Karen Jeans: Hey, everybody, thank you for joining us today. My name is Karen Jeans and I am the director of Regulatory Affairs here in the Office of Research and Development. Also, we have an esteemed panel today with representatives of ORD and ORO, the Office of Research and Oversight. Today we're going to do our discussion of different topics in in human subject’s protections. I do want to start off by expressing my appreciation to the audience for putting up with the delay.

This bimonthly is actually a 3-month course because of an unexpected illness that I incurred the day before our previous session that was scheduled. So again, we do not like to schedule, to cancel our MOVE! [PH] national webinars on very short notice. But unfortunately, they just wouldn't let me do it in the hospital. So I am back healthy again. And there is a lot of things going on, of course, in the agency.

And we're going to take some different topics today, and then there will be time at the end of the session for questions, and answers on different topics. So again, as part of this, this bimonthly series, series, even when we started it, well, one of the focuses was because of the TPOXX, the CDC protocol.

So we are going to be talking about some of the revisions in the protocol that had occurred, but more importantly implementation tools that are coming out of our office in ORD to assist you with this. But also to give you an idea of where the, where we're standing, and in terms of this, this CDC utilization protocol, and why this will be the last session in terms of this bimonthly series where this would be the lead site, or excuse me, lead topic. We're going to be changing to other topics and I'll explain why in just a few minutes.

We're going to be talking as part of the series that we do with this bimonthly series, commercial IRBs issues and resolutions that is a standing part of this agenda, as well as what I really love that, as far as other questions, common questions, and answers from from different individuals, and facilities from our shared mailbox.

And again, what we feel is that if it's important enough to be sent to our Regulatory box, some of these questions, that there's questions that we feel, we feel would be appropriate to share with you, and to learn from them. Because they spike questions. As they spike, hey, well, how do we handle it? So I think you'll find it very interesting today. And that's what we hope.

So we want to start off, of course, with, with, again, giving an idea of where we are with Mpox. And I found that I did not correct one of these and I'll get that corrected. Because that is now what monkeypox is being referred to is Mpox.

And so in terms of the total number of cases that are going on in terms, across the United States, as of yesterday there were 29,643 cases. And when you compare it to where we were when we had our last webinar, which was around mid-September, September 13, there were 21,985 cases, so roughly, about 8,000 cases in the last few months.

Now when you look at that compared to COVID, and the incident rate, that is not even comparable. So what you're not hearing now is a lot of discussion, or you're not hearing a lot of the news about cases, and outbreaks of Mpox. And indeed as part of preparing for this webinar today, of course, we are very fortunate to have a very good working relationship, of course, with Pharmacy Benefits Management.

There is a stock of, of course, Tecovirimat. And I'm going to call it TPOXX because it's easier for me to say. That have we used for our supply? That PPM was able to secure for Veterans who had monkeypox. And we have not, and so we're not seeing a lot of utilization, which is a good thing in terms of the incidents of impacts in the agency.

But again, as part of ORD support, especially when this first came out, to try to organize, and at the national level, again, supporting the enterprise approach, we did indeed, and have, are currently supporting the CDC's expanded access protocol for use of TPOXX for Mpox.

And so we – currently there has been no new sites since our last discussion. We have 81 VA facilities that are currently approved to participate in this protocol, with 79 of them relying on the CDCs, the IRB. And two are using their own internal IRBs. And again, this is an expanded access protocol under an IND, Investigational New Drug Application that's been approved by the Food and Drug Administration.

And the CDC has supported this with a variety of different tools, a dedicated webpage on their website, discussing the protocol, and information that's available. Again, we we along, we being ORD, and ORO established a mechanism so that we could rely upon the CDC IRB for those sites that chose to use a CDC IRB instead of their own local IRBs. And work with them to create a mechanism to do that. Again, as an expanded access program, this use of TPOXX does not constitute human subjects research.

However, again, there are, there are types of activities that require IRB approval, so therefore, that is why this does require IRB approval, which it has. And we also in terms of the institutional issues, it requires VA R&D Development Committee approval. And again, we want to reinforce as always, and that's why we do reference Pharmacy Benefits Management, that we are not involved, neither ORD, or ORO in the procurement or processes to procure TPOXX.

However, we have worked to, with PBM when there are issues from our different pharmacists, and they have questions that are sent to us in ORD about TPOXX, and procurement. We just don't say, "Hey, it's not our problem." We refer those to PBM, and they are very responsive with those type of questions. Again, it's, it's about communication and making sure that we get answers to questions.

