Greetings. This is Elyse Summers, and I'm the Director of the Division of Education and Development at the Office for Human Research Protections. We at OHRP are delighted that you are joining us today on our maiden web-based voyage into the 21st century, as we present our first in a series of educational webinars focused on critical issues in the protection of human research subjects. Stay tuned to the OHRP Listserve and website for more information on future OHRP webinars of interest.

At this point, before I introduce today's speaker, Dr. Kristina Borror, Director of OHRP's Division of Compliance Oversight, I'd like to take a few moments to cover some of the logistical aspects of our program. First, although Dr. Borror will be speaking, during the webinar, your control panel will read "speaking:

Samantha Smith." This is just an unavoidable idiosyncrasy of the software configuration. As many of you know, Samantha is one of our wonderful Division of Education colleagues, and she is the wizard behind the curtain today. I guarantee that in the not-too-distant future when you see the words "speaking: Samantha Smith" it really will be Samantha speaking.

But, I digress. Back to logistics: If you should 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.

In addition, given that there are 1,000 or more of you out there in Cyberland listening to Kristina's presentation, it will not be possible to take questions at any point during this session. Some of you noticed that your reminder email contained a request for questions. We did receive questions in advance and Kristina 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 Kristina's presentation to the general OHRP e-mail box, OHRP@hhs.gov, and we will answer them promptly in our normal course of activities. If you would like to review this video or share it with colleagues, the archived presentation will be posted to OHRP's YouTube website within two weeks. You will find the link on the OHRP website at that time.

Now, it is my utmost pleasure to introduce Dr. Kristina Borror, OHRP Director of.

Compliance Oversight, who will present today's webinar: "When the Feds Come

Program." Kristina is responsible for directing the conduct of compliance oversight evaluations in response to complaints alleging non-compliance with the human subjects regulations, as well as a program of not-for-cause evaluations. She also directs the review of incident reports from institutions regarding non-compliance, unanticipated problems, suspensions and terminations of IRB approval. Prior to coming to OHRP, Kristina was a Science Policy Analyst at NIH within the Office of Science Policy, Office of the Director, National Institutes of Health. Prior to working for the Office of Science Policy she conducted basic cancer research at the National Cancer Institute. Kristina received her Ph.D. in Biology at the University of Pittsburgh.

Go panthers. Okay, then, we hope you're all comfortable and ready to learn. Kristina, take it away.

[slide 2] Thanks, Elyse, it's a great pleasure today to bring you OHRP's inaugural webinar. I'm going to first gave you a little background about our jurisdiction. And how OHRP conducts compliance oversight evaluations, including some details about site visits.

I'm going to tell you some tips for preparing for an OHRP evaluation, some of the common findings of non-compliance that we've made in the course of our evaluations, and we're going to test some of your knowledge of the regulations and of non-compliance findings. And then we'll conclude with some resources that will help you in preparing for an OHRP evaluation.

[slide 3] So OHRP's jurisdiction, as you may know, is for human subjects, non-exempt human subjects research that is conducted or supported by the U.S. department of health and human services. So we have to follow the money.

But in addition to that, as you may know, institutions that receive HHS support for human subjects research have to have an Assurance of compliance with our office and we also have jurisdiction over any research that is covered by that Assurance, and institutions are voluntarily allowed to apply that Assurance to all research, regardless of support. That's sometimes what we call "checking the box." And then we would have, if the institution had checked the box, we would have authority over all research at that institution that involves human subjects. [slide 4] So when we conduct a compliance oversight investigation, we first have to receive an allegation or see an indication of non-compliance. OHRP receives allegations from a variety of sources. One of the most common sources is human subjects themselves. People who are in research and have some concern or family members of subjects. We also receive allegations from internal whistle blowers, such as researchers themselves, IRB members or chairs or staff. We also sometimes get allegations from advocacy groups.

We also can see indications of non-compliance in the press, either in lay press or in medical journals.

When we see an allegation or an indication we first determine whether or not we have authority. As I mentioned we would have jurisdiction if there's HHS support for non-exempt human subjects research or if the institution where it's conducted

checks the box and we would have authority.

And we also have to determine whether or not the allegations are related to our regulations. We also have discretion on whether or not to open an investigation. So if we decide that we're going to investigate, we will send a written inquiry to the appropriate Institutional Officials. That's generally the signatory official on the FWA, the human protections administrator, and any of the internal IRB chairs.

