Lyndi Lahl: So welcome to today's session. Thank you very much for taking the time out of your busy schedule to join us for day one of our 2-day event focusing on human subjects research: policy, clinical trials and inclusion. Our presenters are looking forward to spending time with you over the next 2 days, and we hope that you are going to leave with a better understanding of the HHS regulations and the NIH policies as well as processes, guidance and resources. NIH is pleased to share the stage with our HHS colleagues in the Office for Human Research Protections, which is also known as OHRP. Now, before I formally introduce our presenters, I'd like to share a few housekeeping logistics. Today's session is going to take place over 4 hours, and we will be ending at 4 p.m. East Coast Time. When you log off, you're going to see a quick feedback form pop up. It should take less than a minute for you to complete the form, and it would be very valuable for us in our planning team as we strive to improve the quality and content of our virtual events. Now, during today's live session, we have numerous opportunities for you to be part of the discussion. All questions that you have should be submitted in the Q&A box for our presenters. We're going to try to answer as many questions as we can, but there are going to be literally over 1,000 of you, and we're going to have limited time to answer those questions. We do have saved time at the end of every presentation to try to get to all of your questions, and in addition, tomorrow afternoon, we have an extended period of time with our entire panel of HHS and NIH experts that are going to be ready to dive deeper into the questions that you still have. Now, to help us identify the most relevant questions for those of you in our audience, we invite you to use the thumbs-up feature in the Q&A to up-vote any questions that are also of interest to you. We do have the chat feature that will be open throughout the presentations. It should be used to share comments and answer questions that the presenters may pose to the audience, but this is not where you should be putting your questions in to the presenters. Now, some people find the chat distracting, so if you find the chat distracting, you can just click the little arrow next to the chat tab in the navigation, "Turn off notifications," or you can also minimize the chat box. So you can find all of the PowerPoint presentations in the NIH Grants Conference website and in the NIH Grants Conference event center once you're logged in, so just look for the precon event tab in the human subjects research link, and we'll be sharing that link in the chat periodically. Now, to answer our most frequent questions, will there be a recording? Absolutely, yes. We are recording, and that will be posted in approximately 7 to 10 business days, and it's going to be in the same location as the conference site. Now, our day together today consists of four engaging presentations with Q&As at the end of the sessions as well as a couple of breaks along the way. Our OHRP experts will be presenting on, "How do You Know if a Research Study is Human Subjects Research, and What Does That Really Mean?" and "What You Need to Know About FWAs and IRBs to Get Your Grant Money." And then the second half of our day, we have an NIH expert that will share "An Overview of NIH Policies on Human Subjects" and "Essentials of Single IRB Requirements." Now, this is just a reminder, this is a live event, so we ask that all attendees be respectful to one another in the chat. Please don't enter specific names of people or complaints in the chat. However, we do want your feedback, so if you would like to provide information to us about things that are of concern, please e-mail our team at nihgrantsevents@nih.gov. And that will be put in the chat so you have that e-mail address if you need it. And finally, we hope that you will also be able to join us tomorrow for day two of this event, which is going to run from 12 to 4 p.m. Eastern Time, and it's going to cover clinical trials, diversity and inclusion in human subject research, and at 3:15 p.m., we're looking forward to our continuing conversation with all of you as we bring together our entire panel of NIH and OHRP experts who have presented during this 2-day event for a live Q&A, so don't miss that valuable opportunity tomorrow. Now, we would like to find out a little bit more about the folks that have joined us today, so I want to take a moment for a couple of polling questions. So the first question is, what is your primary role? And then the second question is, what is your experience level? So if you can take just a moment and answer those two questions, that will be helpful to us, so we have a better understanding of the folks that have joined us today. Okay, and it looks like most people's primary role that are with us today are administrative. We have then the second-most, science and programmatic, and then the third is other. So there's a mix. And then what's your experience level? It looks like the majority have more than 5 years experience, and then about a third of you have between 1 and 5 years experience, and then it's split between the rest of them. So thank you very much for your answers in the poll. Now, we know that you're anxious for the main presentations, so I'm going to go ahead and get started. So thank you for joining today's presentation on, how do I know if a research study is human subjects research, and what does that really mean? My name is Lyndi Lahl, and I'm your moderator for today's presentation. I'm the Human Subjects Officer in the Division of Human Subjects Research, which is located within the NIH Office of Extramural Research. I am very please to introduce to you our experts for this presentation who are from the US Department of Health and Human Services, OHRP. So presenting on this topic this afternoon is Ms. Marianna Azar. She is a Public Health Program Specialist from the Division of Education and Development located in the HHS Office for Human Research Protections, which is commonly referred to as OHRP. And joining Marianna for the live Q&A that follows will be Dr. Yvonne Lau. She's the Director of Division of Education and Development in the HHS Office for Human Research Protections. Now, during the next hour, Marianna will be covering some important elements of HHS regulations as they relate to human subjects research and has developed some wonderful scenarios to test your knowledge. This time frame will also include the Q&A portion so we can help get your questions answered. So, Marianna, I'm going to turn this over to you now. Thank you.

