Cyberseminar Transcript

Date: December 18, 2018

Session: PART 2 -The Revised Common Rule, Proposed VHA Directive 1200.05, and the IRB: Focus on Significant Changes

Presenter: Karen Jeans, PhD; Soundia Duche, M.A., M.S.

Soundia Duche: Good afternoon everyone and welcome to today’s training. Petrice has already told you guys what we have in store for you. As she mentioned, this is the second part. It's a continuation of the November 29th training we did which was quite long I know. And so what we're doing is, there were two sections we were not able to get to and so we're going to be talking about those two sections, vulnerable populations and then definitions. Specifically, we're going to be going over the significant changes in the proposed VHA Directive 1200.05. And then we're going to segue into answering about, we had about 16 questions that we were not able to get to during the November 29th training and so we've included those questions here and we'll be going over them today.

I am one of your presenters. I'm also going to be joined by Dr. Karen Jeans who's going to be co-presenting today's training with me. And Dr. Kristina Borror will also be joining us to answer some of the questions on some hot topics that we're going to be going over. Before we get started though in terms of the vulnerable populations, our first major section that we're going to be discussing today, we want to give you a brief update on the revised common rule and VHA Directive 1200.05.

So let's get started here. In terms of the revised common rule, where are we? It's coming folks. We are about, just a bit over a month away. January 21st, 2019 is the compliance date with the revised common rule. It's also known as the 2018 requirements. The reason being, it was originally supposed to be effective this year, January 19th, 2018. If you see that little purple arrow. We were supposed to be already compliant with the revised common rule, but there were a series of delays, two to be exact. Two six-month delays. And so they've pushed out the compliance date to January 21st, 2019. And what that means is that all new studies approved on or after January 21st, 2019, or deemed exempt by the IRB on or after January 21st, 2019 must be in compliance with the 2018 requirements. The one provision that does not go into effect is the cooperative research provision, and that deals with certain requirements for single IRB review for multi-site research. That compliance date was always January 20th, 2020 and that has not changed. So that remains in effect.

VHA Handbook 1200.05. Let's see. My cursor is not moving. Uh-oh. There we go. I'm going to ask Karen if she could chime in here to give you guys an update on where we are with the new directive.

Dr. Karen Jeans: Okay. Hi everybody. This is Karen. And in terms of 1200.05, the new directive, we're very close. We have completed Office of General Counsel concurrence and so we are in the final stage of concurrence by the Office of Labor Management Relations before it goes for signature by Dr. Stone. And so in terms of being able to tell you exactly in terms of days when the final signature will happen, I cannot answer that today, but as we have been committed to giving [unintelligible 3:43] very transparent process, this is where we are and I hope to be able by next week, be able to give a status on where we are with the signatures for Dr. Stone. So as Soundia had stated, this will happen. And as Dr. Longenecker discussed on the ORD field call yesterday, we're also seeking permission from VHA publications to be able to release, since OGC has concurred [unintelligible 04:14-04:15], a copy of what has been submitted to Labor Management Relations because it does represent concurrence from the Office of General Counsel and we do not expect any additional changes to be made. So that's where we are right now.

Soundia Duche: Great. Thank you so much Karen. And so this slide was borrowed from the presentation we just did on Friday. Dr. Petrice Longenecker did one of our first workshops. And I just want to briefly, I know many of you participated in that training, but I want to make sure everybody on this call is on the same page in terms of when we talk about the revised common rule and the 2018 requirements, what does this all mean. Essentially, the most important thing to remember is that we have two versions of the common rule. We have the pre-2018 requirements. Those are essentially what we're operating under now. Our current common rule. And then we also have the 2018 requirements which go into effect, in terms of the compliance date, on January 21st, 2019. And so what this means is, all studies that are currently approved by the IRB or that will be approved prior to January 21st, 2019 will be under one set of regulations. The pre-2018 requirements. And then all studies approved or deemed exempt on or after January 21st, 2019 will be under another set of regulations, the 2018 requirements. And we spent a lot of time over the course of this year going through, we had monthly trainings, both ORD and ORO on what the changes are for each section. Continuing review, informed consent, waivers and so on and so forth. That said, there's also a third category whereby some studies that are currently approved under the pre-2018 requirements, our current requirements, current common rule may migrate, may transition at some point to the 2018 requirements. They're not required to, but some facilities at some point may decide it's worth transitioning the study. So we're going to have a lot of movement. We're going to have a lot of things you have to keep track of. Our take-home message is to know that IRB's will be operating under both sets of requirements for the foreseeable future. And so, making sure you track what study is in which pot. Which requirements apply to which study so that you don't find yourself in a situation of non-compliance. The workshop that Petrice led on Friday really talked about what studies have to be in compliance with the 2018 requirements. And that's this blue side, the right side of the chart. Essentially any study that's approved by the IRB on or after January 21st, 2019 and studies that were reviewed and approved between July 19th, 2018 and January 20th, 2019 that used the burden-reducing provision of elimination of the grant as part of their review process. This is something they consciously did and documented that they were doing that. And those studies have to transition and be in compliance with the 2018 requirements on January 21st, 2019. Now I'm not going to go into that because Petrice has done a great job. She did a presentation in June and July on the burden-reducing provisions and the workshop that was just done this Friday. The June presentation or the July, one of those two, is on the PRIDE Cyberseminar website, the recording. The workshop has yet to be uploaded. We hope that that will be uploaded by the end of the week. So you can stay tuned for that.

Borrowing again from her presentation. In terms of what studies must comply with the 2018 requirements. We've discussed what, but how do you determine the date? Because essentially we keep saying, any study that's approved or deemed exempt by the IRB on or after January 21st, 2019 must follow the 2018 requirements. Now ORD has made a policy decision whereby what we've said is in order to reduce confusion, in order to facilitate our [unintelligible 08:30] who's going or coming, and just allow for better tracking within sites and increase clarity with respect to which requirements apply, what we've said is that any new study that is undergoing IRB review, if it receives its final IRB approval letter or notification that the IRB has approved it, all conditions have been met, any study that is approved by the IRB on or after January 20th 2019, must comply with the revised common rule. I know this can be confusing so I'm going to repeat it again. If the study has undergone expedited review or convened board review and as of January 21st, 2019 or after, all the conditions are met, the IRB designated reviewer or the expedited reviewer can sign off saying yes, everything's approved, all IRB conditions are met, that study, ORD has decided, will fall into the bucket of the 2018 requirements. Again, why have we done this? You can envision if a study is reviewed by the convened board let's just say on January 10th. And it's approved with minor modifications, but the study team does not return the modifications for two or three months, which happens. Happens often. And then you have a study then subsequently down the road sometime in the spring where finally the IRB has said yes, now you've met all the requirements, we can issue our approval letter. Some sites in the VA will say okay, that study is subject to the 2018 requirements because the IRB has issued the approval letter after January 21st. But other sites might say, citing the way you handle continuing review and calculation of expiration dates, you say well this study was reviewed by the convened IRB. And so because it was reviewed by the convened IRB and it was approved with minor mods prior to January 21st, 2019 we're going to make it subject to the pre-2018 requirements. And so we could have our sites doing one or both of these things and they would base it on what, we're not quite sure. But it could create a lot of confusion especially as time goes on in terms of which rule a study is under. And so to help make this more streamlined and increase clarity this is ORD's position. Now, I'm going to say there's a caveat here. We are seeking consultation with OHRP and some of our other sister federal agencies on how to best treat multi-site studies, particularly those where there is a sponsor. Because the sponsors obviously want all their studies to be reviewed as similarly as possible and to be under the same rules and requirements. So, we're in consultation with OHRP recognizing that we want to make sure VA handles these the same as DoD and NIH and everyone. And so we're all in consultation to really determine how are we handling this. The significance is you could have a study, let's say a pharma study. It's been approved in, what are we, we're in 2018, it was approved in 2017. And it's adding sites continuously. And so you have it at a site in 2019. You have it at another site in 2020. Those sites that are added, which rules do they fall under? And so those are the types of discussions we are in negotiation with OHRP. Everyone's giving a lot of thought to this because these are critical issues and we want to make sure that everybody handles these similarly. But from our perspective, for VA research for now, ORD's stance is that final IRB approval on or after January 21st, 2019, the study, whether it's reviewed, approved, deemed exempt, must follow the 2018 requirements. And once we post Petrice's workshop on our web page, probably by the end of this week you'll be able to listen more to the rationale for that and she has some great examples in that presentation.