We also will generally cc the investigator of the research that's being complained about.

We tell them what the allegations are, we ask them to conduct an investigation of their own into the allegations, and to send us a report of that, along with supporting materials. Including relevant IRB documents, and that would include the protocol, informed consent document, meeting minutes in which the study was conducted, et cetera.

We then communicate with the institution as necessary. And most of our communication in the context of an investigation is through correspondence, but we can also do telephone interviews or teleconferences and video conferences, as well as, on occasion, a site visit.

And then we will issue our final determinations.

[slide 5 and poll 1] So now we're going to do a poll to determine, find out a little bit more about the people who are on the call and what kind of compliance oversight interactions you've had with our office.

And so some of the questions that -- that you can have multiple answers. The first one is my institution has had a for-cause OHRP evaluation. My institution has been the subject of a not-for-cause OHRP evaluation. Or, C, my institution has been blessedly free of compliance oversight intervention from OHRP. And you can select multiple choices. For instance, you can select both the first one and the second one if you've had both. And we'll give you a minute or two to respond.

Okay, we're going to close off the voting now and tell you what the results are. So 9% of you have said that your institution has been subject of a for-cause OHRP evaluation. 16% of you said your institution has been the subject of a not-for-cause evaluation. And 77% of you have luckily not had any compliance oversight interactions with our office. As far as evaluations.

[slide 6] So the next slide indicates that when we receive complaints, we can always refer them to other agencies, such as FDA. So even if the research is conducted at an institution that applies its Assurance to all research regardless of support, if there's no HHS support and it is FDA regulated, we will refer that complaint to the FDA. And we also can -- and will refer it to another common rule agency if the research was funded by that agency, such as the Veterans Health Administration or the Department of Defense. And we can also refer it to another HHS agency such as the Centers for Disease Control and Prevention.

[slides 7 and 8]So some tips on how to prepare for an OHRP evaluation. One of the things that we have been told institutions find very helpful is to review our recent compliance oversight determinations. This was updated in 2009 and can

be found at the U.R.L. on your slide. You can also find all of our determination letters that have been issued by our office since July of 2000. They are on our website in the compliance oversight section, under determination letters. And you can see all of the determinations that we've made and some of the corrective actions that institutions have done to address those determinations.

We also recommend that you re-review the regulations, particularly the subparts, if you are conducting any research involving such vulnerable populations. You might want to review OHRP guidance documents to see what we are saying about our interpretation of the regulations and what we would expect as far as following them. You can -- you might want to review your institution's standard operating procedures and update them as necessary, make sure that all of the required written procedures are in there.

You also want to make sure that your institution is clearly and consistently documenting all of the IRB activities. And especially if we're doing a site visit, it would probably be useful for you to designate one contact person at your institution that will interact with our compliance oversight coordinator to coordinate any requests or questions that we have.

[slide 9] So I'm going to tell you a little bit about the difference between for-cause evaluations and not-for-cause evaluations. As I mentioned, for-cause are in response to substantive allegations or indications of non-compliance, most of these are usually done through correspondence. Greater than 90% of them are just through correspondence, although we can do site visits as I mentioned.

Not-for-cause evaluations usually assess institution's compliance in the absence of any specific evaluation. We're looking at the institution at a whole, but they can be partially for cause. For instance, if we've had some previous compliance problems with an institution or have gotten some vague allegations such as “this IRB is in meltdown.”

Some of these are actually through a site visit and a higher percentage of them are through site visit, about one-third. [slide 10] And to -- to tell you a little bit about more about a for-cause site visit, how do we make a determination of when we're going to go on-site. As I said, most of these are through correspondence, but we may decide to do a for-cause site visit depending upon the nature or severity of the allegations, if there's any evidence of systemic problems we're going to be more likely to want to go onsite. Also, what has been the appropriateness of the corrective actions that the institution has taken. And are we sure that they have actually taken them.

Or if we have some -- see a need for having more in-depth discussions with institution staff. Sometimes it's useful to just get -- sit down, face-to-face with folks, to try to find out what is going on.

