Karen Jeans: Thank you Parker. So hi everybody. My name is Karen Jeans, and I am the Director of ORPP&E here in the Office of Research and Development and I’d like to thank you for joining our bimonthly series on HRPP Protections. And I am very…also want to express my gratitude today to other representatives from ORD and ORO who will be part of our panel during the question-and-answer session. This is a webinar series that we set up. This is our third in the series that goes every two months to discuss different topics. It’s not one single topic that is discussed for the entire webinar, it’s to cover different ones. And part of this is that we always have questions about the NCI IRB, the National Cancer Institute IRB, and commercial IRB issues.

And so this month’s focus in addition to those two topics, the primary topic is going to be about the VA facilities implementation of the Centers for Disease and Control and Prevention, the CDC expand access program for use of Tecovirimat, TPOXX for monkeypox. We’ve been running this protocol now for a little over a month and so we’re going to give an update on new emerging issues, questions, and answers, because we’ve got a lot of them. And so we wanted to let you know what’s going on with that and it apprise everybody of that. Again, continuing feedback is another topic in this webinar series is the NCI IRB. Again, we want to…we have 56 sites that rely upon the NCI IRB for NCI \_\_\_\_\_ [00:07:24] studies.

And so we have a relationship with the NCI, and they give us a lot of feedback on issues related to different topics that are relevant to those institutions that rely upon the NCI IRB. This is a forum where we share that information. And also as the majority of our VA facilities with research programs rely upon at least one of our commercial IRBs. We are continually getting different topics and issues that are brought west by you from the VA facilities as well as from the different commercial IRBs himself directly to us that we share because in the end, if it’s one question by one site, it’s probably going to be relevant to multiple sites.

And also, we wanted to give you as part of the ending of this webinar before we go to questions-and-answer is an update on the PRIMA Virtual Annual Conference which is going to be held on December 12th through the 15th in both the Office of Research and Development and the Office of Research Oversight are going to be doing as part of their support of the PRIMA Annual Conference this year. So with that in mind, we’re going to jump into the first topic. And our first topic is about the monkeypox expanded access program using TPOXX.

So when you look at this slide, the first slide is about an update, and you’ll see a link at the bottom where you can at any given time see how many active cases are currently going on in the United States of diagnosed confirmed cases of monkeypox. And the different colors talk about in terms of the density of the number of cases reported for a given state. Now in terms of what we are doing here in VA, roughly a little over a month ago we establish a reliance agreement with the CDC’s IRB. In order for…similar to the Mayo Clinic convalescent plasma protocol for COVID-19 where CDC’s IRB could be the IRB of record for those facilities with research programs that choose to use it to rely upon them for the CDC to core that program for monkeypox.

And the reason we wanted to rely upon the CDC IRB is that CDC itself is holding the IND for this. And they have the investigator who has the protocol. So therefore, it makes it a lot easier to make it all concise in terms of efficiency from regulatory and implementation standpoint to rely upon the CDC IRB. It was not a requirement. If other facilities did not want to rely upon the CDC IRB, that’s their choice. But this was an option that ORD and ORO worked together to make happen. And so at this current time, we had 81 VA facilities that are currently approved to participate in this program. And of the 80, we have two sites that use their own IRB, and the rest are using the CDC IRB. And this again is an expanded access program with an investigational new drug application approved by FDA.

And again, it allows access and use of TPOXX for monkeypox. And as this slide, you’ll see the name of the protocol, which is use of Tecovirimat for treatment of human non-variola orthopoxvirus infections in adult and children. Now while we are not only doing the CDC IRB component here in ORD and ORO, we are also doing what we call the support mechanisms. Again focusing on the regulatory aspects of this. Now again, we are not dealing with the science of it. We’re not dealing with the pharmacology of it. We’re not dealing with the pathogenesis of monkeypox. We are dealing with the implementation to support VA facilities that are indeed involved in conducting this program whether you use the CDC IRB or whether you’re using your own IRB.

Now what is again very…what causes confusion with this program is that, yes, it is under FDA. It is an expanded access program, but it does not meet the definition of research under the common rule. It does not meet the definition of a clinical investigation under FDA. This is not a systematic investigation designed to develop or contribute to generalizable knowledge. It is a treatment protocol using an investigational drug under FDA’s regulations in 21 CFR part 312. So that is where it must require IRB approval prospectively and it also here in VA requires R&D committee approval. But one thing that…also one of the reason we’re also having this topic today is there’s a lot of confusion about the role of ORD.

ORD is not involved in the procurement or the process to procure the drug. We have no relationship with that. Now with that in mind, ORD is working closely with Pharmacy Benefits Management, PBM as we coordinated between our offices to make sure communication is clear and that is one of the roles when we’re doing this type of protocol. But again, we get a lot of questions, my office does about how do we get drug supplies and as many of you know who have asked that question to ORD, we refer you right back to PBM. Or give the information that PBM has given to us. So that is not the role of ORD. We have no ability to get drug.

Now we have a very, very active website. And we have a dedicated webpage that we set up for this program. Again, the analogy for those of you who were here during COVID-19, it’s the same thing we did with the Mayo Clinic IRB. We have a dedicated webpage to which we update a lot. Usually at least once a week describing again, how do you rely upon the CDC IRB if you still…if your facility hasn’t. And we still have VA facilities are in the process of joining the CDC IRB to be part of this program. But also it has a number of tools and support documents to support it. And so this is where we…this is a website that every one of you on this call can access anytime. It is a public facing webpage. And we have a number of groups outside of VA between universities and even some other federal entities which are accessing our page because it is indeed useful, and it has never different types of documents that can be used to facilitate.