Marianna Azar: Thank you so much, Lyndi. Okay. So before we jump into the content, a brief disclaimer that any expressed opinions are my own and do not necessarily reflect the viewpoints or policies of HHS or OHRP. You'll also note that there are going to be several regulatory references made throughout this presentation. For a complete and accurate description of the regulatory requirements, please consult the complete text of the revised Common Rule, which can be found at the link provided on this slide. Okay. Our learning objectives for today are to outline the regulatory definitions for research and human subject and then explain what makes a study human subjects research under the Common Rule regulatory requirements. We'll also go over the conditions for exemption of some human subjects research from the Common Rule regulatory requirements and explain the flexibilities that exemption offers. Okay, so what are the Common Rule regulatory requirements, and when do they actually apply? Well, the regulatory requirements apply when a project is nonexempt human subjects research, which, among other things, means that the human subjects research is required to undergo IRB review according to the regulatory requirements and criteria and that informed consent, unless the criteria for an alteration or waiver can be satisfied, must be sought and documented in accordance with the regulatory requirements. In contrast, the Common Rule regulatory requirements typically do not apply when a project is either not research, not human subjects research or the project is human subjects research but is otherwise determined exempt human subjects research. Now, when we determine that a project is exempt from the Common Rule regulatory requirements, investigators and institutions have flexibilities in the way that they conduct their human subjects research, but even with these flexibilities, the ethical responsibility for protecting the rights and welfare of research participants still remains, and I'll say a lot more about all of these concepts throughout this presentation. So having established that, how do you determine if your project is nonexempt human subjects research? Well, to do so, you need to ask these questions, and I cannot stress this enough, you need to ask them in this order while keeping the regulatory definition for each of these terms in mind, and the questions are, does my activity involve research? If yes, does my research involve human subjects? If yes, is my human subjects research exempt from the Common Rule regulatory requirements? Now, I just said that you need to ask these questions and consider these terms in accordance with the regulatory definitions, so let's now take a look at what these regulatory definitions are. The Common Rule defines research as a systematic investigation, including research development, testing and evaluation designed to develop or contribute to generalizable knowledge. The key words in this definition are systematic investigation and designed to develop or contribute to generalizable knowledge. So what do these things typically mean? Well, when we are conducting a systematic investigation, we might be employing some kind of method to our data collection. There would also likely be a hypothesis behind our investigation, and we probably have plans to systematically collect and analyze our data, and when we talk about an activity that is designed to develop or contribute to generalizable knowledge, we might be talking about drawing general conclusions about our investigation and presenting our findings at a conference or publishing them in an academic journal or promulgating our conclusions in any other number of ways. Now, note that not presenting or not publishing something would not necessarily make the activity a nonresearch activity, so keep that point in mind as we go through our examples. Okay, so let's now take a look at our first example and ask if it is research. So a team of physicians sees a patient with an unusual combination of symptoms. They run a variety of diagnostic tests and procedures, but the results do not yield a known diagnosis. Our physicians write a case summary of their observations, and they submit it to a medical journal for publication. So is something like this research or a systematic investigation designed to develop or contribute to generalizable knowledge? The answer would be no because there is no systematic process to study this condition in this example. The physicians here are merely writing an account to inform the medical community about their observations, nothing more. So the publication of the findings, just like the nonpublication or presentation of findings, does not make this a research activity because the two are not linked or mutually dependent. All right. What about this example? A group of physicians identifies several patients with similar disease presentations. Our physicians have a hypothesis: These patients all suffer from the same disease. Now, to test their hypothesis, our physicians plan to systematically review these cases to identify characteristics and commonalities that would help them better understand this disease. This understanding would allow them to contribute to generalizable knowledge about this disease. Now, I've likely already given away the answer to this question, but is something like this research? Yes, this is likely research because there is a hypothesis or a research question, a plan to systematically collect and analyze the data, and the activity will add information and contribute to generalizable knowledge about the disease or medical condition. Now, I also want to briefly note that the Common Rule details four types of activities that are deemed not research activities. The important thing to note about these activities is that they refer to types of activities and not to entire disciplines. This can be academic, medical or other kind of disciplines. Each of these activities is clearly described and includes specific stipulations that must be satisfied. Now, as the NIH typically funds research activities, I will not go into these four types of nonresearch activities in further detail here, but I do encourage you to view OHRP's webinars on the basics of the Common Rule to learn more about this topic. A link to this webinar will be provided in the final slides of this presentation. All right. So having defined research, how do we define human subject? Well, a human subject is defined in the regulations as a living individual about whom an investigator conducting research obtains information or biospecimens through interventions or interaction with the individual and uses, studies or analyzes the information or biospecimens, or research could also involve human subjects if an investigator obtains, uses, studies, analyzes or generates private information or identifiable biospecimens about a living individual. Now, there's a lot in this definition, so let's unpack it a bit by looking at the terms and concepts that are associated with it. An intervention, as part of this definition, would include physical procedures by which information or biospecimens are gathered. For example, venipuncture or an elevation of room temperature in a study designed to gauge the impact of temperature on academic performance could constitute research interventions. Now, an interaction would include communication or interpersonal contact between the investigator and the research subject. This can be in the form of an interview, a focus group or another form of communication through which the researcher obtains information about the research participant. So what is an example of human subjects research that involves an interaction? Well, say that researchers introduce a novel science curriculum for first-year medical students for research purposes. The researchers in this example are studying the impact of novel curriculums on medical student performance and degree completion rates, and they plan to evaluate identifiable graduation data to gauge the impact of this novel curriculum. Now, the novel curriculum here is introduced for the purposes of research in this example, so the novel curriculum is the research intervention. This type of research also involves use of identifiable private data to gauge the impact of the research intervention, and the use of this private identifiable data for research purposes would also need to be considered as a research activity. Okay, what about an example of human subjects research that involves an interaction? Well, what about a case in which a researcher tests his hypothesis for why there are high resignation rates among hospital nursing staff by conducting interviews and obtaining information from former nurses about their personal experiences and the reasons for their decisions to leave their profession? This would be an example of human subjects research involving an interaction, namely in the form of the interviews our researcher would conduct with his research participants. Now, let's unpack a little bit further. What do we mean by private information? Well, by private information, we mean information about behavior that occurs in a context in which someone can reasonably expect that no observation or recording is taking place. For example, a hospital examination room in which the patient may be discussing sensitive information about herself with her physician may be a private setting in which our patient has the reasonable expectation that the discussion is not also being recorded for research purposes. Private information also includes information that has been provided by an individual for a specific purpose, so for example a sexual history questionnaire completed for one's medical record may be a form of private information which one can reasonably and understandably expect will not be made public or shared with a researcher without one's consent. Now, identifiable private information is information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information. So our sexual history questionnaire responses may be readily identifiable if they include our name, medical record number, date of birth or any other details that may allow a researcher to readily ascertain that the responses came from us. An identifiable biospecimen is similarly one for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen. So blood collected from me and labeled with my name may be an identifiable biospecimen. All right. So let's look at an example to make sense of what we just covered. So say you have a genetic researcher who is studying a possible correlation between environmental exposure and rare cancers. Our researcher reviews patient medical records at her hospital and identifies 30 individuals with documented environmental exposure to toxic dust who are currently undergoing treatment for a rare form of cancer. Our researcher has a hypothesis: The rare cancer has resulted from genetic mutations triggered by the toxic dust exposure. So our researcher wants to perform genetic sequencing on these rare tumors, so she obtains tissue samples left over from clinical procedures performed on these 30 patients. The left over samples are provided to our researcher with patient-identifying information. So in this example, you have a researcher who is obtaining both records and identifiable biospecimens. Even if the biospecimens are left over from routine clinical procedures, you have a case of human subjects research because both the data and the biospecimens are readily identifiable to the researcher and being used for research purposes. So now that you have the definitions, you can ask, are human subjects involved in my research? And to answer this question, you'll first need to consider, who is or are the human subjects in your research? Now, this is going to be the living person or persons about whom you are obtaining information or biospecimens. Now, once you establish that, consider if you're obtaining the information or biospecimens through some type of intervention or interaction with your human participant or if you are obtaining, studying, analyzing or generating identifiable private information or identifiable biospecimens about your human participants. Note again that even without a direct intervention or interaction you can be conducting human subjects research if you obtain private information or identifiable biospecimens about a living person. So with that in mind, is the following example human subjects research? Some researchers want a better understanding of the effects COVID infection has on the respiratory system. So they conduct a detailed examination of health records and lung tissue samples from 200 deceased individuals with a diagnosis of COVID infection at the time of their death. Now, remember, we ask our questions in a specific order, so let's first ask if this is research. Yes, this is research because there is a systematic investigation here and probably contribution to generalizable knowledge stemming from the analysis of the health records and tissue samples, but is this human subjects research? Well, while the research does involve use of private identifiable information and biospecimens, this is not human subjects research because the individuals about whom the private identifiable information and biospecimens are being used for research purposes are not living, and, again, the Common Rule definition of human subject clearly stipulates that the individuals are living individuals. Okay. What about this example? Human trachea and lung cultures are purchased from a commercial entity for research purposes. The samples are sent to the researcher without any information about the individuals from whom they were collected. Now, this is research, as the example clearly states, but is this human subjects research? No, this is likely not human subjects research because the researchers cannot readily ascertain the identity of the individuals from whom the specimens were collected. These are not readily identifiable biospecimens, and so the definition for human subject is not satisfied. Okay, what about another example? What if we purchase identifiable biospecimens, such as strands of hair from famous living individuals? Well, assuming that this is done for the purposes of research, such as, let's say as in this example, genetic testing to test a research hypothesis, we can squarely say that this is a research activity, but is something like this human subjects research? Yes, this would be human subjects research because the research involves purchase of identifiable biospecimens or biospecimens for which the identity of the subject is or may readily be ascertained by the investigator. All right. What about the purchase of data? So say that a researcher purchases hospital discharge data from a commercial entity. The data includes specific clinical and demographic variables but is otherwise, quote unquote, deidentified. Now, this would likely satisfy the definition of research, but would this constitute human subjects research? No, because just like the biospecimens in the previous example, the identities of the individuals in the purchased data set are not, for the purposes of this example, readily ascertainable. Now, note that I said, quote unquote, deidentified. This is because the Common Rule does not include mention of things like deidentified, coded or any of the other common terms that are typically used in this discussion, so for the purposes of this presentation and for the purposes of the Common Rule, our focus is on identifiable private information or biospecimens, and again, this is defined as information or biospecimens for which the identity of the subject is or may readily be ascertained by the investigator. All right. What about another example in which there is obtainment of data about living individuals? So say that you have a researcher who wants to conduct secondary analysis of identifiable medical information about living individuals collected for research purposes under a different study. Now, this is research, but is this human subjects research? Yes, this would constitute human subjects research because there is analysis of identifiable private information about living individuals. The fact that the data in question in this example was collected under a different research study does not change our need to consider if the information or data satisfies the definition of human subject under the Common Rule. Now, I'm going to come back to this example later in this presentation, so do keep it mind. And finally, let's look at a more straightforward example. So let's say that a researcher arranges for biopsies to be performed for her research during surgical procedures that are performed for other clinical purposes. So this is a case in which the biopsies are specifically being performed strictly for the purposes of research. So we know that this is research because we just said that it is, but is this human subjects research? Yes, this is clearly human subjects research because you have an invasive research intervention, the biopsy, that is being performed for the purposes of some research aim. Okay. So now let's say that we've established that you're conducting research and that this research involves human subjects. What does this mean for you? Now what? Well, before we answer that question, let me just stop for a minute and offer a refresher on how we got to this point. So recall the three questions and the order in which we were told to ask them. So we start by asking if something is research, and if we answer no to that question, as we would in the example in which our physicians saw a patient with unusual symptoms and wrote up their observations as a case summary for publication, we would stop our inquiry because we would have established that the activity does not constitute research. Otherwise stated, we wouldn't go on to ask if the patient they wrote the report about was a human subject because we would have established that the activity did not constitute research. Now, on the other hand, if we were to answer yes to the question, "Is it research?" as we would have in the case in which our physicians were systematically reviewing cases of patients with similar disease presentations to identify the characteristics and commonalities about their disease, we would then go on to ask the question, are these patients human subjects? Now, if we were to answer no because, for example, our physicians would only be reviewing records that do not include identifiable information about these individual patients, we would again stop because, while our physicians are conducting research, human subjects are not involved in this research activity. Now, on the other hand, if we were to answer yes and determine that human subjects are involved, as we would in the case of our genetic researcher who was purchasing identifiable biospecimens belonging to living celebrities, only then would we go on to ask if our human subjects research might be eligible for exemption from the Common Rule regulatory requirements, and if we were to determine that our human subjects research is indeed eligible for exemption, we would again stop because the human subjects research is otherwise exempt from the Common Rule regulatory requirements, and so we don't need to ask any additional questions. Now, note that if we were to answer no to the question, "Is it exempt?" as we would likely do when considering the example in which we are performing biopsies for research purposes, we would then determine that our human subjects research is nonexempt human subjects research and that the Common Rule regulatory requirements including those for IRB review, informed consent and so forth do apply. Now, note the importance of the order in which these questions must be asked and answered. One of the most common sources of confusion stems from asking these questions out of order or not establishing if a research activity actually involves human subjects before asking if the activity is otherwise also exempt. Now, another important point that I want to make before I go on further to detail exemptions is that irrespective of whether our human subjects research is exempt or not exempt from the Common Rule regulatory requirements, we need to recognize the inherent ethical tension that is at the heart of any research that involves human participants. The research that we do is presumably done to promote the common good, but it requires research participants to achieve this goal. Now, at times it can be a challenge to manage the competing interests of our research and of course the rights and the welfare of our research participants. Now, the regulatory framework, if it is applicable to what you're doing, does provide a baseline standard for protecting participants in research, but for research that is not subject to the regulatory requirements as well as research that is and that does comply with these standards, we need to recognize that we still have an ethical responsibility to protect the rights and welfare of our research participants, and furthermore that a study that is in compliance may not necessarily be protective of participants or free from ethical concerns. Now, the reason that I stress this point is because while the Common Rule does provide flexibilities from the regulatory requirements in the form so exemption categories, researchers must be cognizant of the ethical responsibility that they have to safeguard and respect human research participants, and this is again irrespective of the level of review or the regulatory requirements that may apply to their research. Far too often, researchers equate the inapplicability of the regulatory requirements to their human subjects research as a determination that their research is somehow free from risk or that they need not concern themselves with the safety and well-being of their research participants, so what I'm trying to convey here is that we must always approach our research in ways that include ethical reasoning and consideration and not merely limit ourselves to considerations on whether the regulatory requirements do or do not apply. All right. So having established and acknowledged this ethical duty, let's now take a look more deeply at when your human subjects research might be exempt from the Common Rule regulatory requirements. Now, your human subjects research is exempt when the entire study meets the regulatory definition for human subjects research but satisfies the conditions for one or more of the eight exemption categories that are described in the Common Rule. So when we say that human subjects research is exempt, what we mean is that the entire study is excused from the typical requirements of the Common Rule, and this includes IRB review and informed consent requirements. Now, some exemption categories do require what is referred to as limited IRB review, and some also require prospective agreement or consent from participants. Now, I'm not going to go into this in this presentation, but if you do want to know more about what this means, I encourage you to check out OHRP's basics of the Common Rule webinar on exemptions, and again the link to that will be provided in the final slides of this presentation. Now, most institutions will rely on experienced individuals in the IRB or what is typically referred to as an HRPP office to make the determination that human subjects research satisfies the criteria for exemption. This is very seldom, if ever, left to individual investigators, and this is also why you would generally submit your human subjects research proposal to your IRB or HRPP office for review, even if you've reviewed the exemption categories and concluded that one or more of them may be applicable to the activities that you have planned. So of course when a determination is made that human subjects research is eligible for exemption from the Common Rule regulatory requirements, this does not equal the project having gone through IRB review or approval. Now, again, this is another common source of confusion for researchers, so be careful not to say that your human subjects research has been reviewed and approved by the IRB or HRPP if you've only received a determination of exemption from the IRB or HRPP office. Now, there are eight categories of research that may be eligible for exemption from the Common Rule regulatory requirements. For the purposes of this presentation and in the interest of time, I will briefly touch only on exemption four and walk you through some of the considerations that an IRB office will have in reviewing your research and considering if it is eligible for exemption under this category. Now, I focus on exemption four because it is the most commonly used exemption for secondary research, which I will say a bit more in just a minute. So if you want a more comprehensive overview of the other exemption categories as well as examples of research that may fit under each category, I again point you to our Common Rule basics webinar on exemptions. Now, note that the question of whether your human subjects research is exempt, and if so, what category of exemptions may be applicable to it is also something that you'll need to address on your NIH grant application forms. So it is important to familiarize yourself with these categories. So before I go any further, as I just said, let me stop and explain what we generally mean by secondary research. Now, when we talk about secondary research, we talk about the research use of private information or biospecimens that have been or will be collected for a purpose other than the original research use. The original purpose of the collection may be for nonresearch activities, such as blood collected for routine clinical tests, census work, education records, public health data or health care quality assurance activities. In addition, secondary research may refer to new research use of information or biospecimens that were originally collected for different research purposes. Now, secondary research is contrasted with primary research, and I'll point you to an example of this shortly. So let's take a closer look at exemption four and what it can and cannot be used for. Now, the key to exemption four is that again it is to be used for secondary research use of identifiable private information or identifiable biospecimens, and again, secondary research is research that uses information or specimens collected for different purposes other than the current research, and identifiable indicates that the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimens. Now, there's the additional caveat that the research can use identifiable private information or identifiable biospecimens if at least one of the following four criteria is met: one, the identifiable private information or biospecimens are publicly available or, two, the information is recorded by the investigator in such a manner that the identity of the human subject cannot readily be ascertained directly or through identifiers that are linked to the subject, the investigator does not contact the subject and the investigator will not reidentify subjects, or the other criteria under which exemption four may be applicable is that the researcher's use of identifiable health information is covered under HIPAA. Now, note that this criteria cannot be used for biospecimens, and lastly, the exemption four may be applicable if the research is conducted by or on behalf of a federal department or agency using government generated or government collected information obtained for nonresearch activities and federal privacy regulations apply. Okay, so now let's look at some examples and see if exemption four could apply, and let's start with our example involving the purchase of hair strands from famous living individuals. So recall that we established that this is research and that it involves human subjects, but could this research be eligible for exemption under category 4(i)? Now, again, recall that 4(i) is for identifiable private information or biospecimens that are publicly available. While our researcher does have to pay for the identifiable biospecimens in this example, the fact that they can be purchased by anyone on the public-facing website does make them publicly available, so exemption 4(i) may apply. All right. What about our prior example involving the use of identifiable medical information about living individuals that were collected for research purposes under a different study? Could our current researcher seek exemption for this secondary analysis of data collected for other research purposes under exemption category four provision two or ii? Well, recall that exemption four is for secondary research, which includes the use of information or specimens collected for different purposes, and this of course includes another research study. Exemption four is also for identifiable information or biospecimens, and this example does involve identifiable medical information about living individuals, so we can check off that box. Now, the information is not publicly available, so we can say that exemption 4(i) would not apply, but exemption 4(ii) might apply. Now, it might apply if our investigator records the information in such a manner that the identity of the human subjects cannot readily be ascertained by him, either directly or through identifiers that are linked to the subjects. Our investigator would also have to not contact the subjects or make efforts to reidentify them. So assuming that these conditions can be satisfied, this is an example of research that might be eligible for exemption under category 4(ii). Okay, what if we change the details of this example a little and see if the same research may be eligible for exemption under category 4(iii)? Okay, so in this modified example, and you'll see the changes in red, our researcher works at a HIPAA-covered entity. Now, this could be a university health system. The original research study under which the private identifiable medical information our researcher wants to use for his study was collected under a different study conducted by another researcher at this same institution. So the primary research was conducted at the same HIPAA-covered entity. Now, in this modified example, could the research be eligible for exemption under category 4(iii)? It's possible, yes, because 4(iii) says that the researcher's use of identifiable health information is covered under HIPAA. So assuming that the research activities are regulated by HIPAA in our example, exemption 4(iii) would allow for the secondary research use of identifiable medical information collected under another study. All right. Let's look at another example, and this time one that involves biospecimens. Now, recall our earlier example of the genetic researcher who obtains identifiable biospecimens that are left over from routine clinical procedures. Our researcher wants to perform genetic sequencing on these samples because they come from 30 individuals with documented environmental exposure to toxic dust who are being treated for a rare form of cancer at her medical center. So could this research qualify for exemption under category 4(ii)? Well, again, it depends, and it depends on whether our researcher could record the information about the biospecimens in such a manner that the identities of the human subjects would not be readily ascertained to her. We don't have enough information here to clearly say that this is the type of research where identifiable information is not needed or where the identities would not be readily ascertainable to the researcher. So this is an example that demonstrates that the devil is always in the details. And what if we were to modify the example that we just looked at and say that our genetic researcher works at a HIPAA-covered entity? Would her research then be eligible for exemption under category 4(iii)? No, because again, recall that category 4(iii) is for information and not for biospecimens, and this example explicitly involves the use of biospecimens. All right. Now what about an example in which a researcher arranges for biopsies to be performed for her research during routine clinical procedures? Now, she does receive the samples with codes, which in theory could mean that the identities of the subjects are not readily ascertainable to her. So is this the type of research that might be eligible for exemption under category four? No, because this is an example in which biopsies are being performed for the purposes of research, so this is an example of primary research. So not only is this not secondary research because the biospecimens are being collected specifically for the research in question, this is also not the type of research that is generally eligible for exemption under any of the exemption categories. This type of research would likely be covered by the Common Rule regulatory requirements and would likely undergo IRB review and include requirements for informed consent from the living individuals on whom these research biopsies would be performed. Now, we've covered a wide variety of examples in this presentation, but of course there's a lot more that goes into considering if your project entails research, if it involves human subjects and if it is eligible for exemption from the Common Rule regulatory requirements. One resource that will help you navigate through these questions is the OHRP human subjects regulations decision charts. These are available on the OHRP website, and the link is provided on this slide, and I did see a number of people asking if slides will be available after these presentations, and my understanding is that, yes, you will have access to these slides. Now, I referenced these videos all throughout, and I now want to say that this is where that link is provided. So for a deeper dive on the topics that we covered, I do recommend checking out OHRP's educational videos, which can be found under our online education - videos tab under the division of education section of the OHRP website. Specifically, again, be sure to watch the basics of the Common Rule featured videos which offer a much deeper dive into the Common Rule regulatory requirements, the basic terms that are used in the Common Rule and the comprehensive overview of the exemption categories and requirements. Now, as you also may be aware, the NIH does require completion of training for all key personnel that are engaged in human subjects research. If you haven't done so already, be sure to complete OHRP's human research protection training, which includes five self-study lessons and the completion certificate that is generated at the end of each lesson. Now, note that OHRP does not keep track of who completes this training, so if you misplace your certificate we will not be able to reproduce it for you, so I'm saying that to say when you complete your training be sure to hold onto that certificate. Now, we also now offer two and soon to be three interactive training programs on IRB review criteria and considerations. So as researchers, if you are researchers, you will find that these interactive programs offer insight into the way that IRBs review human subjects research and consider the review criteria for project approval. Now, last but not least, I also want to point you to our e-mail address where you can send your questions about the Common Rule and other related topics, and a link to our website is also provided on this slide. Now, I also wanted to very briefly mention our About Research Participation page, which includes information, resources about research and research participation. All of these resources are written in very plain language. They're all translated into Spanish, and they were all developed with the general public in mind. Now, I talked a lot about ethical responsibilities and respecting our research participants, and I would say that part of that includes educating our prospective research participants about the concept of research and research participation. So if you are firmly committed to that, as we all are, the use of these tools can be a starting point in this endeavor. And with that, I thank you for your time, and I look forward to answering your questions in the time that we have left.

Lyndi Lahl: Thank you, Marianna. This was a great presentation. We really appreciate you sharing your expertise. Right now I would like to welcome back Dr. Yvonne Lau as well so we can answer some of the numerous questions that everyone asked during their presentation. So if you have additional questions, please go ahead and enter them into the Q and A, but we're going to go ahead and get started here on some of these questions. So there was a question, can an exempt study still be reviewed and approved by an IRB?

Marianna Azar: So, again, assuming that limited IRB review does not apply, and I also want to stress that limited IRB review is not the same as IRB review, an exemption determination is a determination that the Common Rule regulatory requirements do not apply to your human subjects research. IRB review is performed for consideration of the Common Rule regulatory requirements. So typically it's one or the other. Now, an IRB can review a study and make a determination that the study is otherwise eligible for exemption, but if an exemption determination has already been made, it would not make sense for the study to then go on to the IRB for review under the Common Rule regulatory requirements.