[slide 11] And -- when we do a site visit, either for-cause or not-for-cause, they do slightly differ. In a for-cause, as I mentioned, it's triggered by an open compliance case. When we do a for-cause site visit, the team usually includes the OHRP legal counsel, two to five OHRP staff, two to four outside consultants, which can include folks like ethicists, research coordinators, IRB coordinators, IRB

chairs or staff and researchers themselves. These site visits usually last three to four days and there's a dual focus both on the allegations and we're also looking at the systemic protections at the institution. When we do a not-for-cause site visit, there's no open compliance case and the site visit team is usually smaller, one to three OHRP compliance staff, sometimes our legal counsel, plus one to three outside consultants. They are usually shorter, two to three days and the focus here is on the systemic protections at the institution.

[slide 12] When we do any kind of a site visit we're going to do a record review. Prior to the visit, we ask the institution to send us a list of all, at a minimum, HHS supported human subjects non-exempt research. And from that list, we will select 25 to 75 active protocols that we will ask the institution to pull the records for that we can review on site.

We're going to want the entire record of the IRB. We're going to have -- we want to see all of the protocols that were reviewed and informed consent documents, IRB meeting minutes, et cetera. In addition, we also ask the institution to have available the last 25 protocols and amendments that the institution approved by -- under an expedited review procedure and also the protocols that were determined by the institution to be exempt during the past six months, and at a minimum the minutes for all IRB meetings for the past four years.

[slide 13] We will also conduct interviews at site visits. Both for-cause and not-for-cause. We want to -- to interview the institutional administrators and including most importantly the signatory official on the FWA. We also want

to talk to the IRB chairperson. The IRB members, usually separate from the chairpersons, the IRB staff, usually separate from the human protections administrator, and a for-cause site visit we will also interview investigators that are conducting the research related to the allegations.

And for all site visits, both for-cause and not-for-cause, we ask the institution to choose a variety of investigators that submit protocols to the IRB, so that we can ask them questions about the system for protecting human subjects and how they interact with the IRB.

And we may also ask to interview others as appropriate.

[slide 14] When you are preparing for an OHRP site visit, when you are looking at the location to have the site visit, you should make sure that it's in such a place that the requested files can be easily accessible to our team. Either in the room where we're conducting the record review or somehow transportable between rooms. We would also like you to make available some of your staff to retrieve additional requested items that we may need during our record reviews. Also ensure that there's an adequate space for the site visit team to conduct our record review.

[slide 15] When you are preparing the records for a site visit, first look--are all of the files in order? Are they easy for people to follow chronologically? Does your institution have an electronic filing system? Is everything done electronically? Do -- if -- OHRP staff are going to have access to the electronic files? We may ask you if you have such an electronic system, to give us access to that system before the site visit because some of these electronic systems have

a high learning curve and it may take us a while to figure out how to operate them. We don't want to spend time during those precious hours of the site visit trying to figure out how to work your electronic system. So we might want to try it out beforehand. And so it's helpful if the system is easy to follow.

We also want to be sure that the excerpts from the minutes for each protocol are in the file. If they are not in each file, make sure that the minutes are easily accessible for all of the IRB meetings in which any of those protocols we requested are discussed.

[slide 16] As far as the interviews, make sure that the parties that we have requested to interview are going to be available at the specific time. And if we have requested a particular person to be there, such as investigators, make sure that you let them know plenty of time before the site visit so that they can tell you whether or not they're going to be available and so that we can make other arrangements, such as maybe have them included by a teleconference.

And when we have, as I said, we ask the institution to choose some investigators so that we can talk to them just about your general system. Try to choose a variety of investigators. Who -- who -- to -- to submit a variety of different kinds of research protocols to your IRB. And maybe not just your favorite investigators, but also sometimes it can be helpful for us to talk to your curmudgeons.

And if you are going to have some of the people that we want to interview by teleconference, make sure that there are appropriate technological facilities

and capabilities for that.

[slide 17] After a site visit, OHRP will send you a letter with our official findings or we may have additional questions or concerns about what we saw. And you will usually receive that letter within two or three weeks. Your institution will be asked to respond to that letter with a corrective action plan, if we found any non-compliance, or with answers to any of the questions and concerns that we had within about six weeks after we send the letter. And we want to look at the adequacy of any corrective action plans that you propose.

[slide 18] So what are some of the outcomes of any kind of evaluation that OHRP does?

