Cyberseminar Transcript
Date: February 20, 2018
Series: Focus On: Engagement In Human Subjects Research
Presenter: Soundia A. Duche, MA, MS

Soundia: Welcome and good afternoon everyone. Thank you so much for joining us today. Our topic today is going to be Engagement in Human Subjects Research. My name is Soundia Duche and I am a program analyst here in PRIDE, which is the Program for Research, Integrity, Development, and Education in ORD. With me today are my colleagues, Dr. Karen Jeans, who is the Associate Director of Regulatory Affairs for CSR&D, Clinical Science Research and Development, and also with me, Lucinda Shouse, program analyst in CSR&D as well. So, this is, what we are considering this as a relaunch of our core series and let me just explain that for a minute. Our core series are going to be topics that are essentially the fundamentals for regulatory affairs and protection of human subjects. They are not necessarily basic. They are core. They are kind of the things that everybody needs to know when reviewing, submitting, approving, auditing human subjects research. We initially launched the series back in 2013 and we've decided to relaunch it now and incorporate it within our current Cyberseminar structure so we will continue to do specialized topics so, for example, last month Lucinda Shouse did a Cyberseminar on Records Management. That would be considered a specialized topic. Karen Jeans, the month before that, she did a topic on Certificates of Confidentiality, Part 1. We know you're waiting for part 2, we have not forgotten. That's going to be forthcoming. So, within our core series, we'll have a core series and we'll also have our specialized tracks. So, our cores will be primarily geared towards people who are new in the field, we know that there's a lot of turnover in the research office often and so we hope to probably do each topic maybe every year, every year and a half. We will record each of our Cyberseminars, as we do all of them, so this information will be posted on the PRIDE website as Heidi mentioned but by redoing our core seminars often, frequently, then we will enable new people to the field, to this research role, to be able to ask questions and can always tweak the presentations as needed. So with that said, I think we are just going to go ahead and get started.

So, today, what I hope to accomplish today is really to first describe what it means to be engaged, according to the Common Rule. When we say engagement, what does that mean when an institution is engaged in human subjects research. We're going to spend some time identifying the necessary steps you use to determine if an institution is engaged in nonexempt human subjects research and then, finally, we're going to just spend some time going over some case scenarios where we're going to give you all the opportunity to evaluate whether institutions are engaged. So we have about six cases, some of them have multiple parts, but Heidi is going to run the polls for us and we're trying to be a little fancy here, so, we hope it works well.

So now, when we say engaged, what does that mean? Essentially it means that there is at least, and I really want to stress at least, there's at least one employee or agent of the institution that's involved in activities pertaining to the conduct of nonexempt human subjects research and because there's at least one employee or agent at that institution, that institution

is now required to adhere to certain requirements, adhere to certain regulatory requirements, amongst which are; one, that facility must hold a Federal Wide Assurance, secondly, it must identify a local VA investigator for that study, and lastly, it has to have an IRB of record that oversees the study. That IRB of record does not have to be at the facility, but it has to be an IRB of record that that facility has designated on its FWA and that oversees research at that facility. So those are the things that have to be in place if an institution is deemed to be engaged in human subjects research.

Why is it important to know? Well, one, like I just mentioned, you want to make sure that an institution that's engaged in human subjects research, is adhering to the necessary requirements that the Common Rule requires, the three things that I mentioned. When it comes to multi-site projects, you know, you kind of, you have this large pie, and within the pie you have multiple factors, right, multiple slices, multiple factors, people doing different things. Not all slices are equal in any research project, or research team, multicenter project, so some people, some institutions will be doing things that will engage them. Other individuals, will be doing, conducting activities that do not engage their facility. It is very important to be able to decipher who's engaged and who's not so that those who are engaged follow and have in place the necessary regulatory requirements and that those institutions that are not engaged, do not. It's very difficult when you have an IRB overseeing a research project that they should not be overseeing because their institution is not engaged. It creates a host of problems; things like who does one report to? Whose IRB has jurisdiction? It's really important up front, at the beginning to be able to identify whose engaged, whose not, so you can parse out what is required for each institution. Engagement decisions and determinations are complex. Very rarely do you get one that is very black and white. You really have to look at all of the details of the project. The devil really are, in the details here and, sometimes, the details are not in the project application, right, and so you have to ask the right questions in order to get the information, get that information, and incorporate it in the protocol or other study related documents so that you can make a valid determination. So, one, look at everything, look at all the details, ask questions if you don't have enough information. Two, then you have to ask a series of questions in this order. There are four key questions that will help us determine if a facility is engaged in human subjects research. You have to start with that, seeing if a project is research or not. If you determine that it is research, you need to then ask, if it's human subjects research. If you determine that yes, indeed, it's human subjects research, then we're going to ask if it is exempt from IRB review. If the study is not exempt from IRB review, then the last question is, is my facility engaged in human subjects research? I just want to comment on that third point, the exemption. Is the study exempt from IRB review? Many times when we say engagement, we all just say are you engaged? Are you engaged in human subjects research? Rarely does someone say are you engaged in nonexempt human subjects research? But, essentially that's what we're asking. So we kind of throw the terms around, you know, but essentially what we're asking in all those scenarios, it's the same thing, are you engaged in nonexempt human subjects research? And that should become clear because you have to answer these three questions, affirmatively, for the last one you have to say is nonexempt, and then you go to the fourth question, which is are you engaged? So, so, in this lecture sometimes

you hear me say engaged, sometimes you hear me say engaged in human subjects research. I will always mean, are you engaged in nonexempt human subjects research?