Lyndi Lahl: Okay. Thank you very much, Marianna. Another question ...

Marianna Azar: Lyndi, I think Yvonne wanted to add to that.

Lyndi Lahl: Oh, I'm sorry. Go ahead, Yvonne.

Yvonne Lau: Sorry. I just wanted to say that the exemption categories in the Common Rule are provided as a way of making research more convenient for researchers. They are seen as a kind of a flexibility, and if you have an exemption, then you don't, in theory, have to follow all the strict regulatory requirements for IRB review, informed consent. Again, that doesn't mean that investigators and institutions cannot go ahead and still expect some level of oversight or some level of contacting participants to make sure that they are happy with participating, things like that. So those two things are different.

Lyndi Lahl: Thank you, Yvonne. There seemed to be a number of people that have been asking about exemption. So one of the questions is, who makes the exemption determination prior to IRB review? Are there any regulatory requirements or best practice that you can speak to?

Marianna Azar: Yeah, so as I did mention in the presentation, this determination is very seldom left to individual investigators. Now, the Common Rule does not specify who must conduct and make the determination that exemption does apply, but common practice, best practice is that someone who is experienced and trained and knowledgeable in the exemption categories and all the nuances that are associated with each one would make that determination within an institution. So if you are at a university, you might have an IRB or an HRPP office, and within that office, you may have staff that are labeled as HRPP staff or IRB staff who would generally make this kind of determination. Some institutions do rely on individuals who serve as IRB members to make the exemption determinations, but again, I want to stress that making an exemption determination is not conducting IRB review, and, moreover, given the way that this question was phrased, that once you've made that exemption determination, the project does not then go on to IRB review. Lyndi, you're muted.

Lyndi Lahl: Okay. There. So sticking along the lines of exemption, one more question. So if you have an institution that is research-naive, they don't have an IRB, and they're not even sure if human subjects will be involved or if it's an exempt human subjects research study, do you have any recommendations on how they would go about making that determination themselves, or should they be reaching out to somebody else?

Marianna Azar: Yvonne, you want to take this one?

Yvonne Lau: Well, first of all, I'm a little bit worried that if the institution really has so little experience, the question of whether the institution ought to be engaging in human subjects research. I think that's something to think about. I want to just go back, and there's always a start somewhere. So I think to begin with, I guess if you have institutions are coming in new, there are ways to try and get yourself up to par so that at least you understand something about human subjects research and the regulations. Marianna, in her last few slides, mentioned the five lessons training that we have on the OHRP website. That is a set of foundational training giving you an overview of the regulations or the ethics that are involved and what human subjects research really mean. They're easy to go through, and I would really highly suggest that at least you go through that training first and then get a comprehensive understanding of what you're talking about before you actually embark on any research that really kind of involves human subjects, as Marianna has defined.

Marianna Azar: And it occurred to me that we did not mention that this training is free. It is free. You can access it without any associated payment, which I know may be an issue for institutions that do not generally conduct research. They may not have resources for this purpose.

Yvonne Lau: It doesn't mean that you're going to become an expert, right? It takes experience. It takes coming to these classes and so on, and OHRP does actually, anything that OHRP offers online in particular, they're all free of charge, and you should, we have a lot of resources on our website, and if you do actually need some advice, we welcome that you write to us as well at ohrp@hhs.gov.

Lyndi Lahl: Thank you, Marianna and Yvonne. Here's another question that has to do with exempt research. Do the principles of the Belmont apply for human subjects research, even if it meets the criteria for exempt research?

Marianna Azar: Yes, the Belmont Report principles underlie the Common Rule regulatory requirements, and of course the exemption categories are outlined therein, so, yes, the respect for persons, justice, and, yes, you should absolutely be keeping in mind the ethical principles that govern human subjects research irrespective of whether your research is exempt or subject to the regulatory requirements.

Yvonne Lau: I think this may be a good time to say a little bit more about how the regulations work. The Common Rule sets a basic standard of what the minimal expectations may be, and in developing the regulations in the Common Rule, the policy makers are conscious that research actually brings a lot of common good as well, so you don't want to make it so restrictive and prescriptive, regulations being so prescriptive that it becomes very hard for researchers to do research. So there is a balance there, and the Common Rule is a set of regulatory requirements setting some basic standards of what you should meet if you're getting federal money to conduct research by complying with the Common Rule and able to comply with the Common Rule means that you are really just satisfying the basic standards of the expectations. It doesn't necessarily mean that your research has no ethical issues whatsoever, and when things are outside of the Common Rule jurisdiction, the idea that we should still try and think about research and design our research in such a way that it would be ethical is always a good idea, right, because ethics is about how we interact with people in society, and being ethical, being respectful of people, being respectful of all the principles in the Belmont Report will only help you maintain and build public trust in this research enterprise, which is so very much important in the work that we do.

Lyndi Lahl: Great. Thank you. So people continue to put Q and A in our Q and A box, so that's great. So another question: Is it exempt four research when a researcher wants to use medical record data from the medical clinics to conduct research? The records would be deidentified. For example, studying data or medical records to determine any data that could have helped to provide earlier detection of ovarian cancer. So the issue is about the use of medical records to conduct primary research.

Marianna Azar: So, again, keep in mind all the nuances of exemption four and all the conditions that would have to be satisfied, and again, I note that the Common Rule does not use the term deidentified. So it's a question of whether it would be readily identifiable. Now, it would be secondary research because the medical records will be records that were otherwise generated or created for nonresearch purposes, right? So they were created or generated in the course of medical care. So exemption four would still ... may still be applicable because this would be secondary research of information that was otherwise created for nonresearch purposes, but again, it really depends. It depends on the specifics of the case.

Lyndi Lahl: Okay. Thank you. So another question, and it's on exemption 4(ii). I always call it four-two, so good to know. So this is through identifiers linked to the subjects. So the question is, if a coinvestigator has the links to the subject to be able to readily ascertain who is who, would that be exemption four research? If it's the primary investigator does not, but somebody else on the research team does have it.

Marianna Azar: Yvonne, you want to take this one?

Yvonne Lau: So look at research project as a whole. Anybody who's working on the same research project, if they continue to be able to link the private information or biospecimens back to a living individual through whatever means, that would be considered identifiable to OHRP under the Common Rule. So in terms of exemption 4(ii), notice how it's written very clearly that you need to strip the materials of the identifiers that you will not, you have to actually promise, not to go back and contact people. So that separation is quite clear. You really need to not. Everybody who's working on that research project, being on that same research team, they must not ... None of them should be able to actually link the materials back to living individuals. That's really the criterion that we look at when we determine whether it fits into the exemption or not.

Lyndi Lahl: Great. Thank you. So there are several questions that came in when, Marianna, you were doing the part about, what is research? And they were talking about quality improvement activities, and if you could kind of differentiate a little between research and what is a quality improvement activity because I think that that is something that's misunderstood.

Marianna Azar: And now I regret taking those slides out of the presentation. So I will say this, first and foremost, because I don't want my limited response here to be taken as the end-all, be-all. This question is addressed in one of those webinars that I referenced throughout my presentation in detail. So the thing to keep in mind about quality improvement or quality assurance activities is that they are not necessarily activities that don't also involve research. Otherwise stated, you could have research activities that are also inclusive of quality improvement or quality assurance activities. In other words, the two are not mutually exclusive. So the thing to keep in mind is the definition of research. If the definition of research is satisfied but you're otherwise referring to something at QI, QA, that QI, QA activity may be a QI, QA research activity.

Lyndi Lahl: Okay. Thank you. I think that the pointing them to the other presentation is also very helpful. So that's good. So somebody asked a question. Can a researcher deidentify data themselves so they can use that data later on for research that's not human subjects research?

Marianna Azar: Yvonne, you want to take an initial stab at this?

Yvonne Lau: I do not see why researchers cannot deidentify the data that they've collected from research and then hope to use this set of data in the future as not human subjects research. The key, again, is the definition of what is identifiable in the Common Rule, right? So when you say you deidentify, what exactly do you mean? In the Common Rule, we mean specifically that you will not have any means to be able to link the material back to the living individuals. Now, if you can do it in such a way and satisfy that, then, yeah, sure, but if you're thinking, "Well, I'm just calling it deidentify because I put a code. I slap a code, and I have some key somewhere, but I'm never going to look at it." Well, that's not good enough.

Lyndi Lahl: That makes sense. So somebody asked, and we have 2 minutes left. So this may be the last question. Can you do a recap of the difference between exemption and nonexempt research?

Marianna Azar: So very briefly, exempt research is research that satisfies all the conditions that are outlined within the Common Rule and satisfies one or more of the eight exemption categories. So if your research falls under one or more of the exemption categories that are outlined in the Common Rule, your research is otherwise exempt from the Common Rule regulatory requirements. Now, if your research falls outside of those exemption categories, then it may be subject to the Common Rule regulatory requirements, in which case it is subject to things like IRB review and approval and requirements for informed consent or justification for why informed consent must be altered or waived. So the threshold is, it falls under the exemption categories, or it does not.

Yvonne Lau: Yeah, I just want to reiterate what Marianna said about the exemption categories in the Common Rule. So this word exempt is not used in any way in a layperson kind of way. So by referring to something as exempt human subjects research, it means that you have first already determined that the research project is human subjects research, and then when you look at the exemption, the eight exemption categories that are available and defined in the Common Rule, that this whole human subjects research project fit into one or more categories of those exemption categories defined in the Common Rule, and if that happens, then you have a situation where you have exempt human subjects research. If you don't have a situation like that, in other words your whole research project does not fit into one or more categories of the exemption categories in the Common Rule, then you have a situation of nonexempt human subjects research, and that is when the requirements for the Common Rule, the typical regulatory requirements in the Common Rule, IRB review according to the Common Rule criteria, informed consent according to the Common Rule criteria, et cetera, kick in.

Lyndi Lahl: Great. Thank you very much. Well, we are at 1:10, which is the end of the first session, so I want to thank Yvonne and Marianna very much for joining us for this presentation. My name is Lyndi Lahl, and I am your moderator for today's presentation. I am the Human Subjects Officer in the Division of Human Subjects Research located within the NIH Office of Extramural Research. Now I'd like to take a moment to introduce you to our experts for this presentation. Dr. Yvonne Lau, who is the Director of the Division of Education and Development in the HHS Office for Human Subjects Research, will be the presenter for today's session, and joining her with the Q and A that follows this presentation is Ms. Marianna Azar, Public Health Program Specialist in the Division of Education and Development located within the HHS Office of Human Research Protections, or OHRP. Now, I know your audience is anxious to hear this information, so, Dr. Lau, it's all yours.

