ORPP&E Webinar

Date: July 18, 2018

Session: Revised Common Rule: Informed Consent

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**Dr. Kristina Borror:** Hello, everyone. This is the presentation, the Revised Common Rule related to informed consent and I have muted everybody in the audience. If you wish to ask a question, you can submit an instant message and I will try to answer questions as they come in but we may need to leave them until the end. I have started a recording of this presentation so if folks can’t call into this presentation, we are recording it and we will provide a link to that in the very near future. And I did provide the handouts for the slide, or at least the slides in an email and if you didn’t get that email, they’re also in an attachment in this Skype call. And as an additional attachment, there’s an unofficial final version of the final rule with all of the changes and the delays and the transition provision that are also available in that link. And you know, just be aware that you are being recorded and so if somebody has no sound, they can’t hear anything. Can folks hear me?

**Ian:** We can hear you.

**Dr. Kristina Borror:** Okay. So somebody can’t hear. If folks cannot hear, then, let’s see, maybe somebody can provide in the IM one of the call in numbers. So that if folks are having difficulty with the audio, they can call in and still hear the call. I’m going to focus on the Revised Rule in this presentation. This is also sometimes referred to as the 2018 requirements and remember that the VA may have additional requirements. And I’d also like to mention that my ORD colleagues; Karen Jeans, Soundia Duche, and Petrice Longenecker are also on the call and are available to help answer questions. And we have a lot of questions. So what’s up? So folks are using Skype and somebody also put in the phone number and the access code. Wonderful. Thank you so much. So this is just an overview of what I’m going to be talking about today. I’m going to give an introduction about the final rule and a little bit about the transition provisions, some of the major changes to the content of informed consent and the process, talk about broad consent, and waiver or alteration of informed consent, screening, recruiting, and determining eligibility as it relates to obtaining informed consent, posting of informed consent forms, documentation of consent, and legally authorized representatives. And I’m going to give some slide numbers for folks who are calling in. And the slide numbers are going to match what is in the handout which may be a little different from what you see on your screen if you’re on Skype, and that’s because I added some answers to the questions. So we’ll go to slide four.

And that is about this introduction to the revised final rule. So as many of you know, there were revisions to the regulations for the protection of human subjects that were published in January of 2017 and so these revised 45 CFR 46 Subpart A, otherwise known as the Common Rule. For VA, the Common Rule is codified at 38 CFR 16. And the preamble noted that the revisions to the rule were intended to modernize, strengthen, and to make our current system of overseeing research involving human subjects more effective. And the rule had not been changed significantly since 1999. So this was, some said, a long time coming. As many of you know, there were several delays in the implementation of this revised final rule and the final general compliance date is January 21st, 2019. And I’ll talk a little bit more about this in the next slide, which is slide five, but note that I’m not going to go into too much detail. Karen Jeans covered this really thoroughly in a presentation a few weeks ago. But I’m just going to go over some of the key dates and the time periods in this transition.

And the first date is the effective date for the 2018 requirements, which is July 19th, 2018. And although July 19th, which is tomorrow, is the effective date of the rule, please note that you still must follow the current rule, that is the pre-2018 requirements until January 21st, 2019, as I’m going to note in a minute. So this next time period between July 19th, 2018 until January 20th, 2019, also known as the delay period, is a time period where institutions can actually take advantage of some of the burden reducing provisions of the 2018 requirements of the revised rule. There were three burden reducing provisions that came out in this last delay and VA may only follow two of those provisions. The three provisions are the revised definition of research which deems that certain activities are not research. The second one is the allowance of no continuing review annually for certain categories of research. The third one is eliminating the requirement that IRB’s review grant applications or other funding proposals that are related to the research. But as I said, the VA is only allowed, during this delayed period, to apply two of those provisions and that is the revised definition of research and the elimination of the requirement of the review of grant applications, or funding applications, by the IRB. And the third time period is January 21st, 2019, and beyond. And so that date, January 21st is, as I said, the general compliance date for these new revised requirements, as I said, otherwise known as the 2018 requirements. And so any new research that is reviewed and approved by the IRB on January 21st and beyond must follow the 2018 requirements, the revised rule. And also note that any studies that transitioned to the revised rule during the delay period must transition completely to the new requirements, the 2018 requirements in their entirety. So if you implemented any of the burden reducing provisions during the delay period, come January 21st, 2019, that study would have to follow all of the requirements of the revised rule, those 2018 requirements as of that date. There’s sort of no turning back. The other date to remember is the compliance date for the cooperative research provision which is January 20th, 2020. And this is the requirement for a single IRB review. Okay. So it looks like we had maybe a question. So somebody said there’s no Skype on, yeah that’s a problem. The second burden reducing provision is the allowance for no annual continuing review for certain categories of research. VA researches may not apply that provision. So that is not allowed by the VA. So the only two that the VA can apply are the revised definition of research and the elimination of the review of the grant application. Okay. Oh and I just gave away the answer didn’t I?

Okay. So the next thing we have is a question related to this and it says a new study is approved by the IRB on January 21st, 2019. Which regulations may they follow, may this study follow? Is it the pre-2018 or the current rule. The pre-2018 rule plus three burden reducing provisions. The 2018 revised rule. Or either the pre-2018 rule or the 2018/revised rule. And I’m going to put up a stop sharing. I don’t know if this is going to work. Let’s see. I have the poll question for this. So you can answer the question. Okay. So I’m going to. Okay. For some reason it’s not letting me, let’s try this. Okay. So now I’m going to close the poll and show the results. And the results are 96% said the revised 2018 rule. Four percent said either the pre-2018 rule or the 2018 rule, that’s the revised rule. And 1% said the pre-2018 rule plus the three burden reducing provisions.

Okay. And the answer is, this is a little clunky. The answer is the studies approved by the IRB on or after January 21st, 2019, must follow the requirements in the 2018 final rule, the Revised Common Rule. So this is because, as I said, the general compliance date for the 2018 requirements is January 21st, 2019. So any new study that is reviewed and approved by the IRB on January 21st, 2019, or after, has to, they have no choice. They have to comply with the 2018 requirements. And so this, and this example was, this was a new study approved after that. Yeah I know. Okay. So everybody on the call is a presenter and they can see the polls. They are not hidden. Okay. So how do I adjust that? Let’s see.