So we are going to start with, is it research?

The Common Rule defines research as a systematic investigation, including research development, testing and evaluation, that's designed to develop or contribute to generalizable knowledge. I know this is a definition most are familiar with. As this is a core training, we have to, you know, really start at the beginning and build our foundation from there so we are going to spend some time talking about research and what it means to determine if something is research or not research.

We kind of looked into this definition. Two main things that really stand out and that is systemic investigation and generalizable knowledge. So, a systematic investigation is an activity that is planned in advance and that uses data collection and analysis to answer a question. Now, this really applies to most any well thought out project, right? We want to make sure that we've kind of been systematic in our approach, in designing an activity, that we have tools that we're using to collect the data, and that we're using, you know, you know valid data analysis approaches right, to answer the question. So this doesn't really differentiate if something is research or not, but it's important in order to determine if it is research it has to, at least at a minimum, be a systematic investigation. The next part of the definition is generalizable knowledge and that is information that expands the knowledge base of a scientific discipline or other scholarly field and that really is what will really determine, and we're going to hone in on that, if something is research or not, and ORO has a handbook, VHA Handbook 1058.05, it's an ORO handbook, the title is VHA Operations Activity that may constitute research and it's a great resource because they kind of go really in detail about things that might be research or always research or sometimes are research, you know, they have a host of examples but one thing I really love about what they do, is they stress the word designed. A systemic investigation designed to contribute to generalizable knowledge and I think that's something we want to keep in mind as we're evaluating whether something's research. What is the purpose? How is it designed?

So, again, always want to go back to the details, right? Any decision, determination in terms of whether something is research or not, it really depends upon the specifics. And, so, in the handbook it talks about when something, a project is not research if both criteria are satisfied. One, the project is designed and implemented for internal VA purposes, internal being the operative word here, we're not contributing to generalizable knowledge, we're focusing on VA and our internal processes and things that we can do to improve and better understand our approach to the way we run our facility or things that benefit our patients directly because of the way we conduct our clinical care and business here at the VA. And, secondly, that the project is not designed to produce information that expands the knowledge base of a scientific discipline.

So, as I mentioned, the handbook goes into numerous examples of things that sometimes are research, things that are not, things that typically do not constitute research in and of themselves. They give a number of examples, somethings like quality assurance and quality improvement typically do not constitute research. Patient satisfaction surveys, evaluation activities related to policy development, performance evaluation activities, regulatory compliance activities when you have someone come in to audit they're going to talk to people, they're going to look into records, that's not typically research, medication use evaluation. These are things that are typically not research.

Soundia: Karen has a . . .

Karen: I do want to jump on the specifics of this. This is Karen. So these are great examples, it's like Soundia is talking about the devil's in the details. It's like that, that key definition that she's referencing about generalizable knowledge is the key concept here. What makes something generalizable? Just because its presented publicly or in a manuscript does not mean that it's generalizable. It's that, it's like what she said, does it develop or contribute to generalizable knowledge in terms of expanding the knowledge base of the science. So, what she's talking about here, is like these great examples, we can take several of these and we can turn them around by how we take the activity and we could make it research, depending on how we do it. So, so, the catch in here, is don't take this list and say that ORD put it in a slide that all of these are always not research, it's like she has bolded typically, typically.

Soundia: Definitely. Thank you Karen.

Karen: This is getting into the meat of this now. This is the fun part.

Soundia: And she's right. It's all about the details. I'm going to go over like an example that crossed my desk recently. I was helping a facility evaluate a proposal that had come in. It was a simple one pager. It was to determine if something was research or not. In brief, the project involved two drugs that were used to treat a condition, both were on the formulary at the facility. The condition that they were being used to treat was the condition that the drugs were approved for so they were being used in their, you know, approved capacity. One drug seemed to result in happier patients. I mean, apparently you could walk down the hall and you could tell, post-procedure, who had received which drug based on the mood and, you know, the demeanor of the patients and, so, in this one paper that came in, the plan was to give a very brief survey, I mean we're talking four to five questions, you know, to the patient, post procedure to see how they fared and then later on, one would go back into the medical record and then determine who was on which drug, who had received which drug. So that was the plan. They were going to do this. They were going to do this based on the current conditions where, you know, some patients had received drug X, other patients had received drug Y and, apparently, what differentiated the administration of either drug was really just based on physician provider departments. That's what was described in the application at least. They made it clear that that there was no plan to disseminate the results outside of the VA and they were going to implement changes if the results showed that there was a better outcome on the

