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OHRP Webinar "When PIs Come a'Knockin': Everything Investigators Want to Know but are Afraid to Ask"

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>> ***Feige***: The broadcast is now starting. Attendees are in listen only mode.

>> Greetings. This is Elyse Summers and I'm the director of the division of education and development at the Office for Human Research Protections. Welcome to our third educational webinar, When PIs Come A-knockin': Everything Investigators Want to Know But are Afraid to Ask.

These webinars, begun this past February, are an important component of the Division of Education's menu of opportunities, which also include in-person learning activities, such as our major research community forums and our hands-on quality assessment workshops. Keep an eye on our website and your email inbox throughout the year for real-time information about the full panoply of OHRP educational programs.

Today my colleague within the Division of Education and Development, Michelle Feige, will be discussing important aspects of the requirements of the U.S. Department of Health and Human Services regulations for the protection of human research subjects as they pertain to investigators. This webinar is a basic offering, well suited to those of you who are new to the field of human subjects research and protections and those of you who are not so new, but wish to refresh and reinforce your understanding of the HHS regulatory requirements.

At this point, I would like to take a few moments to cover some of the logistical aspects of our program. If you happen to have difficulty hearing the presentation, you may want to switch your audio selection from telephone to voice over internet provider or VoIP or vice versa.

Next, I want to mention that insofar as there may be a thousand or more of you out there in cyberland listening to Michelle's presentation, it will not be possible to take questions at any point during this session. Some of you notice that your reminder email contained a request for questions. We did receive questions in advance and Michelle will make every effort, time permitting, to respond to those within or after her presentation.

As always, you may, of course, send along any questions you have related to this presentation to the general OHRP email box, Ohrp@hhs.gov. And we will answer them promptly in our normal course of activities. Also, if you would like to review in webinar and/or share it with colleagues, the recorded presentation will be posted to OHRP's YouTube channel within the next several weeks. You will find the link to the OHRP website at that time. Many of you undoubtedly know that our first two webinars on, respectively, compliance activities and nuts and bolts, are already available on YouTube.

Finally, I want to thank Lannette Myers and Samantha Smith, who, along with Michelle, are the brains behind this operation and have worked diligently to ensure the smooth production that you are about to enjoy today.

Now, it is my pleasure to turn the mic over to Michelle.

>> ***Feige:*** Good afternoon. It's a pleasure to be with you all today. I want to welcome you to OHRP's third webinar in our series. This one is entitled when PIs Come A-knockin': Everything Investigators Want to Know But Are Afraid to Ask. In this talk, I hope to fill in any information you may have about your responsibilities as investigators and also to encourage you to follow-up in the future to ask us any questions that you might have about the issues that I will be discussing today; or if you have general questions about issues not in the webinar. We very much want to be a resource for you. So my take-home message for you before we even get started is please keep in touch with us.

I know there are about -- about 900 of you out there listening, so since we are such a big group, I wanted to get a sense of the experience level of my audience. So we're about to launch a poll. And I want to ask you how much experience have you had as an investigator conducting human subject research?

So we're going to open the polls and please check the one that applies to you. Or if you are not an investigator, you can check "e." So we're just going to wait a moment while you put in your responses.

Okay. So I'm just looking at your poll. And it looks like 84 percent of you voted and a lot of you actually are not investigators. [Laughter]. So hopefully this will be relevant to you. The next highest majority of you has had about one to five years experience.

Okay. So we're going to close this poll and move on to the next poll. Which is another question I have is what is your relationship like with your IRB? And I hear a range of comments from my IRB is my best friend to my biggest nightmare. So I would like to know what your relationship is with your IRB. So we're going to open the poll.

And the question is: I have a good working relationship with my IRB, very true, somewhat true, not at all true or you don't work with an IRB. Okay. The tally is coming in and most of you have voted and it looks like, fortunately, most of you have a very good relationship with your IRB, which is great to hear. Okay. We're going to close the poll. And move on to the next slide.

So I want to start by going over my outline for today's talk. I'm going to start by giving you a little bit of background about the regulations and then an overview of OHRP and our role, and then speak about investigator responsibilities. In particular, talking about the regulations, what they are, and how to determine when they kick in. And then I'm going to discuss how you can work with your IRB and how you can help each other by understanding your roles and responsibilities. Then we're going to have a discussion on informed consent and waiver of informed consent and then talk about incident reporting and figuring out what you need to report. And then finally I will give you contact information for how to stay in touch with us.