Again, reminding everybody, we do have a webpage in the Office of Research and Development that is updated with forms, and and different types of tools regarding the program. I'm going to be referencing a document today that we've uploaded for VA DocuSign. Again, the link to that page is on the slide.

So in terms of TPOXX, and what we're going to discuss today, I'm going to do a summary of the protocol changes, but really talk about the informed consent topics. And I want to focus on that for several reasons, including the facts that there are issues, and I'm not talking about VA, but at other sites that are participating in the program. Again because VA talked with CDC frequently about different issues involving informed consent.

So that is the two issues we're going to be talking about TPOXX today for this expanded access protocol. So in October, and again, this is December, but a little less than two months ago, they revised, the CDC IRB approved a revised protocol. And it's protocol version 6.2. And it's dated October 24, 2022. And the approval letter for the CDC's IRB approval for those sites that are relying on the CDC IRB are on their web page.

And it can be downloaded directly there. Of course, as part of that as we again stated in ORD, that when this protocol started, and we decided to take this on, that again, there would always be central information security reviews and central privacy reviews that would be available. Regardless if you're relying upon the CDC IRB or not, those are going to be publicly available. And so those are indeed, were done, and posted on ORD's webpage for this protocol.

It is very important that we monitor this site every single day. It did not result in a change in the consent form, even though there were a number of revisions made to the protocol. And so the current – the CDC IRB approved consent form is still version 6.1, which is dated August the 10th, 2022.

Now, in terms of, there were a number of revisions that were made in the protocol, and a lot of the revisions, and I'm not going to read every single one of these, involved fine tuning, eligibility issues, or contraindications to receiving TPOXX for patients who had, for example, renal disease. And, again, better educating and better helping the treating clinicians who are providing TPOXX under it for this protocol, for this expanded access protocol, more defined parameters, more information to indeed help them treat the patients who are receiving this.

But there were also issues in all involving the random, the randomized clinical trial that's being conducted. And so there has been a lot of questions that ORD has received about this. And so one of the reasons I wanted to bring this up today is to, again, give clarifications regarding what it means in the protocol revision when it states that providers should inform as part of the revisions of this protocol, patients about STOMP.

STOMP is the name of the clinical trial, randomized, that is being done by CDC. And it's called a study of Tecovirimat for a human monkeypox virus. And again, as part of this revision with the protocol, it's informing providers that, by the way, you need to tell them, "Patient go into this randomized setting if you can, rather than use the expanded access."

Okay. That does not mean – and there we, we've had a number of questions about this. That if you're at a VA site where this is going on, that you tell them, “By the way, here is this randomized trial," when you, yourself are not participating in it as a facility. So that has a, that is a clarification that we wanted to make sure and reinforce.

Because right now as of the current date, we are unaware of any VA facilities that are participating in STOMP. And again, there is a list of the sites that are participating in the randomized clinical trial using TPOXX for Mpox, which we have made that available to you so that you can also see who was all's all participating in that. So that is an important issue that we wanted to make sure and clarify for your treating clinicians that are in the protocol for this expanded access protocol.

Again, many of the revisions of the protocol had to do with clarifying the children's dosages. But also a really big deal on this was, number two, they wanted to clarify some of the adverse events of interest for monitoring and reporting to CDC, but welcome by all was the implementation of this online registry.

And for those of you, sites, that participated in the Mayo Clinic convalescent plasma for COVID-19, for those of you who remember that, that was where the Mayo Clinic can be operated an online site where many of the forms could be done there, registration. It was very very user friendly. Well, that's, pretty well, exactly what the CDC has done with the incorporation of this new online registry that allows these forms to be done electronically rather than submitting in forms and using a encrypted e-mail box.

And it increases the likelihood of missing something. So again, just to very briefly remind sites that your, your new providers must register if they're coming into this protocol after October 28th, '22, they must register themselves, and to the registry. And again, it allows for the forms that are required by the protocol as well as those that are optional to be done.

But more importantly, it is a really great mechanism to allow the CDC to know you all is working with the provider who also needs access to those forms. And so that has been an issue. And again, when we talked to CDC about information that we need to convey here in VA to reinforce issues that they have seen nationally, not necessarily at VA. And I want to reinforce that. That the provider registers on the online registry.