new drug. Okay? I received this application. I just asked some simple questions. I said, one, I'd like to see a copy of the survey. I asked who was going to be administering the survey? How long would the activity last? And then I said, you know, will patients be given a chance to, or choice to, participate or not? Just want to try to get a better sense of what was going on and they responded and they adequately answered all my questions but in the process and I also told them, please, you know, incorporate your responses in the application because I need the application to basically include everything that you're telling me. I don't want to have look in multiple places. So, as they revised the document, they added some additional information. One of the things they added was, they said, that if the findings suggest a difference then our plan is to develop a randomized control trial in the future. When I saw that, I thought oh no, because now listen we have gone from possibly black and white to oh no, now we're in the gray area because I'm seeing this and I'm thinking oh, this is starting to feel and smell like a pilot study. Doesn't matter how small it is, it doesn't matter that they only want to do four questions. That's not what differentiates something as being research or not, right? It's the intent and how it's designed and whether it's designed to contribute to generalizable knowledge so that was the second point. In the revised application, they wrote that the quality and patient safety groups in this field would find the data interesting. Again, I'm getting uncomfortable. I'm thinking, oh boy, this is starting to smell a lot like a pilot study. Now, I'll be honest, the last thing, the last thing I want to do is have to tell a project manager that, because you want to, you know, and when it's a five question, a five question survey, now you have to fill out a large research, you know, application. But, based on what they had provided to me, there was no way I could say that this was not research. We needed more information and the way they had presented the second iteration was starting to verge on the realm of no, this is starting to sound a little like research. Oh, you can imagine. The project manager was not too happy with me, at all, and honestly, I would have preferred to have it not cross my desk but it was in front of me and I had to do my due diligence so, at that point, we arranged a telephone call and we spoke and as we spoke, it became very clear to me what was going on and what was the intent, which was not what was reflected on the paper so, one of the things that came to light was; one, the situation was such that there were these two drugs, they were both being administered in the facility but the pharmacy had limited the ability to dispense the drug in question, the one that resulted in a better mood because it was more expensive. So the pharmacy was limiting the ability for the physicians to use this drug because of cost control measures. Understood. The physicians, on the other hand, are walking around and saying but our patients are doing so much better. We can see it. Now, what the pharmacy had agreed on, they said, this is what we'll let you do; in order for you to compile some information for us and bring, to support your case, we will let this drug be dispensed for 30 days. So, instead of dispensing the other drug, both remember are approved for the treatment, okay, we're going to allow this more expensive drug to be dispensed for 30 days. Use those 30 days, gather your information, bring it back to us. That's a whole different situation now. So, now, who is our end user? It's the pharmacy. Why are they using and needing this information? To decide for this particular VA facility, if they will allow increased use of this drug, which the physicians were clamoring for but, because of cost control measures, the pharmacy was limiting its use. Again, that information was not presented, so one had to ask additional questions. One had to really get to the meat of what was going on and then, most importantly, one had to make sure that

that was reflected appropriately in the document so that anybody coming after me, would look and be able to say, okay yes, this would constitute, this would not constitute research. So, that's just the more recent example of just really how nuanced, right, these situations really are.

So, I'm going to kind of rush over these next few slides because the information is in the handbook and it's a great handbook 1058.05. It goes into examples of things that are always research. Products funded or supported as research by ORD, or any other entity, right, are research, if you receive money and that money was allocated for research then it's research because that's why they gave it to you. No. ORD does fund non-research. They fund, you know, quality improvement projects, so, just because it comes from ORD, the Office of Research and Development, does not mean it's always funded as research. You want to look at the merit, whether, and maybe Karen can talk a little bit about that, and how that works.

Karen: Yeah. This is Karen. We've actually had the opposite happen. This is what, exactly what, Soundia was talking about where we have the QUERI Program here in ORD and projects are funded within the QUERI Program as not research activities but there have been more than a few times, within ORD, that we will get a QUERI activity that is published and someone who is outside reading it and, again, the community is out there coming back to ORD and saying wait, this was not funded as research, but it sounds like research and, so, it goes back to what Soundia was talking about, about the devils in the details, but when something is funded by research by ORD, it is always research. If its funded as not research, like through QUERI, then it is never research and, if it does cross over into research than that is not appropriate. Then that's not something that should be funded that way, so, you can't change the intent once you get the funding so that's what this slide means, how we fund it determines what algorithm, or what road, it follows.

Soundia: Excellent. Thank you. The other part is clinical investigations as defined under the Food and Drug Administration regulations. Those are always research and so, by that, we are talking about, you know, any experiment that involves a test article in one or more human subjects and that either must meet the requirements for submission to the FDA or whose results are intended to be submitted as part of a marketing application to the FDA. Those are always research.

The handbook then goes into things that are always research.

Karen: Kind of reminds me of adverse reporting. Possibly, probably . . .

Soundia: But, you know what, we laugh, but it's true there are so many shades of gray in this. Right? So it's very hard to say definitively this is always, this is never, you know, there are a lot of things that fall in between there. So, they list a number of things that are almost always research, things like double blind intervention, placebo control trials, prospective patient level randomization to clinical interventions not tailored to individual patient benefit.

These are some of the things that are often, but not always, research. There are a number of things there. A million acts would go into the details of this because the handbook is great. It provides a lot of information. Definitely, use it as a tool to help gauging them in these decisions.

Once we determine that something is research, our next step is to ask the question, is it human subjects research? So, the Common Rule definition of human subjects is, a human subject is a living individual about whom an investigator conducting research obtains either data through intervention or interaction, or, identifiable private information. So, we're all very familiar with the intervention and interaction piece, you know, for the most part, we get that, that, you know, it makes sense to us, right? An intervention, anytime we're intervening with someone that includes both physical procedures by which data are gathered, for example, venipuncture or manipulation of the subjects or the subject's environment that are performed for research purposes. So, you know, you can even think of things like, I don't know, troops, right, you know, a lot of times they have to test the armor, the body armor and stuff that they wear and they have to be subject to different environmental conditions to make sure that it's going to protect them adequately. That would be a form of research. Not one maybe that we see in the clinic but, you know, that's manipulating the subjects environment, you know, to perform research purposes. Interaction includes communication or interpersonal contact between the investigator and the subject. Many times that's things like focus groups, surveys, those types of thing, interviews. So those, typically, you know, those are things that would be considered human subjects research.