**Ian:** Kristina?

**Dr. Kristina Borror:**  Yeah?

**Ian:** It’s Ian. You can go to participant actions, make everyone an attendee.

**Dr. Kristina Borror:** Okay. Okay. Thank you.

**Ian:** You’re welcome.

**Dr. Kristina Borror:** This is my first time doing one of these with Skype so I apologize for any of the confusion I’m having. All right. So as I said, in this example it was a new study and it was approved on January 21st so it has to follow the revised rule.

Okay. So moving on to specifically look at the provisions within the revised rule that relate to informed consent. And those can be found, it’s section 116 and section 117. And if you look at the preamble of the rule when they are discussing section 116, it talks about requirements for the process of getting consent but also what is in consent forms. But remember that when you’re looking at the actual regulations, the requirements for the process are in 116 and the documentation requirements are in section 117. But that 116 actually does include a lot of information about the substance that is going to be required to be in the documentation. And this section of particularly 116, has references that are much easier to cite.

So there’s a section in 116 that in the pre-2018 rule, in the current Common Rule, it was just an unnumbered list of conditions and it was basically saying, you know, here are the requirements generally for informed consent. But in the new rule, in this final rule, the requirements are separate and they’ve been numbered and some new conditions have been added that we’ll talk about in some subsequent slides. And the reason is, it makes it easier to actually reference or cite these requirements.

So here’s just a general look at the updates to 116 and some of the numberings have changed. So 116(a) is the general conditions, as I mentioned, they’re now numbered. There are some new additions that we’re going to go over in the next few slides. So 116(b) has the basic elements of consent and it has a new additional basic element. 116(c) has the additional elements of consent that are only required when appropriate and there are three new ones added. And section 116(d) is a new section about broad consent.

And I’m not going to talk too much about this in detail. Soundia talked about this yesterday in her presentation about waivers. And note that there are plans for FDA to harmonize language. As a matter of fact, the 21st Century Cures Act which was promulgated in 2016, actually requires the HHS Secretary to basically harmonize these differences between the Common Rule and the FDA Human Subject Protection Regulations. And so it’s expected that FDA is going to issue a notice of proposed rulemaking with proposals for revising 21 CFR 50 and 56 and eventually a final rule that will harmonize. You know, note that they have different requirements for waivers, consent processes, and consent foreign language and a lot of that is going to get harmonized. Also in compliance with 21st Century Cures Act, as Soundia mentioned yesterday, FDA is using its compliance discretion now and is allowing for institutions to allow a waiver of informed consent for research if it actually meets the requirements found in the Common Rule. And note that if the research comes under both the VA regulations, if it’s VA research, but it’s also FDA regulated and involves a drug, biologic, or device that you have to follow both FDA regulations and the VA regulations depending upon when the research starts or whether it transitions that will be either the current pre-2018 rule or the 2018 version when they both apply.

So I’m going to talk about the major changes to the informed consent process in this next section. And basically there’s been a lot of acknowledgement that current informed consent documents have some problems. They’re often very wordy, they’re often too long, there’s a lot of boiler plate language in some of them and there is, frankly, some information that only protects institutions from liability. And there are several changes in the final rule that address this. And these are intended to make sure that informed consent documents actually have some meaning and that subjects, or potential subjects, have information that they need in order to make informed decisions.

And one of these new standards is this idea of providing information that a reasonable person would want to have in order for them to make a decision, an informed decision, about whether or not they want to participate. And this idea of reasonable person is not new. It’s been around for a while in tort and criminal law. And it usually denotes this hypothetical person in society and this person exercises average care skill and judgment in their conduct. And this serves as some kind of comparative standard. And it was used for determining whether or not somebody would be liable in one of these cases. And in most cases if a person had greater than average skills, or special duties, to society they’re held to a higher standard of care, for example, physicians. But a reasonable person is the average person who exercises average care, skill, and judgment. And even though there is, you know, this idea of reasonable person and what they would want to know in order to make a decision, there’s still a responsibility for the investigator to provide additional information if the subject requests it. And also they have to have sufficient time and opportunity to discuss the research with the prospective subjects or answer any questions that would improve the subjects understanding. And for certain types of research, particularly if there’s reason to believe that some subjects might find the research controversial or objectionable, there would need to be a real robust description of the research in order to meet this reasonable person’s standard.

And in addition, the information that’s presented in the informed consent process has to be in sufficient detail and also has to be organized and presented in a way that actually facilitates the subject’s understanding. And this is understanding why they might want to participate or not want to participate and it’s not just a list of isolated facts. And this new requirement reminds investigators to present this information during the informed consent process in enough detail and in a way that helps subjects understand. And it’s not just running down a list of risks and procedures. The goal is to foster understanding and to enhance the informed choice that the subject is making. And it also recognizes that there may need to be some flexibility and there may be a need to tailor consent documents to particular research studies. So there’s no imposition of a page limit and there’s no prohibition of certain information from being included in the main body of the consent form.

So the general improvements of informed consent include that there’s a new requirement that key information has to be provided first. And so this portion of the document has to be concise and focused and it has to be this key information that a subject might want to know in order to determine why they might want to participate or not want to participate and it has to be an organized and presented in a way that facilitates comprehension. And it’s generally expected that this presentation of this key information is going to be relatively short. And it needs to be included first and this is a way of emphasizing information that would be most important to someone who was deciding whether or not they want to participate in research. And in contrast to the proposal in the notice of proposed rulemaking, this is not limited to information that’s required by section 116 of the regulations. And it also doesn’t apply to broad consent which we’ll be discussing later. And that’s slide 16. I’m sorry I haven’t been mentioning slide numbers. But that’s slide 16 of the handouts.