Yvonne Lau: Hello, everybody. I'm really excited to be here to be talking to you about this topic on FWAs and IRBs. So first of all, just some standard disclaimer, the opinions expressed here are those of mine and do not necessarily reflect the policy of the Department of Health and Human Services. I've also tried to ...Whenever I mention or refer to the regulations, I also try to simplify them for the purpose of this educational presentation. I would ask you to refer to the language in the revised Common Rule on our website for accuracy and further details. So for today's presentation, I'm going to be covering three topics, basically. So the Federalwide Assurance, FWA, what it is, when do you need it, and what are the options for institutions? I'll talk a little bit about Institutional Review Board, IRBs, and what are the general requirements under the Common Rule, and finally I'll cover a little bit on the concept of institutional engagement, what it is, and what are the implications in a cooperative human research project? Now, you would wonder, why three separate topics? I hope that by the end of this presentation you understand that they are actually very much related, and in a way also that is really important because if you have a good understanding of them, it helps you to be able to get your grant money promptly. So first of all, a bit of information about our office, the Office for Human Research Protections, OHRP. Many of you have probably heard of OHRP, but you probably don't know how we stand in relationship to NIH, FDAs, the giants and the elephants in the room, if you like. So we are also a part of the Department of Health and Human Services, just like NIH and FDA are parts of the Department of Health and Human Services. We are a very small office, and we provide the leadership in protecting human subjects in HHS-conducted or supported research. So we hold the regulatory authority for what is known as the 45 CFR part 46 set of regulations. CFR is Code of Federal Regulation. There are five subparts to this set of regulation at 45 CFR 46. Subpart A is what is known as the Common Rule. It's referred to as the Common Rule for the simple reason that this subpart which provides the basic set of standards for protecting human participants in research have been adopted pretty much across many departments and agencies in the federal government, which means that when these federal government departments and agencies provide funding to support or when they're conducting research that the requirements under subpart A, or the Common Rule, apply as well. Now, for HHS research, we also have the other subparts. Additional subparts in B to D, additional protections afforded for certain vulnerable populations, and then there is a subpart E that provides stipulations on IRB registration. So the OHRP, this office, is all about the authority and making sure that institutions within our jurisdiction are compliant with this set of regulations. The NIH, on the other hand, is a sponsor of research. Now, many of you have heard of NIH policies. Those are policies. They are slightly different and have a slightly sort of, if you like, different set of power compared to regulations, right? And then FDA is a regulator of drugs, devices, biologics, et cetera. They have a totally different function. They also have sets of regulations that protect human subjects involved in research. Their regulations are very similar to the set of regulations under the Common Rule. Now, OHRP is responsible for the regulation for human subjects for all NIH-funded nonexempt human subjects research regardless of whether that particular research is also regulated by FDA. So both the OHRP set of regulations and the FDA regulations could potentially apply to certain research. So the Common Rule regulations typically apply to nonexempt, what we called nonexempt, human subjects research. So these are human subjects research projects that do not fall into any of the exemption categories defined in the Common Rule, and when we say that the Common Rule regulations apply, that typically means that there will be IRB review done according to the regulatory requirements and criteria stipulated in the Common Rule, that informed consent, unless it's waived, needs to be obtained according to what's stipulated in the regulatory requirements, and that institution needs to have an active Federalwide Assurance, or FWA, in order to be able to get the federal money, the HHS money, to support the human subjects research and that there will also need to be certification of the IRB review and approval of the research. So let's say a little bit more about FWA. What is it? So the Federalwide Assurance is an affirmation of an institution's commitment to the Department of Health and Human Services, or other federal agents, Common Rule federal agencies, that it will adhere to the regulatory requirements at 45 CFR 46. Now, for other Common Rule regulatory agencies, if they require you to submit the FWA, it would be an assurance to adhere to the Common Rule, right? For HHS, if you're getting money from HHS, when you submit the FWA, when you file it, it will be a commitment and an assurance that you will comply with the full set of regulations at 45 CFR 46. This includes ensuring appropriate conduct of research by the agents and employees covered by your institutional FWA. Now, FWAs are filed by institutions. It is institutions that get awarded grant money to conduct research, even though it may be the investigators who are proposing the project, right? But it's actually the institutions to which the investigators belong to that actually have the responsibility and when they receive the money. So institutions that receive HHS funds to conduct, again, nonexempt human subjects research need to be covered by an FWA filed with OHRP. These institutions typically include, first of all, your so-called primary awardee. So if you are the primary awardee for a nonexempt human subjects research project, you're about to get your grant money, you need to make sure that you have an FWA filed with OHRP that is active. Now, there are a few very rare exceptions. I'm not going to go into that, but typically if you are the primary awardee doing human subjects research, you will have to have an FWA. Now, sometimes a research project, many institutions are involved in that research project, and apart from the primary awardee, there may be subawardees. Subawardee institutions who are considered engaged in human subjects research activities on that project will also need to be covered by an active FWA. So I'm hoping that you are starting to see why FWA engagement and IRBs all come together now. So let me say a little bit more about what being covered by an FWA may look like. So, first of all, the simplest way would be an institution can file its own FWA with OHRP. The FWA here, there's a hyperlink there, and it will take you to the website with all the instructions. There are videos. There are detailed instructions of how you can do that. Filing FWA with OHRP does not cost you any money. It involves the process, it's not that complicated, but you do need to make sure that you put aside time to do that, right? And typically if you're a primary awardee of a human subjects research, you probably have your own FWA. Now, in order to file an FWA with OHRP, you need to make sure that ...You'll be asked to provide information of your signatory official. A lot of people ask who that person may be, right, in an institution. This will be somebody who actually has the authority to commit the entire institutional organization named in the FWA to legally binding agreement, as you can imagine. FWA is an assurance, is a legal assurance, is a legally binding kind of agreement, right? So the signatory official is somebody usually like the chancellor, the president, the CEO, right? Somebody who is important who can commit the entire institution and who can assure compliance with the regulations. So you need to be ready, and you need to know who that signatory official is when you're ready to file the assurance. The other thing that you need to have ready when you are filing the assurance is that you need to be able to designate an IRB that is currently registered, already registered, with OHRP. So when you file the FWA, you'll be asked to provide an eight-digit IRB registration number, right? Generally, so traditionally in academic institutions, that's not usually a problem because they would have IRBs already set up in the academic institution. Often it's not just one. There are more than one, and then the question then becomes, now, which one should we designate? Right? Usually that would be the principal IRB, the main IRB that is reviewing the majority of these HHS-funded research. Now, notice that not all research in an institutions are funded by HHS or for that matter by the federal government, right? Institutions can be getting money from other organizations that have got nothing to do with the federal government. When we do these presentations with you, I want you to make sure that you understand we're always talking about and referring to HHS, for OHRP's HHS-funded and supported research, and of course most of the time this same thing would apply to many of the federally funded research as well, but not anything that is outside the federal government. So last thing I want to say about FWA here is once you've filed one, it will last you for 5 years, and at the end of that you need to renew it, and every time you come into the system and change something, that 5-year process starts again. The clock starts again. So this is one way of being covered by an FWA. You file one yourself. The institution file one themselves, right? Now, I mentioned that you need to have designated an IRB, and I mentioned that for many traditional academic institutions they would have their own. They would use their own. They set up their own. They use their own, right? So say if - I want to say a few words about IRBs. And so institution review boards under the Common Rule, it's a very well defined organization. The Common Rule has stipulations on what the IRB membership looks like, what are the IRB functions, how they will review research, what kind of criteria they need to satisfy before they could approve research, and then there are also stipulations on how you manage your records and documentations and so on. So these are all defined and described by the regulations, right? So it's kind of you need to be able to satisfy all that. It's not just any organization where I put together a few people and they agree to review research, okay? So it takes time and commitment, right, to be able to create and manage an IRB, and for institution that is really very new to getting federal funds or really just have one set of funding to conduct nonexempt human subjects research, then it's probably not worth their time to go and think about setting up one for themselves and using that. So there are other options, right? So what are the other options? Other options would be rely on an external IRB, an IRB that has not been created internally by your own institution. So what are the external IRBs that are available? So there are many commercial IRBs that you can acquire their service for the review of your research, and then you also have the option if you are very friendly and you know other academic institutions or in fact you're working and collaborating on a project with another academic institutions that have their own IRBs, or doesn't have to be academic institution, but another research institution that you already have their registered IRBs, then you can see if you can rely on these IRBs as well. Now, in order to rely on them is not just to say, "Oh, I know somebody. I know that IRB. I'm going to rely on that," and you name them on your FWA. No, you need to establish some written reliance agreement, right, with them so that they know that you're going to be relying on them, right, and that you know that you will be relying on them so everybody is clear what their responsibilities are, right? So you need to have established written reliance agreement to be able to use and rely on that external IRB. Now, in the revised Common Rule under 46.103(e), it provides you with some flexibilities as to how you set up this reliance agreement, but however you do this reliance agreement, the most important thing is that you use this opportunity to set up clear parameters as to what the institution to which you rely on would be doing and what their responsibilities are and what your own institution's responsibilities are. You want it to be very clear. Now, all this, right, needs you to plan well ahead of time, right, because as the time comes when NIH or other HHS organization tells you, "Hey, we're going to give you this grant," you want to be able to get the money as quickly as possible and to start your human subjects research, right? So you want to think about these things ahead of time so that you don't suddenly then- The time that you're about to get your money, you suddenly wonder, "Okay, now, oh, I was just told I need an FWA. Oh, what am I going to do? How am I going to do this?" So you need to kind of think about all these ahead of time. Just to add this information here at this point, and we'll come back and talk about it a little bit more. So if you happen also to be involved in a cooperative project, as many of us will be, right? Research has become very big and involving many different institutions all working and collaborating together, right? Now, under the revised Common Rule now, there is a mandate, the requirement for the use of a single IRB of record for your federally funded nonexempt human subjects research project, and there are a few exceptions, and I'm not going to go into that, and we'll come back to this topic a little bit more. So chances are that then it may come a time even if all along you might have been using your own institution's IRB, there may be a time when you might need to rely on an external single IRB for the review of the research that you're doing, right? So again, think ahead of time, know what you're involved in and plan ahead of time. So we talked about being covered by FWA, and FWA, the most direct way of doing it is to file your own, for the institution to file their own, but then there is another option, right, and it's called a collaborating individual investigators agreement, IIA. So independent investigators may come under the FWA of a collaborating institution under certain circumstances. The collaborating institution establishes a collaborating individual investigator agreement, IAA, to extend the institution's FWA to cover these investigators who are going to be doing human subjects activities. All right? So this has become more common these days, again, because as I mentioned, research projects has become a lot bigger, and then there is this real initiative to try and bring the research to participants where they are, right? So there is this interest in making use of services, health care providers, services that may be closer to where your research participants are, and when you bring those health care providers or health care agencies in, and you require them to be conducting activities that are considered human research activities, human subjects research activities, right, then those people will need to be covered by this FWA assurance. Now, obviously being individuals and not involved in federal-funded research in their usual sort of business situation, then it's very unlikely that they would want to go through all the trouble to file their own FWA or that requires having an IRB or relying on an IRB, so under those circumstances, that's usually when you might think about this kind of option. So I said that I would say a few words about the Common Rule single IRB review requirement because that is, again, it comes in - It has become much more common, the situation, and that you need to know something about this in order to be able to be prepared ahead of time when you get your federal grants money. So with few exceptions, any institution located in the US, institution located in the United States, that is engaged, right, in cooperative research for the portion of the research conducted in the US must rely on the approval of a single IRB. I bolded most of the terms that you need to pay attention to. All right? So requirement is applicable only to cooperative research projects that are nonexempt human subjects research. So you have a whole group. You have who are going to be participating in this research project. This research project has a purpose, has a design of how you're going to collect data to answer your question. Remember this is the definition of research, right? So that whole research project, you can have many institutions and maybe individual investigators who are involved in that, so that would be a kind of a cooperative research project, right? And for the single IRB review criteria to apply, we're talking about the part that is being conducted in the United States. Now collaborating institutions engaged in human subjects research must rely on the review and approval of a single IRB of record. So all those collaborators are working and participating in this nonexempt human subjects research project, and if the institutions themselves, whatever they're doing, are considered human research activities, then they are required to rely on the review and approval of that single IRB of record for the research, for their part of the research. Now, institutions obviously will have to establish reliance agreements to document the relationship and the responsibilities of each. However, each institution is still responsible for safeguarding the rights and welfare of their individual participants. So when we get to this part, you see how, right, at the beginning of the presentation when I said, "Okay, we're going to talk a little bit about institution engagement," and how that comes into this discussion and become relevant in us trying to get our grant money, right? So a little bit more about cooperative research, right? Again, just to reiterate, this refers to nonexempt human subjects research project that involves more than one institution. It's as simple as that, right? This is what cooperative research means under the Common Rule. I know that I'm not going to say anything about the NIH and how they look at it. They may have a slightly different way of seeing it under their policy, but don't forget the NIH comes under the HHS regulations, the Common Rule as well. So if you like, we are the umbrella, and this really covers it all. Now, so collaborating institutions can each be working on different parts of the research project. Collaborating institutions do not need to be doing the same things, right? So different institutions can be responsible for different parts of this research, can be doing very different things that are still part of this whole research project. They don't, it's not only when they are doing exactly the same thing would they be called collaborating ... It's not only when they're doing the same things they will actually come under this requirement. So it is possible that some collaborating institutions may only be responsible for activities that are not considered human subjects activities. For example, so for this nonexempt humans research project, there will be interactions with human participants to - and then we'll also be doing so apart from asking them questions and getting information, private information, data from them for the purpose of the research. We'll also be collecting, say some biospecimens, blood and so on for the purpose of this research. Now, this material then gets sent to, let's say institution B. Institution B investigators will only be provided the biospecimens without associated identifiable information of individuals. They would be coded, and then the institution B, their investigators are only responsible for doing the analysis of the biospecimens. They are part of the whole research project which is a human subjects research project, right, but then their part doesn't require them to have any access to identifiable materials. So you see how institution B is definitely a collaborator on this nonexempt human subjects research project, but then their part, right, does not involve human subjects activities because they're not, themselves, interacting or intervening with research participants to do anything for the research, and at the same time, they, themselves, are also not receiving any identifiable materials for the part of this research. So this institution B, the investigators are not conducting any human research activities, and their institution would be considered as not engaged in human subjects research. However, they're still part of this umbrella. All it means is that because they're not engaged, there's no activity that they're doing that needs be under the review of the single IRB. That's what it means.

So just a refresher on what human subjects activities are, right? The regulatory definition for human subject is a living individual about whom an investigator conducting research obtains information or biospecimens through an intervention or interaction. So you are collecting, interacting or you are talking to them or doing question or surveys, or you are intervening because you are conducting, you're doing biopsies or you are collecting blood specifically to support the goal of this research, right? So that's primary research. Notice that there is an "or." So if you're not doing that, but nonetheless you have access, you are being given identifiable private information or identifiable biospecimens of this research to work with, right? So either one or the other, you would be considered as doing human subjects activities. So a person, as I've already explained, a person is conducting human subjects activities when, for the purpose of the research, the person conducts any activities that fall within the above definition. For example, they're obtaining informed consent for research participation, or they're administering an intervention for the purpose of the research, or that they have access to identifiable private information of the study participants to conduct the research. So these are some of the examples of what make investigators or/and their institutions be conducting human activities.

So when is collaborating institution engaged or not in human subjects research, right? Collaborating institutions on a cooperative research project may have different engagement statuses. We have repeated that over and over. Institutional engagement depends on whether its employees and agents are conducting human research activities for the cooperative research project. We just defined what human subjects activities are. For example, a collaborator that is only doing lab tests on coded biospecimens sent to them by collaborators who collected the materials for the cooperative research, they are considered not engaged in the research. A collaborator that conducts the study interventions and collect information or biospecimens from research subjects will be considered engaged.

So what are the implications for collaborating institutions, engaged or not in human activities? Now this is all going to tie it back to my initial overview slide, right? Engaged institution, right, needs an active FWA or be covered by the FWA of your collaborating institution. It needs IRB review of the research, of that part of the research that they're doing, and typically this will be referred to that single IRB of record for the review. Institutions that are considered not engaged because their employees and agents are not doing any activities within that big project that are considered - The activities that they do are not considered to be human research activities, such as they don't have identifiers or they're not interacting, intervening with participants directly, right? Those non-engaged institution, they do not need to have FWA coverage, and they do not need to have IRB review of research. So they don't need to have to think about, "Oh, do I have realized agreements and setup, and do I have to refer to that single IRB of record and so on? Or do I even need, for that matter, to have an FWA?" They don't.

So the key take-home message for you is primary awardees for nonexempt human subjects research will need to have an active FWA to receive the HHS funds for the research. So when filing an FWA, right, institutions will need to be able to designate an IRB already registered with OHRP and name an institutional signatory official. Now let me just say we didn't used to talk about this topic very much because most of the research is actually being conducted by big academics research centers, and they would be familiar. Their administrations would already be familiar with this, and because they're big, they're probably getting some federal funding one way or another to support research, and that they probably would already have an active FWA on file, and then they would probably have more than one IRB set up already, and that they would already have designated the IRB when they filed the FW. This becomes much more relevant these days because more money is going out to smaller institutions that may never have actually received any federal money or, for that matter, HHS money to conduct research, right? So if this is kind of, fairly new, and you've really never been involved with federally-funded research, HHS-funded research in particular, then this would be quite new to you, and you notice how, in fact, all this requires thinking well ahead and preparation well ahead of time. So for cooperative research projects, collaborating institutions, including subawardees that are engaged in human research activities will also need to have or be covered by an active FWA to receive HHS funds to do the research. Now, so as I've said, for cooperative research, engaged institutions that do not already have an FWA filed with OHRP because they have not really received any federal funding in the past, so they're kind of new to this process. If they're really part of a cooperative research project, then likelihood is that when they have to file an FWA, the IRB that they would designate would be the single IRB of record. Now what does that mean? That means that you need to be in communication with the principal investigator for that whole research project and know, "Hey, what's the deal here? Which is the single IRB that you guys are going to be relying on?" And so when you then file, when your institution that is new to this game and that you have to file an FWA, for example, and at the time when you meet to then designate an IRB, you need to have that information of which one that will be, and don't forget it's not just naming them. It's also having established communication with that IRB that you'll be relying on or that institution, its IRB you'll be relying on, and that you would have reliance agreements of some sort established with them, right? So again, what does that mean? That means be sure to plan ahead and allow time for communications with all relevant parties. All right?

So these are some resources here for you. You have that on the slides that you received, the PDF files that you received. There is a lot of information there. We welcome you to send us questions about this at ohrp@hhs.gov, and I think that's it, right, for today for me. I'm happy to open this up for questions. Lyndi?

Lyndi Lahl: Yes, Yvonne, thank you very much for that very informative talk. So I do have a number of questions that I've seen in the Q&A, so let's go ahead and get started. We have about 8 minutes left. So there's a question. Are international partners, e.g. a foreign university conducting human subjects research, subject to the same FWA requirements, or does that requirement only apply to US institutions?