The other part of it we might struggle with a little bit more and that is, private information. Right? The Common Rule says that it's identifiable private information but first let's just talk briefly about what private information is. It's any and includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place and it's also information provided for specific purposes in which the individual can reasonably expect will not be made public. So things like, you know, information in your medical records.

The individually identifiable part, however, is key when we're determining if something is human subjects research. Now, the Common Rule defines it one way and the privacy rule defines individually identifiable differently. At the VA, we take into account both. So, the Common Rule, identifies individually identifiable as instances where the identity of the subject is, or may readily be, ascertained by the investigator or associated with the information. The Privacy Rule, when we're looking at whether something is de-identified or not, gives a list of 18 HIPPA identifiers and in order for something to be considered not individually identifiable, or de-identified, that information cannot contain any of the 18 HIPPA identifiers. So, here, at the VA both of those have to apply in order for us to consider something not individually identifiable. So, I just want to have you guys really, a few things I want to mention about this whole individually identifiable, something that we see often here. Many of these times will be, in the protocol, we're told that one investigator at one of the sites in a multi-site study is only going to be sent de-identified information to analyze but, then as we read through it, we'll see

that they want to calculate a certain metric that would require dates right? So if he states, for example, one of the outcomes is the time to achieve X, or the time from administration of a drug to developing a certain symptom or event, you need dates to do that. So, they won't explicitly say oh, we're sending him dates but if he's doing the data analysis and that's one of the metrics in order to arrive at that final metric, in the interim, you need dates and so the issue is, if one is exposed to identifiable information, in this case dates, then that information is not de-identified. Similarly, codes, codes is another thing. We're always told, oh, that investigator is only going to be receiving coded information so they're not involved in human subjects research, they're not engaged, that's not human subjects research, they're only getting coded data. If you look at the 18 HIPPA identifiers, codes is number 17 is it not? It's one of the numbers and, essentially, if they're getting coded information, codes are an identifier unless there's some agreement in place that clearly stipulates that that individual, whose obtaining the information, will not have access to the code and will not be able in any way, shape, or form to link the identity of the subject with the data that they're receiving and so, that's really something to really think, you know, about as you're looking at whether something is human subjects research and, again, often you have to ask additional questions because, as originally presented, you may not get all the information you need in order to make that determination.

Our third step, that we're not going to spend a lot of time on today and that is, if you determine that something is human subjects research, is it exempt from IRB review and oversight? It's important to ask this question because, in order to get to engagement, we only look at something that's non-exempt. So, first we have to determine is the research exempt and what does it mean to be exempt from IRB review and oversight. The Common Rule outlines six instances when, if a project falls into one or more of those six, if all the activities of a project fall into one or more of those six categories then it is exempt from IRB review and oversight. What that means is; one, the IRB does not have to approve the study. They don't have to oversee the study. They do have to make the determination that is exempt, though, so don't forget that. Whether it's the IRB administrative office or it's the IRB chair, or it's a member of the IRB, whatever your SOP states. That decision is made in the IRB or in the IRB office but, once it's determined to be exempt, then it's reviewed by the R&D committee and it's followed by either the R&D committee or one of its sub-committees. That's how we do things here at the VA.

I will say, and this is important to note, and here are your six categories, a summary of your six categories, in a multi-site study in order for the project to be deemed exempt, it is not the same as an engagement and we're going to talk about this. All activities, every single activity that is done in that study, has to be exempt. Everything done by anybody involved in that study, has to be able to fall into one of these categories so that's very important to remember. Again, we're not going to talk about this now. We could do a whole lecture, we've done lectures about exemptions. We're going to revisit this in the future, we just have to figure out the best way to do that given the forthcoming changes with the Common Rule. So, you know, we have it on our radar, we're just trying to figure out the best timing of actually doing the [unintelligible 30:02] core.

So, the last one, the fourth step is, once you determine that the project does not, is not exempt from human subjects research, then is my facility engaged. So we ask, is it research? We determined yes. We said is it human subjects research? We determined yes. We said is it exempt from IRB review? We said no, it's not. Now our fourth question is, is my facility engaged in human subjects research? When you determining whether or not a VA facility, or any institution for that matter is engaged, you really want to consider, and need to consider, what is being done at my institution and who is doing it. Very important and then finally, does the activity that's being done require review and approval by the IRB of record of my institution.

We are going to delve into all of this in this part of the lecture. So, OHRP has a guidance on engagement and that was included in the handout, and that was the slides. The guidance, the purpose of the guidance is to help describe how the Common Rule applies once you have determined that your project involves non-exempt human subjects research. Now, who can engage an institution? I think I touched on this earlier, but we're going to reiterate. An institution's employees or agents. Now, what does that mean? It's any individual that's acting on behalf of an institution. An individual that exercises institutional authority or responsibility or an individual that performs institutionally designated activities. So, if somebody, is employed by a certain VA facility or has some agreement, whether it be a WOC agreement or some type of student related affiliation and they are working on their VA time to do this activity and they are engaged in activities that would be deemed human subjects research, then it is that individual that engages the facility. I also want to say this, again, it only takes one individual. It only takes one, so, sometimes you will have in an institution you will have some people who are not engaged in human subjects research and some who are. Maybe you have a study team that's doing, conducting the research at the institution and, therefore, engages the institution but then you have some other people who are just providing a service. We're going to talk about it a bit more. It doesn't matter. The institution is engaged. As long as there is one individual conducting an activity that would engage, that meets this criteria, the institution is engaged and, therefore, they have to meet the regulatory requirements that we mentioned before: IRB review, FWA, designated investigator at that facility.

