowledge check. So DeRon, if you can, bring up our first poll. I'd like to ask the audience to respond, and the first question is, cost is an acceptable reason to exclude women from an NIH clinical research study, true or false? And go ahead and answer there in the poll. Okay, why don't we go ahead and pull up the results? Great! Almost all of you got this right, okay? Cost is not an acceptable reason to exclude individuals from a study. In fact, the law specifically says that women and members of racial and ethnic minority groups cannot be excluded from a clinical research study due to cost. Very good, thank you. Okay, so moving on, let's do one other quick knowledge check to make sure you understand our policies. Children may be excluded from a study on Alzheimer's disease because the condition does not occur in children, true or false? What do you think? And for this one, I'm going to ask that you use the chat. I think our poll is not quite working for this. You can just put it in the chat. Okay. All right. Very good, I see a lot of trues in there, and you are correct. The answer is true. If the condition does not occur in that group, the Inclusion Across the Lifespan policy specifically mentions this as one reason why you can do a study in a specific group.

So I mentioned earlier that this is really a paradigm shift in that we want you to be thinking about inclusion throughout the entire course of your study, from the time you're developing an application until you get to close out. We want to make sure that inclusion is a part of your study. In terms of the specific requirements for NIH, there's requirements at the time of your grant application or proposal. You'll need to submit inclusion plans and an Inclusion Enrollment Report. That information will undergo peer review and be considered in review. If you're doing a research project grant, that's considered under both approach and additional review criteria, and then for Just-in-Time, if you need to submit any information to NIH, we may request additional information on inclusion. And then finally, when we get to your study monitoring and progress report, you'll need to update us on your cumulative enrollment progress and also any progress that you've made on your analyses by sex or gender, race and ethnicity if you're doing an NIH-defined Phase III clinical trial. Let's talk about these a little bit more in depth.

Okay. All right. So what's required when applying for funding? So if you're developing an application, you're going to need to include plans for inclusion of women and racial and ethnic minorities and plans for individuals across the lifespan. You'll also need to include the minimum and maximum age limits of participants in your study and an Inclusion Enrollment Report. So let's talk about those. So all of this information will be provided on the PHS Human Subjects and Clinical Trials Information form. The relevant information on inclusion is in section two on study population characteristics, and you can see there are questions for the different plans, for the Inclusion Enrollment Report, and you'll also specify your minimum and maximum age limits there. So in your inclusion of women and minorities plan, you'll need to include a description of the plan distribution by sex or gender, race and ethnicity, and you also need to provide a rationale for the selection. Why does the population look the way that it looks? How did you decide what the demographics of your sample should look like? And you'll also need to justify any exclusions in this section. So for example, if you are not including women in your study, you would explain why you're not including women here. You also should describe any proposed outreach programs for recruitment. So if you're working with community advisory boards, or for example, if you have certain methods of recruitment that you're using, you should provide those there. It's also helpful to provide data if you have them in terms of why you're using certain methods and how you expect to be able to reach out to various groups using those methods. And then if you're doing an NIH-defined Phase III clinical trial, you will need to include plans for analyses by sex or gender, race and ethnicity. You'll include a separate Inclusion Across the Lifespan plan, and in that plan you'll need to provide similarly a rationale for the age distribution, so describe the age of your participants. Why did you choose participants of that age group? Explain how it will contribute to the analysis and again justify any exclusions. So if your age limits are, say 16 to 40, why did you choose those age limits? Why is it important to the science that you have participants of those age groups? You'll also want to provide a description of the study team expertise and the appropriateness of the facilities for included age groups. So the purpose of the policy is not simply to include people and try to put them into a study that isn't designed for them, but you want to make sure that you have the right study team expertise to deal with these populations and also make sure that you have the appropriate facilities.

So also in your application, I mentioned, you'll provide an Inclusion Enrollment Report. So the Inclusion Enrollment Report includes both the section with specific fields and some data tables. You have a few required fields. You'll need to provide an Inclusion Enrollment Report title and indicate if you're using the existing dataset or resource, so this is, for example, if you're doing a secondary analysis study or maybe you're using a repository. This is an example of an existing dataset or resource, and so you would answer yes to that question. If you're doing a prospective study, you'll probably answer no. You indicate whether enrollment is domestic or foreign. If you are including participants both within the U.S. and outside the U.S., you'll need to provide that separate tables for those populations. Then you'll include data tables both planned and actual data tables for your planned enrollment which is usually what you provide in an

application, but if you do have actual enrollment, for example, if you are working with an existing dataset, you can provide that as well.