So the next slide, slide 17, is a little bit more about what key information is. And the preamble actually has a brief description of five factors that might be in the beginning of an informed consent process or in the form that would encompass this key information including a concise explanation that consent is being sought for research, that the subjects participation is voluntary, what’s the purpose, how long is the subject expected to be in the research, what are some of the reasonably foreseeable risks and discomforts, what are the benefits that they or others might reasonably expect, what are some alternative procedures or courses of treatment that might be advantageous to the subjects. And the description of risks in this should identify the most important risks, not just an exhaustive list of the risks. This might be similar to the information that a doctor might provide in the clinical context.

So as I mentioned earlier, the basic elements of informed consent have had one new element added, and on slide 18 it shows what that is and that is a notice about possible future use of either information or biospecimens after they have had all identifiers removed. And that you have to notify subjects, or prospective subjects, that their information or biospecimens could be used in future research and that no additional consent will be obtained for that future research use. And also notifying them that, or if they’re not going to be used, notifying them that they won’t be used. So currently, under the current rules, there can be secondary use of non-identified research information or biospecimens without informing subjects that this secondary research can take place. And this is just a notice. And make sure the subjects understand that this can take place. If someone doesn’t want this future use, they can’t say well I’m just going to cross this part of the informed consent document out, no. If they object to that future use then they can just choose not to participate in the research study for which their consent is being sought if it does have a notice that it can be used for future research. And again, this is once the information or biospecimens have been stripped of identifiers so it’s no longer human subjects research.

Okay. So I am going to do this with the next question and go to the poll and that is. Okay. So this question is, is the new element of informed consent about possible future research use of information or biospecimens stripped of identifiers required in all informed consent documents. Is this true or is this false? Give it a few moments for folks to answer. Okay. It looks like the responses are slowing down. So I will close the poll and I will show the results.

And the answer to the question about whether this new element of informed consent with the possible future research use of information or biospecimens stripped of identifiers is required in all informed consent documents, 80% said it was true and 20% said it was false. And so we will go back to the presentation.

And the answer is true, so the 80% were correct. And as I mentioned, this is a basic element of informed consent so it has to be present in all informed consent documents unless the element is altered or waived by the IRB.

So as you know, there are additional elements of informed consent. These are generally not required in all informed consent documents. The IRB requires them when they’re appropriate. And there were no changes to the six previous additional informational elements of consent but these three new requirements were added. And the first two were actually proposed in the notice of proposed rulemaking. And those are that notice of whether there’s any clinically relevant research results will be provided to the subjects, and that could include individual research results and would explain under what conditions those would be provided. And the second one that was also proposed in the NPRM is notice about whether there might be some commercial profit from research involving biospecimens and whether or not subjects will share in that profit. And the third one was not in the NPRM but it’s notice about whether the research might include whole genome sequencing. And this is, again, just for research involving biospecimens. And this third one is recognized that this whole genome sequencing can actually provide important insights about health not just of the individual’s but also their biological families and it could have important implications many years later that might not have been anticipated. And so the reason why this was added as an additional element of informed consent that IRBs can require when they think it’s appropriate is because this information might be needed in order to, for an individual to decide whether or not they want to participate in research and that it would be relevant to them if the research involves biospecimens.

So we’re going to switch gears a little bit to the section of the regulations related to broad consent. And provide a little bit about the background and the history of this concept of broad consent. You may remember that the notice of proposed rulemaking for revisions to the final rule actually proposed a fairly big change to the definition of human subject. And it would have included as human subject research, any research in which an investigator used, obtained, studied, or analyzed biospecimens and that was regardless of whether or not they were identifiable. And so under that proposal, if it had gone through, then any research involving biospecimens, even if it was stripped of identifiers, would have been considered human subjects research. And because they realize that would be a big change, the NPRM also proposed to allow broad consent which would cover the storage or maintenance for any secondary use of these biospecimens regardless of whether or not they had identifiers or not and also of identifiable private information for basically the secondary research. And that’s research that we’ll go over in a little bit more detail in subsequent slide.

I have a couple of questions here. Where does potential access by third party commercial entities work into this requirement? Oh we have a couple of other questions. Are you talking about the requirement about if there’s commercial profit? That would be, you know, related to any rules that the government, the VA in particular, has related to access to that information.

And under the Revised Common Rule, will it still be possible to offer participants the option to allow future uses of their information or biospecimens stripped of identifiers or do they just have to be told that such uses could happen or that such uses will not happen? So yeah, they could still have an option. That would, I suppose, be the best of all possible worlds to say, you know, even though we don’t have to give you this option. You can always go beyond the regulations and say, you know, we’re going to give you the option of whether or not to do that, whether or not you allow that.

So let’s go back to the genesis of broad consent. And in the revised final rule that proposal in the NPRM to include biospecimens in the definition of human subject even if they’re not identifiable, was one of the most commented on in the NPRM. Almost 30% of folks who commented, commented on this. And 80% who commented were opposed to it. And you know, one of the concerns that folks had was the concept of broad consent. And so in the final rule, there were changes to the definition of human subjects but mostly just for clarification. I want to be clear that the definition of human subject does not include all biospecimens regardless of identifiability. So if you have a biospecimen that has been stripped of all identifiers and there’s no codes or keys to the code, that would not be considered human subjects research. So we’ve talked a little bit about secondary research, what exactly is that?

So that’s research use of either information or biospecimens that were collected for research studies other than the proposed research or for non-research purposes. So that would include information or biospecimens that were collected for clinical care, public health, or education but then are going to be used for that future research, otherwise known as secondary research.

I think we have another question. Let’s see, oh so Karen Jeans is jumping in, she says for MVP, MVP was approved as part of the pre-2018 requirements. It has a consent that is under the current Common Rule and would probably require a re-consent of almost 700,000 subjects if it was transitioned to the 2018 requirements. So for MVP, the current IRB consent form specifies how data will be shared. So let me see if I can make Karen a presenter so that she can, I don’t know how to do that and I don’t see her name on the list here. Okay. So I will, I will invite Karen and others from ORD to type in things, sorry about that. Okay. So this concept, so Ian says to right click her name and choose to make her a presenter. Let’s see if I could find her name I could do that. Oh well. I can’t find it. Okay. So we will go on. I’m sorry for this.