Yvonne Lau: So regardless of whether you are domestic or international, if you are going to be getting money from the Department of Health and Human Services to conduct nonexempt human subjects research, in other words human subjects research as defined by the Common Rule, that does not come under one-off exempt categories in the Common Rule, then you need to file an FWA. If you're not covered, if you're not under an FWA, an active FWA, you'll not be able to get your HHS money, and this applies similarly to if you're getting money from other Common Rule federal agencies and departments, but I'm not going to speak for them because they may have additional requirements. Let's stay in the space of HHS money. So if you're getting HHS money to conduct nonexempt human subjects research, whether you are international or domestic, you need to have an active FWA to get your money. Or rather you need to be covered by an active FWA, right?

Lyndi Lahl: Great, thanks, and I do want to mention that the chat was very informative. We have a number of folks from different countries that have joined us today, so this topic, I think, was relevant for a lot of folks that are attending today's session. Okay, so another question about FWAs. Would a component of an institution with an FWA be eligible to be a primary recipient, or must the award go to the assuring institution itself?

Yvonne Lau: Okay, before I answer this component question, I just want to say something to the last one as well. Again, I just want to remind you even if you are international, right, if you're getting the federal, If you're getting the HHS money, you need to be covered by an active FWA, and what that means, that means that you are assuring the Department of Health and Human Services that you would comply with the HHS regulations of 45 CFR 46 when you conduct human subjects research. I say that because recently we had questions about equivalency, whether we follow some other ethical principles, whether we still have to comply with that regulations. Yes, you still have to, and remember how I also said that if your research happens to also be regulated by FDA? Let's say it involves an innovative device or a new drug that you're testing, right? So that comes under FDA regulations, right? Even if that research comes under FDA regulations, but if you're getting HHS money for it, you still have to comply with the 45 CFR 46 regulations. The good thing, however, is that 45 CFR 46 regulations are very similar to the FDA regulations, but there are things that are additional to the FDA regulations. So both sets of regulations you need to comply with. Coming back to the component question, reason why I kind of was delaying my response is that I really hesitate to answer questions like that because it's very hard to know what you mean by this being a component of an organization. A lot of that depends on the structure and legally how you're structured within that organization, and the best person to ask that question as to whether you're under, whatever that organization you're referring to as a component, is to ask the lawyers at the institution, right? I'm really not in a position to answer. First of all, you'll notice in my background that I'm not a lawyer by training, although I've studied some health law and so on, but in no way do I have the knowledge to be able to answer that particular question.

Lyndi Lahl: Okay, thank you. So a question, how long does it take to get the IRB registration done? Are there any factors that would influence how fast it takes? And then a part of the question is, do you have to have an FWA to register your IRB?

Yvonne Lau: No. Requesting an FWA coverage or filing an FWA or registering IRBs, those are processes. All right? I want to first say that when you register an IRB, right, you just have to follow the process. You kind of provide the information that are required on the form. By registering an IRB, it does not mean that your IRB has gone through some sort of level of accreditation, that you have satisfied some sort of accreditation process. This is strictly a registration process so that OHRP knows where to find you and who to contact, right? So it's a filing process, and I believe that if you have all the information that are required for that form to be completed, then you should be fine. It should not take very long. Our colleagues here at OHRP, there are specific colleagues who look at the information that you provide, do a basic level of verification, right, to make sure that you've completed everything and that things are factually correct in general. Then they should be able to provide you with the eight-digit number, I guess, to say that your IRB is registered, right? So it should not be complicated. The thing with FWA is when you register an IRB, you do not need to already have an FWA. In fact, that is probably the first process. So if you're thinking that, "I need to file an FWA," and you're not thinking that- So again, come back to it. So if you're thinking of filing an FWA, you do need to have two sets of essential information that you might not be able to get just right away, right? You need to know who your signatory official is, right? So it's not just, "Oh, I'm the PI. I'm going to file it, and I am the signatory official." Unless you're also the CEO of the company that is actually going to be receiving the research money, right? So you need to know who that person is, and the other thing that actually may need more thoughts and consideration is that you need to know what already registered IRB you'll be using, you'll be designating on this FWA, right? Probably that's not going to happen to you, but if you are the typical academia institution, where you have many IRBs to choose from, then your question is really, "Okay, which one should I designate?" And the one that you need to designate would be the IRB that is reviewing the majority of the HHS or federally-funded research that your organization is doing, right? But usually that is more a question for smaller institutions who are new to the game, who are just potentially getting their first HHS grant, right? So then your question is, "Okay, which IRB?" Most likely, you don't have one, right, in-house. So that really presents a question to you, right, "So where do I find one?" Now that is a question for you. Where do you find one? I've already given you some indications of where you find one, right, but you need to be able to establish that fact where you have time because that involves you knowing which IRB that has already been registered with OHRP that you can use. You need to have already spoken and have communications with that IRB and already probably set up written agreements, a freelance agreement of some sort so that the other IRB knows that you'll be using them and relying on them and so on and so forth, right? So there is a whole lot of things that need to go on before you come to the point where you know which IRB you can designate. And hence this, that's why I keep saying, right, and at the beginning, it seems like I'm talking about three different things completely, but they're all linked, and they're all interrelated, and it all can eat into your time that you have before you can actually get your grant money to start your human subjects research which, of course, to you would be the most important and relevant part here.

Lyndi Lahl: Great, thank you very much, Yvonne, and to Marianna as well. It is 2:01, so this concludes this session. Thank you again to our OHRP colleagues for this informative presentation and to our audience as well. So the PowerPoint and related resources are located in two locations, on the NIH Grants Conference website and inside the virtual NIH Grants Conference Center. Look for the Human Subjects Research pre-con event page to find this information.

Pamela Kearney: I'm Dr. Pam Kearney, Director of the Division of Human Subjects Research in the NIH Office of Extramural Research. I'm pleased to be your moderator this afternoon. I'd now like to introduce you to Ms. Lyndi Lahl. Lyndi is a nurse practitioner by training, and she has extensive experience in human subjects research requirements both professionally and independently through serving as an IRB member. She is currently the NIH Human Subjects Officer in the Office of Extramural Research at NIH. Lyndi, you have the floor.

Lyndi Lahl: Thanks, Pam. So today, as Pam said, I will be doing an overview of NIH policies on human subjects. So during this session, I'm going to be covering three topics; one, identifying NIH policies pertaining to research involving human subjects. The second is reviewing considerations when applying for an NIH award for research that involves human subjects, and the third, identifying NIH resources for investigators conducting research involving human subjects. So the first thing we'll do is talk about those policies that involve human subjects.

So NIH has a lot of policies pertaining to human subjects research, but during this presentation, I will be introducing the policies related to human subjects in clinical research. Now please note that the NIH policies on clinical trials and the policies on inclusion will be covered in separate sessions during the December 7th pre-con seminar, so I recommend that you attend the Overview of NIH Policies on Clinical Trials and the Including Diverse Populations in NIH Clinical Research to learn more about these policy topics.

So the first question that you want to ask is, you need to know when the NIH human subjects policies will apply. Depending on what you're doing will define exactly what you have to do. So during Marianna's session, she provided you information on, how do you know if a research study is human subjects research, and what does that really mean? So she went through those three questions. Does it involve research? Is it human subjects, and is it exempt from the regulations? Now the information will be helpful when determining if the human subjects are involved in this research activity, and then tomorrow, in Dr. Kearney's session on clinical trials, she will go through the questions for determining if a human subjects research study is a clinical trial. I do want to note that the NIH human subjects policies are complementary or in addition to the Common Rule requirements.

So the first policy I'm going to talk about is the NIH policy for education on the protection of human research participants. It's been a requirement for over 20 years. All key personnel, which include all individuals responsible for the design and conduct of the study, must have completed training in the protection of human subjects. Now, this educational requirement also pertains to key personnel at alternate performance sites, including non-U.S. sites as well as key personnel that begin after the award is funded. Now, NIH expects the key personnel receive the required training before they are involved in the research. Now please note that NIH does not mandate any specific course that the key personnel need to take or the specific content that's included in the course. This is a one-time training requirement, and as Marianna shared with you during her presentation, OHRP has a free training on human research protections that will satisfy the NIH educational requirement for key personnel.

Now, all NIH-funded research that is ongoing or awarded on or after December 13th of 2016 and is within the scope of the NIH Certificate of Confidentiality policy - I will often call this CoC or Certificate, talking about the same thing. It's deemed to be issued a Certificate. Now, as an investigator of a NIH-funded research study, it is your responsibility, along with your institution, to determine if your research is collecting or using covered information, since that's what the Certificate protects, covered information. Now, covered information includes the name or any information, physical document or biospecimen that contains identifiable sensitive information related to a research participant, and in addition, if there's at least a very small risk that the information, document or biospecimen can be combined with other available sources to determine the identity of an individual, these are also protected by a Certificate. Now I want to note that covered information that is collected or used by a subrecipient who receives funds to carry out part of your NIH award are also protected by the Certificate, and in addition, secondary researchers that receive information protected by a Certificate are also required to uphold the CoC protections. As the investigator, you will need to inform any subrecipients that the CoC protections apply and any secondary researchers that you're providing that information to when it is protected by a Certificate. Now, the protections of a CoC last in perpetuity, so that means that the data that you collect during your NIH funding will remain protected by the CoC even when your NIH funding ends. Now please note if your research continues after your NIH funding ends, and you continue to collect new data or enroll new participants, that newly collected data or those newly enrolled participants will not have the benefit of protections by a CoC. However, you can request a Certificate to provide CoC protections for that data that is covered after your NIH funding ends, and there's more information about requesting a CoC for research that is not funded by NIH, which would be the case if your NIH funding ends, and it can be found on the NIH CoC web page.

So this topic is so important, I have a second slide on it. So you and your institution are prohibited from disclosing or providing information protected by a CoC, and that would be in any federal, state or local civil, criminal, administrative, legislative or other proceeding or to any other person not connected with the research. Now, there are limited circumstances when you or your institution may release participants' identifiable sensitive information. Such disclosure is only permitted when required by other federal, state or local laws such as for public health reporting of communicable diseases or child or elder abuse reporting, or if it's made with the consent of the subject, or if it's necessary for the medical treatment of the participants, and it's made with the consent of the participant, or if it's made for purposes of scientific research that is compliant with the human subject regulations. Now I do want to clarify something that I just mentioned. Disclosure of identifiable sensitive information protected by a CoC must be done when the disclosure is required by other federal, state or local laws. Now, there is a distinct difference in receiving a subpoena or request from law enforcement for information covered by a CoC, and you are prohibited from disclosing under those circumstances. However, let's say there is a public health reporting requirement at the state level that you report the name of a participant with a communicable disease. It's mandatory reporting, so you must report under those circumstances.

Okay, so you heard a little bit about single IRB under the revised Common Rule with our last session and Dr. Lau, but I do want to make sure you are aware that there are two similar but separate requirements for use of a single IRB for non- or for NIH-funded nonexempt human subjects research. Now, the NIH single IRB policy became effective in January of 2018, and the compliance date for the revised Common Rule Cooperative Research Provision was in January of 2020. Now, you can learn more about these two single IRB requirements on the NIH single IRB for multi-site or cooperative research web page, or better yet, stay for the final session of the day which immediately follows this session, and that is going to cover the essentials of single IRB requirements.

So delayed onset generally means that human subjects research is anticipated within the period of the award, but the application or the proposal that you've submitted does not include any definitive plans for this involvement, and please note that a delayed onset research does not apply to a study that can be described but is not going to start immediately. This is called delayed start. Kind of makes sense, right? Now, if you have any questions on whether your research, in your application, is delayed onset research, I recommend that you contact your program official listed in the Funding Opportunity Announcement for guidance. Now, if you are recipient of a single-project award, and you have a delayed onset research, this may be because you are waiting for results from initial preclinical research before the human subjects research can be fully planned. You will need to submit a prior approval request in writing to your grants management officer for the funding institute or center no later than 30 days before the proposed change. Now, this will need to be signed by your authorized organization representative in accordance with the NIH Grants Policy Statement. Now, you'll need to provide a newer revised human subjects section that clearly describes the risks, methods, protections and the importance of the knowledge to be gained by the revised or new activities, and in addition, you're going to need to provide other applicable documentation such as the certification that the key personnel have taken appropriate education for the protection of human subjects and a new or revised inclusion plan for women, minorities and children.

Now, there are two other awards that are associated with delayed onset research. This includes cooperative research or multi-project awards and award mechanisms that allow a portion of the budget to support small human subjects research projects that is awarded to a different institution, and those are often known as pilot projects. Now, you'll need to follow the instructions from your funding institute or center for prior approval of your projects, and note you'll also need to submit appropriate inclusion enrollment information as well, as well as any other requirements that the institute or center has.

Now, although human fetal tissue isn't exactly human subjects research, I thought it was good to include this information as well. Research involving human fetal tissue is defined as research involving the study, analysis or use of primary human fetal tissue, cells and derivatives and human fetal primary cell cultures that are obtained from elective abortions. Now, if you are submitting an application for research involving human fetal tissue, you need to justify the need for the use of the human fetal tissue for the proposed research, and you'll need to include sufficient details in your description that allow a meaningful evaluation by NIH. You'll also need to include all required information, such as a detailed budget. Now please note if you're proposing research involving the use of human fetal tissue, you cannot use the PHS 398 Modular Budget Form. Instead, you'll need to use the R&R Budget Form, and I do want to note also that these additional requirements must be met within the existing applicable page limit, and if your application does not address all the information that is required, it is going to be withdrawn, and it will not be reviewed.

Okay, I have a couple of polling questions within this slide set, and this is the first of three. And the polling question, is it true or false? Investigators and all key personnel involved in human subjects research that is determined to be exempt from the regulatory requirements in 45 CFR 46 must meet the protection of human subjects educational requirements. So DeRon had launched the poll. Thank you, DeRon. And I want you to go ahead and answer true or false. Do you think that the investigators and all key personnel need to have the human research education if they are conducting exempt research? Okay, the poll is closed, and 82 percent of you said true, and that is accurate. So let me ... Whoops. Uh-oh. I went too far. Okay, there. So the correct response is true. Similar to the educational requirement for nonexempt human subjects research, investigators and all key personnel involved in human subjects research that is determined to be exempt from the regulatory requirements of 45 CFR 46 must still meet the protection of human subjects educational requirement, and this also includes key personnel at performance sites as well.

Okay, so the next polling question, it's also a true or false. NIH will provide a physical certificate for my NIH-funded research project to document CoC protections. So thank you, DeRon. You just launched the poll. This is a true or false question, so please go ahead and answer if you think that NIH provides a physical certificate when you have an NIH-funded research project that has covered information and offers CoC protections. Okay, the poll is closed, and 28 percent people said true, and 72 percent said false, and the majority of you were correct. The correct response is false. NIH does not issue a physical certificate for NIH-funded research projects. Now, it's the NIH CoC Policy, the Notice of Award and the NIH Grants Policy Statement, if you have a grant award, and the NIH DGS Contract Handbook-Special Contract Requirements, if you have an R&D Contract, and those documents will provide the documentation of the CoC protections. Now please note that institutions and their investigators are responsible for making the appropriate determination as to whether the research that you're conducting involves the collection or use of identifiable sensitive information and is subject to the CoC policy and is therefore deemed to be issued a Certificate. So NIH will not tell you if the policy applies and if you have CoC protections. It is up to you to make that determination.