Again, this slide just reiterates what I've just said. With expedited review it's always pretty straight forward because it's the date the reviewer deems everything to be met. So if the reviewer deems all conditions have been met before January 21st, 2019 it’s straightforward. It goes by the pre-2018 requirements. If it's after January 21st, 2019 it will go by the 2018 requirements. But convened board can be a little trickier. And that's why we've come up with this position to help clarify things. If anything changes, we will be sure to let you know. You can be sure of that. But this is our way forward in terms of how best to handle making sure all our sites proceed in a similar fashion.

And these two questions relate to that. These questions came in at the end of the November 29th training and we were not able to get to them. So let me just read out the question. The first question was, does the date of January 21st, 2019 for compliance with the 2018 requirements apply to final approval by the IRB or by the R&D committee? And so just want to stress, even though here in the VA we do have R&D committee approval which is required before you can start the study, the common rule really deals with IRB, right? So, the revised common rule states that anything approved or deemed exempt on or after January 21st, 2019 by the IRB. So what we're looking at is the final approval by the IRB. We completely recognize and accept that you'll have studies that are approved January 15th, 2019 and they may not get R&D committee approval until weeks later. Those studies would still be subject, if it was prior to January 21st, 2019, to the pre-2018 requirements. If it was after it would be the 2018 requirements. But it's the IRB approval date.

And then the second question asks a very legitimate question. Isn’t the IRB approval date for a study the date that the convened IRB votes to approve the study and not the date of the designated review? That is the way most IRBs function and the study, if approved, is approved for a time period from the date of the convened meeting. This simplifies the tracking of expiration dates as well. From my reading of the handbook, the IRB determines in their SOPs how they want to address this. Is this a misinterpretation? And I'm so glad [unintelligible 14:55] individual who asked this question because no, no you're not misinterpreting it. What you're doing is absolutely in line. And we are not changing any of that. How you calculate your expiration date, how you calculate your convened board date, your continuing review date, whether it's based on the date the convened board approves the study with minor mods or you base it on the date when the final IRB approval is given, that's for your SOPs to spell out and you abide by what your SOPs say. What we are stating here in this approach is that, in terms of determining which regulations your study falls under, we are saying that for that purpose and that purpose alone, if a final IRB approval is issued on or after January 21st, 2019 that study should be subject to the 2018 requirements. Does not change how you handle your continuing review date. Does not change any of that. This is specifically to determine what requirements apply.

So again, I hope we've clarified that. We will continue to clarify that as often as possible. And if anything should change we will let you know for sure. But that is our current thinking. And so now, we're going to move. Oh, Karen do you want to say something [unintelligible 16:12].

Dr. Karen Jeans: I wanted to [unintelligible 16:13]. Can we go back to the last slide just for a second?

Soundia Duche: Yeah, absolutely.

Dr. Karen Jeans: So I also wanted to add to Soundia's comments here. There's the approval date for purposes of continuing review. And then there's what is common called the effective date. The date that the study is ready to be initiated from an IRB standpoint. And so when you're looking at that first time that the IRB, and the study requires convened IRB review. When it's approved by the convened IRB, but it requires modifications, in terms of the IRB approval date, yeah it's approved at the convened IRB meeting. We haven't changed that. And then when those modifications are reviewed by the designated reviewer, because I want to answer [unintelligible 17:10-17:11] designated review. That's why I want to comment on that question. That is the date that that initial IRB approval will become effective because all of the conditions have been met. And what is interesting here is that until 2015, when the previous version of 1200.05 went into effect, we did establish an ORD policy on how continuing review dates would be set in relation to the date the IRB reviewed the study and approved it with modifications for example, when it had to require a review by a convened IRB for establishing the dates that you would set the continuing review intervals. Now, in 2014 we aligned ourself with OHRP who issued guidance in 2010 on how those continuing review dates would be set. And we are now in alignment with them. But as Soundia is reinforcing the process that you use has to be in your SOP. It has to be transparent how the continuing review date will be set. So just reinforcing what Soundia is stating. It's critical. We're not changing the requirements from the 2014 requirements and the current 1200.05 regarding how continuing review dates are set. We are just reinforcing it has to be transparent in your standard operating policy. So that's my comment Soundia.

Soundia Duche: Great, so thank you Karen. Thank you. Yeah and I quickly glossed over that because I was focusing on the date of compliance but she is absolutely right. So if you have further questions please we can get to them during the open Q&A session because we can talk all day about [unintelligible 19:06]. We don't have a problem. We want to just make sure everybody understands the approach. Right so that said now we're going to move on and wrap up the training part one. This is part two and we're going to be talking about vulnerable populations and Karen is going to be leading this. So Karen when you're ready you just let me know when I should advance, okay?

Dr. Karen Jeans: Thank you. So next slide. Okay so the first issue that we are going to make some revisions on in the proposed Directive 1200.05 involves the conduct of research in VA when it includes pregnant women. Now currently we have a requirement that the VA medical center certifies, certifies means in writing, that the medical facility has sufficient expertise in women's health to conduct the proposed research as an absolute. If you're surveying, your research involves surveys of women who are pregnant, it's currently required. So we're trying again to use an approach that is more within the spirit of what is intended. To let the facility director have basically come to a scope of attention an immediate scope [unintelligible 20:25] attention when certain types of VA research are being conducted in the facility, as he or she is the institutional official for that research. And so what we are doing is taking out those activities involving like surveys or when you're, for example we're following up women who become pregnant [unintelligible 20:47] for example in a clinical trial that's being conducted in VA. And then we'll take them out of the active intervention part but we'll just do follow-up for pregnancy outcomes and how the newborn is, the neonate. And so all we're doing now is basically reducing the facility director certification requirements to only involve VA research for pregnant women when it involves interventional studies that they are involved in or invasive monitoring of pregnant women as subjects. But we are doing an absolute if it involves research at all involving the neonate, we'll still require with these current requirements, facility director certification. Next slide.

A major change in VA research policy in the Office of Research and Development is now a reversal of the prohibition that we currently have in ORD involving research involving the provision of in vitro fertilizations. And this is directly related to the expansion of VA medical care benefits to allow for VA to pay for in vitro fertilization as part of our medical care benefits package with the condition [unintelligible 22:21] described in the medical care package regulations. So what we are doing is indeed allowing that to happen. And 1200.05 will go into very specific caveats on what can be done during the in vitro fertilization research and align it with other federal agencies, but the big issue is that we are reversing it to align ourselves with the changing healthcare needs with the Veterans that we taking care of, particularly the women Veterans. Next slide.

Fetal and human stem cell research. Again a major area of expansion that VA will now allow. VA had an absolute prohibition in our current policy that we will not allow the focus of research to be fetuses. You cannot use the human fetal tissue and really we do not allow the use of embryonic stem cells in VA research. So again, as a result of different changing needs of women Veterans and also a lot of input, all of our handbooks and directives are reviewed by different program offices including Ethics and Women's Health, legal, multiple patient care services. And so we are increasing or expanding the ability for VA researchers to be able to conduct research involving fetal tissue, embryonic stem cells. But it will be in alignment with our sister agencies, particularly the National Institute of Health. So if we're going to use embryonic stem cells or stem cells in general in fact, they have to be registered with the NIH. Now, here's a very important issue that literally is evolving as we speak on this topic. We are very aware that in terms of use of stem cells, embryonic, that how the federal government is allowed to use these in VA research directly comes from executive orders of the White House. And so we are always going to only be able to do what the White House allows us to do. As that changes our policy changes. So recently, for those of you who've been reading the Washington Post or also reading different types of scientific journals, you may be aware that there have been some recent prohibitions that have been placed by the White House on certain types of tissue, stem cells that are being allowed to be used in research that is funded by the National Institute of Health. And so, again as we evolve through this, we would be in alignment with that. If the White House changes and says you cannot do this, then that's exactly what will happen. So we will always be in alignment with what the White House directs us to do because we are a federal agency. Next slide.