So, the Guidance Document provides examples of situations in which an institution would generally be considered engaged and, also, not engaged. There's two sections, IIIA and IIIB, that deal with that. The Guidance Document says that these scenarios are not all inclusive. They're examples. And, as you know, we have previously described, engagement decisions can be extremely tricky. We're going to talk a little bit about some of the examples. I didn't list all of them, but some of the examples that we see often, you know, in our normal, you know, everyday human subjects work here in the office and what you are most likely to see in your institutions.

So, section IIIA, gives examples of situations that would engage an institution in human subjects research. One of the things would be obtaining data about subjects through intervention or interaction with them. Obtaining identifiable private information about the subjects. Obtaining the informed consent of subjects for the research. Essentially these are engaging with a human

subject in research at your facility. If somebody is obtaining data, obtaining private information, obtaining the informed consent, they are engaged with that subject and obtaining human subjects, well, they're engaging with the human subjects in human subjects research. If an activity is funded or otherwise supported as research, as we said, that's human subjects research and they would be engaged, that facility would be engaged.

Number of examples of activities that typically would not engage in institution. This list is not all encompassing. There are some additional examples that I did not include here. I really tried to just focus on things that we typically see and get questions on. So, performing a service for an investigator that the institution typically performs for non-research purposes. For example, if you use a transcription service. A transcription service provider that this is what they do, this is their business, and we need someone to do the transcription for our research study and you enter into a contract with them to do that work, they're performing a service for you. Similarly, often laboratories, right? You have a laboratory that's running blood or processing the blood or analyzing, you know, separating the blood for you, what have you, if they're doing this, this is what they do, they do this for clinical purposes, and you need them to assist you with this because you don't have capability in house, then you're using them as a service provider. They are not engaged in the research. They are providing a service for you. If you're going to inform a prospective subject about a recent project, you're going to provide prospective subjects with information about the research, or you're going to obtain their permission to be able to send their information, or let an investigator know that they're willing to be contacted. Those are activities that would not typically engage an institution. Now, caveat there okay? As long as the individual is one, not a member of the study team, and two, is not acting as an agent of the investigator. So simply saying, in the process of clinical care, oh, I'm aware of this study that you might find interesting, would you like me to have them contact you, or giving someone a flyer, or giving someone a brochure. That interaction does not engage the institution. If that's the only activity being done, right? [unintelligible 36:22] already being engaged because they have a study team that's performing the study at the facility. Those actions alone would not typically engage an institution but it's very important that's it very clear in the protocol the extent of these interactions and, many times, we'll have to go back and forth with a study team to ask them, to clarify exactly what level of interaction is being done with the patient by these non-study team members because we need to make sure that they truly are not performing activities that would make them an agent of the investigator and then really a member of the study team.

Karen: And this is Karen. I want to . . . . this is so incredibly critical because that line is so thin between informing and providing perspective to patients basically, who are prospective subjects about information or about a research project and then becoming their agent and also, let me give you an example where we're seeing this. As many of you know, many of our VA investigators are also clinicians. That's what we are, a healthcare organization who has dual appointments. So, sometimes we'll see, and it's never done in maliciousness. Let me say this right now. We have an incredibly wonderful research community but, a lot of times, an investigator will not want to open up the study at both sides of the street, the proverbial street, and so we see some creativeness going on where the investigator is running it at the university

and the investigator doesn't want to run it at the VA, so, he or she just wants to tell his VA patients about it and say, oh by the way, here's a study I'm running over at the university. That is not permitted; you're basically self-referring to yourself. So, when you are, you know when you're finding out about this, it's like what Soundia was talking about, you need to ask questions. One of the questions you need to ask about, is, by the way, are you part of a research study on the other side? So, so, just very interesting.

Soundia: Very good. Some additional examples that we've chosen to cite, that we see often, that come up often during our review of projects or just questions that we get from the field, is permitting investigators from another institution to use your facility to conduct their research and, in line with that, also releasing identifiable private information or specimens to investigators at another institution. This always is a huge source of confusion and, honestly, I get it, we get it, you know. IRB's are somewhat contested and it makes sense why. Right? They are charged with protecting subjects primarily at their institution. And so, when someone from another institution comes in and says, oh, we're here to do research on your patients and, by the way, you don't have to do anything, we're covered, you don't have to oversee, you don't even have to review the project, we've done that, you know. The IRB's get a little nervous, you know, and we get it. But the fact is that that activity really does not engage the recipient institution. We're going to touch a little bit more on that after we do our cases but I just want to say that it can really create a great deal of confusion again when you have multiple IRBs reviewing a project, particularly when one institution is not engaged in research and then you have their IRB involved. It really tends to open up a can of worms but that does not mean that that institution has no rights and we're going to talk about that, you know, later one.

Lastly obtaining coded information or specimens from another institution that has documentation preventing the release of the code to anyone at your institution. Here we go, you guys, we've seen this before, this coded information. So what this is saying is, we've talked about if the information is coded and there's a key and the recipient is not allowed in any way, shape, or form to ever have access to that key to be able to decipher and link so that that information, while coded, there's no other identifiers than that is not human subjects research. We've talked about that earlier. So what this is saying now, if you obtain such coded information where there's documentation preventing the release of the code, then you're not conducting human subjects research, your institution is not engaged in the conduct of human subjects research.