Okay, and the third and final polling question, so under the CoC Policy, an investigator may release a participant's identifiable sensitive information, and we have five different answers. Is it A, if required by institutional policy; B, if the participant consents; C, if the investigator decides it is appropriate to disclose identifiable sensitive information; D, all of the above; or E, none of the above? So go ahead and respond, tell me what you think. When can you release a participant's identifiable sensitive information? Okay, it looks like the poll has closed, and it looks like almost half of you said it's when the participant consents, and over 1/3 of you said none of the above, and then there's a mix, a few that said everything. So the correct response here is B. Under the CoC policy, an investigator may release a participant's identifiable sensitive information when the participant consents to such disclosure. An institutional policy does not give the investigator the authority to release the participant's identifiable sensitive information, and an Investigators cannot decide on her or his own that the participant's identifiable sensitive information can be released. Now please note that when other applicable federal, state or local laws require disclosure, as we talked before about communicable diseases and public health disclosure of that, disclosure of identifiable sensitive information protected by a CoC must be disclosed. I recommend that you see the NIH CoC website, Investigators and Institutional CoC Responsibilities, and there is a hyperlink here, for the limited circumstances under which an investigator or institution may release participant's identifiable sensitive information and other responsibilities as well. Now, you can also go back and view slide eight in this slide set, and that's posted now for the day one, and that will include the limited circumstances when disclosure is permitted.

Okay, we're going to go on and think about review considerations when applying to NIH for an award that will support research involving human subjects. So as you know, or as you may know, the HHS regulatory requirements of 45 CFR 46.120 says the department or agency will evaluate all applications and proposal involving human subjects that are submitted to the federal department or agency, and the department or agency can utilize experts and consultants as determined to be appropriate, and for applications and proposals submitted to NIH, the agency that will conduct the evaluation is NIH. Now, this evaluation will take into consideration four specific things, the risk to the subjects, the adequacy of the protection against these risks, the potential benefits of the research to the subject and others and the importance of the knowledge to be gained, and on the basis of this evaluation, NIH may approve or disapprove the application or proposal or enter into negotiations to develop an approvable one.

So in the next two slides, I'm going to be focused on the plan protection of human subjects that you'll need to address in your NIH application. Risks, you need to consider if your application adequately describes human subjects involvement, the characteristics and design, the source of material and potential risks, so think about the following things. Do you have a description and justification for the proposed involvement of human subjects, including your planned enrollment numbers, the age range of the participants you plan to enroll and the health status of those participants? Do you have a rationale for the involvement of vulnerable populations, such as pregnant women, children, prisoners or institutional individuals? Is the role of any collaborating sites described? And this would be where research is going to be performed outside of your institution. Do you describe and justify the research procedures that you plan to do? Do you describe research materials, data and information you plan to collect? Will you have access to personally identifiable information that is collected and retained? Have you identified all potential risks to the participants, including the likelihood and the seriousness of those risks when it comes to physical, psychological, financial, legal and other risks? And do you address how you will handle incidental findings that may occur during the research? Now, the second piece, adequacy of the protection against those risks. You need to think in your application, are you adequately describing the recruitment and the informed consent and the protection against the risks? This would include, how are you recruiting your participants? Do you describe the informed consent, parental permission or assent that you're going to be obtaining, or do you plan to request a waiver of consent from your IRB? How will you minimize the risks that you've identified? What additional protections do you have for any vulnerable populations that will be part of your research? And do you have the necessary medical or professional folks available if there is an adverse event that you need to address when a participant has an AE? So potential benefits of the proposed research to the participants and others, so does your application adequately describe how potential risks to the participants appear reasonable in relation to any anticipated benefits? And I do want to note that financial compensation of participants should not be presented as a benefit of participating in the research. In the fourth and final plan for the protection of human subjects that you want to make sure you address is the importance of the knowledge to be gained. So does your application adequately describe how potential risks to the subjects appear reasonable in relation to the importance of the knowledge that may result from the study?

Now, many of the concerns that have been identified by peer reviewers are due to the lack of information or inadequate description of one or more parts of the plan for the protection of human subjects. So that's why you need to include the details that will provide the reviewers sufficient information, so they understand that the protections that will be available to your participants. Now, there are some common concerns involving human subjects that are often identified during peer review. Now, the most common concern by peer reviewers is that the application had general deficiencies in the protection of human subjects section. Now, that's not very helpful because general deficiencies probably mean there's more than one piece that wasn't sufficient. Surprisingly enough, there's missing or inadequate data in safety monitoring plans that is often a problem when it comes to clinical trials and peer review. They don't have good Data and Safety Monitoring Plans. There may not be any information addressing incidental findings which is vital in these plans. The risks may not be adequately addressed, and that would include all those risks I talked about in the previous slide. There may be inadequate protections for vulnerable populations. The source of the specimen or data is not addressed, or the application did not clearly delineate whether investigators have access to participant identifiers, and you can think about the first two presentations that we had today with Marianna and Yvonne, and it's really important for the reviewers to understand whether or not human subjects are involved. If you do not get any identifiers with your specimens, human subjects may not be involved, and if that's the case, then the protections aren't relevant because there are no human subjects involved in the research, and then the planned recruitment activity sometimes appears to be coercive.

So when NIH needs additional information from a grant applicant, the Just-in-Time period provides a tool to facilitate this purpose. So Just-in-Time, sometimes called JIT, allows you and the signing official to submit certain elements of a competing grant application at a later date in the application process. This is done after peer review and when the application is being considered for funding. Now, there are several pieces of information that are collected at Just-in-Time. This includes the Federalwide Assurance Number if the institution has proposed nonexempt human subjects research, and you heard all about FWAs in the last session, the certification of IRB approval, and that's satisfied by submitting the latest IRB approval date. Now, for most this is going to be your initial IRB approval date, but we do sometimes fund studies that are ongoing, and it may have been more than a year since the initial IRB approval, and if that is true, you would need to submit the latest IRB approval date, and then of course the institution needs to provide certification that all key personnel involved in the human subject research has completed the educational requirement in the protection of human subjects. Now, this is also the time in which you will submit a request for an exception to certain policies. Now, if the project is exempt under Category 5, your program official is actually the one that will be prompted to submit this policy exception request for Exemption 5, and I'm going to talk a little bit more about this in the next slide. Now, if you want to request an exception to the single IRB requirement, this will be the time that you will submit this request, and stay for the next session, as I mentioned before, to learn more about the relevant information that needs to be submitted if you decide to seek an exception to the single IRB requirements. And this is also when a policy request, and this again is going to be done by your program officer, for Public Health Surveillance Exclusion would be submitted, and if you remember back to Marianna's presentation, this is one of those exclusions that if you're doing public health surveillance, you're not doing research because it is excluded. NIH developed a process for this earlier this year, and I recommend that you look at the NIH website, Public Health Surveillance Exclusions, for additional information. Now please note that it is rare for NIH to receive or approve any of these policy requests.

So let's go back and talk about Exemption 5 for just a moment. So Exemption 5 is research and demonstration projects that are conducted or supported by a federal department or agency and are designed to study, evaluate, improve or otherwise examine public benefit or service programs. Exemption 5 research activities must be posted on a federal website prior to the research being initiated, and NIH will post NIH-supported Exemption 5 research activities when the activity is designated as such. However, a determination of Exemption 5 research is typically made in error. It seems that folks get a little bit confused, and it's expedited Category 5, not Exemption 5 research. At least that's what we've found, so NIH is going to review a determination of Exemption 5 to confirm it's appropriate, and today, since the revised Common Rule went into effect, NIH has supported zero Exemption 5 research activities. So we have not seen any true Exemption 5 research, and we do not anticipate that we are going to receive any because it's not something that NIH will do in general.

So if you will be involved in a multi-site study, you need to be aware of information that is on this slide. So in general, the prime recipient of a NIH award is considered engaged in human subjects research even when all activities involving human subjects are carried out by employees or agents of another institution, and, of course, Yvonne talked about this a bit in the previous presentation. I recommend that you review the OHRP guidance document, Engagement of Institutions in Human Subjects Research, if you'd like to learn more about engagement, and the link to this guidance document can be found in the resource document that's listed on the resource slide at the end of this presentation. Now the reason that this is relevant is because all sites that are engaged in nonexempt human subjects research need to be covered by a Federalwide Assurance, and again going back to Yvonne's presentation, she included the information about FWAs. In addition, each of these sites will also need to have their activities reviewed and approved by an IRB, and when there's more than one US site that is engaged in the research, the single IRB requirements will apply.

Now, a subaward allows a different institution to perform some of the activities under the NIH award, and if you're the prime recipient of an NIH award, it is you and your institution's responsibility to supervise these activities that are being done by your subawardee. Now, there's going to need to be a formal written agreement that addresses the specifics of this arrangement, and this will include identifying who is the lead investigator and other individuals who are responsible for the research activity along with their roles as well as any financial aspects of this arrangement. Now, the subaward or a pilot project investigator must obtain IRB approval before involving human subjects in the nonexempt human subject research activities, and please note the single IRB requirements may apply. Again, the next session will delve into that. Now, it's going to be the recipient institution that submits progress reports to NIH that includes relevant information on all the subawardee activities, including these pilot projects, and lastly, I do want to note that all applicable NIH policies and applicable regulations will apply to subaward and pilot projects. This includes the NIH regulations at 45 CFR 46, the educational requirements for human subject protections and the NIH Certificate of Confidentiality Policy amongst many others.

Okay, well, we are getting close to the end, so objective three was to identify NIH resources for investigators conducting research involving human subjects. So a few years ago, after the revised Common Rule came into effect, NIH developed a quick decision tool that can assist you in determining if your research involves human subjects, if it may be exempt from the federal regulations or if the activity is not considered human subjects research. Now please note that this tool should not be used as the sole determination of whether your study is exempt from the regulations, and the tool is available on the NIH Grants and Funding website, and there is a hyperlink here to be able to get to the tool from this slide.

So the resource page, I had mentioned that third bullet resource document. That's a compilation of a lot of different resources, both on the NIH site and on the OHRP site, and it will be very helpful to you, and this hyperlink will get you right to that. In addition, the NIH Human Subjects Research Home Page and the Office for Human Research Protections Home Page also have a lot of information that is available to you. So I would be happy to take any questions at this time. Pam, I am going to turn it over to you, so you can tell me what questions we might have.

Pamela Kearney: Great, thank you, Lyndi, so much for that interesting talk. We have a number of questions in the Q & A. I doubt we'll get to really even close to all of them, but we'll give it a shot. Why don't we start with: Someone was asking if you could clarify that, for cooperative research, whether the requirement for single IRB extends to include protocols that receive limited IRB review.

Lyndi Lahl: That's a great question, and I'm actually going to mention this in the next presentation, but I'm happy to mention it here as well. So limited IRB review is something that's done for certain exempt research activities, and I think there's four different exemptions and then underneath that exemption, it's not all Category 2 exempt research that will need limited IRB review, but certain parts of it. So the short answer is no. The single IRB requirements do not apply if there is a limited IRB review that's required. It's only when it's nonexempt human subjects research.

Pamela Kearney: Okay, thank you. So here's another question about research conducted outside of the U.S. Does the CoC also protect - And here's an interesting phrase. Does the CoC also protect investigators conducting research outside of the U.S. from disclosing identifiable information required by that country's government officials? If such an instance occurs, what should the investigator do?

Lyndi Lahl: Yeah, so that's a good question. We do get this question on occasion, and the bottom line is the policy was developed to protect all the participants in NIH-funded research. However, outside the U.S., the CoC protections may not be applicable. So if your country's laws mandate disclosure, a CoC is likely not going to provide the protections it would if the participants or data are located within the U.S. The CoC is also made to protect participants. It is not designed to protect the investigators or the research staff either, so I want to make sure that I get that part in. I've heard horrible instances of when there has been disclosure outside of the U.S. But it was done on behalf of the government where the research was being conducted, that's not in the U.S., and there, really the CoC is not going to be able to help you with that.

Pamela Kearney: Lyndi, as a follow-up to that, can you talk about the consent requirements regarding CoC coverage? Because that sounds like it would be something that participants would need to know.

Lyndi Lahl: Yeah, absolutely. So NIH expects that the investigators are going to inform their participants when there is a CoC in place. Now, that would likely be through the informed consent. It needs to be through some mechanism. So NIH has sample language on the CoC website that you can use, or you can adapt to your use, but we do expect that you are informing participants, and most likely you'll want to work with your IRB because the IRB may have specific ways not using NIH language, maybe their own language, to be able to inform the participants of those CoC protections, and it's not just the protections that need to be addressed in the consent. You also need to address any limitations to those protections. So if, let's say you are doing research on a vulnerable population. Let's say it's children that have been abused, and you find out that there has been abuse for this child participant. There is going to be a mandatory disclosure that you're going to have to disclose that information. You would have needed to put that in the parental permission form, and if you're getting child assent, you would need to have included that because that is a limitation to those protections.

Pamela Kearney: Mm-hmm. Okay. We have a couple questions asking about examples of incidental findings.

Lyndi Lahl: Okay. So incidental findings, in case you don't know, are something that happens, that you find out, that you weren't looking for, you weren't anticipating, but you found out anyway, and it's something that is about your participant. So let's say you are doing some research, and you're doing some MRIs of the brain, and it's because you're looking for some cognition, and in the course of doing this MRI, you notice that there is some abnormality. If it's actionable, you're going to want to disclose that incidental finding to your participant. You likely will have the information of who referred that person, if the person came from a medical provider, and when I talked about the incidental findings and what you plan to do if you have them, this is exactly why you would want to include those plans in your human subject protection plans in your application because you need to know what you're going to do. You need to have a plan in place.

Pamela Kearney: Mm-kay, thanks, Lyndi. Let's see. We have a couple more here. Okay, here is a question about patient consent for disclosure, and the attendee asks basically, how relevant is the patient consent to release the information if others don't consent to it, as it relates to the CoC, and I'm not exactly sure what they mean by others. I'm thinking family members. I'm thinking maybe other researchers or that sort of thing.

Lyndi Lahl: Okay, so I want to make sure that I have the question. So if your participant consents to disclosure of their private, identifiable sensitive information, but let's say their spouse or someone else does not agree to that disclosure, what do you have to do? Is that kind of the ...

Pamela Kearney: That's what I'm assuming.

Lyndi Lahl: Okay.

Pamela Kearney: I just read it to you basically the way it came in.

Lyndi Lahl: Yeah. So .

Pamela Kearney: But I think it ...

Lyndi Lahl: So I ... Yeah.