Research involving children. So in terms of revisions to the Directive 1200.05 inclusion of children in VA research, we have not made significant changes except to clarify the difference between a neonate and a child in reference to what policies apply. So we have defined neonates as infants who are in the first 28 days of life. We have clarified that the children's research policies do not apply to neonates and they call that out specifically. And so those are the major changes or clarifications that have been made for research involving children. Next slide.

Another major change involves the research the VA does. A large number of our studies involve individuals with impaired decision-making capacity. VHA, the current 1200.05 handbook has numerous policy requirements that are VA specific on what must be done in order to include individuals, and those individuals are targeted, individuals with impaired decision-making capacity in VA research. And what we have found as we have lived with these different policies for over a decade, because versions of this have been in the prior VHA handbooks preceding the one that's currently in effect, the 2014 issuing of the one that we are living with right now, is that these policies again do not serve the purpose for which they were intended and that they really do not, they interfere or they are duplicative with other policies that apply to research involving individuals with impaired decision-making capacity. Primarily those that involve evaluating risk benefit, that ratio, to individuals with impaired decision-making capacity. And looking at [unintelligible 28:11] selection of subjects. Looking at research design. And we found that these requirements that we have currently in 1200.05 are being misinterpreted. And so what we have done is take out those requirements because we do believe that these are covered under the IRB approval criteria. Next slide.

Research involving prisoners. Believe it or not, VA does research involving prisoners and the majority of those research studies involve what I call the non-targeted inclusion of individuals who are prisoners. That is to say that we include prisoners as research subjects in VA when they have been originally consented when they were not prisoners, whether that be, and primarily we're talking about clinical trials or in different types of longitudinal studies. VA does, ORD does have a requirement that if you are going to include prisoners in your VA research study, that it does require, in addition to the review according to the applicable sub-part requirements, that we also require waiver approval from the chief research and development officer. And this will actually be delegated to Dr. Klote. What is missing from the current 1200.05 that you have that's currently in effect is what do you do? How do you do it? And so what we did is, none of the requirements have changed, but we have added the waiver process. How they must be submitted, who submits them, what are all the [unintelligible 30:08-30:09] that are required to do this so that it can be evaluated here in the Office of Research and Development? So that is the major change that has occurred in 1200.05. Next slide.

Soundia Duche: Perfect. Thank you Karen.

Dr. Karen Jeans: You're welcome.

Soundia Duche: So the last part of the training before we go into the questions that we weren't able to get to are the definitions. And so what I've done here, and I hope and pray I've been comprehensive, I certainly tried my best, I made a little chart where I've gone through the proposed 1200.05 and the current 1200.05 and I documented for you here which definitions have been changed, which are new, where there have just been minor clarifications so that as you go through your SOPs, I don't know if, I think each site proceeds differently. Some have a definition SOP or some have all their definitions associated with a particular activity at the beginning of that SOP. But this should be a comprehensive list of what needs to be changed. I know you're going to have to wait to see 1200.05 for some of these, but at least you can flag what you will need to change. The third line here where I say revised per 2018 requirement, those definitions are revised verbatim per the 2108 requirements. So you can go to the common rule, the revised version, and you'll be able to make those changes based on the definitions. Anything that's not on this list should not be changed. So we're just giving this to you to be helpful and make your job a little easier because I know you guys are very busy, doing a lot of things getting ready.

All right. So now we're going to move on to the outstanding questions. And as I mentioned we had about 15 or 16 of them from November 29th session, and then we'll open it up to open Q&A session. Now what I've done is I've grouped questions together by topic and so in order to help frame the issue to remind people what changes are, the presenters, and it's going to be me, Karen and Kristina are going to take different topic. But they'll go over what the changes are and then they'll proceed and address the question. And so Karen, I think you're up with IRBs of record.

Dr. Karen Jeans: Okay. So the major change that ORD has made in the proposed 1200.05 is, in addition to the IRB of records that are currently permitted under ORD policy to be an IRB of record for a VA facility, we've expanded it. In preparation for the single IRB cooperative research provision compliance date of 2020, this is the beginning of that movement. And so one the policy changes that we have made is that we are going to allow, for multi-site research protocols in which VA is participating, including those with non-Vas, an IRB that is not affiliated with that VA can be the IRB of record for the study. We can allow that to happen if that IRB has been specially designated by ORD as an IRB that makes [unintelligible 33:40] to site IRB for VA facilities. In other words, for purposes of policy, ORD approval is initially required in order to say that this IRB which is not affiliated with your VA medical center may be used as an IRB of record. So next slide. I think we'll get to the questions then related to this topic.

Okay. So I'll read the questions. Will there be a list of academic IRBs that are already approved by ORD on January 21st, 2019? The answer to that is no. What we will be doing is we already have three IRBs (this policy was created for them) that we will be working with to see whether or not they will be willing to do this. And this is part of the TINs, the Trial Innovation Networks that is part of the NIH national clinical trial initiative. And they had approached us six months ago about again very much wanting to include VA sites in all these different studies that are part of the clinical trial initiative. And so these include the University of Utah, Vanderbilt, John Hopkins University. Those are the three that this policy was originally written for, but it does not mean that there will not be others that we would include as we vet them and as we discuss all the arrangements that would be necessary. So how can we get academic IRBs that are not on this list to be added to the ORD list? Again, we will go through an approval process and we have a criteria that we will be using. And again, we will be working with the Office of Research Oversight because it involves both of our program offices. So I've mentioned three of these, but if there are other academic IRBs that you're aware of as you get into these different types of situations that could be allowed by policy, you would request this and we will have a process to request the approval. For right now, please direct those requests to Dr. Klote and to myself, C.Karen.Jeans@va.gov.

The next question. Will all current IRBs of record be required to request inclusion on the list? No. No, no, no. I'm really glad this question was asked. This is not like SMART IRB in which even if you're part of the SMART IRB platform, any of those IRBs that have agreed to be part of the SMART platform [unintelligible 36:25-36:26] IRB. So no, that is not true. And there's a huge responsibility that is incurred when an IRB is the multi-site IRB. So, no. The answer is no.

You mentioned that four new IRBs are being considered as an external IRB for VA. Yes. In the previous call I did say four. Originally when the TINs, the Trial Innovation Network came to VA, they had referenced four. We know of three. And so that's why I mentioned three today. But I did mention four so you were correct, in the previous [unintelligible 37:05] meeting. Are any commercial IRBs? No. Not at this time. In fact, the proposed directive 1200.05 continues the current exclusion of commercial IRBs. However, please be aware that we are in the active process, and I do mean active, of creating the different policies, in alignment with the applicable program offices, to be able to use commercial IRBs. It's just not a simple issue that we can deal with immediately. We do have a variety of different situations that we need to deal with in order to allow this to happen. But yes, you can expect, in fact Dr. Klote has spoken on this as well, that we are moving toward the model of being able to use commercial IRBs. That's my comments.

Soundia Duche: Thank you Karen. I think you're still up with privacy officer and ISO [unintelligible 38:04-38:06] question. ISO and PO review. So you're still on.