Soundia: So, now, we get to what we hope is the fun part. We have some case studies. Heidi is going to work her magic and I'm going to read the case and then she's going to magically pull up the polls and you should be able, if all goes well, to answer the polls and then we can talk about them, you know, the scenario.

Our first case study we have the Old Glory VA Medical Center they have established a special geriatric clinic and they want to implement a process to refer patients for special services; for example, vision care and physical therapy. Now, nurse Nicols, for internal quality assurance, she is going to audit patient's charts to evaluate whether the referral process is working and

she is also going to survey patients to evaluate their satisfaction. Our question is, is this research?

Heidi: And the options are yes, no, or more information is needed. So, as the responses are coming in, we'll give everyone a few moments to respond and we will go through the results.

Karen: Perfect. Thank you Heidi.

Heidi: And it looks like we're slowing down so I'm going to close that out and what we're seeing is 4% of the audience saying yes it is research, 50% saying no it is not research, and 46% saying more information is needed. Thank you everyone.

Soundia: Thank you, thank you, this is great and it worked beautifully. Thank you Heidi. So, the answer, is this research, we said no, so we agreed with the majority. I think it was 50% and they said no and the reason being is, yes, the project meets the criteria for a systematic investigation in that it was planned in advance and it uses data collection analysis to answer questions, but it does not meet the criteria of generalizable knowledge because, as we stated, the activities are planned for internal operations only. I think in the description it said internal quality assurance, Nurse Nicols is doing this activity for internal quality assurance. So, it will not expand the scientific understanding for the knowledge base of, or scholarly field. It's really designed to assess their special geriatric clinic and what they need to do to improve the referral process.

Lucinda: I have a question. Ben would like to leave the scenario up for a few more moments so they can think about it. The next, the next one so they have time to think about.

Soundia: Okay. Is that possible Heidi? People are asking for a few more seconds to keep the poll up because I don't think maybe some folks wanted to provide a response and do not quite have enough time.

Karen: To the poll or to the slide?

Lucinda: The question is can you leave the scenario up for a few more moments so we can think about it before the poll pops up?

Karen: Absolutely.

Soundia: Okay, you got it, got it. Thank you Lucinda. So case #2, I'm not going to move, well . . .

Karen: They get harder.

Soundia: Yeah. They're going to get harder. I'm going to try to leave this up. Unfortunately, I think what happens though in order to open the poll we have to move from my screen so

maybe before we open the poll, we'll try to give you guys a few more seconds before we open the poll. I think that's the best way to do that. So case #2 is the same as case #1, remember we have this internal process right, the geriatric clinic, referring patients, nurse Nicols was doing internal quality control to assess the referral process. So, now, nurse Nicols wants to pull some extra data, that's not needed for QA, he found some interesting things and so he now wants to compare their process to another intervention done at the Red, White, and Blue VA. So there may be, you know, there are areas for improvement here. He plans to compare and analyze the two interventions to construct a predictive model for how best to treat geriatric patients. We're going to give you guys. . . . Can we give them 30 seconds Heidi, before we close the poll?

Heidi: Well, we can but that's going to add up after a little while, just so you know.

Soundia: Alright. The answers are going to be yes, no, or more information is needed. I think that's our standing three choices for all of these cases. So, if Heidi, you can go ahead and open up the poll.

Heidi: Yep, here we go. And responses are coming in. Again, we'll give everyone a few more moments to respond before we go through the results. Also, just a reminder, that we did in the reminder that was sent out this morning, several links to the handouts and if you want to download that we do have the case study questions in there so that if you do want even more time, we do have that available if you want to download them from there. And it looks like we've come to a stop so I'm going to close that out and what we're seeing is 58% of the audience saying yes it is research, 12% say no it is not, and 30% says more information is needed. Thank you everyone.

Karen: Thank you.

Soundia: Thank you. Alright great. Well, we agree with the 58% if I'm right that said that it is research and why was that? They met the criteria for systematic investigation, activity was planned in advance, and it uses data collection and analysis to answer the question, and we also felt that it met the criteria for generalizable knowledge because now by going outside of the RBA and getting information on another VA's practices on another process, and, as he said, he plans to compare and analyze the two interventions to construct a predictive model for seeing geriatric patients. So, his intention now, is to find a better way to treat geriatric patients. That's more than just internal now to his clinic or, even really, internal to the VA. This is applying the knowledge that he's obtained from these two VAs and presenting it and seeing how best can we treat geriatric patients. So that would be expanding the knowledge base of the field, in this case, geriatric care.

Karen: Right. So think about that, it's Karen. Think about that, that last phrasing about the predictive model. It is indeed, as Soundia is talking about, it's not intended to benefit the patient's that's under his or her care. It's really intended to improve the lives of future patients by developing this model of care. So that is a great example of generalizable knowledge. The word generalizable knowledge is not organic, you know, it's not something that's easy to

conceptualize so, so it can come in any form and so this is one way it can be, be done through this.

Soundia: Excellent. Alright for the third case I think we're going to leave nurse Nicols now and we've gone on to Dr. Thomas. So we have Dr. Thomas and he wants to conduct research on interventions for gastric ulcers in patients at the VA. He requests coded data from a VA database which tracks private identifiable healthcare information about living VA patients. Dr. Thomas can readily ascertain the identity of patients and he plans to pull additional patient data from CPRS to correlate the results for his study. The question that we're going to ask is, is the activity human subjects research? We're going to ask Heidi if you could please open the polls.