So when it comes to what I’m going to go through next is, I have taken a variety of common questions and answers that ORD has received in the last month, and I divided up into three different categories. Pharmacy related, Informed consent issues, and then miscellaneous. And so what I’m going to do for this portion of this seminar today is go through some of the common questions in each of these categories starting with pharmacy related questions. And each of these questions are high-volume questions that we’ve received. And by far one of the most high-volume questions we received is, is completion of a VA form 10-912, which is called the Investigational Drug Information form required for the use of TPOXX in the CDC expanded access program? And the answer to this is no. While it is an investigational drug and usually when you’re looking at investigational drugs, you have a VA form 10-912. But it’s not because this drug is also approved for the use of smallpox. For treatment of smallpox. And as long as there’s a package insert for this drug; you do not need a VA form 10-9012.

So that is why a VA form 10-912 is not required to be completed for the use of TPOXX for this CDC expanded access program. Now this is also…because it seems what I just said seems to be contradictory Karen. Is TPOXX considered an investigational drug? See if I said yes and no just now. And the answer is yes and no. It depends upon how it’s used, what condition it’s approved for. Is TPOXX an investigational drug when it’s used for the treatment of smallpox? The answer is no. It’s FDA approved and marketed for treating smallpox.

But when this situation is occurring where you have an approved drug which is used in an unapproved indication, this is only being allowed to be given in the United States by the Food and Drug Administration through their FDA regulated expanded access investigational new drug mechanisms. So in this situation, when TPOXX is being given for the treatment of monkeypox at the current time, it is investigational. And it’s investigational not because a quote VA policy. It’s investigational under FDA regulations. So this is not a VA policy issue. It is an FDA regulatory issue backed up in FDA regulations.

Now another confusing issue is the difference between EUA which is an emergency use authorization versus expanded access investigational new drug. And so why is the difference with that? Because recently as many of you on this call know, Jynneous is a vaccine, and it’s a vaccine that was recently given an EUA, emergency use authorization for monkeypox. So what does that mean in terms of EUA versus EA and EIND, expanded access? Are they the same? They are not the same at all. The only similarity between the two is it still involves an investigational drug. When you’re doing an EUA and expand access IND, they’re both investigational drugs. But they’re done under different authorities.

When you have EUA, it is granted as part of a public health emergency and in that situation, it is granted when there is no adequate approved are available \_\_\_\_\_ [00:18:26] that exists. And the known and potential benefits outweigh the potential risk. EUAs are not analogous to what we have currently with TPOXX, which is under an IND. As you’ll see in this next slide, I’ve underlined very, very clearly and I normally don’t underline, but it’s so critical to reinforce it. The current use of TPOXX for monkeypox is not under an EUA. Now that does not mean it could not possibly be that in the future. We saw that with convalescent plasma as an example for COVID-19. It went from being under an expanded access IND nonemergency to a EUA. But at the current time, this is not under any EUA, so please do not confuse the two for TPOXX.

Again, one of the biggest difference with an EUA versus what we have with TPOXX which is under an IND is that IRB approval is not required when you use a medical product under an emergency use authorization. But again, that’s not the case. Not for TPOXX. And so TPOXX is being done under a nonemergency IND, so therefore it requires prospective. Prospective means before it’s given, it requires IRB approval. And that’s why the CDC has the IND, they have a principal investigator who holds it. There is an IRB approved protocol and a facility can initiate treatment with TPOXX for monkeypox, you have to have IRB approval. This does matter if it’s VA or if it’s a non-VA facility. This is required by FDA regulations.

Now we’ve had already some situations where…and we’re going to talk about informed consent here in a little bit where we have some individuals…again, nothing is ever done maliciously. It’s just okay, how do I make this work? And people are thinking, well, it’s going to be too difficult for me to get informed consent. And oh, I don’t know if whether or not I’m going to get IRB approval yet. So I’m to go ahead and call this an emergency IND, and therefore I don’t have to get prospective IRB approval. And I probably don’t even have to get informed consent either. That is wrong. That it’s not correct. FDA determines whether or not the IND is emergency or nonemergency. It just can’t be flipped.

We as individuals, as VA, as ORD, as treating clinicians, as investigators do not have the ability on any IND to say oh, by the way. Now I’m going to flip it to an emergency IND. So this is FDA’s determination and classification when they approve an IND involving a drug. So that’s a very important part that I also wanted to reinforce today because there is misconceptions about making it…can someone flip it. Can a treating clinician decide what’s an emergency, so therefore I’m going to not get IRB approval. So that is a key part in understanding about emergency versus nonemergency INDs.

Now there’s also…we’ve got a lot of questions about the FDA form 1572. And the question is, are prescribing pharmacists required to be listed as principal investigators on the form? They are not required to be listed on the forms. That is not, not at all. Also in terms of their activities when the pharmacist are indeed doing what they’re doing as required by their physicians, which is dispensing drug, they are not considered to be involved in the conduct of the research as a member of a study team. Or as in this case, a member of the treating clinician’s team. They are not required to meet ORD’s needs training requirements for completion of training in human subjects protections ethical principles.