Pamela Kearney: I think it has to do with the autonomy of the person to give their consent to release it, is the way I'm taking this.

Lyndi Lahl: Yeah, so under the CoC Policy, you are permitted to disclose that information, and I think it's kind of expected that if the participant says that you can disclose to, let's say the police because the police are asking for this, then you can disclose that. If it's for other medical purposes, let's say there's an incidental finding, the participant will need to consent, and then you're going to be able to release that information to their medical provider, who is not a researcher. It might get a little uncomfortable if, let's say the spouse doesn't want you to disclose that, but it really is, as you said, Pam, it's the autonomy of the participant.

Pamela Kearney: Okay. We had a follow-up question to one that was answered just by typing the answer in, and it had to do with the definition of identifiable sensitive information. The link was provided, and an excerpt of the definition was provided, and the follow-up question is relating to genetic information or tissue samples, and the question specifically is, does every study that includes genetic information or tissue samples, are they considered sensitive information, and therefore, would that necessarily need a CoC?

Lyndi Lahl: So the short ...

Pamela Kearney: Or would it be deemed issued to have a CoC?

Lyndi Lahl: Yeah, yeah, yeah. Yeah, so the short answer to that is yes. Likely it is going to be deemed to be issued a CoC. It's not just about having those identifiers. You don't have to have the person's name or other type of sensitive information. If there is a very small chance that you can identify someone with the information that you have .. . And when I say information, that's broad. That also includes specimens, data, et cetera, and it can be combined with anything else, then it is also deemed to be issued a Certificate. So I don't want to say 100 percent yes, but it is most likely.

Pamela Kearney: Okay, thanks, Lyndi.

Lyndi Lahl: [Indistinct] Mm-hmm.

Pamela Kearney: Thanks, Lyndi. Someone else is asking if you could address the question of patient samples that were collected while the patient was alive, and there was a CoC issued, but now the patient is deceased, but the patient was consented and was part of this CoC, and data and information was collected under that CoC, but now the patient is deceased.

Lyndi Lahl: Yeah, so going back, when I talked about Certificates, you might remember I said Certificates are, the protections are in perpetuity, so that means that they are going to protect even the data from a deceased individual. So you cannot just release the deceased individual's private sensitive information. You would need to then look at your state laws and regulations on who can give consent if you want to release that information and probably talk with your institutional lawyers about how you would go about being able to release that information if it's appropriate or if you want to do that.

Pamela Kearney: Okay. There are a couple of questions that I'm not really sure what is being asked, so I may come back to those and just ask a question the way I think it was going to be asked. There is a question here that - It was actually a two-part question, and the question reads, "IRB training is separate from HIPAA training, but both are needed, no?" So I think the question is, is IRB training needed, and is HIPAA training needed for NIH-funded studies?

Lyndi Lahl: Well, so NIH is not a covered entity. NIH is not OCR, Office of Civil Rights, so NIH is not going to require that you have HIPAA training. Now that being said, most IRBs serve as the privacy group that and is HIPAA language in addition to looking at the research and looking at informed consents. Again, NIH policies don't really speak to IRB training, and this would have been a great discussion with Yvonne because she is from OHRP. I can tell you as an IRB member for over 10 years, and, Pam, you were an IRB chair for many years, I hesitate to say IRB training for your IRB members is not required because I shudder to think that there are IRB members out there that are not being trained, but it certainly is not an NIH requirement. And you can add if you have anything else to say about it.

Pamela Kearney: And we're getting short on time, so we only have time for a couple more. Another question is, how long should a principal investigator hold on to the identifiable information? And I'm always going to put on the end of that "for NIH-funded studies" because that's what we're talking about so ...

Lyndi Lahl: Yeah, so it really is going to be between you and your IRB how long the identifiable sensitive information is retained. You're going to do the research. You are going to maintain that information in a place where you're going to be able to secure it, and you're probably going to want to go back and do some QA to make sure, when you're doing your data analysis, everything is good, but in terms of NIH requirements, there's not a specific requirement that says you must retain it for a certain length of time. Certainly look to the FDA, if you're doing FDA-regulated research. They have requirements under I&D, how long you need to maintain it. If there was ever a question, you would want to be able to have the information to be able to defend what you had done, so I wouldn't be getting rid of it right away, but again, talk to your IRB about what information you're going to retain with identifiers and how that information is going to be maintained.

Pamela Kearney: Okay, and we probably have time for maybe one or two more. We had a couple of people up-vote a question about the one 18 letters in the Common Rule and whether or not it can be used if IRB approval hasn't yet been secured at Just-in-Time. We might need one of our colleagues from Grants to answer this one, but I thought I would throw it out and see if you have the answer to that, Lyndi.

Lyndi Lahl: Yeah, so I think they're talking about the delayed onset research.

Pamela Kearney: Mm-hmm, yeah, Dawn is shaking her head yes. So Dawn is up there, yeah.

Lyndi Lahl: Yeah, so and, Dawn, let me talk a little bit, and then if you want to add on, you're more than welcome. So it may be that the grant can be awarded with restrictions that no human subjects can be involved until such time that you have submitted that information that's needed, that the IC has been able to review and make sure that everything is acceptable, and then they would take the restriction off the award. So, Dawn?

Dawn Corbett: Yeah, Lyndi, I think you covered it. I think that's right. You would just need to submit that information when it becomes available and you can describe the protocol, and then that restriction can be lifted.

Lyndi Lahl: Great, thanks.

Pamela Kearney: I think we literally have about 30 seconds, so I am reluctant to go into another question. So I'll stop here and thank Lyndi very much for a great talk, and I want to thank all of you for joining us today for this talk. The PowerPoint and the related resources are located in two different locations. You can find it on the NIH Grants Conference website and also inside the Virtual NIH Grants Conference Center. Look for the Human Subjects Research Pre-Con Event Page.

And I am Dr. Pam Kearney. I'm the Director of the Division of Human Subjects Research in the Office of Extramural Research. I am going to be your moderator for today's presentation. I'd like to introduce you to Ms. Lyndi Lahl. Ms. Lahl is a nurse practitioner by training. She has very extensive experience in human subjects research requirements, both working professionally and independently as an IRB member. She is currently the NIH Human Subjects Officer in the Office of Extramural Research. And, Lyndi, take it away.

Lyndi Lahl: Thanks, Pam. So as Pam mentioned, I'll be doing the Essentials of Single IRB Requirements. So the objectives that I'm going to cover during this session are reviewing the single IRB requirements under the revised Common Rule and the NIH Single IRB Policy. I'll be reviewing scenarios, so you'll be able to recognize when the single IRB requirements apply to an NIH-funded study, and I'll be identifying the type of justification needed for a single IRB exception request both to the revised Common Rule and to the NIH Single IRB Policy.

So let's talk about those single IRB requirements. So I'm going to first start off talking about the NIH Single IRB Policy. Now, this was initially released in June of 2016, so it's been around for over 6 years. Now, the effective date of the policy was changed a couple of times, and this was to provide institutions more time to ready themselves for the single IRB requirements. So the final effective date for the NIH Single IRB Policy was for competing grant applications with due dates on or after January 25th of 2018 and for contract solicitations issued on or after this date. Now with note, ongoing noncompeting awards with more than one domestic site conducting the same protocol are not expected to follow the policy until the recipient submits a competing renewal application. So this means that the date of the noncompeting award must be - that it must be compliant with the NIH Single IRB Policy would be the date that the competing renewal award is issued, and we've been seeing a number of those in the last year or so that have been coming up for competing renewal, have been renewed and started off they were not subject to the Single IRB Policy, but now they are. And the whole purpose, the reason that the policy was written this way was, it was the expectations that all multi-site research being done in the U.S. would eventually fall under the single IRB requirements. Now I do want to note that if an application that proposes an ongoing multi-site human subjects research study being conducted in the U.S. that did not previously have NIH funding but now has received funding, it will become subject to the NIH single IRB requirements when that award is issued. So even if it didn't have a single IRB in place when it started because there was no requirements because it was not NIH-funded, once they receive NIH funding, then the single IRB requirement would likely apply if there's more than one U.S. Site conducting the same research protocol.

So let's talk about a little bit more detail on the NIH Single IRB Policy. The policy applies to domestic sites of a multi-site study when those sites are conducting the same nonexempt human subjects protocol. Now, there are some built-in exclusions to the NIH Single IRB Policy requirements, and these include international sites that are conducting the same multi-site protocol as domestic sites. The international sites do not need to be part of the NIH or do not need to fall under the single IRB. This also includes certain awards. Career development or K awards, institutional training awards or T awards and fellowship awards or F awards were not subject to the Single IRB Policy requirements. In addition, the NIH Single IRB Policy does not apply to other transaction awards or OT awards. Now, there are three types of exceptions to the Single IRB Policy. The first two exceptions are automatic, and that means that if automatically accepted, there's no need to submit a single IRB exception request. So the first automatic exception is when a single IRB review is prohibited by federal, state or tribal law, regulation or policy, and the second automatic exception is a time-limited exception for ancillary studies that are associated with multi-site ongoing studies. Now, the parent study and the ancillary study will become subject to the single IRB requirements when that ongoing parent study has its competing renewal award issued, and then the other type of single IRB exception must be requested by the investigator and will need to include a compelling justification, and we're going to talk about requesting exceptions a bit later.

So note that the Single IRB Policy applicability is in part when sites are conducting the same protocol, so I want to talk a little bit about what that means. So in general, the same research protocol means that the protocol is addressing the same research questions involving the same methodologies and evaluating the same outcomes. Now note I did not use the term identical when I was describing same protocol because there may be some variations in the protocol procedures due to local context. Also, to be conducting the same protocol, it doesn't mean that one award is funding all the sites that are conducting the same protocol. There can be multiple awards, including a different award for each site that is conducting the same protocol, and sites don't have to be conducting the entire protocol to be considered conducting the same protocol. They can be conducting only part of the same protocol and still fall under the NIH single IRB requirements. An example of this would be a site that is only recruiting participants, determining their eligibility, obtaining informed consent from the participants and performing select study procedures. This site would most likely be considered to be conducting part of the same protocol and then would be subject to the single IRB requirements when it's a multi-site study that involves more than one U.S. institution. I also want to talk about prime recipients. So when a prime recipient has subawarded all nonexempt human subjects research activities to another domestic site, now note that the prime recipient must perform a substantive role in the conduct of the planned research. They cannot just merely serve as a conduit of funds to another institution or party, and for this reason, NIH considers the prime recipient to be conducting the research as well, and therefore the Single IRB Policy applies.

So the original NIH Single IRB Policy required that applicants and offerors include a single IRB plan in their application or proposal. Now, the single IRB plan was intended for the applicant or offeror to describe the plans for use of the single IRB that will be selected. Now, since the release of Forms F and other later grant application packets, applicants no longer need to submit a plan that describes the use of a single IRB at the time of application submission. Now that being said, applicants that are required to use a single IRB are required to provide the name of the single IRB during the Just-in-Time submission before the award is issued, and I talked a little bit about Just-in-Time submission during the last session. Now when the applicant provides the name of the single IRB, this satisfies the Single IRB Policy requirement for a single IRB plan, and I do want to remind you that although applications no longer require that a single IRB plan is included, this does not mean that the applicant doesn't need to have a plan in place. Applicants will still need to develop and carry out a plan for using a single IRB when applicable because without a single IRB plan, a recipient will most likely have delays in implementing the portion of the research project that involves human subjects, and I have to say that I have seen this a number of times, and there isn't much that we can do except tell them, "You just need to get it in place."

So let's move now from the NIH Single IRB Policy to talking about the other single IRB requirement under the revised Common Rule. Now, the revised Common Rule at 45 CFR 46 was published in January of 2017, and the single IRB requirements in the revised Common Rule are found at 45 CFR 46.114, and these are known as the Cooperative Research Provision. Now, the compliance date for the Cooperative Research Provision pertains to research subject to the single IRB requirements that receives initial IRB approval on or after January 20th of 2020, and as was asked in the last session I want to repeat it here. Institutions conducting the same exempt research protocol and that need limited IRB review are not subject to the single IRB requirements. They can all use their own local IRB for exempt research that's being - multi-site research that's being done at more than one institution.

So now let's talk about the details for the revised Common Rule single IRB requirement. Any institution located in the U.S. that is engaged in cooperative research must rely upon approval by a single IRB for that part of the research that is conducted in the U.S. I know this sounds familiar because Yvonne talked about this as well. So I have one word and a phrase that I'm going to focus on, and it's not what Yvonne focused on. So the term engaged, this term is used in the phrase that the institutions are engaged in the cooperative research. Now, OHRP considers an institution engaged in a particular nonexempt human subjects research project when its employees or agents either, one, obtain data about the participants of the research through interventions or interactions with them, or two, obtain identifiable private information about the participants of the research, or three, obtain the informed consent of participants for the research. Now the phrase that I want to highlight in this same section is cooperative research, and this is defined by the revised Common Rule as research projects that involve more than one institution. Now please note that the single IRB requirements apply to all domestic multi-site nonexempt human subjects research regardless of funding mechanism. Now, just as the Single IRB Policy has exceptions, the revised Common Rule also has some exceptions to the single IRB requirements, and the first is when more than a single IRB is required by law, and the second is when any federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular research context. Now please note that the federal department or agency for HHS-supported research is OHRP. It's not NIH. NIH does not have the authority to make determinations on exceptions to the revised Common Rule unless OHRP has determined a particular category for which the cooperative research single IRB requirements are not appropriate, and this leads us to the third exception. So the last type of exception to the revised Common Rule single IRB requirements is limited during the COVID public health emergency. This is the only exception for which NIH can review and potentially approve the use of this exception. I do want to note that this exception can only be used during the ongoing COVID public health emergency, so once the public health emergency is declared over by the Secretary of HHS, NIH will no longer have the authority to approve exceptions for research that is subject to revised Common Rule single IRB requirements.

Now, similar to the NIH Single IRB Policy, institutions that are the prime recipient of an NIH award directly from NIH for nonexempt human subjects research are considered engaged in the research project. This is true even when all activities involving human subjects are carried out by employees or agents of another institution. So if both institutions are located in the U.S., the revised Common Rule single IRB requirements will apply.

Now I want to spend a moment talking about reliance agreements. A reliance agreement or IRB authorization agreement, which is what OHRP calls them as well as how they're referred in the Grants Policy Statement from NIH, is a written agreement that details the responsibilities of the institution that's relying on the IRB and the reviewing IRB's responsibilities under that institution or organization that is serving as the single IRB of record and performing the IRB review. Now, to be eligible to serve as the IRB that is reviewing any NIH-supported research, the IRB must be registered with OHRP, and you did hear that from Yvonne with the last session. So it's the responsibility of the NIH recipient to ensure that there is a reliance agreement in place and ensure that there is a mechanism established for communications between the single IRB and the participating sites. The recipient will need to maintain a copy of the reliance agreement to document compliance, and I did see in the chat with the last session that somebody had mentioned SMART IRB, and SMART IRB is a mechanism that helps facilitate that reliance agreement, and if you don't know about it, you can go to the NCATS website, N-C-A-T-S, write SMART IRB, and you can learn more about this SMART IRB platform.