Well, we can find that protections at your institutions are in compliance. It actually happens. We can also find that you are in compliance, but we may recommend some improvements. These first two in which we don't find any non-compliance at your institution happen about 10% of the time. So it's not extremely rare, but it's not the most common thing. The most common is that we identify non-compliance and we require institutions to take corrective actions to correct it.

The next thing that we can do and the more serious is that we identify non-compliance -- and this is serious non-compliance and we will restrict or suspend your Assurance pending required corrective action.

And restrictions can range from requiring quarterly reporting of your institution to a complete suspension of your Assurance so that all non-exempt

federally funded human subjects research at your institution must stop. Except when -- when it's necessary for -- for the best interests of the subjects to continue in research if they are already enrolled.

(slide 19) The next more serious outcome from a compliance oversight investigation are that we identify non-compliance and we withdraw approval of the Assurance. And this is a pretty serious thing. We haven't done this in a number of years. Back when we had done some withdrawal of Assurances, it was at a time when OHRP had multiple different kinds of Assurance mechanisms. And so say an institution had a Multiple Project Assurance, which allowed them to conduct many different projects that were HHS supported and we withdrew that Assurance. What we would do is require them to apply for a Single Project Assurance for each single project that was HHS supported after that fact. And those Assurances would come under closer scrutiny by our office.

We now only have one Assurance mechanism, which is the Federalwide Assurance, so withdrawal of approval of Assurance would be a much more serious thing today. We can also, in increasing seriousness, are -- to recommend to appropriate HHS officials that an institution or investigator be either temporarily suspended or permanently removed from a particular project. Or we can ask that the HHS to notify peer review groups of an institution or investigator's past non-compliance, OHRP has never done these two things, but it remains something that we can could do. [slide 20] Then the most serious of the possible outcomes is that OHRP can recommend debarment of an institution or investigator, which means that they would be declared

permanently ineligible to participate in HHS-supported research. This is the most serious thing that we could do, although we have never actually recommended debarment of an institution or an investigator.

[slide 21] So ... the next is some little compliance data. As a former scientist, I just can't resist showing data when I can. People also like to see what are some of the trends in our compliance oversight activities.

[slide 22] And this slide shows the number of new cases we have initiated each year from 1990 until 2011. And if you look at the scale on this, it goes up to 100 and you can see that in the late '90s or early 2000s, it was at the highest level of the office, approaching 100 cases per year. And you can see that since then, the number of new cases has been declining. We often get asked why do you think there is that decline? We can't say for certain, but we think that some of the reasons include the -- the ability of institutions to “uncheck the box.” That is to say that their Assurance no longer applies to all research, regardless of support, but only to federally supported research. And that reduces effectively the amount of research out there that we have authority over.

Also, we have started within the last five or so years, instead of when a research study does -- we do have authority over it at an institution, that has “checked the box,” but if it's not HHS supported and FDA regulated, we will forward that complaint to the FDA and not elect to -- to investigate it, also.

We also like to think that the reason why there's been a decline in new cases is that more institutions have gotten the word and are doing the right thing and

we hope and we think that there is actually less non-compliance out there.

[slide 23] The next slide shows the number of site visits that we've done in the same time period. And I want to point out that the scale on this is very different. This the top of the scale is only six where the other was 100. So you can see we do far fewer site visits than we do compliance oversight investigations. And the most that we have ever done in any single year is six. Last year we did three. And you can see that during the time period in which we had a high level of new cases, we also had a higher level of site visits. But it's never been higher than six per year.

[slide 24] The next slide shows the numbers of suspensions or restrictions of Assurances in that same time period. And, again, the scale here is the highest at seven and then in the time period when we were opening a lot of new cases, we also had a higher number of suspensions and restrictions in the late '90s and early 2000s. But you can see here that we haven't had a suspension or a restriction of Assurance since 2007.

[slide 25] So next I'm going to switch gears a little bit and talk to you about some of our common findings of non-compliance.

Our determination letters can be found on our website and OHRP has the determination letters from -- since as I said, July of 2000. We also have significant findings on our websites in which you can see some of the most common findings that we've made in the last five years or so.

In addition, we have two publications that have been authored by compliance

oversight staff in the last eight or so years. There was one in 2003 and we did an update in 2010, which is a summary of that.