And again, ORD has developed a special set of slides for those treating clinicians that can be used in lieu of CITI when they are involved in the conduct of this program. And the link to that slide set is in the hyperlink that you see on the slide for this…in this presentation. Now again, lots and lots and lots of questions. These next two questions are probably the most common ones that both the Office of Research and Development and ORO as well have gotten about 1572s and that’s what do you do with it. So you have a form FDA 1572, all the treating clinicians who are going to be prescribing that drug are listed on that 1572. What do you do with it next? Does ORD need to get a copy of it? And/or are we required to upload that document into VAIRRS? The answer to both of those questions are no. You are not indeed required to send that question to…send that form FDA 1572 to ORD. Nor does it go uploaded into VAIRRS. If you want to upload it, that’s your business. But again, it’s not a requirement.

But the next question that you see on the screen is a yes. Does your VA facility’s treating clinicians need to submit a copy of the form FDA 1572 to the CDC? It is not a need. It is a must. The answer is clearly yes. And one of things I want to reinforce and why I'm citing the exact paragraph within the CDC protocol is, the protocol drives what happens. While ORD has a webpage and we reference the protocol and we’re making supporting tools, it never replaces the IRB approved protocol. And so as per paragraph seven of the current protocol, which is version 6.1 dated august 10th of this year, it is the responsibility of the treating clinicians to complete that form FDA 1572 and return to CDC.

Now they would like, like is a key word here to get it prior to the initiation of TPOXX to the patient who has been diagnosed with monkeypox. However, they recognize that many times that’s not feasible. So therefore as per the protocol, it is allowed to be done, sent to CDC within seven days of TPOXX initiation. And again, this is required per protocol. So this again, when you do not do this, you’re non-compliant with the protocol. This is again, not a VA policy requirement, this is a requirement of the IRB approved protocol. So again, it’s very important to follow the protocol. And again, I had talked to CDC even before this webinar and they wanted to reinforce, VA is not it…it has not been an issue with VA facilities, but again, only one form is required. So if you have nine treating clinicians listed on that form FDA 1572, there is no requirement, nor does CDC want nine separate 1572s. Okay. Let me try to advance my slide.

Okay, so now we’re going to a very, very large topic area in terms of questions. And the questions really are…well, there’s a lot of questions. They all sir around three primary issues. And so I bet you can already guess what is the most frequently asked question ORD has received about the CDC program using TPOXX related to informed consent. And I think you could probably guess it because the slides went out ahead of time. But even without that, the question in many various forms is, can verbal consent—and I literally took this from a question I even received yesterday—waiver of documentation of informed consent be used to obtain informed consent for the CDC expanded access IND TPOXX program? And the answer is no. And I want to really reinforce this, because ORD has been asked this question over and over. Sometimes different people with ORD, a different version of the same question, but it’s this question.

And so I went to really emphasize this point. No. No. No. It is not an option. It does not exist. The criteria are not met. This is not something that falls under VA policies of 1004.01. This is not a clinical consent. This is indeed an IRB approved consent involving investigational drug of an expand access program which is under FDA regulations. That is what this is. So again, I’ve had some individuals…again, nothing malicious but again, it’s being confused about what policies apply. It’s not policy. Its regulation. The regulations as per the CDC IRB approved protocol, which that protocol must follow.

So then you get into, why is this question being asked so often? And the answer is simple, because unlike what we saw with COVID-19, when we were dealing with all the different expanded access programs and indeed clinical trials where you had most…many of these patients were in-house unless we were doing long-term follow-up. Many of these patients as we’re seeing in VA when they come into, or they present to a clinic VA, and they have a test. And it’s not for 24 or 48 hours later that we find out and we call them at home, the treating clinician and says oh, by the way. Karen, you have monkeypox. Now I’d like to talk to you about this expand access program using TPOXX to see whether or not you would be willing or would like to be in this program.

Now again, TPOXX is infectious. And it’s not something where usually you had the patient come back into the hospital to, here’s the consent form. Here. I’m going to hand you a consent form that has my signature on it. That could be potentially contaminated. Also as per the CDC recommendations that again, I’ve cited on the slide, the recommendation at the current time. If you’re not in the healthcare setting in terms of if you’re hospitalized that if you have monkeypox that you isolate at home or another location if you can. And so that is part of the issue involving this type of protocol. And again, reinforcing that sharing a paper is problematic.

Now CDC has made it very clear again, IRB approved protocol that it is explicit in the protocol. That’s why I always go don’t…you don’t have to believe Me. Believe the protocol because the protocol clearly states, it is the protocol requirement is for patients or their legally authorized representative to sign and date the CDC IRB approved protocol prior to treatment unless an exception from informed consent applies. Now I’m going to…I’ll talk to you a second what it means by an exception from informed consent. Because that is going to be very rare if at all applicable in this protocol as what we’re seeing right now in VA. But in terms of again, a lot of questions we’ve received about the executed subject signed and dated informed consent forms, those forms are not required to be returned to the CDC.

The only time as per protocol that the CDC must be sent the subject’s…I mean the patient’s signed and dated informed consent forms is when the facility or the institution that is conducting this program cannot maintain the forms. That’s not going to be applicable for any VA facility. That is not what we…we’re able to do this. So if you’re reading that statement in the protocol, it doesn’t apply. And in terms of what is required to be kept, a copy of the entire subjects executed consent form, not just the signature pages must be kept by the VA facility. And we’ve had a problem with that as well where there’s been misunderstandings that we only have to keep the last page. Now I made a reference about exception from informed consent.

CDC has allowed an exception for informed consent. That only applies when the patient is unable to respond because of physical and capacity. Let’s say they I had sepsis, and they were in the ICU, and they’re ventilated, and they can’t make their wishes known about hey, do I want to be…I have monkeypox and therefore I would indeed to receive TPOXX under this expanded access program. And there’s no next to kin or LAR available and the treating clinician and a clinician who is not involved in this program document…both document that the patient’s life is in a life-threatening condition. It’s not feasible to obtain consent and there is documentation that is required. And in this case, CDC requires…this is one of those situations where that document must be sent to the CDC within three days of the initiation of the TPOXX treatment.