Dr. Karen Jeans: Thank you Soundia. Okay. So what we have done right now in the current 1200.05, there is an entire section about the responsibilities of POs and ISOs. Privacy officers and information security officers, [unintelligible 38:28] review of research. And it goes into pre-reviews and when do they do it and final ISO reviews and final PO reviews. And what we have done here is take all of this out to make it to where, as again, with the idea, we are moving toward the single IRB model and using different types of IRBs. The primary issue is that all VA research must be conducted in compliance with all applicable requirements, regulations and policy. That's the underlying requirement. And so we cannot put a requirement in that POs must serve on IRBs because we don't utilize all internal IRBs. What we wanted to do is be able to say through our policy that as a protocol is going through review, understanding that many more of these protocols that currently require IRB review will no longer require IRB review because they will be exempt. That PO and ISO review is flexible. It can occur when it is needed. For example, I have a protocol right now, literally got an email this morning from an investigator who is submitting a protocol to their local IRB in VA, asking about hey, I have this app I want to use. Can I do it? And my first question back was, have you contacted the ISO? And so we're making it flexible to where the ISO consultation, privacy officer consultation is part of the IRB review process as applicable to the protocol as needed. Same thing goes with all these protocols that will no longer come under IRB review in terms of the IRB being the oversight committee for these studies involving human subjects. There's also a lot of studies that are not human subjects at all. They will never go to an IRB. We also want to put in a requirement that's very important to us when it comes to disclosing names and other information to firms, in terms of industry. For example, that investigator’s contract with, we want the PO to be involved in this process. We're very concerned here. We're hearing the concerns here at the national level among different offices about information that's being disclosed from our VAs outside the agency when it's [unintelligible 41:37] supposed to be de-identified or it's identifiable and there is not the authority under the privacy regulations and laws for that to happen. And so we have indeed put a requirement in to address the specific issue that's at risk to the agency.

Next question. Okay. So is the review still required for new VA protocols submitted to the IRB? The issue is not is their review still required. The issue, does the research involve a privacy officer or an information security officer issue? An issue involving information security and privacy officer for which their expertise is required. Because at the end of the day, all VA research again must be conducted in compliance with applicable regulations, requirements and policies. So, again we've introduced a flexibility into this so that if the protocol requires, involves for example an app, yes you're going to need to get consultation from the information security officer to ensure that this app can be used for the VA research protocol. Same thing with privacy. If the research involves, for example, disclosure of PHI outside the agency, is there authority under the privacy act and HIPAA to allow that disclosure to happen so that we do not have violations, breeches of the privacy rule or that we're not in violation of the privacy act.

Now the next question is a really good one that I want to get to. Do the PO and ISO still have to fill out the Department of Veterans Affairs checklist for reviewing privacy, confidentiality and information security in research. And I will show my age here and say that I was around when this was created. This was created by Dr. Cuccherini in consultation with the VHA Privacy Office and the Office of Information and Technology. Again as a response to a major non-compliance issue that the agency had. It was designed as a checklist. It was never put into policy as a requirement. It has never been in ORD policy as a requirement. I am not aware, and I did a search through the OI&T directives and handbooks and VHA Privacy directives and handbooks and memorandums. So if there is a policy requirement for this please let ORD know. But it's not coming from ORD. If you have a local policy requirement, again local policy can always be more restrictive, but there is no national policy that I am aware of at this time, and please inform us if we are wrong, that specifies the use of this checklist. It was designed as a voluntary worksheet. And speaking for ORD policy, we have nothing in policy that requires it.

Is PO and ISO input required for exemptions requiring limited IRB review to ensure there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of their data? The question is it depends. It truly does depend upon the type of research that is being reviewed under the limited IRB review and whether or not there are privacy and or information security policies that are applicable to the research. And I know that's an it depends answer, but it truly does depend upon what is being done under the limited IRB review. Next slide.

Soundia Duche: Thank you. So the next question we've got is regarding limited IRB review. And so I know many of you guys don't have this slide because I added it about two hours before the presentation. I will upload the final slide deck when we post the recording, so no worries there. You'll get it. But I just wanted to briefly go over limited IRB review and what's required and then we'll segue into answering the question. And so limited IRB review is a new approval criteria, well there is an new approval criterion in the 111 criteria that's specific to limited IRB review. So it's 111(a)(8). And limited IRB review is specific to certain activities that are eligible for exemption. So with limited IRB review, the IRB does not have to ensure that all the 111 approval criteria are met, but instead they have to look at just certain things and I've included them here, in order to determine that a particular exemption is eligible for that exempt category. So there are four instances when limited IRB review is required in order to determine that an exempt research activity can be exempted. That's in exempt category two slash three or sub-three, and exempt category 3(i)(c). Exempt category 2, that's our one that deals with surveys and interviews and exempt category three is this new category, benign behavioral intervention. And in both cases, when one is collecting identifiable information that could potentially place subjects at risk, they require limited IRB review in order to ensure that adequate provisions exist to protect the privacy of subjects and to maintain the confidentiality their data. That's the only thing that the IRB review has to ensure. And that could be done by expedited review or convened board review. Exempt category seven. That's a category that deals with secondary storage for secondary use when broad consent has been obtained. And in order to qualify for exempt category seven, the IRB has to conduct a limited IRB review and again determine certain things. What do they specifically have to determine? They have to determine that broad consent was obtained in accordance with the requirements. That it was appropriately documented or documentation is waived. And here in VA, it has to be documented. And Kristina will be talking about that in just a few minutes. And if a change is made for research purposes in the way the identifiable information or specimens are stored, that there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of their data. So again, specific things that the IRB has to determine as part of this limited IRB review. Limited in the sense that they only have to look at this. If these criteria have been met then the study is eligible for exemption and one makes sure that it meets the exempt category seven if that was the one you were looking at. And then exempt category eight is again secondary use of specimens or data that were obtained under broad consent. And in this case the limited IRB review requirement is that the IRB has to determine that the research is within the scope of the broad consent and again, that there are adequate provisions that exist to protect the privacy of subjects and to maintain the confidentiality of their data. So that's just a quick primer on limited IRB review. Kristina did a great presentation earlier this year that again you can find on the Cyberseminar website all about exemptions and limited IRB review.

But the question that we received was, do you have suggestions on what a limited IRB review form should look like? What specific questions need to be answered? And then they asked, especially if we are transitioning an expedited project to exempt, like a simple chart review study. So let me start by saying that the regulations say that the secretary of HHS is going to issue guidance on what are adequate provisions to protect the privacy of subjects and maintain the confidentiality of their data, what things you should consider. We don't have that guidance yet, but we expect to receive it. However, if you look at the specific criteria, what the IRB is looking for, one of the things was when appropriate there are adequate provisions to protect the privacy of subjects and the confidentiality of their data. That's our current approval criteria. That's IRB approval criteria 111(a)(7). So that hasn't changed. So the same things that the IRB is looking for in order to ensure that that criteria is currently met, at a minimum that's what they'll be looking at again for limited IRB review. The other things, if you recall, were related to the broad consent. Determine if broad consent was obtained. Determine if it was appropriately documented. So while we don't have a form we can direct you to right now, that's something we can work on though. This is what your form would need to include. And so literally if you take this slide which you will get when we upload the presentation to the web and create a form that has this information and I realize that there will be additional guidance in terms of if there's anything else that the IRB really needs to consider when they're looking at protecting the privacy of subjects and maintain the confidentiality of their data. But at a minimum this is what you need to look at. So hopefully that's helpful.

Just want to point out the question asked also, especially if we are transitioning an expedited project to exempt like a simple chart review. So when you're transitioning a study, and this is for a research study that's subject to the pre-2018 requirements and the IRB and the investigator have decided that it's eligible for transition to the 2018 requirements, you have to make sure that it meets all the requirements of the 2018 requirements. And if you're trying to transition it to an exemption, you need to make sure it meets the exempt criteria. In the example given it just so happens that a simple chart review, I'm assuming they're talking about looking at data, which I believe that would probably be exemption four. And it just so happens that that one doesn't have a limited IRB review requirement. But let's just say they were looking at transitioning a study that was eligible for exemption two. If it required limited IRB review because it met the criteria of two slash three, then you would have to conduct the limited IRB review and ensure that there are adequate provisions to protect the privacy. So what you would be doing is looking at that. You would have it in your form and your IRB member, whether you do it by expedited or otherwise, would look and make the determination that that criteria is met and that the study does fall into the exemption and all activities related to that study fall into one or more exemptions. So hopefully that's helpful.