All right. So this concept of broad consent actually allows a new flexibility for secondary research. So under the current rule, investigators can use, you know, biospecimens that have been stripped of identifiers. They are not identifiable and so it’s not human subjects research and so they don’t have to get consent. And they can do research with coded biospecimens and data. And this isn’t human subjects research if they can’t be linked to specific individuals by the investigators either directly or indirectly through coding systems. So if it’s coded and they don’t have the key to the code, then that’s not human subjects research also and there’s no need for consent. Also researchers can do research with identifiable biospecimens and data either with waiving informed consent or getting a study specific consent. So under the new rule, investigators still have these options for secondary research. And in addition, there’s a new alternative with this new broad consent.

Okay. Let’s see what are the discussions that are going on now. Okay. Regarding your slide on the required elements of informed consent, there is a California state law, California Health and Safety Code, that has funding sources required element. Even though it’s not required by the Common Rule, it is required by California. VA facilities follow state law on this or is it just recommended? So there is a provision about the current rule and the revised rule that basically says that the Common Rule doesn’t overturn any requirements, both state and local, that go above and beyond and are in addition to the protections that are here. So you would still have to follow those California state laws.

So this new broad consent for secondary research it is optional. That’s very important to note. It’s not required to implement broad consent. It’s an alternative to actually getting traditional informed consent or waiving informed consent for storing, maintaining, or using secondary research use of identifiable private information or identifiable bio-specimens that were collected either for a different research study or for non-research purposes. So this is flexibility in the future. And this concept of broad consent actually plays a very different role than was proposed in the NPRM. Because remember in the NPRM, consent would almost always have been required for the use of biospecimens, even those that didn’t have identifiers because that was going to be human subjects research. And in response to public comment, this new flexibility is an alternative to either obtaining study specific consent or getting a waiver of consent. And it can be used to meet two new exemptions, exemptions seven and eight, which I’ll talk about in subsequent slides. And broad consent includes elements of consent from both the basic and the additional elements of consent and some that are unique to broad consent. And the goal here is to be meaningful informed consent even though specific research studies do not need to be described. The broad consent actually has to provide a general description of the types of research that may be conducted by giving sufficient information to allow a reasonable person to expect the broad consent would permit what types of research to be conducted. And when information about specific research is not provided, the broad consent has to tell subjects that, you know, you might have chosen not to consent to some of those research studies. But at the same time, the broad consent requirements in the revised rule are actually more simple and less restrictive than were proposed in the NPRM.

So I think we have some more questions. Where to get copies of the slides? I sent them out but they’re also in the attachments. In the, excuse me, so if you go to the paperclip at the bottom, oh that’s a file to send, where is it? Where are attachments? Where do folks see the attachments? Is it in the paperclip? And if you can’t find them on the Skype, you can email me.

So then we have another question about MVP. So the current MVP consent does not need to be re-consented. Is this state specific to prevent all from redoing?

So to get the slides, Ian says go to the manage content icon, it looks like a computer screen with a red dot and you should find the slides there.

And so do we have an answer to the “current MVP consent not needing to be re-consented question? I think what Karen was saying is that with the advent of the new Common Rule, there’s certain new requirements to consent. And I think Karen was saying that those requirements don’t have to be met for re-consenting of people who were enrolled before January 21st, 2019. Although she can clarify if I’m wrong about that.

So more about broad consent, the requirements for actually what’s in the broad consent includes that you have to describe the types of research that may be done. And again, this is just sufficient information that a reasonable person might understand what the consent would allow. What are the materials that might be used? And these are the identifiable materials that we’re talking about here; whether those materials might be shared and, if so, with what types of institutions or researchers, and what period of time those materials are going to be stored, maintained, or used for research.

So there are some caveats for broad consent. If broad consent is used, the IRB can’t omit or alter any of the requirements that are described in section 116(d) related to broad consent. They have to be there. And if an individual is asked to provide broad consent for future use of their biospecimens or data and they refuse to give broad consent and a researcher downstream wanted to use that individual’s data or biospecimens data for human subjects research, the IRB could not waive consent for that secondary use. So if you ask somebody to give broad consent and they refuse, then that’s it. You can’t, the IRB can’t waive consent for that individual. And remember that this is only permissible for secondary research and no other types of research. So one of the things that this really, one of the major caveats to broad consent is that in order to implement its use, you really have to be able to track who has provided broad consent for future use and who hasn’t. So if you’re doing a research study and you’re thinking that, well you know, we’re collecting information and we’re collecting data from these folks and we might want to use the samples in the future and we don’t want to go back and get consent for that use, and so we’re going to have a separate document to get broad consent for that study. And if you do that, and the person says, no I’m not going to give broad consent for the future use of my samples, you have to know that this person’s information and biospecimens cannot be used for that secondary research and so you have to have a way to track that. And so that’s going to be probably one of the biggest caveats for using broad consent. And I think that it’s going to require a lot of logistical, you know, and technical things to try to follow and to track that. And this is slide 28. I’m sorry. I haven’t been good about telling you the slide number.

So we have another question. So I am going to bring up the next quiz. Okay. So the question is, you can use broad consent for research that involves drawing subjects blood, true or false? And you can, you know, click on the little button right next to the true or the little button next to the false to vote. Ah-hah. So I found Karen and I made her a presenter. So Karen, you may speak if you wish to. Okay. It looks like we’re slowing down so I’m going to close the poll and show the results. So 59% said true and 41% said false. Okay. And let's go back to the presentation.

And the answer is false. So remember that broad consent is permissible only for secondary research and no other types of research. So if there is research that actually involves drawing a subject’s blood that is primary research. The data and biospecimens that you’re going to be collecting from that research, that’s not secondary use of those. So that is false. The answer to that is false.

And I think there was a question, oh it’s Karen, Karen has responded it looks like. Yes. For the Million Veterans Program, my prior response related to transitioning with use of a broad consent. If MVP wanted to transition, the current consent form does not meet the 2018 requirements for its primary consent and there is no broad consent because it doesn’t currently exist. So if it is transitioned, the IRB that oversees it would have to decide whether or not all previously consented subjects would have to be re-consented. So it is possible that all 700,000 subjects would have to be transitioned depending upon what the IRB decided. For example, the current Common Rule does not have a broad consent. So if a study like MVP wanted to utilize a broad consent, it is possible that re-consent of the previously consented subjects could occur, depending upon the IRB of record. Thank you, Karen. As I said, I made you a presenter so in the future if you want to chime in, you can feel free to do so. And we will go back to the presentation.