All right. So let's do another quick knowledge check. In the justification section of my inclusion of women and minorities plan, I should explain that the distribution of participants is based on local demographics. So what do you think, true or false? Okay, while we're answering, you're answering that, I will address, I'm sure, Polly's question. In a hospital setting that doesn't treat children, does the study still need to include children through collaboration? So, yes, if your scientific question is not limited to adults, so it really depends on the question that you're asking. All right. Let's look at the results of the poll. Okay, most of you got this right. Well, actually most of you maybe got it right. This was a bit of a trick question. So most of you said true, so my answer was a little different, tricking you guys a bit, which is false unless additional information is provided. So again, it's a bit of a trick question. You can explain the local demographics, but what we're looking for here is, what is the population that's appropriate to your study? And so this is something that we often see, and reviewers often comment on it, that the plans don't really include the rationale for the population that they're including. So in some cases, your local demographics may not be the appropriate population for your study, and you may need collaboration with other sites to be able to get the appropriate population, so keep in mind we usually expect participants to look like the people with the condition. If your local demographics don't necessarily support that, you may need collaboration plans. So unless you gave me some additional information, again, I would still need to know why did you just choose people based on your local demographics? How do we know that's okay? And you might give me something like prevalence or incidence and some evidence that people of your local demographics will actually participate in the study.

All right. So I'm going to move on. So the information that you submit in the application, as I mentioned, will all go to peer review. We have guidelines published on our website which indicates what peer reviewers are looking for when they're looking at your inclusion plans. Inclusion is considered in the score. It's reviewed both under approach and additional review of criteria for research project grants. For training and other awards, it may just need an additional review criteria. So review, besides including considering it in the score, will also consider whether each application is acceptable or unacceptable, and they do this through a series of codes that appear on your summary statement which are, as you can see here, at the bottom of the summary statement, there's codes for gender, minority and age. Each one of those will get a code. The first number just describes the population, but the second one describes whether it's acceptable or unacceptable. So you'll get an A if acceptable, a U if it's unacceptable. If you receive a U code from peer review, that application cannot be funded until any concerns are resolved, so that's something to keep in mind if you see a U code. You will likely have to provide some additional information to NIH before your study could be funded.

So let's do a quick knowledge check. For my RO1 application, peer review will consider my inclusion plans under approach and additional review criteria. True or false? All right. DeRon,

can you show us the results? Good! So you all did very well, much better on this one. Most of you answered true, so yes. For an RO1 application, inclusion plans are considered under both approach and additional review criteria, and they are factored into your overall score.

Okay, so let's talk about Just-in-Time. So you made it through peer review. Now your application has - We've asked you for some additional information because it scored above a certain threshold generally. So some things to consider in Just-in-Time, for most of you, you will not need to submit anything during Just-in-Time, if you've provided all of the required information. However, if you did get an unacceptable code in peer review because they found your plan was not acceptable, you have to resolve those concerns prior to funding, so your Institute and Centers staff will likely be reaching out to you to discuss those concerns. And then if any information that you submitted maybe was changed either due to review or programmatic concerns or adjustments or maybe something was missing, the IC may reach out to you to ask or provide that information as well.

And then, now we've gotten to the NIH award. Congratulations. So once you've been awarded, now what do you need to provide? Well, every year in your progress report, you will need to provide cumulative actual enrollment data. So you'll provide us Inclusion Enrollment Report, and you'll tell us who you've enrolled over the life of your grant, and then for some situations, there are some additional requirements. So if you're doing an NIH-defined Phase III clinical trial, you will also need to report on the status or the results of analyses by sex or gender, race and ethnicity. And as I mentioned earlier on, if you're also in an NIH-defined Phase III clinical trial and an applicable clinical trial, then you'll also need to report those results on clinicaltrials.gov within 1 year of the study's primary completion date.