So what is the Office for Human Research Protections and why should you care?

Our mission is to provide leadership in the protection of the rights, welfare and well-being of research subjects and we strive to provide clarification of the regulations and guidance on how to interpret them. And we realize sometimes it can be confusing and sometimes there are gray areas that we all struggle with.

So we're here again to hope to clarify some of the confusing areas.

We also develop educational programs and materials to assist you in furthering and expanding your knowledge about the regulations. We also have a lot more information on our website. So if you go to the education tab on the OHRP website, you can find more information on our activities.

And why is it important that you care about who we are?

Because you've probably heard of our compliance division, which maintains the regulatory oversight over your institutions. So in cases where the regulations are not being followed, OHRP has the authority to restrict, suspend or even terminate your institution's federal-wide Assurance which enables you to get HHS funding for your research. So hopefully that last statement woke you up sufficiently so that we can get into more details about the regulations.

So even though I'm going to be talking about mainly your responsibilities as investigators, clearly it "takes a village" to make research run smoothly and ethically.

The institution, research staff, IRBs, families and subjects all play a vital role in ensuring the protection of the subjects and integrity of your research.

So let's start off with perhaps an obvious and simple question: Who are you and what makes you an investigator?

The term "investigator" refers to an individual performing various tasks related to the conduct of human subject research activities, such as obtaining informed consent from subjects, interacting with the subjects and communicating with the IRB. Investigators can include physicians, scientists, nurses, administrative staff, teachers, students, amongst others.

In every human subject research study, investigators have responsibilities regarding the ethical treatment of human subjects, which is what this talk is going to focus on.

So what are your responsibilities as an investigator?

First and foremost, you are responsible for conducting ethical research. In some cases, there may be debate or some confusion about what ethical research is. And one primary and fundamental "go-to"

resource for knowing how to conduct ethical research, besides the regulations, is the Belmont Report on which in large part the regulations are based.

In 1979, the National Commission issued the Belmont Report, which was a groundbreaking document outlining ethical principles and guidelines for human subjects protections. Today the Belmont Report continues to be an essential reference in order to ensure that the research meets the ethical foundations of the regulations.

And for any of you out there who have heard me speak before, you know that I am a huge fan of the Belmont Report and I highly recommend you read it if you haven't. And if you have, reread it. It's a very beautifully written document and is very inspiring and thought provoking.

The Belmont Report identifies three fundamental ethical principles for all human subjects research. Beneficence, which is an obligation to protect persons from harm by maximizing benefits and minimizing risks. Justice, which is a fair distribution of the benefits and the burdens of research, that subject selection should be careful and equitable and that you should ensure that certain classes of individuals are not systematically selected or excluded unless there are scientifically or ethically valid reasons to do that. And thirdly, respect for persons, which is recognizing the autonomy and dignity of individuals and the need to protect those with diminished autonomy. And when reading the regulations at 45 CFR Part 46, you can see strong echoes in the language of the regulations from the Belmont Report.

So besides conducting ethical research, another key responsibility that you have as an investigator is to follow the rules. A logical next question would be which rules do I follow? And that can sometimes be a complicated question and in some cases, several sets of rules may apply. So it's important to know which rules apply and when they apply. As you know, the focus of this presentation is on the HHS rules at 45 CFR Part 46 and I'm going to talk you through how to figure out when they apply.

The meat of the regulations fall under Subpart A which talks about IRB membership, IRB review, informed consent, et cetera. These regulations are often referred to as "The Common Rule" and it's called The Common Rule because 17 additional federal departments and agencies have adopted these regulations

and used them as their own. Listed on the slide are the agencies or departments that have adopted them. You may notice that the FDA is not included on the list of agencies that have adopted The Common Rule. They have their own set of regulations. And since they do, I won't be discussing them, but would encourage you to contact the FDA when you have questions that pertain to FDA regulated research. In addition to Subpart A, the regulations have three additional subparts, which provide added protections for special populations. Pregnant women, fetuses and neonates are covered under Subpart B, Subpart C covers prisoners, Subpart D covers children.