To my knowledge, this has not been on a single time in this protocol for any VA facility. And again, as you can see from the slide, it would be very, very unlikely it would be done. Because again, they have to basically be unable to respond, there’s no LAR, and again, treating clinician and someone who’s otherwise involved in the care of the patient under this IND protocol have to make statements affirming that this is indeed necessary to do. So that’s why exception from informed consent does not apply or is highly unlikely for patients who are going to be…who are diagnosed with TPOXX unless they were indeed in the hospital from another condition or something else happened. So that’s why it’s not…it’s not equivalent to a waiver of documentation of informed consent.

So that gets into okay, we’ve talked about the issue with paper. Why we do it here. So iMed. We are working with the VA iMed team to place a CDC IRB approved template into iMed and deploy nationally. We are close. I wrote on the slide today; I don’t have a timeline for deployment as of today’s date. I should have a timeline for that by next week. So we’re working with this incredible…again, the incredible gifted team with iMed. And again, when we get that ready for deployment, again, just like we did with the DocuSign, which I’m fixing to talk about in a second, we will send notification to everybody. In terms of DocuSign, the CDC IRB again, process and documentation of informed consent required by the IRB is under the oversight of an IRB. So that is why ORD again, sought approval through an amendment to the CDC IRB to allow the use of DocuSign.

We have developed in coordination with \_\_\_\_\_ [00:35:02] the Identity and Access Management team a streamlined approach that will allow rapid implementation of the VA DocuSign for this expanded access program. And ORD develop detailed instructions in coordination with IAM the five steps, and we’re not getting to go through all five steps today. If we need to have a dedicated webinar just for DocuSign, we can do at a later time. But these instructions go through it in excruciating detail. And you should be able to…again, if there’s questions about the ORD DocuSign portal, those questions can be sent to the regulatory box or to me personally. We have also in terms of making that easier to fill out the DocuSign portal for ORD, I am very, very…I was very fortunate to have an incredible group from the CSP group who are now working with me to again, deploy tools.

And as part of the handouts for today and one of the handout will be of course on the supporting documents and tools on that webpage. There’s also a one-page table on how to fill out the ORD portal that gives you the fields right there in a single page, so that you don’t have to go through the entire ORD guidance document. Which is referenced in the last bullet. That makes it much easier to fill out the portal very quickly. This guidance document is again located on that webpage that I referenced. You also have a link as you saw on the prior page. And so again, we know that we’re getting a lot of requests.

Brandon Alexander is part of this group today. He’s been receiving a lot of your requests for DocuSign for this program, and so we’re processing those and then those are going forward. The reason that this is going a lot faster than if you were not…have a normal request I call it is that DocuSign templates for this program which include not only the CDC IRB approved consent form, but also the VA form 10-5345, the HIPAA authorization form. They’ve both already been set up in DocuSign and there is a process that’s already set up when usage or request ORD approves your request, and you forward that to Identity Access Management using the email address that is in that guidance document with the table. They have accelerated process to be able to put you in a sandbox and be able to start…give you the materials you need to be able to implement. So there’s not a lag in terms of needing to setup the templates because they’re already setup.

Now I’m going to cover two more very important issues related to informed consent. One is the issue about the informed consent addendum. Now right down the addendum is not approved and it’s working well right now for the information to be conveyed by treating clinicians that by the way, you’re not going to get charged for a treatment or procedures that are part of this expanded access program. Now if you have copayments that are due as part of your usual care, there still going to have to do that. But also, if you are injured as a result to be in this program, we’re going to cover you. VA is going to treat you or arrange for that treatment to be covered. Bottom-line, you are not going to have to pay. So why is it that we’re requiring this to be set? Why is it that we say, well, why do you have to do this? And the issue is because of language that is in the CDC IRB approved consent form that is indeed required.

That CDC IRB approved consent form cannot be modified, and it is not modified. Again, remember we’re a federal agency, so the consent form was written for all institutions. It’s not written…there’s not a federal version versus a nonfederal version. And so in that consent form as you will see with some of the yellow highlighted lines, there’s statements concerning cost and what happens if you’re injured where it basically states, you may have to pay for it or your insurance companies. We are not an insurance company. We’re VHA. And so that’s why we tell the patients, by the way. You’re signing a consent form that says you may have to pay, but we’re letting you know, you’re in VA and you’re a veteran. And we are going to cover any costs related for research related…for related injuries for this program. And any costs related to this program, we’re going to cover. So that is why we have those statements why that information must be conveyed.

Now also even before I go to miscellaneous, I want talk about another topic that again, we’re getting ready to issue an FAQ on this, but it’s another frequent question. And indeed it’s related to the issue of how to convey informed consent and how to obtain it. Okay, so let’s say you don’t have DocuSign. It’s not set up yet. iMed is not yet ready. Okay. So the issue of what like we did with COVID-19 where we had photographs taken. So I want to talk about that and indeed we’re planning…we should have an FAQ issued on this next week. But I wanted to go through this. It is indeed and the CDC IRB has approved for VA obtaining a digital fit image of each page, and I do mean each page of the CDC IRB approved consent form. And of course again, the 1053…10-5345. Again, that’s not an IRB issue, but that’s VA’s.