And the next special situation is delayed onset studies. So these are studies where they can't be described at the time of application, so you don't have full information on them. Often you'll have a restriction on your award for delayed onset studies, and you can't start them until you get approval. So once you can describe a delayed onset study, you'll need to provide all of the information you would provide for any other study. You need to provide the full PHS Human Subjects and Clinical Trials Information form once the study can be described, and that will include all of the inclusion information I mentioned earlier. In progress reports, if you come under the Inclusion Across the Lifespan policy which means you submitted your application January 25th, 2019 or later and you were funded, you will need to provide individual-level participant data. As I mentioned, those data are on race, ethnicity, sex or gender, age at enrollment. So it looks a lot like this, like a spreadsheet. It's submitted in a CSV file and uploaded into our system which Rebecca will tell you a little bit about in the next session.

Okay, let's do another quick knowledge check. Which of the following participant characteristics does NIH require to be reported in progress reports? Select all that apply. So your options are A: sex or gender, B: disability status, C: race, D: ethnicity, E: primary language and F: age at enrollment. So again, you'll select all that apply here. Oh, it only allows one answer, Daniel? Oh, okay. Well, thanks. All right. Well, you know what? You can put it in the chat if you want. I know

it's quite a bit. All right. So why don't I just move to the answer then? DeRon, you can close out the poll. Thank you. So you need to include sex or gender, race, ethnicity and age at enrollment, not quite all of the above, Rosie. These two here, disability status and primary language, you do not need to provide for the purposes of the inclusion policy, but you do need to include sex or gender, race, ethnicity and age at enrollment. Okay. All right. So thanks, all of you. All right. Let's do another. Let's test your knowledge again, this time with a case study. I'm going to ask you to put on the hat of an NIH peer reviewer, and you tell me what you think about these situations, if you're a thumbs up or a thumbs down, I think, in your poll. Your answers will be yes or no. So if it's thumbs up, you can put out a yes. If it's a no, you can put a thumbs down. So our first case study, a research proposes a study investigating risk factors for eating disorders that will exclude males because the prevalence of eating disorders is lower in males than females. Yes or no, what do you think? If only peer review were this simple, I know, but we're simplifying it for today. And feel free to comment in the chat if you have a maybe answer. Okay, no. Okay, very good, right? So I like, Daniel, how you put it, "Lower does not mean nonexistent, and reporting is really bad in males, so it's probably underrepresented." Something that I keep in mind when I'm thinking about inclusion is, who's going to benefit ultimately from this information, and will there be gaps, right? So yes, the prevalence of eating disorders is lower in males, but that doesn't mean that it doesn't exist, and so I would need some kind of stronger justification than just this if I were going to exclude males from a study. And, Alex, you said, "What if, in this case, the justification has to do with something other than prevalence, different age of onset?" So this is an important point, Alex, and one of the conditions in which you can exclude populations is if a separate study is preferable and warranted. So the investigator may be able to make a case that a separate study in males is preferable and warranted because maybe the age of onset is different. Maybe the symptoms are different in severity. I don't know eating disorders, isn't my field. Yes, so absolutely the investigator can make that case. They haven't done it here, but they could make this better. Okay, let's try another one. Okay, so I give that one a thumbs down. Let's go to case study two. All right, DeRon. You can put this one up. So in case study two, a researcher proposes a study for a new drug that will exclude individuals over 60 because of the likelihood of hypertension in this age group. Yes or no, what do you think as our peer reviewer? And I will say don't assume any other information in these, just what's provided. Okay, this one is evenly split, yes or no, and I'm not surprised to see that. So I will say if I just saw this, I'm going to say no. Know why? So is hypertension a reason to exclude someone from a study? Well, certainly there are many studies for which it's appropriate, if there's a safety concern. The problem here is we're making an assumption that every individual over 60 has hypertension, right? What else could you do? Can anyone think of something else you could do besides excluding everyone over 60? How else could you think about this? Maybe you could exclude people with a certain blood pressure, right? You could do screening, exactly. So this is something to think about, and there may be cases where this would be appropriate, but I would suggest, based on this information, my preference would be that you do some screening of individuals. Not everyone over 60 has hypertension, and there are certainly people under 60 who do. So think about the people that