It's very important to remember that in order for research to be approved by your IRB, when working with any of the populations covered under the subparts, not only do the regulatory findings need to be satisfied under Subpart A, but additional findings under each subpart would need to be satisfied as well. So, for example, if you are working with a pregnant, incarcerated teenager, you would need to fulfill all of the requirements under all of the subparts.

Earlier I mentioned that at times there may be more than one set of rules that apply to your research. What is important is that you know if they apply and what those additional rules and policies are.

So some examples of rules that may come into play: the FDA regulations -- and again those would come into play when research involves FDA regulated products, drugs, devices and biologics; and other departments or agency rules. So, for example, if you are doing research that's funded by the Department of Education or the VA, they may have additional requirements that go above and beyond the HHS regulations and you need to be aware of those. There may also be state and local laws, and again those are important to be aware of. There may be laws that address specific issues about conducting research in your state or local jurisdiction.

And then finally, institutional policies, which would need to be followed.

Under the regulations, an FWA holding institution is required to have written policies and procedures. And I highly recommend reading your SOP's and knowing in detail how your institution deals with important issues concerning the research that you are conducting. So, again, I encourage you to go to your

IRB office and ask them for a copy of your policies and procedures.

So now that you know what you need to be mindful of in terms of the many levels of rules that come into play, I want to move on to a discussion of how you figure out if the HHS regulations, apply to your research activities.

So the HHS regs apply when you are conducting HHS-supported non-exempt human subjects research. So basically, if you are being funded or supported by HHS, NIH, for example, and are conducting non-exempt human subjects research, the regulations kick in.

Besides following the money trail, the regulations may also kick in if your institution has voluntarily agreed to apply the regulations regardless of source of support, which also is referred to as “checking the box”.

That would mean that you would need to follow the HHS regulations for all non-exempt human subjects research at your institution, whether or not it was HHS supported. So clearly it's very important that you know if your institution has or has not checked the box. So if you don't know, I would suggest that you try and find out.

So moving on, let's assume that your activities are either HHS supported or that your institution has checked the box. We still don't know if you are conducting non-exempt human subjects research, so how do you know when you are? What you would do is you would ask these three questions that are on this slide and it's very important that you ask these questions in this order. And I'm going to go over each of these questions briefly in the next few slides. But I want to also refer you to the decision charts that we have on our website that will really help you think through some of these questions.

So the first question is: Does the activity involve research?

And the regulations help you out by giving you a definition of what research is according to the regulations, which is: A systematic investigation designed to develop or contribute to generalizable knowledge. And that includes research development, testing, evaluations and pilot studies.

So in order for the activities to meet the regulatory definition of research, they must both be a systematic

investigation and contribute to generalizable knowledge. If one of the prongs is met but not the other, it would not be considered research. If after looking at this definition it is determined that these activities do not meet the definition of research, you don't need to go on to the next question because you know now that the regulations will not apply.

So the next question is: Does the research involve human subjects? And before we get on to that question, let's do a quick poll looking at this question. So we're going to launch the poll. So pick one answer. Human subjects are involved in my research when I obtain: a, identifiable private information about a subject; b, obtain data through an intervention with the subject; c, obtain identifiable private information about a deceased subject; or d, a and b only.

Okay. So I have a very smart group of people here. And almost all of you picked d, which is the correct answer.

None of you picked c and you all knew that the regulations define a human subject as a living individual. So let's move on to the next question, which is, does the research involve human subjects?

Again, the regulations provide you with the definition, which is "a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or private identifiable information."

That private information must be individually identifiable, which means that the identity of the subject is or may readily be ascertained by the investigator or associated with the information. So, again, if your activities do meet the definition of research, but not of a human subject, you can stop here, as the regulations would not apply.

However, if you discover that you are indeed conducting human subject research, you move on to the next question.

So the next question is: Is the human subject research exempt?

And the regulations provide six categories of human subjects research activities that are exempt from IRB review and they can be found at 46.101 (b,) 1 through 6. Unfortunately due to time limitations, I don't have

time to go into them, but we do have decision charts on our website and you can always call us or email us if you have questions about them.

But basically if your activities fall into one or more of these categories, your research would be exempt from the regulations. Just a quick note about the exemptions and the subparts. If prisoners are involved as subjects, exemptions do not apply; and all of the exemptions can be applied to Subpart B which covers pregnant women, fetuses and neonates. And there are some limitations when conducting research with children, in particular under Category 2, and I would recommend that you see our FAQs on that topic. And just one quick word about who can make the determination about whether or not the regulations apply. The regulations are actually silent about who at an institution may determine that the research is exempt or not. And I would refer you to our FAQs on that topic and would suggest that you check your policies and procedures or with your IRB office about who can make that determination at your institution.