Dr. Karen Jeans: And this is Karen. Can I add one other thing?

Soundia Duche: Yes, please.

Dr. Karen Jeans: Okay. So in terms of, as Soundia referenced, the regulation states that HHS will be providing guidance. We have clarified with HHS that the regulation does not say when. And so while guidance may be issued in the future, it will not be issued prior to January 21st, 2019 because as Soundia has referenced, we're already using the IRB approval criteria that are in play here concerning privacy and confidentiality. So it's not a, you don't look at it differently in terms of the research activity in regards to how to apply that criteria because the criteria regarding privacy and confidentiality which is a(7) is the same regardless. Whether it's a limited IRB review or whether or not it's a study that does not qualify for limited IRB review in which it must undergo an IRB review under all of the IRB review approval criteria. So that criteria does not change.

Soundia Duche: Excellent. Thanks Karen. We're going to move on to broad consent. We had a question about broad consent and I'm going to turn this over to Kristina.

Dr. Kristina Borror: Hi. Thanks Soundia. Hello everyone. This slide is just a little reminder about broad consent and what the revised common rule, the 2018 rule says about this. And this is specific to certain exemptions related to storage, maintenance and secondary use of identifiable data and biospecimens. And in the revised common rule it says that this data or biospecimens could have been collected for research or non-research purposes. But we'll see how the VA is implementing that. And this is a kind of consent that can be used in place of getting very specific consent for each study. And there are elements that are outlined in the 2018 rule, 12 of them. And they all have to be included if you want to get broad consent. They can't be waived or altered. And that's described in 116(d). So the proposed VHA Directive 1200.05 specifies that broad consent can only be used if those data or biospecimens were collected solely for research purposes. So that is a restriction compared to what's in the common rule. And another restriction is that this broad consent has to be documented. The directive does not allow IRBs to waive that documentation and those 12 elements that are required in the revised common rule are basically aligned in 1200.05. Those are the same requirements and elements that you're going to see in 1200.05. And there's a clarification that it can be either a separate form, the broad consent form can either be separate from the study-specific informed consent document. But it says that if you do combine them then it has to be clearly discernible from the research-specific consent. And so this is somewhat related to one of the questions that we're going to see on the next slide.

So the first question is, what's the definition of broad consent? And we would love to give you a very clear definition, but the 2018 common rule and the proposed 1200.05 don't actually provide a definition of broad consent. The preamble to the 2018 rule does give us an idea of what it is, what it means and the preamble refers to it as seeking prospective consent to unspecified future research. And as I mentioned for VA this broad consent is only for secondary research on information or biospecimens that were originally collected for research purposes. And, as I also mentioned, this broad consent does have to be documented. That in the VA broad consent documentation may not be waived.

The next question is, can facilities decide not to adopt broad consent as long as it is documented in their SOPs? And the answer to that is yes. Broad consent is optional. There is not a requirement that facilities allow the use of broad consent or that investigators get broad consent. But in order to use exemptions seven and eight you do have to allow broad consent. So, that would be the only caveat. So if your facility wanted to allow the use of exemptions seven and eight, they would have to allow the use of broad consent.

The next question is, for VA-approved research can broad consent be used for the collection of samples or information for research purposes? And broad consent can't be used for research in which samples or information are obtained through a direct interaction or intervention with an individual for that particular study. The information, so remember broad consent is basically for unspecified future use. And the information or biospecimens have to have been collected for a previous research study. And for the VA it has to be a research study. It can't have been collected for clinical purposes. However, if you're getting study-specific consent for a study that involves interaction or intervention, you're actually getting information directly from somebody and you are getting samples directly from them. You're getting study-specific consent for that interaction or that intervention, you can also at the same time seek broad consent for this future unspecified research, use of that information or biospecimens that you're collecting now for the current research study that you're also getting individual study-specific consent for. So hopefully that's clear.

And the fourth question on broad consent is, if broad consent is combined with a traditional informed consent form, does the broad consent need its own signature block for the participant to sign? Does it have to be separate from the signature block for the traditional informed consent document? And basically the answer was alluded to the in the previous slide and it's yes because the subjects have to be able to decline or have the ability to decline broad consent for unspecified future research even if they want to participate in the current research study. So they have to be able to somehow delineate that okay, I'm saying and giving consent. I'm signing because I want to be in this specific research study where you're getting my specific consent for this collection of this data and these biospecimens. But you have to be able to say, delineate from that, from the fact that they are consenting or not consenting to this unspecified future use, this broad consent. So it has to be clear on the form which ones they are signing for.

Soundia Duche: Thanks so much Kristina. So we're going to move on. We received a question about just the regular, traditional informed consent. I'm not going to go over this whole slide, but just as some background, make sure everyone's aware under the revised common rule there's some additional requirements for informed consent, and specifically that informed consent has to start with, it has to include at the beginning of the consent form or the consent process inclusion of a concise summary presenting key information that subjects should know about the research study. So that's something that's new. And all studies approved by the IRB on or after January 21st, 2019 will need to be compliant with this. There are also some additional elements of informed consent that you can see here that are now required. And VA is in full alignment with all of the elements, both the new elements that are required for research subject to the 2018 requirements as well as the key information. VHA Directive has removed a few VA-specific elements that have been eliminated. So you see those on the right-hand side. I just want to say with all of this, with the changes to the revised common rule as it pertains to informed consent, there's nothing in these changes that conflict with the current requirements for informed consent in terms of the elements and forms. So it goes above and beyond what we're currently required to do. And again remember there's always nothing wrong in general with going above and beyond. And so nothing prevents a site from starting to revise their informed consent form template so that they're consistent with the 2018 requirements. And you can start using this new format now. So that's just something to keep in mind.

But the question we got was specifically, will there be clarification re: regarding what needs to go in the key information section for informed consent under the revised common rule. So remember I mentioned you have to have this key information and what's expected is that this key information is a concise and focused presentation of the most important information that's most likely to assist a prospective subject in understanding the reasons why they may or may not want to participate in the research study. The revised common rule says that this information should be organized in a way that facilitates comprehension and there's an expectation that it's key. So it's short. But of course as we all know, short is relative and it's really study specific. Because if you have a clinical trial that's involving a risky procedure, if the traditional form was 20 pages, well your key information might be a couple of pages versus let's say a pretty benign study that's just doing surveys where the whole consent form is maybe two or three pages. I don't know if that exists or not. A consent form that's two or three pages, that’d be nice. But anyway, we don't have guidance yet in terms of what the key information should entail, but in the preamble to the final rule, they do suggest certain key things or certain pieces of information that they would consider would constitute key information. And one, that's the fact that the consent is being sought for research and that participation is voluntary. That should be upfront. The purpose of the research, the expected duration of the prospective subject's participation and procedures to be followed. Any reasonably foreseeable risk for discomfort and what I've read is that really it should be your most prominent risks. You don't have to list all the risks in your key information section, but the most prominent risks. And then the benefits to the prospective subjects or to others that may reasonably be expected. And then the appropriate alternative procedures or courses of treatment, if any, that might be advantageous. Now, like I said, this is what's in the preamble. Our hope and our goal here is to have one of our new workshop sessions that we just rolled out where we can focus on consent form and consent requirements in the near future. So look out for that. We hope to get guidance from OHRP, but as Karen mentioned they haven't given us a sense of when that would be. In this case they're not required to provide guidance on this, but it's something we're all hopeful for. But in the meantime we do hope to help you all with that so look out for something from us on a workshop on this topic.

With respect to HIPAA we got a question about combining the form, so I just want to really briefly talk about what some of the changes in proposed VHA Directive 1200.05 as it relates to HIPAA. Currently, for VA research, if there's a HIPAA authorization required, you have to use the VA form 10-0493, the Authorization for Use and Release of Individually Identifiable Health Information. Currently now we know the consent form and HIPAA has to be separate. We're not able to combine them. But going forward, once the new directive is published you will be able to combine the forms into one. In our November 29th training we talked extensively about situations where it may be beneficial to combine it and situations where you may not want to. I won't go into that now, but I really encourage people who were unable to attend that training to listen in to that recording.