When you have a subject for example, a patient…I keep calling them subjects. They are patients. Who again, let’s set it up. They’re at home, they’ve been called two days after coming to clinic that they have monkeypox. Okay, the treating clinician gets on the phone with them and says okay, I would like to be able to do this. I sent you…I have a copy of the consent form that you have. But now I’d like you to be able to…we need to be able to sign it and date it and we need to get it back. Now I just told you about the fact that patient let’s say he lives alone and he’s not going to come into the facility and deliver that piece of paper, nor do we want him to. And I’m him saying he. It could be he or her.

So what you can do here is, the VA patient in this situation signs the CDC IRB approved consent form and the VA form 5345 at home and they take a digital image to send via My HealtheVet. Okay, that’s the first and best option. My HealtheVet secure messaging. It’s wonderful. Okay, here we got a problem. They don’t have My HealtheVet. Okay, step two. Treating clinician says okay. Alright, let’s get on Videotel. Let’s have the treating clinician or a delegate like study nurse or a nurse clinician or someone who’s helping them take a screenshot of each page as the patient holds up the page on the screen at home. Now the treating clinician or whoever is taking it for VA, cannot use their own personal phones. It has to be government furnished equipment. So that’s option two.

Let’s say that’s not an option. Okay, so now we go to the image of can a patient, that same patient whose at home take the image using their personal cellphones. Okay, so here’s the trick with this and here’s the information you need to understand. Okay, as we know, that informed consent form is going to contain sensitive information. It says the patient has monkeypox. That is sensitive information by the way. It’s protected health information. Now VHA cannot say the only way you can be in this protocol is if you send this information nonsecurely. that is not the way it works. That is never going to be an option. We cannot require or demand that a VA patient or there legally authorized representative include…send PHI by a nonsecure method in order to receive treatment.

However, if the VA patient wishes to use his or her personal computer or phone to send those images to VHA, then the patient is to be told ahead of time okay, please know that if you’re using your personal cellphone or your personal computer to send those images that that’s insecure. And there’s always a risk of loss of control of the documents. For example, it could be intercepted or received by a non-VA system. But if the patient then wishes to send it using their personal cellphone or a personal computer, then it becomes the patient’s choice to send how to return the form. And indeed, we will except those images of the form. You have to get every page. I cannot emphasize that enough.

So now the issue also is when you’re doing this images issue is that when you look at the CDC IRB approved consent form, the CDC IRB has a requirement which is unique to the IRB and they require the signature, date, and again signature of the person obtaining consent. So this again is an IRB requirement. It is not something that you can just say oh, no. I’m not going to do it. So therefore what happens then is, the treating clinician has a copy of the CDC IRB approved consent form, one that they run off right there that you can download instantly from the website.

And the treating clinician signs and dates that consent form as the person who is obtaining consent. And then that is matched up as part of the patient’s file with the images of every page of the consent form and the VA form 10-5345 and that is the documentation that you do when you’re doing images. And again, we are going to be issuing an FAQ on that. I did not want to put that in until we issue the FAQs formally, but that is also a common question that we’ve received concerning the images. And we’ve been working with VHA privacy and ITC date on this.

Now next also, that’s informed consent. There’s still other issues. Miscellaneous issues. There is confusion about require versus optional forms. Again, part of this is that the CDC changed their protocol on August 10th to where they made forms that were required into optional forms. Again, the best way for you to remember whether it’s required versus optional is to always read the most current version of the protocol. Here in ORD, we are always going to be…we monitor that website. We also have close communication with CDC, and when we find out that the protocol has changed, we will let you know. We also know that the CDC IRB will also inform you when their protocol has changed.

But this is on this slide a little snapshot again, of what is required forms versus optional forms. And again, the protocol is always…this is as per protocol, the definitive document in terms of the protocol itself on what is required versus optional. Don’t \_\_\_\_\_ [00:47:45] somebody else tells you…if you talk to somebody else and say, well, I heard from this person, it’s the protocol. The protocol drives everything. There’s also been questions about because we are relying upon the CDC via the IRB, many facilities, 79 of them was \_\_\_\_\_ [00:48:02] the local IRB.

There cannot be two IRBs that are both doing regulatory required review of a single protocol. So there is no local IRB regulatory review if the CDC IRB is the IRB of record for your facility. So we wanted to reinforce that. Also this is again a treatment protocol. And while it is an investigational drug, the treating clinicians are not required to fill out the research financial conflict of interest form, which is OGE form 450 Alternative VA. Now since this is protocol has started, we’ve had a lot of revisions to the standard operating practice. Again, with the incredible work from the Office of Research Oversight, both ORD and ORR developed a SOP, standard operating practice for reliance on the CDC IRB that includes many of these steps in terms of operationalization.

Whenever the CDC changes their protocol or whether or not we indeed like that recently the VA DocuSign, we include that information. We revise the SOP immediately. Whoever are the points of contact that are listed for that protocol, receive that SOP automatically. You don’t have to request it. So that is again, an operations issue of how our offices are again trying to support this protocol by making sure that the VA facilities connecting this program have the most recent information in terms of procedural steps on how to implement the protocol primarily focusing on the human subject regulatory aspects. It does not cover procurement; it does not have anything related pharmacy in it. Because again, we do not do procurement. So that is also something that we wanted to make sure we conveyed just part of this webinar.

Now moving on to the other two topics, are not going to take as much time, but indeed they’re relevant and important because of issues that we continue to get from these groups. And then we have a large number of facilities that use, rely upon the National Cancer Institute’s IRB for the NCI \_\_\_\_\_ [00:50:28] studies program. And we have a very good NCI helpdesk which is again, maintained my NCI which has VA specialist who are dedicated to working with VA institutions. And so they developed an expertise and knowledge of how VA works and it’s really amazing. This is something they’ve implemented recently that indeed it makes it easier for someone who’s not used to working with federal agencies to work with federal agencies.