I also want to again encourage you to read your SOPs. Some institutions have actually decided to go above and beyond the regulations and require the review of exempt research, so again it's important that you know what is required of you at your institution.

And here are some links that can help you with this decision. The human subject regulations decision charts, the FAQs on quality improvement activities, and also guidance on engagement.

So now you know that you need to follow the regulations for your research. So what happens next? You need to be aware of both what the regulations require of you and what your IRB and your institution requires of you. The regulations actually give quite a bit of flexibility to IRBs and that's another reason that it's so important to understand and follow the procedures from your institution.

So let's do another quick poll. As you know, you and your IRB need to work together. Before we move on to understanding a bit more about how your IRB works or how you can work together, let's look at when you need to obtain IRB review and approval. Again, pick one. Okay. And most of you are correct that the answer is d, all of the above. So we're going to close the poll. And move on to the next slide.

So you as investigators are responsible for obtaining IRB approval on several occasions: before

beginning any non-exempt human subject research or initial review; at the time of continuing your review; and prior to making any changes to the approved research, unless it is to eliminate an apparent immediate hazard to the subjects. If investigators change the research in order to eliminate apparent immediate hazards to subjects without prior IRB approval, you should report those changes promptly to the IRB. It's important to remember these required times that you need to go to the IRB because if you don't get IRB review and approval under the above circumstances, you'll be in violation of the regulations.

So just briefly, what are the different types of IRB review that you could expect? When submitting your research to the IRB, you should be aware that there are two types of review that could be conducted and it would depend upon the type of research that you are submitting and when you are submitting it.

The first type of IRB meeting is called a convened meeting, which consists of a meeting where a quorum of IRB members are present. It's also sometimes referred to as a full board meeting. Approval in a convened IRB meeting is by a majority present and a convened IRB can disapprove research. The second type is expedited review. An expedited review requires same substantive and meaningful review as a full board review, except that it is commonly conducted by the IRB chair or one or more experienced reviewers designated by the chair.

In conducting expedited review, the IRB reviewers may exercise all of the authorities of the IRB except that they may not disapprove the research. A research activity may be disapproved only after review by the convened IRB in accordance with the non-expedited procedure. Anyway, in order for a protocol to qualify for an expedited review, an activity must involve no more than minimal risk and be found on the list of expedited review categories, which you can find on our website, or be a minor change in previously approved research during the period of one year or less for which approval is authorized by the IRB.

So, again, going in it's sometimes helpful to know what type of review your research will undergo.

So besides knowing that you need to submit your research to your IRB, there are things that you can do to help the IRB help you and perhaps even expedite getting your research through the IRB.

First of all, it's helpful to know what documents or information your IRB expects you to submit to them.

Check with your IRB office to see if they have a checklist or if they might be willing to create one if they don't have one yet. Once the IRB receives your submitted research information, for example your protocol, consent, grant application, recruitment information, et cetera, the IRB must fulfill its regulatory obligations, including making the required determinations under 46.111, which are listed on the slide and applicable Subparts B, C and D. One thing that you can do to help your IRB and work well with it is to ensure that your submitted documents have addressed the issues found at 46.111. If you have not addressed these issues and the IRB cannot make the required findings, the IRB cannot approve your research. So knowing up front that this information needs to be addressed can save you and your IRB valuable time.

Some other considerations for working well with your IRB are: Do you understand your IRB's expectations and policies? Have you provided sufficient information and materials to the IRB? Are there certain requirements that go above and beyond the regs that your IRB requires or that you need to be aware of? If you have a conflict of interest, have you worked with your IRB to recognize and manage it? Have you complied with the IRB's decisions and requirements? Have you responded to your IRB's requests in a timely fashion? Again, all of these considerations can help you and your IRB work well together.

So now you have gotten through the initial review and your study got approved, so congratulations! But wait, there's more. The regulations go on to say that an IRB must conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. So as I'm sure you are well aware, what that means is that you need to have your research reapproved every year or in some cases, if the IRB requires, more than once a year. If you don't get your materials into the IRB in time to review it prior to the expiration date, there would be a lapse in continuing review, which means that all of your research activities involving human subjects must stop, unless it is determined to be in the best interests of already enrolled subjects to continue participating in the research. You also cannot enroll new subjects after the expiration of IRB approval.