[slide 26] So what are some of the most common findings that we have made in our office in the last few years?

One of the most common ones is we have found deficiencies in informed consent documents, particularly with respect to how they describe the risks and discomforts but also problems with other elements. Another most common finding is that the IRB has received insufficient information that it needs in order to make the determinations required for approval under 111. Another common finding that we have made is that the IRB does not have adequate written procedures that the regulations require.

[slide 27] The next most common findings are failure of the investigator to obtain the legally effective informed consent of the subject and this is when informed consent could not appropriately be waived.

Also, more common are protocol changes made without prior IRB review and approval. We've also seen problems with failure of the IRB to conduct continuing review at least annually and this is in cases where research was conducted during that lapse in approval.

We also see problems with inadequate IRB meeting minutes.

[slide 28] The next most common findings are failure to report non-compliance, suspensions or terminations of IRB approval and unanticipated problems.

Also, we've seen expedited review conducted by someone other than an

experienced IRB member as required by the regulations. And also the most -- one of the more common ones is failure of the IRB to make and document the required findings for waiver of informed consent. [slide 29] So we're going to test your knowledge a little bit and -- and there is -- um ... what these next slides are going to go into, some of the -- some of the consent documents, deficient with respect to risks and discomforts. [poll]

And the regulations state that when seeking informed consent, that they have to provide to each subject a description of any reasonably foreseeable risks or discomforts to the subject. And we have a poll here and which of these risks and discomforting need to be in the informed consent document? First is risks associated with additional PET scans, the risks of standard of care if it's dictated by the protocol, any new findings of risks in a study arm, or the risks of violation of confidentiality, if it could damage a subject's reputation, or none of the above. And note that -- that you can have multiple right answers, so you can select multiple answers to this question.

Okay. I think we're going to close voting. Almost 80% of you have voted. And here are the results.

93% of you said the risks associated with additional PET scans would need to be in the informed consent document. You are correct. Those would need to be as a risk. And the next one is risks of standard of care if it's dictated by the protocol. And 72% of you thought that that needed to be in the informed consent document and those 72% are actually correct. That was probably the hardest one

that some of you thought wouldn't need to be. The reason it needs to be in the informed consent document is because it's dictated by the protocol. It's not any old way of doing standard of care, but the protocol is saying exactly how that standard of care should be delivered to subjects. 93% of you thought that new findings of risks in a study arm needed to be provided. That is also correct. And 92% of you thought that risks of violation of confidentiality if it could damage a subject's reputation needed to be in there and that is correct, also. And only one percent thought none of the above.

[slide 32] So the -- the next one that we're going to talk about when the IRB gets insufficient information to make the determinations under 111. As you may remember, 111 has the criteria for IRB approval. And this includes that the IRB needs to determine that risks to subjects are minimized and reasonable in relation to benefits, that subject selection is equitable, that informed consent is sought and documented unless it can be appropriately waived or altered, that there's adequate provision for monitoring and for protecting privacy and for safeguarding vulnerable subjects.

[slide 33] And we're going to have another poll here about this. And this would be -- what this question is asking is can the IRB approve research if they have questions or conditions and can they do it without re-review by the convened IRB.

So could the IRB say that -- that an IRB chair or an IRB administrator could sign-off on these questions or concerns. Let's say if the IRB had concern about

supervisors encouraging their employees to participate in research, could they approve that without re-review by the convened IRB? Or if they had wanted to know information about where on a subject's bodies biopsies were going to be taken from, could that be approved without re-review by the convened IRB? What if the IRB had precise language changes to the protocol or to the informed consent documents, could that be approved without re-review by the convened IRB or with substantive changes with clearly stated parameters that the changes must satisfy, could that be approved without coming back to the convened IRB?

So I'm going to give you a minute or two to select your answers. Again, you can select multiple answers, multiple answers may be correct for this question.

Okay. We're going to cut off voting. Only 65% of you have voted -- now it's up to 71, but I guess this one was a little harder. So 31% of you thought that if the IRB had concern about supervisors encouraging employees to participate that that could be approved without re-review by the convened IRB. Actually, that cannot because this is directly related to the criteria under 111 related to risks to subjects and also to whether or not the informed consent process is not unduly influencing or coercing subjects, so that would be something that would have to come back to the convened IRB for review.