So regarding the combination of informed consent and HIPAA form, you can now combine them. If however you're going to not combine the documents and you're going to have a separate HIPAA authorization form, then you have to use the 10-0493. So that's something we'll still be requiring in cases where you elect not to combine the form. So 10-0493 is not going away, but you do have some flexibility where you can now combine the documents.

So our question was, or statement rather, for all practical cases, it doesn’t matter for the vast majority of research studies whether the informed consent form and HIPAA authorization form are combined or not. They are usually handled as a group of documents requiring signatures in different places.

Now, I understand from a research perspective when you're out there and you're consenting people yes, you have your stack of documents and so you go through the consent process and then you bring in the HIPAA form. The reality though, we all know, forms don't get signed. A signature is forgotten. A date is forgotten. You use the wrong version of one of the forms. The informed consent form is right, the HIPAA form is outdated. So practically speaking, being able to just have a subject sign one form actually could be pretty beneficial. At least in terms of reducing non-compliance in many instances. There is a caveat. There's always caveats. And that is, there are going to be cases where it does not make sense to combine the document, particularly in cases where you may have to have different individuals sign the document. So for example, if you have a subject where there's a legally authorized representative because you may be dealing with someone with a fluctuating decision-making capacity issues. Well in that case, that subject may have an LAR who would be eligible to sign the consent form, but they may not qualify as the personal representative who would be eligible to sign the HIPAA authorization form. So in cases like that you may not want to combine the form and we’ve talked at length about that previously. Also, we reached out to privacy on this and they suggested in cases where there are optional components of a research study, such as data banking or tissue banking where you require additional signatures, not saying that you can't combine the form, but in that case you need to have probably more than one signature where first they consent to the main study and then they consent to the HIPAA component. I'm sorry, the data banking or tissue component. And so there are going to be instances where it may or may not make sense to combine the form, but I don't think it's fair to say just that it doesn't make sense because we all know, and I think investigators appreciate this, IRB appreciates this, if you can cut down on non-compliance incident, hey that's a good thing.

All right. Collaborative research. Karen, I'm going to ask you to please comment on this question. Karen?

Unidentified speaker: Karen, try to unmute yourself now.

Dr. Karen Jeans: Okay, I'm on?

Unidentified speaker: Yep.

Unidentified speaker: Yep.

Dr. Karen Jeans: Okay, thank you. All right. This is actually a very, this is a really important question because the question is that the proposed 1200.05 has removed the language that states collaborative research involving non-institutions may not be undertaken without a signed written agreement that addresses such issues as the responsibilities of each party concerning ownership and reuse of data. Key question, does this requirement for collaborative studies no longer exist? Or will this requirement be included in another handbook or directive? There are major issues that we are engaged in as the Office of Research and Development with the Office of General Counsel involving what needs to be done [unintelligible 1:11:25] document the relationship to ensure that the agency's rights are being protected in these collaborative relationships. And so, while we removed it from this current directive because we do not want to put into a policy a requirement that we can't comply with or that we cannot define. Will this requirement be included in another handbook or directive, or guidance documents? The answer will be yes, as we work with the Office of General Counsel to be able to define what those agreements will look like. So the answer is, you will have in subsequent policies what is needed. It does not mean that for purposes of the research that's conducted involving other institutions, that we don't have to have agreements when those agreements are legally required. It does not mean that DUA requirements required by 1200.12 do not apply. It does not mean that the requirements for storing VA data on non-VA equipment do not apply. But what we're trying to do in terms of another handbook besides 1200.05, because collaboration involves research activities that include [unintelligible 1:12:48] also non-VA subject research activities a better place to be able to address this issue.

Soundia Duche: Thanks Karen. And then our question is about policy. If revised 1200.05 requirements contradict another handbook, for example 1200.12, the data repository handbook, which handbook do we follow?

Dr. Karen Jeans: So this is Karen. I'll take that. So the key issue is, don't make the decision yourselves. If there is an ORD policy conflict between two of ORD policies, please notify ORD. For example, in 1200.12 there is a requirement that unless the research is exempt, it must undergo continuing review. And so that's one of the requirements of 1200.12. Now as we know, in the 2018 requirements there is going to be a large group of studies that by default will no longer require continuing review because they're minimal risk. And so in those situations the IRB is indeed not going to be required to conduct continuing reviews for those activities because 1200.05 requirements will supersede 1200.12 because 1200.05 [unintelligible 1:14:32] the policies for the conduct of continuing review. So what I do ask all of you to do is [unintelligible 1:14:41] and we are actually developing a list of all these type of conflicts that we are aware of so that we can indeed document these and put these out. But if you are aware of, as you come up against these, we will keep a running list of this. We will publish these. Please let us know and we will add this to the tool and FAQs that we will ongoingly be publishing. Because I think as you can see from this conversation we're having, we don't have all the answers. We're working with it all together along with all the other common rule agencies. So just please let us know when these conflicts exist so that we can indeed step in and we can mediate those so you don't have to guess. Thank you.

Soundia Duche: Okay, thanks Karen. All right. So we've come to the end of the main session. Here's some resources. We always include relevant links. Just want to mention yes, we've come to the end of our scheduled trainings. That does not mean we are done having trainings. We have just not finalized the 2019 calendar yet, but as soon as we do, we'll publish it. I will say, just to give you a heads up, we're likely to continue to hold our monthly Cyberseminars on the third Tuesday of every month and as we introduce the workshops more frequently we'll be filling in and having some of those to supplement the monthly Cyberseminars.

All right. This is where you can find all the trainings. And as I mentioned the workshop on Friday will be loaded, that occurred on Friday, will be loaded hopefully by the end of this week. Now, we have a number of questions here. It is 3:17. If everyone is on board we can go till 3:45 so that we can get these questions answered. All right, so Petrice if you can start?

Dr. Petrice Longenecker: Sure. First question. Waiver for consent for screening and recruitment is no longer required under the revised common rule. What about HIPAA waiver.

Soundia Duche: Great question. As I mentioned earlier, this is Soundia, I'll take this one. Remember the revised common rule is not about HIPAA. HIPAA is the privacy rule. So HIPAA continues to apply. We are a covered entity. If you're collecting, accessing, using identifiable protected health information HIPAA applies. You either need an authorization or you need a waiver. So if that's for screening or recruiting you need a waiver. For any other activities, again remember HIPAA, identifiable protected health information which is identifiable by nature. HIPAA applies. You need the authorization or you need the waiver. Thank you.

Dr. Petrice Longenecker: Also I'm going to unmute Kristina so that you can mute and unmute yourself if you'd like to weigh in on any of these questions, okay Kristina? So you're now self-muted.

Dr. Kristina Borror: Okay, thanks.

Dr. Petrice Longenecker: Okay. The next question. What about SOP approval dates? If IRB approves SOPs for revised common rule prior to January 21st, 2019 but R&D has not yet approved them by that date. Does IRB have to wait for approval of SOPs prior to approving a study under 2018 rule?

Dr. Karen Jeans: So this is Karen. I'll take this one. So the issue of SOP approval for R&D committees under 1200.01 is not an explicit requirement. Now again, if this is a local requirement that is a local issue. But, while we require written procedures for recurring processes as part of the R&D committee, we do not indeed require the R&D committee to explicitly approve these type of IRB SOPs.

Dr. Petrice Longenecker: Okay. Is there going to be a list of at least the topics that the VA-specific guidance will cover? And with the caveat, hopefully provided soon.

Dr. Karen Jeans: I'll take this one again. This is Karen. So again, we were preparing to publish a list. Right now all resources are going into publishing the product that Dr. Klote has referenced. And then after that product has been issued, we will work on issuing a list.