Now this is the third webinar we’ve had in the series, and I know some you are saying this is the third time Karen you’re bringing up issues with completion of the annual signatory institution worksheets. Why are you bringing it up again? And the reason is because again, as we talk with the NCIC IRB, they again want to bring examples and convey information as to here are the issues they’re seeing and what impact it has. So in the last month, we’ve communicated with the NCICIRB and based upon the feedback VA is receiving, it has been conveyed by the NCI that there is continuing to be issues. It does seem to be stabilizing right now in terms of the number of issues, but it’s either related to content or technical reasons. But the issue is, when those signatory worksheets are rejected, they have come back in. It’s like a new submission. So many of you on this call are from the IRB world, if not send back for modifications, it’s start over again.

So that is where what has happened recently is that some these worksheets when they’re being submitted by VA facilities, they need to be turned around quickly. And the problem is, they can’t be turned around quickly because there’s issues. So that is why it can take two to four weeks and remember there’s a large number of sites that are doing this. Because while NCI has VA specialist, they also have other institutions beside VA. So that’s why when you’re looking at well, I need this by next week. It may not be possible to get that turned around in one week, because of the workflow that these groups are working with in trying to turn these around.

And as the NCI helpdesk wanted me to convey today, if you’re a VA site that has not yet had your signatory institution worksheet approved, you will continue to use your prior one including your prior VA boilerplate informed consent language with the VA addendum until all of that is approved. So that’s where they are right now in terms of the status of issues. They are working actively. They try very hard to facilitate these issues, but we’re still having issues with completion of the of boiler sheets. Boiler plate language and also the signatory institution worksheets. And this is an example that was given to me last week. And again, I want to reinforce, we do not bring these examples to…these are not to make fun of anyone. They are teaching moments and that is why we do this. Because again, it may be something we all learn from each other.

So the NCI helpdesk came to me and said, Karen. We got this answer on annual signatory institution worksheet from one of the VA facilities that are updating their worksheet. And on the questions on the worksheet is question five. What are the other state or local laws that govern the conduct of research at your institution? And the VA facility responded with the following. Not applicable. VA is a federal agency. State and local laws will never apply. And I want to emphasize that word never. So the NCI helpdesk instantly contacted ORD and said, we want a statement from ORD that state laws never apply when it comes to human subject protections regulations when a VA facility is conducting human subject research. And of course ORD could never say that because it’s not true. Applicable state laws may apply depending upon whether those laws apply additional protections. What do I mean by that? What is the basis of me saying that?

A few months ago, VA issued a guidance document. An FAQ which we coordinate with the Office of General Counsel Special Team Advising Research in which we were talking about the inapplicability of a specific state law. California state law involving specific comments related to the HIPAA authorization and also separation of the informed consent and HIPAA authorization. Now the reason I’m bringing that out is because again, one is the reason when we do or do not follow state law when it comes to human subject protections.

And what we do as a federal agency is we look to whether there is a basis in federal law to apply state law. And when we’re applying it to what I just talked about for question five in that institution worksheet, it goes back to the common rule regulation which VA codified as 38 CFR part 16. In which it states in regulation that the federal regulation, the common rule doesn’t affect any state or local laws or regulations that may be otherwise…that may otherwise be applicable and that provide additional protections for human subjects.

So what does that mean is that, if you’re in a state that indeed states, if you have an individual with impaired decision-making capacity, and if they can only have this requirement, they have to have a \_\_\_\_\_ [00:56:28] in order to get informed consent for a research procedure, than that applicable state law is going to be followed because it requires additional protections. Again, one of the most common example of course is state laws that apply is the age of majority. So that’s why that statement is not accurate. The initial response was not accurate and why indeed there is applicability of state law under the common rule when it particularly applies to informed consent when those state laws provide additional human subject protections to the subject.

The NCI helpdesk has also provided feedback that there seems to be confusion what you can and cannot put in the boilerplate. And this is not talking about VA specifics, this is talking about the boilerplate itself. So as a result of that, again, NCI is working with us so hard to try to facilitate this because it helps them. It helps all of us. We all want to get our research done. And so they provided a guidelines for permitted boilerplate language additions. They updated that document in January of this year. We have uploaded that to the ORD, ORO, NCIC IRB SharePoint site. The link is located on the slide. It’s also in the reference text that document. You can also access this from the ORD webpage dedicated to the National Cancer Institute CIRB.

And then the last section were going to cover before we go to question and answers is a few questions related to commercial IRBs utilized by VA facilities as ORD approved commercial IRBs. And so I have several examples here. Again, it’s working well. We have a lot of communications with the commercial IRBs. Again, it’s a learning curve. And so again, we continue to grow to learn how to use them as they grow to learn how to use us. But these are some very interesting situations, which again happen just in the last month. And so again, these are teaching moments that we can all learn for because I’m going to be honest, some of these…this one that I’m going to talk about right now had never happened before.

One of the commercial IRBs contacted Dr. Workman and myself because a number of VA facilities were using the VA informed consent template VA form 10-1086 for IRB submission. Now all these facilities have used this commercial IRB before and so, the commercial IRB was going, what’s going on? I know these facilities. They know us. And so when the sites were contacted, all the facility said the same exact thing. They had been told by the industry sponsor that yes, you can use the VA form 10-1086. That’s fine with us. And so what did ORD do? ORD told the commercial IRB well; they’re doing it because the sponsor told them to do it. So the commercial IRB went straight to the sponsor and had a discussion with them.