Heidi: Yup. Here we go. And the answers, again, are yes, no, or more information is needed and responses are coming in. Again, we'll give everyone a few more moments to respond and then we'll close the poll question out and it looks like we've slowed down here so I'm going to close that out and what we're seeing is 89% of the audience saying yes, 6% saying no, and 6% saying more information is needed. Thank you everyone.

Soundia: Thank you, and excellent. We agree. Is the activity human subjects research, we agree with about 90% of you who said yes and the reason being, the information is about living individuals, that information is individually identifiable, and the information is private. So, we are sticking with Dr. Thomas.

Same details as case #3, so we've established that it involves human subjects research. Now, we're going to add that Dr. Thomas now wants to send the information he collects to his co-investigator at the Old Saybrook VA to assist him with data analysis. Our question is going to be, is the Old Saybrook VA engaged in human subjects research? Heidi if you can open up the polls.

Heidi: Certainly, and again, the answers are yes, no, or more information is needed and responses are coming in. We'll give everyone a few more moments to respond before closing the poll question out and going through the results. It looks like we've slowed down so I'm going to close that out and what we're seeing is 41% of the audience saying yes, 14% saying no, and 45% saying more information is needed.

Soundia: Excellent. That's exactly the response we wanted so I think we got a good taste here. So, more information is needed we felt. The results were perfect because really we just don't quite know enough, right? It looks like he most likely is, you know, engaged in human subjects research. He is a co-investigator so, at a minimum, he's involved in research, you know, but what we don't know is what he's receiving, right? We don't know if the information that was sent was de-identified. Was it identifiable? We don't know if he received coded information. We didn't include that information in our case and we don't know if he did receive coded information, can his co-investigator get access to the key to decipher the code. We didn't say

anything about whether any agreements were in place to limit it. So, in this case, we just really don't know what was said and, I'll be honest, we see this all the time.

Karen: Yeah, and it's very complicated because, even as Soundia is talking about, well do you need the key to the code, it's also important, like we're reinforcing, what coded information are they getting then. So it's important not only to ask whether or not they have the key but also what's in the data set and that goes back to that second, the third bullet, is it identifiable? So all of these together will go into this why more information is needed.

Soundia: Right. Alright. Leaving Dr. Thomas and we're visiting our friend, Dr. Everett. So, Dr. Everett, and his study team, who are located at the Great Plains VA, they plan to conduct human subjects research on endocrinology patients who are treated at the Great Plains VA and four other VA facilities. Now, only clinical data will be obtained by Dr. Everett and his study team from the electronic medical records as patient's visit the endocrinology clinic over the next five years. So no research data, they're going to be going into the medical records. No subjects will be contacted. The research presents no more than minimal risk to human subjects. Our question is going to be, which facilities are engaged in human subjects research? Before we move from the case, I'm just going to read the answers. The answers will be only the Great Plains VA is engaged, only the four other VA facilities, all five VA facilities are engaged, or more information is needed.

Karen: Remember what is Soundia is saying. There's four other VA facilities involved, so think carefully about this and ponder it before we open the polls.

Soundia: [unintelligible 54:19] Heidi.

Heidi: Okay there we go. We'll give everyone a few moments to respond before we close the polls and go through the results, and it looks like we've slowed down here so I'm going to close the poll question and what we're seeing is 45% of the audience saying only the Great Plains VA, 1% saying only the four other VA facilities, and 31% saying all five VA facilities, and 24% saying more information is needed. Thank you everyone.

Soundia: Excellent. Thank you. Yeah, this was a bit complicated because, well, we only had so much space to give you guys information on the case, so, in terms of which facilities are engaged based on the information we gave and understanding that, you know, additional information might change this determination but the Great Plains VA is the only facility engaged based on the information and we recognize that we gave you very little information. Why is that? The data is being obtained by the study team at the Great Plains VA. We said that Dr. Everett and his study team, who are located at the Great Plains VA, so we limited it to the Great Plains VA consisting of the study team. Right? Everybody is at the Great Plains VA. The other four VA facilities are not engaged and why is that? Because personnel located at the other four VA facilities are not involved in the conduct of research. Okay? They are not obtaining research informed consent. They are not interacting or intervening with subjects for the purpose of the research. They are not collecting any personally identifiable data for the

purposes of the research. Everything is being done by Dr. Everett. Now, whether those VA facilities will have to actually release the information or if Dr. Everett and his team can go in and get the information, is immaterial because, even if they have it, if someone in their informatics office at each of those four VA facilities have to release the information, releasing information does not engage a facility. So, I think that's probably where the people who asked for more information, that might be one of the factors you were looking at, and I'm glad, you know.

Karen: Yeah. It is because a lot of times you'll look at the scenario and you'll say, oh, four other sites are involved so they must be engaged but the purpose of this presentation today is to go methodically through the steps. Again, it goes back to what is being done, who is doing it, does it constitute institutional engagement in human subjects research for purposes of activity, and as the bullet shows, there's no one at these other four facilities that are doing anything that engages that facility in human subjects research.

Soundia: Excellent. Alright #6, case #6, we have two questions for case 6. This is our last case okay?

Karen: This is hard.

Soundia: Case 6, a VA investigator, at the Stars and Stripes VA, is conducting a study on different modalities for administering PTSD support to veterans. Subjects from 10 VA facilities across the country will be enrolled in the study. There's also a VA Coordinating Center that will be used to manage receipt and processing of returned surveys and they are going to be assisting with data analysis. Now, information from the subjects' medical records will be collected from CPRS and sent to the Coordinating Center to collate with the surveys. The other nine VA facilities will only release information from subjects medical records. Our question, first question, there's going to be two. Our first question for the first poll is going to be, is the coordinating center engaged in human subjects research. And our choices are going to be as before; yes, no, or more information is needed. Heidi, if you can open the polls.