Another question, however, if Karen speaks you will need to repeat what she says since those on the phone will not be able to hear her. Oh. Okay. Really? I don’t know why that would be but okay. Ian says they will be able to.

Okay. So next, as I said, the broad consent can be used in conjunction with two new exemptions, exemption seven and exemption eight. So first we’ll go over exemption seven. And this is for storage and maintenance for secondary research use for which broad consent is required. And this is basically identifiable private information or identifiable biospecimens that are being stored or maintained for potential secondary research use. And in order to use this exemption, broad consent has to have been obtained as outlined in section 116(d), as I mentioned earlier, and there has to be this new concept of limited IRB review. So some of the new exemptions are not completely exempt from IRB review. Some of the new exemptions, including exemption seven and exemption eight, require limited IRB review. And I’m going to talk about the exemptions in September. So if you’re a little confused about the exemptions, don’t worry, you’ll have another chance to learn about those. And this limited IRB review is looking at the broad consent process on the form to make sure that it is, you know, appropriate under 116(d) and also is looking at the privacy and confidentiality considerations that are found in section 111(a)(8). But that’s only required, looking at the privacy and confidentiality considerations are only required if there’s going to be changes to the storage and maintenance of those biospecimens or identifiable data. And so let’s say you have an investigator and they want to store information in a databank or they want to store biospecimens from a pathology laboratory into a research repository. They could use this exemption assuming all of the relevant conditions are met. And it can also be used in conjunction with exemption eight that I’m going to talk about in the next slide to use that stored information in secondary research.

Okay. So we have some more questions. But MVP is not secondary to research so broad consent would not be possible, they are drawing blood. And somebody else said, maybe you would have two consents; one for primary research and another for secondary use of data. And Karen says actually the Million Veteran Program does qualify for broad consent if it was transitioned because there is secondary use of data. Thank you, Karen.

Okay. So that’s exemption seven. And as I said, there’s another exemption, exemption eight, that you can use broad consent for. And this is secondary research use for which broad consent is required. So this is actually, exemption seven was for storage and maintenance of identifiable private information or biospecimens and exemption eight is the actual secondary research use of identifiable private information or identifiable biospecimens. And so, in this case, you would have to get broad consent. You would have had to have gotten broad consent for the storage and maintenance and secondary use of these biospecimens and information. And there would have to be a limited IRB review of that broad consent and to see if the secondary research use falls under that broad consent. There would have to be a documentation of waiver, a documentation of broad consent or documentation of waiver of the consent provisions and that’s just waiver of documentation right, not waiver of consent. You still have to get consent, right? Remember. So this is another situation where the exemptions do require some limited IRB review. So they’re looking at the broad consent. They’re looking at the documentation of that broad consent or waiver of documentation and it’s also looking at the privacy and confidentiality safeguards. And there’s also a provision here that the investigator, in order to use this exemption, the investigator doesn’t include returning individual research results to subjects as part of the study plan. But this provision doesn’t prevent an investigator from abiding by any legal requirements to return individual research results. So let’s say you have an investigator who wants to use information that is in some databank or use biospecimens that are in a pathology lab. So for instance, the databank or pathology lab that we talked about related to the previous slide. They could use this exemption, again, assuming that all the relevant conditions of the exemption are met. And it can be used in conjunction with exemption seven, as I mentioned, for use of this information or biospecimens that were stored or maintained for secondary research in a research repository, for example, as I mentioned.

So we’re on slide 32 and now slide 33 talks about waiver or alteration of public benefit or service program. So I’m not going to talk in great detail about the waivers because Soundia talked about this in fair amount of detail in her presentation yesterday. But I just want to mention first the waiver or alteration for public benefit or service programs. This new waiver or alteration looks a lot different, the way it’s organized is different. These changes were implemented to be more clear about the effect of each requirement but this is not a substantive change to this waiver of consent for public benefit or service programs as Soundia mentioned yesterday.

And then there’s the general waiver or alteration of consent which is going to be, you know, the vast majority of waivers of consents are going to be under this general waiver. And the general criteria for waiving consent are actually, are tightened in a few ways. And these changes reflect major revision in the content and format and the organization of general waivers or alterations of informed consent that were in the previous rule under 116(d). Now the four existing waiver conditions that are in the current Common Rule are basically unchanged. And they’re found in 116(f)(3) and you may remember that those existing waiver conditions are that the research involves no more than minimal risk to subjects. The research cannot practicably be carried out without the requested waiver of alteration. The waiver or alteration will not adversely affect the rights and welfare of the subjects. And whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation. So as I said, those four existing conditions are still in the new rule. But an additional criteria has been added. And this is for research that involves accessing or using private identifiable information or identifiable biospecimens. And this is that this new waiver criterion is that the research could not practicably be carried out without accessing or using such information or biospecimens in an identifiable format and that, whenever possible, non-identified information whereby a specimen should be used in order to protect confidentiality and information or biospecimens. And this new criterion is very similar to one of the criterion for waiver of HIPAA authorization. And this is for access or use of private information or identifiable biospecimens.

Okay. So I am going to switch to do another poll. Okay. So it says this fifth criterion for waiver of informed consent and that is that the research could not practicably be carried out without accessing or using identifiers, is required for all research including research that does not collect identifiable data, true or false? Okay. So it looks like we’re slowing down a little bit. So I’m going to close the polls and show the results. So we had 38% of folks say that that’s true and 62% said that that’s false. Okay. So let's go back to the presentation. So this is, what the heck.

So the new fifth criterion for the waiver of informed consent, that the research could not be practicably carried out without accessing or using identifiers, is required for all research including research that does not collect identifiable data is actually false. This additional criterion is only required for research that involves accessing or using private information or identifiable biospecimens.