Dr. Petrice Longenecker: Okay. Is there now a requirement to state in the informed consent form that deidentified information and specimens either may or may not be used for future research? Given that VA must comply with FOIA requests, must VA informed consent forms always indicate that deidentified information could be used for future research?

Dr. Karen Jeans: Hi, Petrice this is Karen. I missed part of the question. It was at the phrasing, now that VA must. Can you read the latter half?

Dr. Petrice Longenecker: Sure. So I think the first part of the question is referencing the new required element of the consent form. So element number nine I believe.

Dr. Karen Jeans: Great.

Dr. Petrice Longenecker: And then it goes on to say, given that VA must comply with FOIA requests, must VA informed consent forms\_

Dr. Karen Jeans: FOIA.

Dr. Petrice Longenecker: FOIA, sorry. FOIA requests.

Dr. Karen Jeans: Yeah, so FOIA is a separate issue entirely. FOIA is, and actually under FOIA we have been able to, and this is Karen again. What we've been able to do as an agency is when, if we have a request for individual [unintelligible 1:20:55] data, even deidentified, because the risk of identification is so high, the agency does not just approve all FOIA requests given to it. So that's a separate discussion, but the bottom line, the answer to the question is no. Just because we have information that's subject to FOIA does not mean that by default VA must always put in the informed consent forms that your deidentified data or deidentified biospecimens could be used for research. But as referenced in the question, the earlier part, it is now a requirement under the 2018 requirements that the subjects be informed that their biospecimens and/or data could be used for future research stripped or they either will not be used. It's one or the other that have to be given as a disclosure to the subjects that they have to be informed about.

Dr. Petrice Longenecker: Okay. Next question. Is there any new information regarding certificates of confidentiality? This is Petrice. I can take this one. So, no. You can fill in if you like Karen. Would you like to take it?

Dr. Karen Jeans: No, I want you to take this one.

Dr. Petrice Longenecker: Okay, great. So the VA and other federal agencies have been in touch with HHS, so the Department of Health and Human Services, who is the only agency that can issue certificates of confidentiality. And we've been in communication. We had a meeting in August to facilitate movement on this front. However, we've met a stalemate and we have not, there's no movement yet. So the current policy remains the same. If you believe your study or one of your investigator's studies needs a certificate in hand, an actual piece of paper, we strongly recommend that you continue to apply to NIH if it's a health related study or FDA if it's a study that is regulated by FDA. So at this moment there are no changes to certificates of confidentiality and process even though I know everyone knows about the 21st Century Cures Act. Karen, do you want to say anything.

Dr. Karen Jeans: And also. Well if it's NIH funded then it automatically is issued a certificate if the facility determines that it's covered by that, right?

Dr. Petrice Longenecker: Yep, absolutely. So if your study is funded by the NIH and it meets one of the four criteria of the studies that would automatically receive a CoC, it automatically receives a CoC. You should not apply for a CoC. You can reach out to your program officer at NIH for additional information if there are any questions.

Okay, next question. Research involving prisoners, I may have missed it but is it still true that if a subject enrolled in a study becomes a prisoner during the course of the study, they can still be a subject if there are no logistical issues?

Dr. Karen Jeans: I'm going to ask Kristina to also add comments to this. In terms of can they still be a subject if there's no logistical issues, first we need to address the human subjects components in terms of logistics. Logistics are not the issue. First of all, is it necessary to continue the inclusion of the subject? Because when the person is a prisoner their autonomy is automatically reduced, altered. And so they're no longer in an environment that is what they were in. And so that research must be, in order for that subject to continue in the study, must be reviewed by an IRB that's constituted with the prisoner representative according to subpart C. And then it also requires approval from the CRADO. Now this is not about logistics. This is the regulatory framework that's required in order to protect the human subject, the ethical rights of this prisoner. And so many times the logistics of continuing it are an issue in terms of whether or not if they're in a clinical trial, that in terms of administering drugs. The issue at play is when you find out that a subject that is in your study is now incarcerated, the IRB must immediately be notified and the study has to be reviewed under a sub-part C requirements and a CRADO approval must be obtained in order to allow that prisoner to be maintained in the study. Otherwise that individual must be removed. And Kristina, I'd like you to comment if you could please.

Dr. Kristina Borror: Sure. Yeah, Karen is absolutely correct. And the requirements for review under subpart C involve, as she mentioned, that the IRB has to have a prisoner representative on the board when they review it and there's other requirements that the research has to meet. And these requirements are not met for all research studies so it's entirely possible that for some research the person who is now a prisoner may not be allowed to continue in the study if it doesn't meet all those requirements.

Dr. Petrice Longenecker: Okay, next question. So do we still need to use the ISO/PO checklist.

Unidentified person: I think we answered that one during the presentation.

Dr. Karen Jeans: So this is Karen again. There is no ORD policy that I'm aware of and it's not in the 1200 series. But if you have a local requirement to use it, then you follow local policy. But, we are not aware of a national policy that requires it to be used. Thank you.

Dr. Petrice Longenecker: Okay, thanks for the clarification. Next question. For studies, usually pharmaceutical studies, there's a website that study staff upload data deidentified to the sponsor. Does the ISO need to ensure that the website is secure per ISPS 140-2?

Dr. Karen Jeans: So this is Karen. I'll take that one. In terms of, if it’s compliant. As a federal agency we are subject to FISMA, the Federal Information Security requirements. When VA agrees to disclose or it shares information and it's VA data, or we're sharing a copy, more importantly, of VA data, our responsibilities in terms of information security apply to the transmission of that. So in regards to what level of security is required for that transmission, that is an information security determination. And so information security should be consulted as to whether or not, when it's deidentified, because there are different security requirements under FISMA for transmission of deidentified versus identifiable data, whether or not what security requirements will apply to that electronic transmission. Excellent question, thank you.

Dr. Petrice Longenecker: Okay, next question. You indicated that review of all research is not always required by ISO and PO per [unintelligible 1:29:10] proposed revisions to 1200.05. However, under paragraph 13 of 1605.01, so I think that's directive 1605.01 it says and I quote, "the information security officer and facility privacy officer must also review the research to ensure it is in compliance with all applicable security and privacy requirements related to the security safeguards and confidentiality of the information to be used and disclosed." Which directive will we follow? 1605.01 or revised 1200.05?

Dr. Karen Jeans: And again, it's not in conflict with what I just stated. If there are no information security and privacy issues related to that protocol, their review would not be applicable. So that's the issue. So if there's no privacy officer issue it doesn't need to be applied. Again, we took it out of 1200.05 to make it a mandate. Does not mean that other requirements will apply applicable to the research. So if there's an information security or privacy officer issue that's applicable to the research then that must be followed.

Dr. Petrice Longenecker: We've got a couple of ISO/PO questions. I'm going to skip them and see if we can come back to them because we've got one now. I am seeing embedded broad consent in pharma studies. If we do not permit local PIs to use broad consent can we just allow this for pharma studies?

Dr. Karen Jeans: So I'm going to start commenting on it and I'd also like Dr. Borror to comment on this. There is a misconception regarding broad consent in terms of there's broad consent and there's regulatory broad consent. Regulatory broad consent under the common rule does not exist and it will not exist until January 21st, 2019 in terms of being able to be effective and complied with. And so what a lot of times we see in these, can I use my research for future use, can we use your biospecimens for future use, can we use your data for future use, it's not a regulatory broad consent. And it usually involves the reuse of deidentified data and not identifiable data. You can refuse even now for reuse of identifiable data and do waivers of identifiable data, identifiable biospecimens with waivers of informed consent. But regulatory broad consent does not exist at the current time. And Dr. Borror I'd really like to ask you to add on to this.