you really do need to exclude and try to make your criteria as close to that as possible rather than using age or something else as a proxy. Okay, so great job on that one. Okay, now let's go to our last case study, and, DeRon, you can put up our last poll. A researcher proposes a study of glycemic control in adolescents and young adults 13 to 24. Other ages will be excluded because the study will target individuals at a unique developmental stage with higher risk of poor glycemic control than other age groups. What do you think, as the peer reviewer? Is including only individuals 13 to 24 appropriate here, yes or no? Okay, great! I'm very happy to see almost all of you got this right. Yes. What's different? Why? Why is this one okay and the other one wasn't? In this case, because a separate, right, they've provided a justification that a separate study is preferable and warranted in this group, and they've given us some information based on the science of why we need a study in this specific group. So they provided a justification where in others' cases, they haven't. I will say sometimes we think reviewers can just assume that a study may be appropriate or not, or they'll understand. Don't make assumptions, write your justification down in your inclusion plan. You don't have a page limit there so spell it out, so that they understand why you're including the groups that you're including.

Okay, so let's move on then from the case studies. I did want to make - Before we go to Q&A, I did want to give you all some resources when you're writing your inclusion plans and some things to think about. We had an Inclusion Across the Lifespan Two workshop back on September 2nd, 2020, and in that workshop we identified a number of recurrent themes of, kind of common sticking points for inclusion and things that could make inclusion better, and these are things that I think are helpful to think about as you're writing your inclusion plans. First is limiting inclusion and exclusion criteria are often a barrier to inclusion. So as we gave the example, instead of excluding individuals over 60, maybe you need to exclude individuals with hypertension or with certain measurements. So that's something to think about and also thinking about weighing the risks of exclusion versus participation. Yes, children are considered a vulnerable population. We need to make sure that we have protections in place when we include children. However, we also need to consider that if we don't include children, we're not going to understand how our knowledge applies to that group and eventually how treatments work in that group if they're not included, and so we need to make sure this is considered. Also, when you're designing your study, think about maybe your participants' experience in that study and caregivers' experience and thinking about minimizing participant and caregiver burden. It can be hard, as someone who's been a clinical trial participant and a caregiver of a participant, when you have multiple study visits, multiple procedures. These are the kinds of things we need to think about in terms of, how can we minimize the burden to the participant and to their caregivers? Also consider there's diversity within populations, and so groups are not a monolith. It's really important to have relationships with your local community and understand their individual needs and assessing and adjusting your recruitment and retention. So I would highly encourage you all to make sure that you're monitoring enrollment over the course of your study, not just once a year but regularly taking a look at it and thinking about, is

this okay? Do we need to make adjustments or change course? And then finally they recommended researcher training and resources which today is one example of that. I also want to point you to our NIH inclusion data. So we take all the data that you provide us every year, and we aggregate it all, and we provide it for the public and for Congress on our NIH report site. We also provide this by research disease or condition. So I encourage you all to take a look at it if you're interested, and you can see who's included in NIH research. Finally, I want to point you to some resources before we get into the Q&A. Please take a look at our website. We have links to training, many resource documents. One document I want to point, in particular if you're developing an application, is on resources on the recruitment and retention of women, racial and ethnic minorities and individuals across the lifespan, where we've taken a number of resources across NIH that are available to investigators to help you think about these issues. Thank you.

Rebecca Favor: All right. Thank you very much, Dawn, for that very informative presentation. So we have quite a few questions in the chat or in the Q&A box. So I'll go ahead and read some of those so we can get started. The first question is, how do you determine who falls into the racial and ethnic minority group category?

Dawn Corbett: Yeah, so for NIH, we use the OMB categories which are mandated by the Office of Management and Budget for all federal agencies to use. So in terms of what you report to us, the categories that are considered racial and ethnic minority categories are American Indian or Alaskan Native, Black or African-American, Native Hawaiian or other Pacific Islander and Asian. So those are the categories provided. I will say that depending on the context that you're working, those may not be the most relevant categories to you, and it's always fine to collect more granular data as long as you aggregate those into our categories, and you can use fragmented subpopulations with which you may be working in your Inclusion Enrollment Report comment.

Rebecca Favor: Okay, great.