Okay, so there are a lot of similarities between the two sets of single IRB requirements, and this slide and the next compare the single IRB requirements to show the similarities and highlight the differences. So the applicability of the two single IRB requirements is similar. Now, the effective dates are different. As I mentioned, the NIH Policy has been around for longer. Its effective date was January of 2018, and the revised Common Rule was January 20th of 2020. Now, the revised Common Rule does not have automatic exceptions for certain types of funding that are found in the NIH Single IRB Policy. The revised Common Rule also does not include any language that mentions the need for a single IRB plan. The revised Common Rule limits automatic exceptions to when more than a single IRB is required by law. Now if you think about the NIH policy, it says that when it's prohibited by law, regulation or policy, so the revised Common Rule does not allow those automatic exceptions if it is from a regulation or policy, only if it's a law. And under the revised Common Rule, new ancillary studies are not grandfathered in, and they will be subject to the revised Common Rule single IRB requirement. Again, if it meets the requirements that it is cooperative research being done at more than one U.S. institution, nonexempt human subjects research, and the exception request justification is different depending on which single IRB requirement the research project is subject. So speaking of exception requests, let's now spend a little bit of time talking about exception requests and justifications and other logistics.

Now, the applicant, offeror or the recipient will need to include the correct type of justification for the single IRB exception request, and this will be dependent upon if the research is subject to the NIH Single IRB Policy or if it's subject to the revised Common Rule single IRB requirement. Now, if the research is subject to the revised Common Rule single IRB requirement, the justification will need to address why a single IRB is not practical during the COVID public health emergency. If the research is only subject to the NIH Single IRB Policy, the exception request will need to include a compelling justification. Now please be aware that if the research is subject to both single IRB requirements, the exception needs to address the revised Common Rule justification. If an exception request is approved for research that is subject to the revised Common Rule single IRB requirement, it is also automatically approved for exception to the NIH Single IRB Policy. This means that it is not necessary to include a compelling justification for an exception to the NIH Single IRB Policy when the research is subject to both requirements. I do want to make sure I state this last sentence on the slide. Exceptions to the use of a single IRB are rare.

So let's talk about the details for the revised Common Rule single IRB exception justification. Now, research that is subject to the revised Common Rule requirements and that is ongoing or initially reviewed by the IRB during the COVID public health emergency is eligible for consideration of this exception. The justification needs to describe why reliance on a single IRB would not be practical during the COVID public health emergency. Now the request should be consistent with the scenarios found in the OHRP Guidance Document on Exceptions During the COVID Public Health Emergency, and the guidance includes the scenarios for which OHRP anticipates that it may not be practical to rely on use of a single IRB during the ongoing public health emergency. I recommend that you review the guidance for additional information, and I want to remind you once again that once the public health emergency is over, NIH will no longer have the authority to approve exception requests for research that is subject to the revised Common Rule single IRB requirement.

Now, if the multi-site protocol is only subject to the NIH Single IRB Policy, the request will need to provide sufficient information that demonstrates a compelling justification to the Single IRB Policy, and this justification should include why the single IRB cannot serve as the reviewing IRB for a particular site that's asking for an exception and why the local IRB is uniquely qualified to be the reviewing IRB for that specific site.

So I want to talk now about submitting an exception request. So during the pre-award phase, the process for submitting a single IRB exception request will start with the applicant sending a written request to the program official or program director. Offerors will need to follow the instructions in the RFP for submitting an exception request. So in general, the request will be submitted as an attachment with the contract proposal. Now please note the applicants and offerors do not submit the single IRB exception request directly to the NIH OD. They will need to submit the request to their respective PO, PD or CO. I also want to mention that applicants and offerors should not assume that their exception will be granted when they're considering what single IRB costs to include in the proposed budget. In other words, the proposed budget needs to reflect all necessary single IRB costs without an approved exception. And after an award is issued, the grants and cooperative agreements recipient seeking an exception to use of a single IRB should submit a prior approval request in writing to the NIH Grants Management official, and that needs to be done no later than 30 days before the proposed change and signed by the Authorized Organization Representative, and that's described in the NIH Grants Management Grants Policy Statement. NIH contract recipients should submit the single IRB exception request and justification directly to their contracting officer.

Now for NIH-conducted or supported research, NIH will review the exception request and determine if the exception can be approved. So it's the NIH Office of Director staff that process all exception requests. The OD staff will review the request to ensure the request includes all required information and confirm that the appropriate justification was included with the exception request, and it's OD officials that determine if the request meets the requirements for exception. After that's done, and it's done at a meeting, OD staff will notify the applicable PO, PD or CO of this determination via email. Now for grants and cooperative agreements, it's going to be the program officer or program director that will notify the applicant or the recipient of this determination, and for contracts, it's the contracting officer that notifies the offeror or the recipient of the determination.

So NIH OD staff and reviewing officials see a number of common issues with exception requests, and these issues include incomplete information that is submitted with an exception request. Perhaps there's no single IRB of record identified or there's no plan to put the single IRB in place or not all sites that need exception are listed. There could be an incorrect justification such that there's a compelling justification that is provided for a study that is subject to the revised Common Rule single IRB requirement. The one that should be submitted is why it's not practical during COVID to have a single IRB. There may be a justification based on the cost of the single IRB or the inconvenience to the researchers. Those are not appropriate justifications, and they will not be approved. And the last thing I have on for this bullet is that there is a decision requested within a few days of submission because, "Gee, the award needs to be issued within a couple of days, so we need to get this exception request approved so we can issue the award." Well, that doesn't work very well. It takes a minimum of a couple of weeks from the time the OD receives the request until the meeting where the OD officials review, and then there is a letter that's written. So it does take a few weeks, and sometimes it takes months because we're not getting the information that we need.

So I do have some single IRB resources on the next page. There are a number of NIH guidance documents on single IRB. Certainly the revised Common Rule is also a good resource, and that OHRP Determination of Exception During the COVID Public Health Emergency is another one. When you have questions, I would direct you first to your program officer, program director or contracting officer for questions about single IRB. If you have questions that they cannot answer, there is a single IRB policy mailbox that you can submit those questions.

And now the last activity that we'll do before we go to the question and answer session is reviewing a few single IRB case studies, and I do want to disclose that all these case studies are based on actual scenarios that occurred with NIH awardees. So case study number one, you have applied to an NIH funding opportunity announcement with a due date of January 20th of 2023. You respond to question 3.2 in the PHS Human Subjects and Clinical Trials, or HSCT, Form, "Is this a multi-site study that will use the same protocol to conduct nonexempt human subject research at more than one domestic site," with a response of no. Your application identifies one domestic collaborative site where all nonexempt human subject research activities will be performed. This site has not yet received IRB approval. There are two questions for this poll. Is the study subject to the single IRB requirements? And two, which single IRB requirements apply? So thank you, DeRon. You just launched the poll. So I would like you to answer the two questions, and you need to type your answers in, limit of 200 characters for each. Is the study subject to the single IRB requirements, and which single IRB requirements apply? So we'll wait about 30 more seconds. Oh, and the poll just closed. Okay, so let's go ahead and look for the answers. So question one, is the study subject to the single IRB requirements? So the answer is yes. The study is subject to the single IRB requirements, even though you answered no in that question, and it looks like the majority of you got that right, so good job. Now the second question, which single IRB requirements apply? And it looks like there's kind of a split answer here. The study is subject to both the revised Common Rule single IRB requirement and the NIH Single IRB Policy. Now, the receipt date or due date for funding opportunity announcement is after January 25th of 2018, and the initial IRB approval date will be after January 20th of 2020. So this is a case where you're not only subject to the two requirements, it's because the applicant who is being considered for funding will be engaged in the nonexempt human subjects research when all human subject research activities will be conducted at a subrecipient institution. Remember, prime awardee that subs out everything to another U.S. site is considered engaged and under both NIH and the revised Common Rule, and therefore the single IRB requirements apply.

Okay, let's go on to case study number two. You are the PI of an NIH-funded multi-site domestic study with an award date of September 22nd of 2022. You received initial IRB approval from your local IRB in November of '22 and have begun to enroll participants. However, your IRB decides that they do not want to serve as the IRB of record for the other two sites. You submit a compelling justification that the study will be delayed if all sites must rely on a single IRB, and this is going to negatively affect the study accrual. You also state that the budget does not include the fees for a commercial IRB. There are two questions for this poll. One, which single IRB requirement applies, and two, is the single IRB exception request or exception justification sufficient? So please go ahead and write your short answer responses to this. We'll give you a little bit of time to address this, and when you're done ... Okay, it looks like the poll closed and ... waiting for the results, and okay, thank you. So for question one, which single IRB requirements apply? So it looks like most of you put that both requirements apply, and that's true. The study is subject to both the revised Common Rule single IRB requirement and the NIH Single IRB Policy. So the initial IRB approval date is after January 20th of 2020, and although the receipt date for funding opportunity announcement is not included in the case study, I know that it was in January of '22, and that means that the study is subject to both single IRB requirements. So, sorry for not giving that second piece to you, but it looks like most of you figured that one out on your own. Okay, so ... Whoops. Oh, there, okay. So now you have that. So let's go on to question two, and is the single IRB exception justification sufficient? And it looks like a lot of you said, no, it's not sufficient, and that's true. It is not sufficient. There is no information about why having a single IRB is impractical during the COVID public health emergency, so this request would not be accepted. It wouldn't even be considered. The request does not mean that the compelling justification would be met either if it was only subject to the NIH Single IRB Policy. Now, the PI should have been aware that the single IRB requirements would be applicable when she or he submitted the application and had months to get the single IRB in place, and cost is not considered a compelling justification from the NIH single IRB requirements. And as unfortunate as this is, I must say that I think the investigator would have benefited from having a single IRB plan in place. It probably would have been very helpful to them.

Okay, the third and final case study; you are the PI of a competing renewal application with an estimated award date of January 20th of '23. The original grant was awarded in May of 2016 and received initial IRB approval in June of 2017. There are seven sites involved in the research, including three in New York, one in Maryland, one in Washington state, one in Puerto Rico and one in Canada. There are three questions in this poll. One, which single IRB requirements apply? Two, which sites do not need a single IRB? And three, which single IRB exception justification must you address? So thank you, DeRon. You launched the poll. So we have three questions. They all require or they all ask for short answers. So please go ahead and take a moment to address if you think the single IRB requirements apply, which site would not need a single IRB, and which single IRB exception justification will you need to address? So we'll give you a little bit longer before the poll is ended. Okay, so the polls ended. So let's go ahead and see the results, and it looks like the majority of you said yes, the single IRB requirements apply. So that is correct. So this award is subject to the NIH Single IRB Policy only. Note that the initial IRB approval date is before January 20th of 2020, so the revised Common Rule single IRB requirements do not apply. Now, when the competing renewal award is issued, the NIH single IRB requirements will apply, so the recipient will be expected to comply with the policy on the date that the award is issued. Okay, and now for the second question, which sites do not need a single IRB? And it looks like everybody or almost everybody said Canada. That's correct. Now I see a few that identified Puerto Rico as not needing a single IRB. So it is the site in the Canada that will not need a single IRB. I want to mention that Puerto Rico is a territory of the U.S. and therefore counts as a U.S. site, so Puerto Rico would fall under the single IRB requirements. And then for question three, which single IRB exception justification must you address? And it looks like the majority of you put compelling justification, and that is correct, compelling justification, since this study is subject to the NIH Single IRB Policy. So excellent, thank you very much.

So we are down to the end here. I had mentioned before that we have a single IRB policy mailbox, if you do have questions after the session, that you can send it to, and now I'm going to turn this over to Pam to see if we have any questions that I can address. Thank you.

Pamela Kearney: Great talk, Lyndi. We actually have a ton of really good questions in the Q&A, and we'll go to about 3:57-ish. I think it won't take us very long to wrap up. So the questions, as I was sorting through them, are kind of grouped together, so I'm going to try to get the general gist of some of the questions, but one of the questions that we have ... and there was at least four that were in this same vein about, which one should I follow, the NIH Policy or the revised Common Rule? That's the general gist of about four or five ones, and so I'll just throw that out to you. Which one should we follow?

Lyndi Lahl: Okay, well, it just depends. I don't like when I get the answer, "Just depends," but it's so applicable for this because it depends on when your NIH funding came in and when the initial IRB approval date was. So remember you have those two dates, and so you have to look and see when it's applicable. So if you're subject to both, guess what? You have to follow all of the requirements. If you're only subject to the Single IRB Policy, you need to follow the Single IRB Policy. If you're only subject to the revised Common Rule, and that does happen sometimes when ... think about an other transaction award, it's not subject to the Single IRB Policy. It would only be subject to the revised Common Rule. Then you'd have to follow the revised Common Rule, but essentially if you're subject to either one of those single IRB requirements, you have to have a single IRB in place for any site in the U.S. that is conducting the multi-site research.

Pamela Kearney: So and then, specifically there was a question about our training awards, the KTNF awards and which ones should they follow because the NIH policy doesn't include them, but there was a guide notice a little bit later that said, "If you are subject to the revised Common Rule, then you would have to have a single IRB." So that if you had IRB approval on or after January 20, 2020, then you would have to have a single IRB for the Common Rule. Another question, can the single IRB be associated with one of the participating institutions, or does it have to be an outside commercial IRB?

Lyndi Lahl: Great question, and we certainly don't mandate that a certain IRB is going to be serving as the single IRB of record. We see often that it is one of the sites that is conducting the research for the award, so it could be the participating site. What we see sometimes is when there's a prime recipient, and they sub the award with all the human subjects research being done at a participating site, often the participating site will be the one that serves as the single IRB of record. So they would be reviewing on behalf of the prime recipient and on behalf of the research that's being conducted there. There, as Yvonne said earlier, commercial IRBs are another option. They tend to be on the costly side, but that's why you have to have your single IRB plan and you have to budget, and in your budget when you submit your application.

Pamela Kearney: We had about four or five questions regarding the prime awardee and the sub sites and what happens if one is doing one part or if the prime awardee was only doing analysis. Would these folks have to have single IRB? You basically answered that, but just because we had so many questions, why don't you address it again?

Lyndi Lahl: Yeah, so you remember the prime recipient of an award, even when all the human subject research activities, nonexempt human subject research activities, are being done not in the institution but in the subawards, they would still be considered engaged in the research, and therefore, if it's more than one domestic site, then single IRB would apply, and there would need to be single IRB for all of those domestic sites that are engaged in the research.

Pamela Kearney: Sadly, there's a whole bunch more, but you guys will have an opportunity. We have a big question and answer at the end of tomorrow's sessions where it's going to be all of the panelists. You can try to fit your questions in then, if your specific question we didn't get to it, but right now we need to wrap up. So a great big thank-you to Lyndi and the other panelists from today.