So it's clearly in your best interests to get your materials in on time.

Continuing review is required so long as the research study is ongoing. That is until research-related

interactions and interventions with the human subjects or obtaining an analysis of identifiable private information described in the IRB approved research plan have been completed.

So at the time of continuing review, what do you need to do? You would need to follow your institution's policies and procedures and report progress of approved research to the IRB as often and in the manner prescribed by the IRB. You are also responsible for submitting sufficient materials and information for the IRB to meet its regulatory obligations and should follow the institutional procedures for continuing IRB review of research. Generally this information is submitted in a progress report, which might contain the information on this slide. Of note, if there's any new information since the last review that might alter the IRB's ability to continue to approve under 46.111 criteria, which we discussed earlier, that is critical information to provide to your IRB.

So moving on to another area of investigator responsibilities that protect your subjects, informed consent. So one question that you might have is: Do I always need to obtain and document informed consent? And the answer is generally, yes.

You are responsible for obtaining and documenting informed consent unless the IRB approves a waiver of informed consent or a waiver of documentation of informed consent. In addition, you must give a copy of the informed consent document to each research subject or the subject's legally authorized representative (or LAR) and keep a copy for your records.

So what information needs to be included in the informed consent documents?

As we discussed earlier, under 46.111, the IRB must make the required findings in order to approve the research. One of the 46.111 findings is that informed consent will be sought in accordance with 46.116. So what does 46.116 say? 46.116 are the basic elements of informed consent required under the regulations. You would want to address and give a description of the elements noted on this slide as appropriate. And this is another area that you can help your IRB help you.

When submitting your consent for review and approval, your IRB will look to make sure that you have included these required elements. So ensuring that you have submitted a consent which includes them may

increase the likelihood of a smooth approval process. In addition, the regulations list several additional elements which should be included, again, as appropriate. For example, any risks related to pregnancy, any circumstances under which the subject's participation may be terminated by the investigator, any potential additional costs to the subjects from participation, a description of any consequences of withdrawal, a statement that any significant new findings will be shared with the subject when appropriate, and the approximate number of subjects in the study.

So, as I alluded to, there may be times when you believe, for the sake of your research, that informed consent should be altered or not obtained at all. The regulations do allow for the IRB to waive or alter informed consent or documentation of informed consent and I'm going to spend the next few minutes going over these options.

So under the following specific circumstances, the IRB can waive or alter informed consent. If the IRB finds and documents that the research involves no greater than minimal risk, the waiver or alteration will not adversely affect the rights and welfare of the subjects, the research could not practicably be carried out without the waiver or alteration and when appropriate, subjects will be provided with additional pertinent information after participation.

And just as a note, the threshold for practicability is relatively high and doesn't mean just inconvenient or difficult.

I wanted to briefly mention a rarely used provision that allows for the IRB to waive informed consent when the research project itself contemplates the involvement of people who are unable to give informed consent. For example, a research study looking at the issue of head trauma in the emergency room. So for more information on this, I would recommend you look at our OHRP guidance on emergency waiver on our website.

Another question we get asked is what can I do when I believe my research would be better served if I didn't need to document informed consent? Under certain circumstances, the IRB may waive the requirements for an investigator to obtain a signed consent form if it finds either that the only record linking

the subject and the research is the consent document and the principal risk would be potential harm resulting from a breach of confidentiality; or that the research presents no more than minimal risk and involves no procedures for which written consent is normally required outside of the research context. So again if your project meets either of these circumstances, your IRB may waive documentation of informed consent. Even though I've focused on when consent is not required, in general it is required. So what should you be aware of when obtaining informed consent? A few comments about the consent process. First of all, in general, consent should be an ongoing educational dialogue between you and your subjects. You want to be aware that there may be circumstances where it would be appropriate for you to update the consent form or when it is mandated by the IRB. As I mentioned earlier, you must provide a copy of the consent to the subject or their LAR and if you are conducting research with children, Subpart D will kick in and the regulatory verbiage looks a little bit different. You would now be attaining assent from the child or parental permission from the adults. Again, I would recommend that you look at our FAQs and guidance for more information on this.