Dawn Corbett: I should also mention the categories are currently under review by the OMB. So there may be some updates, so stay tuned.

Rebecca Favor: That's good to know. Thank you, Dawn. All right. The next question is, how do you report or what do you report - Do you report sex at birth or do you report gender identity or both in your Inclusion Enrollment Report?

Dawn Corbett: So our policy gives you a lot of flexibility to report the information that's most important in the context of your study. So you're actually - You can report either sex or gender, and in terms of the time point at which you report that, that's really up to you. We don't specify it has to be gender at enrollment or that kind of thing. So you can set that based on the needs of your study and report it to us in the categories that we provide.

Rebecca Favor: Thank you. Along the same lines, there were a few questions related to more gender-inclusive definitions, and so for example, people who are nonbinary, both how they should report that and also kind of just what NIH's thoughts are at the moment.

Dawn Corbett: All right. And so we certainly have been hearing a lot of feedback about this, and there's been feedback across federal agencies. I know NSF has been working on this as well, and so we've been working with our federal partners in thinking about the best way that we can answer, we can ask these questions and get the information that we need. For now, if you are nonbinary, if an individual identifies as nonbinary, there's a couple of different ways that investigators usually use to report those individuals on our forms. One is if you're collecting sex assigned at birth, for example, you can report the sex assigned at birth of that individual. If you're reporting gender, and that individual does not identify with the female or male categories, you can include those in the unknown or not reported for now.

Rebecca Favor: Okay, thank you. And what you mentioned about having the IER comment there, that might be another way for them to specify, if they expect that there's a large number of people that identified that way, so thank you. The next set of questions, generally there were several questions about kind of what to do if your local population is not particularly diverse. So what would be something that researchers can do in that situation?

Dawn Corbett: So if your local population is not very diverse, or the clinic that you're working at or the university medical center does not have a diverse population, you're probably going to need to establish plans for collaboration. There are a lot of different ways to look at this. It kind of boils down to tapping into community leaders, either in your local geographic area or elsewhere, and you - that may mean partnering, for example, with another university. It may be partnering with a clinic somewhere else. So it kind of depends, but I encourage you to reach out to individuals within your institution to get a sense of who you might partner with and also to your NIH program officer. This is something that you can talk to them about as well. In addition to that, I'll mention we do have a number of resources on our website which you can take a look at which might give you some ideas about how to go about doing that outreach.

Rebecca Favor: Okay, great. Thank you, Dawn. All right. We have another question that asks, does NIH envision that in specific situations, researchers are encouraged to include prisoners?

Dawn Corbett: So I think certainly NIH supports research on prisoners, and I think there are study questions that are unique to prison populations. That being said, there are special protections in place for prisoners, and you need to make sure that those are followed. So, yes, there's no reason not to include prisoners in your study unless there was a concern, but you do need to keep in mind that there's special permission needed. There's special protections that are going to apply.

Rebecca Favor: Okay, great. Thank you.

Dawn Corbett: Sure. I will just use that question just to plug that because special protections apply to a population is not necessarily reason to exclude that population. We generally, for

example, in excluding children, maybe it's a little harder to get consent, but there are ways to do that, and again, we have some resources on our website to help. Individuals, for example, with mental illness, there are ways to consent individuals with mental illness, and so I would really encourage you, before excluding groups of people because they have special protections, to look into see if your study can address those special protections.

Rebecca Favor: Okay, great. Thank you for that addition. So we had a few questions about studies that involve cohorts. This particular question is that if a cohort is an established cohort from a previously funded NIH study, but only part of that cohort is being included in a proposed study, is that an existing dataset or resource, or is that considered not to be?

Dawn Corbett: Yeah, they can get pretty complicated. I don't want to give you kind of a one pat answer here during the talk because I need to look at your study and if you're following up with people again and that kind of thing, but often if you're just doing a type two, and it's the same cohort, it's usually not an existing dataset or resource, but again, we'd have to look at particulars there.

Rebecca Favor: Okay, thanks. And so in that case, would it be best for them to just contact their program officer for additional information? Okay.

Dawn Corbett: Yeah, yes, please talk to your program officer, and we can look at the specific case.