Okay. So let’s go on and talk a little bit about broad consent and general waiver or alteration. As I mentioned earlier, the IRB cannot waive informed consent under broad consent. And it can’t omit or alter any of the required broad consent elements. And also if someone is asked to give broad consent, either to research with biospecimens or, wait a minute, did I, am I on the wrong slide here? The IRB, I am on the wrong slide. And if they were asked to give broad consent and they refused, then the IRB can no longer waive the consent requirement for the use of their identifiable information or biospecimens. And that’s slide 36 on the handout.

So a little bit more about this general waiver or alteration of consent. Note that unlike a complete waiver of consent, if you alter informed consent, so if you’re like altering it and leaving out one of the basic elements for instance, or altering one of the basic elements, the IRB can’t actually omit or alter any of the general requirements including those new format requirements. So they can’t waive or alter the requirements of the key information, that has to be in the front of the informed consent process, for instance. And the general waiver, though, applies to the general requirements of informed consent, the basic elements of informed consent, and the additional elements of informed consent. So this is if you’re just waiving consent completely. So that’s one of the changes that in the current rule waiver and alteration are lumped into one section. In the revised rule, waiver is in one section and alteration is one section. So it makes it a little more clear.

So I’m going to talk a little bit about screening, recruiting, or determining eligibility. Again I’m not going to talk about this in great detail because Soundia talked about this yesterday. But slide 39 shows that this is a new addition and although it’s under the section of, you know, right under the waiver section. This addresses waivers of informed consent to obtain information or biospecimens when you’re actually screening subjects, or potential subjects, to see whether or not they’re eligible for research. You’re recruiting, contacting them, or trying to determine whether or not they’re eligible. And there are certain requirements for this. That the investigator will obtain information through oral or written communication with the prospective subject or identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens. So you wouldn’t be able to use this exception to informed consent if you were doing a blood draw for instance. And it was determined that previously requiring IRBs to waive informed consent to, you know, say look at medical records to find information about who to contact about, you know, whether or not they might be interested in a research study or determining whether or not they were eligible, that this was burdensome and it wasn’t really protecting subjects and this also wasn’t consistent with the FDA regulations.

And slide 40 talks about these conditions that must be met, as I mentioned. You can only get information by either communicating directly with the subject or accessing records or biospecimens that are stored. And this is not a waiver of the consent requirement, it’s a rather an exception to the requirement. So IRB’s still have to ensure that the 111 criteria are met. And including that, when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. And you would still need a HIPAA waiver if the research involves the use or disclosure of protected health information. So let me share the next poll.

Okay. And the question is. The IRB does not need to waive informed consent for research activities involving recruiting and screening without obtaining informed consent, true or false? Okay so things are slowing down a little bit so I’m going to show the results. And 56%, although now it went down to 55%, said that this is true. And 45% said it was false. I’m surprised it’s so close. Well let's go back to the presentation and see what the answer is.

The answer is true. This is not a waiver of the consent requirement but it’s rather an exception to the requirement. And the whole reason that this was put in was to reduce the burden of requiring IRBs to actually go through the waiver process and say oh does it meet the requirements of waiving informed consent in order to do this very low risk activity. And often it completely makes no sense to go and get consent from subjects in order to look at their medical records in order to see if they’re eligible for this study. For a lot of reasons it didn’t make a whole lot of sense and so this was added to the revised rule. And the IRB does not have to go through a waiver of informed consent in order to allow researchers to obtain this information without getting informed consent.

So we’re going to switch gears a little bit and talk about posting of consent forms. And slide 43 talks about these new requirements and the consent form from a clinical trial has to be public, made public. And this is on a probably available federal website and it’s going to be basically a repository for clinical trial consent forms. And in the preamble it says that clinicaltrials.gov might be appropriate choice. A lot of the trials are going to have a record in the database and so there would be less burden to posting the informed consent document. And the goals here are to increase transparency and trust and ultimately, hopefully, to improve the quality of informed consent. It’s not actually intended to help perspective subjects during the conduct of the trial but to lead to better consent forms. Because the people that are writing them are going to know that they’re going to become public and people are going to be picking them apart. And again, this only applies to clinical trials and only those that are conducted or supported by a federal department or agency. And the consent forms that are posted have to meet the requirements of section 116. Also that includes having this concise presentation of key information at the beginning. And it looks like HHS is going to use clinicaltrials.gov and also a docket folder on regulations.gov for the publically available federal websites that are going to satisfy this posting requirement that’s found at 116(h).

And it looks like we have a question. What is the definition of clinical trial regarding this posting requirement? Don’t get me started on that. The definition of clinical trial has some people tied up in knots. And I will read it to you. And it is, if I can find it, clinical trial means a research study in which one or more human subjects are prospectively assigned to one or more interventions which may include placebo or other control to evaluate the effects of interventions on biomedical or behavioral health related outcomes. And this definition is very similar to, or it’s basically the NIH definition. And as I said, it’s causing some angst among some folks. And this is in part because many folks who are doing these kinds of studies on behavioral outcomes had not considered those studies to be clinical trials. And so this is going to increase some of the studies that are going to come under this requirement for posting informed consent documents. Well of course, nobody’s required to post informed consent documents now. But some studies that had previously considered themselves to be clinical trials are going to have to post their informed consent documents.

And the, so who has to do this? It’s actually the awardee that is responsible for doing it. Or it could be the federal department, or agency, that’s conducting the study. In that case it would be the VA. And it has to occur no later than 60 days after the last study visit by any subject and that’s the study visit as required by the protocol. And if the federal department or agency that’s supporting or conducting the clinical trial determines that certain information shouldn’t be made publicly available, they can permit or even require redactions of the informed consent document before it’s posted. And in some rare cases, the federal department or agency may determine that the existence of a particular clinical trial shouldn’t even be made public and, in which case, there would be no posting of that consent form for that trial.

And only one IRB approved version of the consent form for each trial has to be posted. And it doesn’t even necessarily have to be the final one. You know if there are several sub-studies or, you know, different consent forms for different arms, only one of them would have to be posted on this federal website. And remember there’s a new single IRB review requirements and if there’s a multi-institution study, which most clinical trials are probably going to be done at multiple institutions, there only has to be one posting for that study. And again, it’s not expected that if there were, you know, say a different consent form for adults and a consent form for children that both of those would have to be posted.