Dr. Kristina Borror: Sure. I agree 100% with Karen. And this was covered a little bit on a presentation that I gave related to informed consent. So as she mentioned, there are under the pre-2018 rules that we're under currently, you can either get consent, specific study-specific consent for use of information. The IRB can determine that it's appropriate to waive informed consent under certain circumstances. If you completely strip it of all identifiers and you can't determine who it came from, then that's no longer human subjects research and informed consent is not required for that. But in order to get true, as she calls it, regulatory broad consent, you can't do that until after January 21st. And it's possible, if you had a regular informed consent document that had all the required elements of broad consent, right? So you're collecting information. You're getting study-specific informed consent and in addition, you're also getting additional information like you would in a regular broad consent study. I suppose it's possible that it could meet all those requirements if it had all those 12 elements and so forth and so on. But I don't know if VA would allow that. I think that this would have to occur after. Now if we're talking about after January 21st and your facility said look, we're not going to use broad consent. We're not going to allow broad consent. But then you get this informed consent from industry where they have it and it includes broad consent. Remember that in order to use broad consent, one of the things that a lot of institutions are saying we're not going to implement this is because it's not just getting the consent. You have to track every single person that you obtain broad consent from whether or not they said yes or no. And you have to be able to track all their data and all their specimens as to whether or not they said yes or no because if they said no, you cannot ever use that information in the future for research because you can't waive informed consent for that. So it's much more complicated than just saying we're going to allow broad consent for this study because you still have to be able to track it. And that can be very complicated.

Dr. Petrice Longenecker: Okay, thank you. Will repositories need to be created for data/specimens for broad consent? So there the question is [unintelligible 1:34:57] need or I guess will they be required?

Dr. Karen Jeans: So this is Karen. For broad consent in terms of VA, broad consent is about storage use of identifiable biospecimens and data. Now, you don't have to have a broad consent in order to do that. You can do it right now with the current consent forms which can be used now and will be used after January 21st, 2019. But the premise of why broad consent was used was about putting this into data repositories and identifiable biorepositories for the reuse of identifiable biospecimens and identifiable data. So that's the primary use of broad consent. But currently you can do the same thing, and it is done right now in regulatory compliance with the consents that are not broad as approved by the IRB.

Dr. Petrice Longenecker: Okay, I'm going to shift to HIPAA. If combining HIPAA into the consent form, does one still need to use the revocation of HIPAA authorization form?

Dr. Karen Jeans: So under HIPAA, this is Karen. A revocation, in order to, if a subject wishes to withdraw they have to submit a written revocation. And so a written revocation is required. Now I do want to comment on this because there is a big misconception going across VA that subjects cannot withdraw consent without written revocation and that is not true. Nor is it ethical or consistent with the common rule. And so if a subject states, for example if I went up to Petrice right now and she's the investigator and I'm the subject and I said Dr. Longenecker, I want out of this study. She would say okay, you're out. That would be it. I don't have to write a written request to say withdraw me. And nor do I have to submit a written revocation for her to stop collecting PHI in medical record if that was obtained. Because once I say no, it's no. So yes, HIPAA requires a written revocation, but please, I'm really glad whoever asked this question, do not also translate that to the common rule component because the common rule does not require [unintelligible 1:37:49-1:37:50] for a subject to submit a written request in order to withdraw their consent from a study.

Dr. Petrice Longenecker: Can you think of any cons to having a combined informed consent document and HIPAA template with one signature block, other than when the LAR is different for informed consent and HIPAA and when subjects are required to be re-consented with no changes to HIPAA?

Unidentified speaker: I think one of the examples that I stated in the presentation, and this is straight from privacy, was situations when there's maybe future use being asked and the subject can opt in or out of that. I wonder if HIPAA treats that differently. I know a lot of times in consent forms you just see a checkbox, but I wonder if one would need a specific signature for HIPAA forms and that's why they brought that up as an example of when you would need more than one signature.

Unidentified speaker: I think we would, to be able to answer this question fully we also need input from VHA privacy. So I'd like to defer that question per consultation with them so that we can give a more comprehensive answer.

Dr. Petrice Longenecker: Okay. Regarding the required consent element about whole genome sequencing, one of the new additional elements, is it correct that even if part of the genome is sequenced the subject must still be informed?

Dr. Kristina Borror: I think not. I think whole genome sequencing means sequencing of the entire whole genome. But, I don't know if others want to comment on that.

Unidentified speaker: I agree with you Kristina. I'm pulling that up right now in terms of what is the basic elements in informed consent and the issue was whether or not the whole genome is going to be sequenced.

Unidentified speaker: The language says, will or might include whole genome sequencing i.e.: sequencing of a human germ line or somatic specimen with the intent to generate the genome or exome sequence of that specimen. I think it would have to be the entire genome being sequenced in order to require that to be in the informed consent.

Dr. Karen Jeans: I absolutely agree. It's just not partial snips, so.

Dr. Petrice Longenecker: Okay. Regarding collaborative research. Isn't ownership of the data usually straightforward? For example, if the university is the coordinating center of a collaborative research and VA is a sub-site, isn't it clear that the university owns the data? It would be similar to a pharmaceutical-sponsored study that VA is participating in, or am I missing something?

Unidentified speaker: No, I wish it was that simple. Ownership is actually quite complex because, for example in the scenario that was described about we're collecting data for a study all right. But when VA or, when we produce the data we create a federal record. We own the federal record. So then the issue becomes what can be done with those different records. VA owns the federal record which produced the data, and then, which is being paid for by whoever is the collaborator. So the issue of ownership is not simple because there's many different variations on it. And it also gets into the issue about when does VA disclose versus when does it share. And when we're sharing a copy of data with others, what control do we have over that? If we exert control, how much ownership rights are we going to give to the group that is [unintelligible 1:42:06] the copy? And that ownership also evolves into intellectual property. So it's not just ownership. It's also about the [unintelligible 1:42:14] that's involved and whether or not [unintelligible 1:42:15-1:42:16]. So it's a multitude of issues. But I'm really glad you're bringing that up because if it was straightforward we wouldn't have the issues that we have. Nor [unintelligible 1:42:26-1:42:27] as we are sometimes involving these collaborative relationships and whether or not VA has the right to exert rights over these [unintelligible 1:42:34].

Dr. Petrice Longenecker: Okay. Is there guidance for judging whether existing, signed consent forms involving future use of data or biospecimens satisfies the 2018 requirements for broad consent? Also, can you confirm that an unsigned addendum describing future use procedures does not qualify as distinct?

Unidentified speaker: Kristina, do you want\_

Dr. Kristina Borror: Well we don't have guidance, right? I mean we don't have guidance out yet. Certainly you can look at the 2018 rule and it has pretty clearly what the elements are of broad consent. And as I said you can't waive or alter them. But we and OHRP don't yet have guidance that explains exactly what that might look like. And what was the second part of the question?

Dr. Petrice Longenecker: Can you confirm that an unsigned addendum describing future use procedures does not qualify as distinct?

Dr. Kristina Borror: Does not qualify as what?

Dr. Petrice Longenecker: Distinct? D-i-s-t-i-n-c-t.

Dr. Kristina Borror: I'm not sure I understand the question.

Dr. Petrice Longenecker: [Unintelligible 1:43:55] separate consent process. So I think, well I think the one thing we should remind folks is that broad consent, the regulatory broad consent does not start until January 21st, 2019. And so, even if you have all the elements in a consent document now, today December 17th or 18th, it would not count as broad consent until it's approved by the IRB on or after January 21st, 2019. And so I think the issue of adding an unsigned addendum is something that the IRB could determine on or after January 21st. So it's not something that we could say it can't be added today as a distinct broad consent process because broad consent does not truly exist yet. Would anyone like to add further?

Unidentified speaker: I think you said it well Petrice.

Dr. Petrice Longenecker: Okay. Well it's 3:45. I'm going to send it over to you Soundia to wrap us up.

Soundia Duche: All right. Thank you everybody. Thank you so much for joining us. And please stay tuned for updated trainings in the new year and possibly even before the end of the year. We thank you all. Everyone have a wonderful, safe holidays coming up. Thank you. Goodnight.

Dr. Petrice Longenecker: Thank you. I'm going to close out. And please stay tuned for the survey that should pop up. Thanks again.

[ END OF AUDIO ]