How about if the IRB didn't know where the biopsies were being taken from. 31% of you thought that that could be reviewed without coming back to the convened IRB. And that is incorrect, actually. The IRB would need to know that information in order to be able to ensure that risks to subjects were minimized and that risks

were reasonable in relation to benefits.

As far as precise language changes to the protocol or informed consent documents, 69% of you thought that that could be approved without coming back to the convened IRB and that's correct, because the IRB is saying this is exactly what needs to change and then the IRB chair or IRB administrator could then say whether or not, yes or no, that those changes had been implemented and that could be approved without coming back to the convened IRB.

And as far as the last one, substantive changes with clearly stated parameters that -- that those changes must satisfy, 24%, interestingly, this was the -- this was the lowest number of people who said that this could be reviewed without coming back to the convened IRB and approved and that is actually correct. It can be approved without coming back to the convened IRB. And this is because the IRB has clearly stated what parameters the changes must satisfy. And you can get more information about this on our contingent approval or restricted approval guidance on our website.

[slide 34] So the next common finding that we're going to talk about are the inadequate written procedures.

And as you know, the regulations require that institutions have written procedures that the IRB will follow for initial and continuing review, for how they're going to report their findings to the institution officials and to the investigators, which projects need verification that no changes have occurred since the last review by the IRB, and how to promptly report how the IRB is going to ensure

that prompt reporting of proposed changes is made and that changes are not made before IRB review and approval, except when necessary to eliminate apparent and immediate hazards to subjects. They also require that you have written procedures for how you're going to report unanticipated problems, suspensions or terminations of IRB approval and serious or continuing non-compliance.

So we're going to have another poll here. And this poll is whether or not the regulations require the following written procedures.

Do the regulations require you to have procedures for determining when to audit research? Procedures for determining exemptions? Procedures for reporting suspensions by the DSMB? Procedures for approving research involving prisoners? Or none of the above. And remember that you can select multiple responses because more than one answer may be correct.

And I wanted to add that many of these examples come from actual findings of non-compliance that our office has made in the course of evaluations.

Or if -- they've also come from -- from non-compliance and problems that institutions have reported to us, either because they were required to under the regulations or because their institutional policies required them to be reported. So I'm going to give you another minute or two to answer whether or not you think the regulations require those written procedures.

Okay. So we're going to close the voting. About 74% of you have voted. And 53% of you thought that the regulations require the -- the -- you to have procedures for determining when to audit research. And actually this is another one where

the -- one of the lowest amounts of you voted for it, but we believe that the regulations do require you to have this and this is related to the requirement to have procedures for determining which projects need verification that no changes have occurred.

And the best way to do that is to audit research.

The next one is 88% of you said that the regulations require you to have written procedures for determining exemptions. And this is incorrect. The regulations do not require us to have any written procedures related to exemptions. As a matter of fact the regulations don't even require that the IRB review exempt research to determine whether or not it's exempt. Although we do recommend that somebody other than the investigator review it to determine whether or not it's exempt.

74% of you thought that the regulations require written procedures for reporting suspensions by a DSMB. This was kind of a trick question. It's actually wrong. That the regulations require you to have written procedures for reporting suspension by the IRB, not by other entities.

Now, you may have to report such a suspension by the DSMB if it also was related to some other problem that needed to be reported.

The 91% of you thought that the regulations require you to have written procedures for approving research involving prisoners. And that was the highest percentage of people who thought you needed written procedures and actually this is incorrect. There are no requirements in the regulations for having such written procedures. Although we recommend that you have them. And 2% said none of the

above. That's incorrect because the first one you are required to.

[slide 35] So now we're going to have another poll. And this is which of the following events actually need to be reported to our office.

And the first one is that subjects' confidential contact information was used inappropriately by study staff. Would that need to be reported to our office? Next one is non-exempt human subjects research conducted without IRB review or approval? Would suspension or terminations of sponsor approval need to be reported to OHRP? Or would study drug dosing errors or do none of these actually need to be reported to our office?

I will give you a minute or two to respond to the poll.

Okay. We're going to cut off the voting. 69% of you have voted.