Heidi: Yup. Here we go, the poll is open. Let's give everyone a brief moment to respond and then we will go through the results. And it looks like we're slowing down so I'm going to close that out and what we are seeing is 52% of the audience saying that yes the Coordinating Center is engaged in human subjects research, 17% saying no they are not, and 21% saying more information is needed. Thank you everyone.

Soundia: Excellent. So in answer to the question, we said yes. The Coordinating Center is engaged in human subjects research. And why is that? Oh, typo there, sorry about that. They are performing an activity that they do not typically do for non-research purposes. They are receiving identifiable data. How do we know? Well, they have to collate the results of the survey with the results from, I think it was CPRS and, therefore, in order to do that, there has to be some identifier there and so, we know that they are going to be receiving that. They are assisting with data analysis. Again, so they would be engaged in human subjects research and so, therefore, they would have to have an FWA. They would have to have an IRB that oversees

the research. Now, what's interesting here at the VA central IRB, which is in PRIDE, in cases like this, we include the Coordinating Center as we have an application that they would fill out that would cover them and the VA central IRB would oversee the Coordinating Centers. They'd be the IRB of records to them as well as any of the other facilities that are engaged.

We have a second part to this question. I'm going to actually go back to the description as I read the question. Our second part is, are the other nine VA facilities engaged in human subjects research and should a local LSI be assigned to each site? All right Heidi, if you could open up the polls.

Heidi: Okay and our answers again are yes, no, or more information needed. We'll give everyone a few moments to respond. Responses are coming in. It looks like we've slowed down here so I'm going to close the poll question. What we're seeing is 47% of the audience is saying that yes the other nine VA facilities are engaged in human subjects research. 58% saying no, and 15% saying more information is needed. Thank you everyone.

Soundia: Perfect. This is great. Alright, we agree with those who have said no. Are the other nine VA facilities engaged in human subjects research, and should a local LSI be assigned? And we said no. The reason being, their only involvement in the study, remember is the release of information from the subjects medical records, and that was in the case. I understand, you know, I apologize for those who don't have the case in front of them because I know that it can be challenging when you don't have all of the information in front of you. But, they were only involved in releasing information. A local LSI would not be required because the facility is not engaged in human subjects research. Now, the facilities of those nine, those nine VA facilities may require that the PI provides specific documentation including a copy of the IRB approval prior to releasing of the information of the data centers at each of those facilities are going to have, you know, their own SOPs in terms of what they require to have on file before they release subject information. But, in terms of are those facilities engaged, our answer is no. So I think that we've come to the end of our cases.

Karen: I want to back up.

Soundia: Yeah, sure.

Karen: That one right there. I want to spin this two different ways, the slide before.

Soundia: The slide before? Perfect.

Karen: So one thing that we see is okay, let's talk about if you have your investigator at the primary site and that was at the, pull this up, let's go back to the original case.

Soundia: Stars and Stripes.

Karen: Stars and Stripes, because this is what happens a lot as well. So they're conducting this study and let's say that the investigator at Stars and Stripes VA is sending out people from Stars and Stripes VA to go out and conduct the surveys at the nine VA facilities, the Coordinating Center doesn't count. Okay. Alright. So, does that mean that the nine VA's are engaged since the VA investigator at Stars and Stripes is sending people from his study team to go out and conduct the surveys at the nine VA facilities which include your facilities on the phone. No? No. That's because it gets back to that issue are they doing something that would constitute engagement of that facility, of your facility. Do they need an appointment from your VA facility in order to do those surveys with the patients. The answer is no. That's not what you need a VA appointment for. Now, if you were doing a physical. If you were getting into data management systems that's a different situation. But, just because they're coming on site doesn't mean that I need a WOC appointment without compensation appointment in order to do that activity at your facility. What they do require is under VHA Directive 1200.02, there has to be approval from your VA facility director, or equivalent, to allow that to be done on the premises. Now, again, taking the spin one time further. What would make the sites engaged. Let's say, that let's take it one step further on what I just said. The VA investigator from Stars and Stripes is sending those people to your VA facility but he is asking you to help identify the patients who will be a part of this survey. You are now acting as an agent of the investigator because you are helping to, and you are obtaining individually identifiable information, let's say from CPRS in order to track down patients and ask them to be in the room for the survey. So that is how, what Soundia is talking about this whole thing, how one sentence can change it all.

Soundia: Right. Varying a lot.

Karen: Yeah, varying a lot. It's very interesting how this can go

Soundia: And we received a question about this question about this case, I believe, and the question said well wait a minute now, whose consenting the patient because, yeah, we didn't include that in our description. In this case, for our example, it really didn't matter because we said that the other nine VA facilities will only release information. Right? But, let's be clear, if anybody at the nine VA facilities is an employee, right, of any of the nine VA facilities was consenting the subject for participation in the study, then they would be engaged in human subjects research. Right now, the assumption, unwritten, is that the study team of Stars and Stripes are the ones doing consenting because we haven't said. We said that the other nine VA facilities only release of information, but yes, consenting would change if any of those other VA facilities were consenting the subjects than they would be engaging their institution.

Lucinda: We have a question specific to case 6?

Soundia: Yeah. Sure. Let's go.

Lucinda: I think that_

[END OF AUDIO]