So can the VA facilities use the VA informed consent templates since a sponsor is allowing it? No. No. No. So while the VA facilities were following the instructions provided by the sponsor, it’s the IRB that approves the process and documentation of informed consent and the commercial IRBs do not use the VA form templates. That is a known. And so this case was a sponsor who had not provided the correct information to the VA facilities. There was \_\_\_\_\_ [01:00:17] bad. It was nothing malicious again, but it was just an error in communication. And so what happened after this communication issue was corrected, is the VA facility submitted not using their VA form 10-1086, study approved, all is well. Okay.

This is also an interesting case that happened. Again, these are again unique cases which if they’re happening at one facility, they may be happening at other institutions, and this is not unique to VA as we talked to the commercial IRB layer. So what happened here is again, an ORD approved IRB contacted ORD and said, hey. We’ve got an endorsement letter from a VA facility with a multisite protocol sponsored by one of the major industry partners. Great. The issue was that this is a multisite study. There were no other institutions participating in this study that had submitted to this commercial IRB. Most importantly, the sponsor had never submitted the study to the commercial IRB. The commercial IRB didn’t know whether or not they would single IRB or not.

So what actions were taken to address this issue? What we did is we inform the commercial IRB to put a hold, don’t process that IRB submission until we go back to the facility and find out what’s going on. And what we found again was again, just a misunderstanding. There was a misunderstanding of which commercial IRB was overseeing the study. It wasn’t the one that it was submitted to. And what happened in this case was the commercial IRB that was being used by the sponsor was not an ORD approved commercial IRB. So in this case, the IRB review for this specific study is being done by the VA facility’s primary IRB of record because it takes…it’s going to take too long for ORD to set up a master agreement with this other commercial IRB that’s not currently approved for us to use. We are always working on that, but this is what will be done for this case.

And then the last one before we go to question and answer is one that’s not just applicable to commercial IRBs, it’s applicable to any study. It does happen sometimes and again, never malicious. I want to emphasize that. Again, teaching examples that we all learn from. So we had a study in which the principal investigator for a clinical trial…in this situation, the clinical trial was being overseen by one of ORD’s approved commercial IRBs. They took a leave of absence. But that’s fine. That’s great and wonderful. But the problem is that the VA PI left before another VA PI could be approved by the commercial IRB.

So the question is, is this a reportable event to the IRB? And the answer is yes. There always has to be PI to oversee the study. So it’s not an option to say well, the PI left so therefore it’s okay. We can continue to run the study and not tell anybody until we get someone approved. You got to tell the IRB then. And so it is a reportable event. And in many sponsored studies, such as this clinical trial, the sponsor of these clinical trials and a lot of times you’ll see it in \_\_\_\_\_ [01:03:59] language, the research agreements which are executed between the VA facility and a sponsor that the sponsor has to approve any change in PI prior to the IRB approving it.

And then part of that is the responsibility under FDA regulations. If we’re dealing with an investigational new drug, application, or an investigational advice exemption that the sponsor is responsible in a clinical trial to select investigators who are qualified. So it comes back to sponsor responsibilities. So this is \_\_\_\_\_ [01:04:34] again, nothing malicious, but when your PI leaves, it’s not something that you can sit on. So always inform the IRB immediately when something happens to this effect. Okay, and then the last thing I will briefly go through is again, the Public Responsibility In Medicine and Research, PRIMA commonly known as annual conference is now going to be a virtual event. That’s going to be held at the end of December.

ORD and ORO are supporting this conference by doing two different activities. Number one. We are going to be taking an on-demand session and our session is going to be called A Dialogue with the Department of Veterans Affairs: A Federal Agencies Challenges and Solutions and Working with External IRBs to Facilitate Implementation of the Cooperative Research Provisions. Now it is an on-demand session. So it will be available to people who register for PRIMA, but it will not be available until December 12th. The session will be listed on the agenda for December 12th 11:45 am to 12:45 pm eastern, but it is an on-demand session.

But the other thing that…the other activity that ORD is doing to support this with ORO is we’re going to have a federal agency office hours. Now the past two years when it’s been virtually, we’ve done it multiple times. So instead of trying to break it up and ORD does it this time and ORO does it this time and we do an hour here and an hour there. We are doing it one day on December 13th which is on a Tuesday. The PRIMA starts on the 12th from 2:30 to 4:00 pm eastern time and that’s where representative from ORD and ORO will jointly be in the virtual chat room when they set this up, so that we can answer questions and you visit with those who were able to attend.

And so that’s what we’re doing as our support for PRIMA this year. And so with that said, again, we are continuing to work on your guidance and tools in a number of areas. We know there’s a lot of different things that we need to be getting out and we’re trying to prioritize based upon the most critical needs at a given time. Again, we continue to work with our commercial IRBs and NCI IRB on almost a daily basis. And again, part of the reason we like his bimonthly seminar is that we’re able to give you real cases of issues that have come on, so that you yourself can take part of those and say okay, this one applies this. Or maybe it have happened with commercial IRB, but this may also be happening with a noncommercial IRB study. Because again, it’s about human subject protections and processes.