So switching gears to documentation of consent. Slide 47 on the handout talks about signatures and the short form. And the main changes here are that now you, the rule explicitly allows electronic signatures. It says that you must give the subject a written copy and that that written copy can be electronic, in electronic format. And also the new rule also requires that when you’re using the short form, that that short form also has to begin with this concise and focused presentation of key information. So remember this has to be at the beginning of informed consent documents. So this applies not just to the regular long form informed consent documents, it also applies to the short form. And it also requires that this part of the consent form be organized in a way that facilitates the prospective subjects understanding of the research. Okay. It looks like we have a question.

It says a written copy of the signed consent form or unsigned consent form? The rule does not specify whether or not it has to be signed or unsigned so it could be unsigned according to the Common Rule but, again, VA might have additional requirements.

And there is a new waiver of documentation of informed consent which is on slide 48 in the handout. And this allows a waiver of the subjects signature on the form if the subjects are part of a cultural group or community and, in that group, signing forms just isn’t normal. And this also allows this waiver of documentation of broad consent, although, I expect this to be rare.

So this is in addition to the two existing mechanisms for waiving documentation of informed consent. Those are unchanged in the new rule and Soundia went over those yesterday. The first one is that the only record linking the subject and the research would be the informed consent form. And the main risk of the research would be the potential harm that could result if there was a breach of confidentiality. And the other one is that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. So this is a third waiver of documentation alternative to those two.

And it looks like we’ve got another question. It says can you give examples of groups that don’t sign? So as Soundia mentioned in her presentation, this could be in international research, probably the most common one, so this may not be as common in VA research. There may be cultures in which, you know, they don’t have a culture of, you know, documentation of things. And so they don’t, you know, they don’t have that in their culture and so it would be odd to ask them to sign something.

Okay. So the last little part of my presentation is about legally authorized representatives. And slide 50 on your handouts gives some information about the definition of legally authorized representatives. So as you may know, that in some states there aren’t any laws; either statutes, regulations, or court decisions about who can serve as a legally authorized representative for clinical decisions. And yet clinical decisions are made every day using institutional policies. And so for the purpose of the Common Rule, there could be different outcomes occurring in states that have laws versus states that don’t have laws. So the definition of legally authorized representative in the final rule has been changed. And this is mainly to address jurisdictions in which there is no applicable law that authorizes an LAR to provide consent on behalf of prospective research subjects. And in those jurisdictions, if an individual is recognized by institutional policy as being acceptable for providing consent in the non-research setting, subject to the subjects participation and the procedures in the research, they would now be considered a legally authorized representative for the purposes of research. And the definition is, I’ll read it to you, it’s legally authorized representative means an individual or judicial other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedures involved in the research. This is the same, if not identical to the current Common Rule, but then a new thing was added. And that is, if there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject’s participation in the procedures involved in the research. So that allows institutions to use their institutional policy that is applicable to the clinical context for the research context.

And here are some references and the links to the Revised Common Rule. You can also find some Common Rule educational materials that OHRP has posted at that link. And also the CITI program has some resources on the revised final rule.

And here is a list of the tentative scheduled of Cyberseminars. The ones in white have already occurred and you can see there are some coming up in September, October, November, and December. So I will, let’s put this back here and let’s go back and look at some of the questions.

I will go backwards, let’s see. When will VA provide guidance on how VA will deal with the Revised Rule? If new studies that are submitted after January 21st, 2019, need to follow the new rules, won’t everything need to be in place by that date? Do we need our SOPs ready to go by that date or will there be a grace period? So I have made Karen and Soundia presenters so they can speak if they’d like, or they can type in. But I think the answer is basically stay tuned.

And somebody asked wouldn’t a signed informed consent document violate confidentiality? So that depends. That’s why there is the provision in the waiver that allows waiver of documentation of informed consent for research in which the only record that would be linking the subject and the research would be the consent form. And so that is a situation in which you could waive documentation of informed consent.

Okay. And another question. Can you please talk about the changes for continuing review for minimal risk studies? That is something that I do not have time for. This is only about informed consent document. I actually gave an overview of the changes to the Common Rule and talked a little bit about continuing review in that, the changes to continuing review in that, and those were recorded and so you can email me offline and I can send you the links to those. Karen, I cannot hear you. I’m sorry. Do I have to do something to unmute you or something?

Let’s see I can un-mute audience but I can’t un-mute presenters. Let’s see. I don’t know why. No we cannot hear you so I’m afraid you’re going to have to type in because I cannot figure out how to un-mute you. Put mic on on telephone. Karen, have you tried clicking your microphone to un-mute yourself? Yeah. I don’t know. I don’t know how to do that.

Okay. So let’s look at some of the other questions, where will this recording be available? I will send the link to that once we have posted it. It will probably be on the PULSE website. That seems to be the easiest way for us to make those available.

It says can you respond to the question asked earlier, what if you are accessing identifiable information but not collecting identifiable data? I’m not sure what that’s in relation. Which slide was that relating to?

Can someone send the link to yesterday’s waiver presentation as well? I don’t know if there’s a link for that. I think you have to have received it by email or you can request it from Soundia.

The presentation for waivers will be posted on the PRIDE Cyberseminar web page in about a week.

Okay. So it’s being suggested that I un-mute the audience and then Karen or others can speak. There was this question about, oh and here’s another question about, where was it? Okay. Regarding your slide. I got that one.

**Dr. Karen Jeans:**  So hi Kristina, this is Karen.

**Dr. Kristina Borror:** Hi, Karen.

**Dr. Karen Jeans:**  Hi. So I wanted, while you’re looking at that to answer the question about guidance,

**Dr. Kristina Borror:** Thank you.

**Dr. Karen Jeans:** So the question that was asked, a very good one, when will VA provide guidance on how VA will deal with the Revised Common Rule? New studies that are submitted after January 21st, 2019, okay, I lost the question, basically, I had it here a second ago.

**Dr. Kristina Borror:** They’re basically saying that, you know, they’re going to have to be ready to go before January, right?