There are several key elements to be aware of in the consent process. You want to ensure the full disclosure of the nature of the research and the potential risks involved. These are generally spelled out by the required elements found in the consent form. The regulations require that the information given to the subject or their LAR is in a language understandable to them, so figuring out how to facilitate understanding is important.

Conveying to subjects that their participation is voluntary and that exculpatory language is not permitted and you must minimize the possibility of coercion and undue influence.

Okay. So you've done a great job submitting your research, getting it approved, obtaining consent and now you have begun your research study. So what are your responsibilities now that the study is active? So listed on the slide are just some of the things to consider during the course of your study to continue to protect your subjects. Ensure that the informed consent process continues, assure that privacy and confidentiality is maintained as described in the consent form, continue to monitor the rights and welfare of

your subjects, submit timely continuing review documents to the IRB, safety monitoring should be in place as necessary, report incidents to the IRB, which I'm going to go over in a minute, and uphold and act upon any additional safeguards that were put in place to protect vulnerable populations.

As I mentioned, there are reporting requirements, so what are your responsibilities for reporting incidents to the IRB? The regulations require that institutions have written policies to ensure that the following incidents are reported properly to the IRB, appropriate Institutional Officials, the department or agency head and to OHRP: unanticipated problems involving risk to subjects or others, serious or continuing non-compliance with the regulations or IRB requirements, and suspension or termination of IRB approval. And I'm going to discuss the first one on this list, what are your responsibilities as investigators to report unanticipated problems to your IRB.

What I'm going to focus on is where you would mainly come in as an investigator. So in order for the IRB to meet its reporting requirements, it needs to hear from you first. You are required to inform the IRB when unanticipated problems or UP, involving risks to subjects or others take place. In my experience, many investigators don't know the definition of an unanticipated problem and are therefore either under or over reporting to the IRB. So I want to spend a few minutes going over the definition of a UP so you know when to inform the IRB when they occur. I need to start briefly with going over something that's not even in the HHS regulations but is a term that is commonly mistaken with a UP, and that term is an adverse event or an AE.

The term adverse event in general is used very broadly and includes any event meeting the following definition: Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign, symptom or disease, temporarily associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. Adverse events encompass both physical and psychological harms. They occur most commonly in the context of biomedical research, although on occasion they can occur in the context of social and behavioral research. An AE is not necessarily a UP and it's important that you understand the difference.

So what exactly is an unanticipated problem? A UP is any incident, experience or outcome that is unexpected, in terms of its nature of severity and frequency, related or possibly related to the research and suggests a greater risk of harm than was previously known or recognized. So it's important to understand the differences between an AE and a UP and I would suggest that you look at our guidance document on this topic for further clarification.

This diagram shows what needs to be reported to your IRB and to OHRP and that most AEs are not UPs and would therefore not need to be reported to OHRP. Your IRB can help you with this as can our guidance document on this topic.

Finally, what are your responsibilities once your study is completed? If all research-related interventions or interactions with human subjects have been completed and all data collection and analysis of identifiable private information described in the IRB approved research plan have been finished, then your study has been completed. When it's been completed, you no longer are required to obtain continuing review and approval of that study by the IRB. You should follow any applicable institutional policies and procedures for notifying the IRB of the study's completion.

Be sure to comply with the requirements for the retention of records as required by the IRB or your institution. And again it's important to look at the regulations as well as your institution's policies and procedures.

The regulations require record retention for three years after the completion of the study. But your institution or state may have additional requirements. So it's important to find out what they are. You would want to store study data consistent with the IRB plan and ensure privacy and confidentiality of data and records. And, finally, you should be sure to honor any other commitments that were agreed to as part of the research, the approved research. For example, providing information about the study results to research subjects or honoring commitments for compensation to research subjects for their participation. So in conclusion, I would encourage you to read and follow the Belmont Report, federal regulations, IRB and institutional procedures and policies, obtain document and retain legally effective informed consent,

promptly report changes to the IRB, ensure ongoing protections for your subject and understand your role when reporting incidents to OHRP.

And, most importantly, please keep in touch with us. I would encourage you to join our listserv, which you can find under the newsroom on the OHRP website and again feel free to call us or email us with any questions.

As a reminder, as Elyse mentioned, this webinar will be posted on our website in two to three weeks. Again, thank you for joining me today and I wish you all a lovely day.