So 40% of you thought that you would need to report to OHRP if subjects' confidential contact information was used inappropriately by study staff. And we would say that's correct. That would need to be reported to us because we would consider that an unanticipated problem involving risks to subjects or others. Remember that risks are not just physical risks. They can be, you know, social or psychological risks. And they are not just harms that actually befall a person. That they are -- you know, it includes risks.

The next one is non-exempt human subjects research is conducted without IRB review and approval. And the highest percentage of you, 75%, thought that needed to be reported to our office. And that's correct. We have said that this is generally to be considered serious non-compliance, as you know serious

non-compliance needs to be reported to our office.

How about suspensions or terminations of sponsor approval? 34% of you thought that needed to be reported to OHRP. In general, that's incorrect. Because if that's all that it is a suspension of termination, it's the sponsor that's suspended or terminated and it's only IRB approval suspensions or terminations that need to be reported to us.

Now, you may have interpreted that to say well the sponsor was terminating or suspending it because of an unanticipated problem, but that would only need to be reported to our office if that unanticipated problem happened at your site.

And then 29% of you thought that study drug dosing errors would need to be reported to our office. We think that this is actually correct, that this would be an unanticipated problem involving risks of subjects or others that would need to be reported to our office. Surprisingly 14% thought that none of these things need to be reported. So maybe you need to look at our guidance on adverse event reporting.

[slide 37] So next we're going to talk a little bit about protocol changes without IRB review. And as I mentioned, the regulations require that you have written procedures for ensuring that proposed changes in a research activity don't occur without IRB review and approval. And that -- except when necessary to eliminate apparent and immediate hazards. So we're going to do another poll to test your knowledge about this regulation.

And the first one is whether -- they are all whether or not these -- the

following changes would require IRB review and approval before being implemented. So would you need to get IRB review and approval before enrolling ineligible subjects? What about if you wanted to add a laboratory test to look for an emergent urgent risk, would you need IRB approval before doing that? Do you need IRB approval to increase the enrollment limits or to add a new recruitment advertisement or would you not need IRB approval for any of the above? This of course you can add -- you can respond multiple answers, multiple ones may be correct. So we'll give you a minute or two to respond to this poll.

Okay. We're going to close voting, about 75% of you have voted. 83% of you thought that before enrolling ineligible subjects, you would need to get IRB review and approval. And that is correct. You would need to get because that would be a violation of the protocol and a change to the protocol.

Next one is adding a lab to test for an emergent risk. And the lowest percentage of you thought this needed to be approved and indeed it doesn't need to come to the IRB because it's sort of an emergency, it's an urgent thing, so this is something, as I said, the only changes that don't need IRB approval are when it's necessary to eliminate apparent immediate hazard to the subject and we're assuming here that this would be an emergent risk, an immediate hazard that would need to -- that we'd need to test for and so you could do that without having IRB review and approval. But to increase enrollment limits or add new recruitment ads, you would need to have IRB review and approval. And 90 and 91% of you knew that.

Okay. So we will go to our next one, which is required findings for waiver

of informed consent.

[slide 39] As you know, that the IRB can approve a research procedure that doesn't include all of the elements. Or it alters some or all of the elements if it meets four specific findings. Including that the research is no more than minimal risk, that the waiver won't adversely affect the rights and welfare of the subject, that the research can't practicably be carried out without the waiver and that when appropriate subjects are provided with additional pertinent information after participation.

So we're going to do another poll and see whether or not you think that the following studies could be conducted without informed consent.

Would it be appropriate for the IRB to waive informed consent for a record review study, for research involving couples therapy and alcohol treatment, for a study on teaching vascular surgery interns vascular surgery skills, for deception research or would the IRB not be able to waive informed consent for any of the above? Again this is -- you can have multiple answers that you can select and multiple answers may be correct. So I will give you a minute or two to enter your responses.

Okay, we're going to close voting on this. About 74% of you have voted. So 83% thought that you could -- it would be appropriate to waive informed consent for record review study. In general, that is true. That is correct. That most such studies are no more than minimal risk. It won't adversely the rights and welfare and in many cases, most cases perhaps, you can't practically carry out such record review research without a waiver.