**Dr. Karen Jeans:** That’s true. Exactly and that’s why we’re in the middle of the revision of VHA Handbook 1200.05 which will be VHA directive 1200.05 in order to meet that need. And so we are working currently on revising, making multiple changes to our guidance. Again we do not know what the final policy will be as it’s going through concurrence so we’re trying to, you know, say exactly how some of the specifics will be. But yes, will VA provide guidance? We have to. And as part of the Revised Common Rule we work together with the other Common Rule agencies on that guidance. So for example, the guidance that we’re currently getting ready to issue on the three burden reducing provisions for the final rule, it will be going through HHS so that they are on track with what VA is issuing because there’s some guidance that is specific to VA. So all along this time period we will be issuing guidance. There’s some VA specific guidance that we have to wait until we have a firmer idea of what will be the final policy in terms of VHA Directive 1200.05. But otherwise, you’ll be seeing guidance come out all along this period. And so that’s the answer to the question to that.

**Dr. Kristina Borror:** Great. Thank you so much, Karen. So we have, this question is off topic but I figure with many experienced people on the call I would try to get an answer. Yesterday the IRB made a determination of continuing non-compliance with local IRB policy on a drug study that is not under an IND. Would the FDA require to be notified? 21 CFR 56 says nothing about IND but some FDA link guidance says when reporting suspensions or terminations of IRB approval, please include the IND or IDE number. I was thrown off because I found nothing that says to include IND number for unanticipated problems and serious or continuing non-compliance. I don’t know the answer to that question. It is off topic.

**Dr. Karen Jeans:** This is Karen. I can answer that one. In fact, because I’m former FDA, but don’t speak for the FDA currently so this does not come from FDA. The answer is yes. If the study is under FDA regulations and, again 21 CFR 50, 56, it doesn’t just apply to IND studies or IDE studies. If it’s not a 312 or 812 regulation, you still have to report in terms of the guidance you’re referencing. It is saying that for those studies that involve IND or IDE’s you have to include those so that it will get to the proper branch within FDA, for the IND land and IDE land. But yes, if this study, and there’s many studies we do, approved drug versus approved drug, many of our oncology studies. Again if you’re doing non-compliance, suspensions, or determinations by IRB approval, unanticipated problems involved in FDA regulated study regardless if it’s an IND or IDE, these do have to be reported to the FDA. So the answer is yes. Good question.

**Dr. Kristina Borror:** Thank you.

**Dr. Karen Jeans:** You’re welcome.

**Dr. Kristina Borror:** Okay. So this other question I think I understand it now. So the question is what if you were accessing identifiable information but not collecting identifiable data? And I think this is related to the determining, the screening, recruiting, or determining eligibility exception from informed consent. And this might be related to whether or not the activities are preparatory to research. And if they are preparatory to research under VA directive, then it’s not research and then it doesn’t need to come to an IRB or have informed consent. But if it is research and you are accessing identifiable information in order to do screening, recruiting or determine eligibility, then you can use that exception from informed consent. I hope I understood the question.

And let’s see did I miss any other, any other questions? I don’t see any.

Okay. If modifications to current studies are added after January 2019 and the mod includes new consent forms, will those need to adhere to the Revised Common Rule? So if the study was reviewed and approved initially by the IRB before January of 2019 and the institution did not transition to the burden reducing provisions, then the study could continue to be under the current Common Rule, that is the pre-2018 requirements, and they wouldn’t have to make the changes to the consent forms. However as I said, if they, during that delay period between July 19th and January 20th, 2019, if they decide they want to utilize those two burden reducing provisions that VA is allowing, then come January 21st, 2019, they would have to transition. Even if there wasn’t a modification. They would have to transition that entire study to the new rule. I hope that’s clear. So I think that has a lot of people saying I’m not going to use those burden producing provisions because it’s going to require everything to sort of on a dime revert to all of the new rules.

Question on slide 35 about the new fifth criterion for waiver of consent, assume one would still need a HIPAA waiver for viewing identifiable information if one does not plan on collecting identifiable information. Is that correct? That’s my understanding and if somebody understands differently, they can chime in. I believe that’s correct.

And do you have links for past recordings and slides? ORD, I believe, has links for those recordings and slides. For the ORO ones, if you want to send me a request I can send those.

Okay. Let’s see if there’s any other questions. And Soundia says the presentation for waivers will be posted on the PRIDE Cyberseminar in about a week. I already got that one. And they also provided a link to the PRIDE Cyberseminar webpage on the conversation bar. And it says recordings on all ORD led Cyberseminars can be found there and that they’re usually posted about a week after the training. Yes, I think I got that one.

So the question about accessing identifiable information but not collecting identifiable data was about the fifth criterion for waiver of informed consent, slide 35.

So this is, the additional criteria is that this is research that involves accessing or using private identifiable information or identifiable biospecimens. So if you’re accessing it, even if you’re not recording it, you would still have to meet that requirement.

How will changes to the Common Rule 2018 revisions affect the 2018/19, IC auditing elements? That’s a very good question and we welcome your thoughts on it. You know ORO is having a series of workshops for Research Compliance Officers and that’s one of the things that we’re covering in that workshop. You know what are some of the possible changes to the auditing requirements? So wait for the workshop to come to a place near you.

The next question says the first of the following criteria doesn’t say minimal risk, does that mean that the first can be used for greater than minimal risk studies? I’m assume you’re talking about the first, oh wait a minute, it’s the following criteria, the IRB may waive the requirement for the investigator to obtain a signed consent form for some if the only record… Yes. That can be used for greater than minimal risk research. Yes. If the only record linking the subject to the research is the informed consent form and the main harm would result from a breach of confidentiality there is no requirement that that be minimal risk in order to use that waiver of documentation. The second one does have to be minimal risk and that’s when there’s procedures for written consent are not normally required outside of the research context.

Okay. Any other questions? I think we’re over time so if you have any other questions you can email them to me. As I said, I will send out the link to where these are going to be posted within the next few days, hopefully. And thank you very much for your attention and have a great rest of your day.

[AND OF AUDIO]