Again, as Parker said at the beginning of the conference of this webinar, we do indeed tape these. They’re available on our ORPPE Cyber Webinar website. We keep them archived. Questions about this webinar should be sent to the regulatory box. And again, there is a number of different references which I’m including in this slide set which will be posted. And so with that said, I thank you all for listening to this discussion. And I’m going to stop sharing my screen and I’m going to open the floor for questions and ask my panelist to also join me. Thank you very much. Okay, so this is Karen. Here’s the first question we have on the screen and the question is, if not covered, has the special VA consent page for the TPOXX consent been approved yet? And the answer is no. We are still indeed requiring the information to be conveyed orally. And so that is the answer to that question as of today’s date. Thank you.

Next question. I appreciate the comment. Okay the question is, minor correction to what Carrie just said about Jynneos. The EUA is for intradermal administration of the vaccine. Jynneos has FDA approval for the prevention of monkeypox. Yes. It is about the…yes, that’s a…and I appreciate the clarification. It is about a route of administration which is specific to the EUA for Jynneos for monkeypox. So I appreciate the person who wrote this. Thank you so much. Next question. Do you have a better understanding of how CDC’s alternative consent form a short form is to be used obviously for when a translator is required. But is there any situation when it can be used for a competent English speaker? So great question, but that’s really not the purpose of using a short form. Short forms are actually not to be used in those situations.

We are working with the sponsor that has given…the question is, we are working with the sponsor that has given us the option for either using the local IRB approval our external IRB. I assume this should fall under single IRB. Should the sponsor even give the option for local reviews to take place? So this is a good because I don’t know what’s meant by external IRB. The single IRB cooperative research provisions apply to research that is supported or conducted by a federal agency. Or federally funded. So let’s say that this is a study…let’s say that it’s…let’s use a name of a sponsor for example. Only example purpose. Let’s say it’s an AbbVie. A study involving AbbVie. Okay, it’s a pacemaker study and your sponsor is saying, okay. I’m and give you a choice. You could either use Advarra which is a single…the commercial IRB we’re using for the study, or you could choose to use your own.

Now in terms of the cooperative research provisions…and we’re paying for it. The sponsor is paying for it. That’s a critical thing. In terms of the cooperative research provisions, it’s not going to apply at first, firsthand because it’s not federal funds. That’s first. The only way it’s going to apply is if another federal agency or another federal institution like two VA’s or maybe DOD is going to be involved. So it doesn’t automatically fall under single IRB cooperative research provisions if is not supported or conducted by federal agencies involving federal funds or more than one federal institution such as multiple VA’s. So that’s the setting for that question. So it is indeed an option.

And so I’d be asking this sponsor if…again, it’s a choice. Again, we support the use of a single IRB whenever possible, and that is ORD’s position. So if there is an option, unless there is an indicator \_\_\_\_\_ [01:12:39] sponsor is paying for it, ORD’s guidance is always going to be towards using a single IRB. And in this case if it’s a commercial IRB whenever possible. If it's an external IRB in which we’re talking about let’s say another university IRB, it’s really difficult to set up very quickly, a new reliance agreement with a university IRB that we have no prior relationship with. That’s going to take time. So that’s a situation where I’m going to defer Dr. Workman and that would be a conversation that I would ask you to take place with Dr. Workman.

Dr. Workman: Sure. So really the practical issues are that it rarely is a quick response for getting a reliance agreement like that in place. And so like Karen said, the preferences for single IRB if that’s an option, that would be the option to pursue.

Karen Jeans: Thank you. Next question.

Parker Cunneen: Karen, as right now, that’s the last question on our list.

Karen Jeans: Oh, that is great. That is ecstatic. So that is fantastic. So again, I’ll wait a minute here. But again, I very much value people’s time. Don, yes.

Dr. Workman: Parker, I was just going to note there appears to be one person with their hand up. Ashley, can you type your question into the chat if you didn’t already? That was my only comment. Thank you.

Karen Jeans: So in the meantime while we’re seeing whether or not that can be typed in, again, just want to reinforce how grateful we are to the VA research community. This is a time of change. There’s a lot of challenges and we know there’s a lot of things to keep up with. And so again, we don’t exist without you, and we appreciate all your questions and comments and your commitment to veterans. It makes a difference, and we are indeed improving the lives veterans through research, so it’s something that I wanted to make…I’m glad I had the opportunity to talk about today to make sure you know you are valued, and we do recognize all the work you’re doing, and we appreciate it. So are there any other comments or questions? Parker or Brandon, are there anything else? Otherwise, I’m going to end the session.

Parker Cunneen: That’s it right now. One just literally just came in. I’m sure Brandon is pulling it up, but I can…oh, there you go.

Karen Jeans: Oh, interesting question. Will the sites be able to talk with ORD about some of the concerned issues we are having the sponsor level submissions to the commercial IRBs that do not adhere to VA restrictions or limitations at our site? I have been giving these to my local director to give to ORD, but I don’t know if they had been communicated to you. Dr. Workman and I are always available to talk about any concerns with commercial IRBs. That’s why we have an office set up to support this. So we would very much like…we don’t know…I don’t know what I’m talking about here, but please follow up with us afterwards. We very much would like to talk with you. And we thank you for adding this comment. Thank you. So unless there…are there any more Brandon or Parker?

Parker Cunneen: Nope.

Brandon: That is the last one.

Karen Jeans: Okay, then I’m going to say thank you very much for joining this webinar series. And then I’m going to hand it back to Parker to close us out.

Parker Cunneen: Karen, I think you’ve given a better thank you than most of us and said perfectly. So I think that’s it. And if our guest can just take the time to fill out that post-webinar survey, we would much appreciate it. And thank our other…thank you to our other panelists for joining us. And that’s it. Have a great afternoon everybody.