As far as research involving couple therapy in alcohol treatment, only 13% of you thought that you could waive informed consent. And -- and that's incorrect. That -- that usually you have the couples right in front of you and so -- so there would be no -- you couldn't -- you couldn't argue that you can't practicably carry out the research without the waiver. You have them in front of you, you can get their consent. As far as a study on teaching vascular surgery interns surgery skills, 37% of you thought that you could waive informed consent and that's incorrect. Because again you have the surgery, the interns in front of you, so it's not impracticable to do the research without the waiver.

And as far as deception research, 40% of you thought it was appropriate to waive informed consent. That is correct. It is -- that's actually one of the -- one of the main reasons to waive informed consent is for deception research, if it's no more than mineral risk and the waiver won't adversely affect the rights and welfare. This is one of the key ones where it's not practicable to do the research without the waiver, because if you were to get consent, you would be biasing them some way, you would be letting them know, so they would be responding in a way that's not natural. And also, this is where that last requirement, when appropriate subjects are provided with additional pertinent information after their participation, is the most appropriate. So if you do deception research, that fourth requirement should probably be met. And seven percent of you thought that none of the above would be appropriate for waving informed consent. Some of these it might be appropriate to alter informed consent for some of the elements of

informed consent but this is a question about whether or not it's okay to waive.

[slide 41] So we're going to -- wrap up with some concluding slides and including some solutions to correct any non-compliance or maybe even prevent non-compliance.

[slide 42] And one of the most important things that we see and that we often require as a corrective action when we see non-compliance is education. So make sure that all of your investigators are educated and that all of your IRB chairs and staff and IRB members are well educated. And OHRP has a wonderful education program that I'll tell you a little bit more about that can help you.

Also, ensure that you have enough IRB staff and that they all have adequate resources. And that there are a -- an adequate number of IRBs. Sometimes if you have a ton of protocols then the IRB is overworked or having meetings that are lasting hours, hours, hours and having many different meetings, one of the ways to relieve that is to have additional IRBs. Also make sure that you have adequate IRB documentation, in particular look at your IRB meeting minutes and make sure that they are okay. You want to periodically do a self assessment of your system for protecting human subjects and OHRP has some tools to help you with that. Also want to make sure that you have adequate written procedures and you can check out our website, we have a really good guidance document on written procedures, both what are the actual absolute requirements and what are some suggested, recommended ones that you may want to add. And we think that the institutional officials can be really good to help set the culture of conscience at an institution that will help

non-compliance, nip it in the bud before it even occurs, and they can help set the tone for how the institution views compliance and ensures that they are not out of compliance.

It doesn't have to be the institutional officials, but certainly we wouldn't want any institutional officials standing in the way of the IRB from doing the right thing. The next couple of slides show some of the resources that we have. [slide 41] 43] Our education resources include our research community forums, which we do about three times a year, they're in different regions of the country and usually the host, will help us set the agenda for those fora. We also will respond to speaking invitations where we'll go to a site, if there's a large enough audience, or we can do webinars such as today. You can also go to our website and you can find lots of guidance. You can send an email query to our OHRP email box and the address is there. We also have a quality assessment program, which I'll tell you a little bit more about in the next slide. Also check out the website for training videos and other materials that can help in educating yourself and those at your institution. [slide 44] A little bit more about our QI program, we do have a quality assurance self assessment tool on our website that you can through to make sure your institution is doing the right thing. This is free, it doesn't cost you anything, and we can also help you interpret that self assessment tool results or you can just use it in-house. We can also do a QI consultation, which can include a phone consultation and we can also go on site to your institution. This is in what safe mode where the educational staff will generally not report anything to

compliance oversight unless they see something that is very serious and then they will talk to the OHRP director before doing so.

We also have some quality improvement standard operating procedures workshops. And these are very helpful, it's a whole day event that we have at various places around the country. And these will help you in developing written procedures and for writing meeting minutes and doing some of the nuts and bolts of -- of running an IRB.

We also have, as I mentioned, guidance on our website on how to draft IRB written procedures. [slide 45] So last slide is our contact information, website address, our toll free telephone number and our email address that you can send us any questions. [slide 46] So I know that not everybody who wanted to be on this webinar was able to attend or there may -- they maybe want to revisit it. All of our webinars are going to be recorded and available on with our website within one to two weeks after this presentation. You can check our website for more information. Also the slides from my presentation will also be available on our website.

So thank you very much for your attention. And keep up the good work. And thank you for your commitment to helping protect human subjects.

Goodbye.