Rebecca Favor: Okay, sounds good. All right. So we have a question here that is about multiple studies. So the person said, "As an administrator, how do you determine if you need a study record for each of the studies versus having a new Inclusion Enrollment Report?"

Dawn Corbett: Well, I think Rebecca might be touching on this a bit in our next talk, but what I will say is you can have multiple Inclusion Enrollment Reports on a single study. We may see this, for example, in a study that involves mothers and children. You may want to monitor them separately, and so you have one table for mothers and one for children. I always tell people, "Can you fill out the form completely and accurately?" And when you get to the point that you can't do that, that's probably a good indication you need a new study record. So if it really is a truly separate study, and you can't provide accurate information on the form because you can't fill out all those fields in the same way for both studies, then you'll probably need another study record.

Rebecca Favor: Okay, great. Thank you. So one more question here, this is actually similar to one of the local population questions, but this is a little different. So what is the policy if risk is far less in one group versus another, and so there's difficulty in enrolling participants in one group versus another on a study that's already occurring?

Dawn Corbett: So I - It's a pretty broad question, so I'm not sure how well I can address that. What I will say is your IRB will - I think I would talk to your IRB if there's concerns about risk to your participants, but risk may or may not be a barrier to participation, and I think one thing that we always want investigators to do is to be minimizing that risk. But I'm not sure if I

understand the question. Rebecca, feel free to chime in, if you think there's something that I missed.

Rebecca Favor: Sure. I think that the person might be kind of alluding to what to do if they have low enrollment in a particular group during - while a study is occurring because they're not meeting their enrollment targets as they should.

Dawn Corbett: I see. So if one - if a certain - If you're not meeting your enrollment targets in a certain group, what can you do?

Rebecca Favor: Right.

Dawn Corbett: So if you're not meeting your enrollment targets in a certain group, I think ideally this is something that is addressed during study design. It's a lot easier to address it at that point. However, there are times that the best-laid plans of mice and men don't always go the way that we think. I would encourage you to reach out to your program officer to talk about what you could do. You also want to make sure that you're working with your IRB if you're going to be, for example, adding sites or new cohorts or that kind of thing, but again, at that time, there's a couple things that I've seen. One is you may need to establish a new collaboration if you're not able to recruit the population you need with the population that you had anticipated recruiting from. Another - Sometimes people will hire consultants, and those can often be very helpful, to help them strategize and come up with ideas or execute programs for outreach to diverse populations.

Rebecca Favor: Okay, thank you. So I think we have time for maybe one more question, and so we had a couple of people ask about consequences for not meeting your enrollment targets. Is there a way that researchers are held accountable?

Dawn Corbett: Yes, so your enrollment targets are part of your terms and conditions of award, and as I mentioned, in your progress report every year, you'll need to report your actual enrollment. While different ICs have different policies and ways of looking at this, the bottom line is absolutely if you're not meeting your enrollment targets, NIH can take a number of enforcement actions. Usually the first action will be talking to you and finding out what's going on, maybe seeing what we can do to change things, but for continued or serious problems, it can get as serious, for example, suspension of an award or funding.

Rebecca Favor: Okay, thanks. And then I think we have time for one more final quick question. Is there any flexibility related to the policies when it comes to feasibility or pilot studies?

Dawn Corbett: Well, there's not flexibility in the sense that the policy applies to everyone, right, and so I think your program officer is always going to be looking at your population, and peer review will be looking at your population in the context of the scientific question that you are asking, and so the context is going to be different perhaps for a pilot study or a feasibility study than an NIH-defined Phase III clinical trial. So that will be part of the consideration, but the bottom line is it needs to be justified in the context of the science, and that requirement is the same for all studies.

Rebecca Favor: Okay. Thank you very much, Dawn, and thank you to everyone for participating in this presentation. Remember that the PowerPoint and the related resources are available in two locations for you. The first is on the Grants NIH Conference website and then also inside the Virtual NIH Grants Conference Center. You can look for the Human Subjects Research Pre-Con event page for that. So now we're going to take a 15-minute break which will allow you to stretch, refresh or visit the Human Subjects Research booth along with others from all of our other awarding institutes and centers. That'll be in the Virtual Exhibit Hall, and there's also some available resources and helpful information that you can add and save to your swag bag. Thanks, everyone.