And as part of this registry that they themselves, the provider lists the staff members who are going to be working with him or her with this, this program. And so that is to prevent the staff members from having to put in their own separate online registrations into the registry, so that they can get access to these electronic forms. So they made it so it was as user friendly as possible.

Now, for those providers who were in this activity, and again, for VA, we came on very quickly. Treating providers should have been, got, had received from the CDC, an electronic link saying, "Okay you are now in the online registry," we've put you in there. Again, if they did not receive that or if they have any questions, they can send an e-mail to the mailbox at, that I have at the bottom of the slide there. Or they can register online.

And if they try to register online, it will let them know if they've already been registered. And it's extremely good system because I tried to break it myself. I went in there to, to to see if I could register, and what would happen. And again, the biggest issue that has been communicated to us by the CDC is that those individuals who were working with the providers to assist them, that they are, indeed, are trying to do their own self-registrations.

And so that is why on the online registry when the provider goes in, there is a specific way for providers to go in, and add staff, even if it changes after they initially registered. And so even if they registered once, and they need to add people, there's a way for them to go back in, and basically edit their information.

But, really, the focus of of what I really want to talk about when it comes to TPOXX, and the CDC's expanded access protocol involving this is the informed consent. Again, the reason we're talking about this is issues that have been raised for non-VA institutions, and the the ability for us to also let you know what's going on, and also discuss, make sure that you're aware of these issues, so they're not repeated at your VA facilities.

Again, we're dealing with a low volume protocol right now, which is good. But it, also, we, of course, as we all know, when there's not something that's been used frequently, it increases the likelihood of errors. So that's why we wanted to reinforce that today because there, there have been issues.

Again, in terms of this expanded access protocol for TPOXX, there is no such thing as a waiver of documentation of informed consent. There must be a written informed consent form signed and dated by the subject. I mean, by the patient or the patient's legally authorized representative unless an exception from informed consent applies.

Now, Mpox is not sociated with a high morbidity or mortality. And so the likelihood that a patient who is eligible for this expanded access protocol would meet the criteria of an exception from informed consent, which involves a life threatening condition, and that there's no one available, and it's time sensitive, that is extremely unlikely.

And when I talked to CDC about whether or not there were a lot of uses of exceptions from the informed consent for this protocol in this program, they basically couldn't tell me a case that they were aware of at the time that I asked them. Again, reinforcing because this has occurred, a few VA facilities, again, they're not, they're not, there is no anger.

There is no, "You didn't do anything wrong, but you overdid." Your VA facilities are not required to send a copy of the CDC's IRB-approved consent form that's signed and executed by the, the patient, or the patient's LAR to CDC.

There are some sites, and I'm talking about non-VA sites, that are participating in this protocol where that is indeed relevant, but it does not apply to VA. And again, what we, what is required, again, is for this to be part of the medical record. This is a consent. It's a clinical care consent even though it's an investigational drug.

And again, you won't see it in protocol, the program because, again, we're a covered entity. But a VA Form 10-5345 is typically completed, again, that goes in the patient's VHA health record.

One of the issues that has been, arisen as a result of this informed consent document that has been approved by the CDC IRB is a signature that is not required by FDA regulations. It is not required by the Common Rule. But again, as those of you on this phone know who are IRB specialist, an IRB can always exceed that which is required by federal regulations as long as it doesn't contradict it.

And so the CDC IRB did indeed require as part of this informed consent that's approved by them, the signature of the individual who's obtaining consent. That printed thing of that individual also must be present.

Again, in discussing the CDC, they said they have seen some quality improvement, quality assurance issues in which this is not being done, even though it's on the same page as the consent with the patient's signature. And some of that is a result of use of remote technology, and remoteness of obtaining consent.

So again, one of the reasons that we wanted to reinforce this today is please make sure that the individual completing consent does indeed sign, and date the consent, and that they, they print their name where it's legible. But again, this has been an issue because whereas in VA, and we've discussed this with a number of sites; again, a low volume protocol right now, program. That in most cases, many, many cases, consent is obtained remotely and not in a face to face physical interaction.

So that indeed has produced its own issues regarding how to make sure that a copy of that executed informed consent form signed and dated by the subject, or their LAR, and the VA Form 10-5345 gets back to the treating clinician, so that it can be put in the medical record.

And so when you talk about how are different ways that this can be done? Of course, you have a physical return where that, that copy, that's consent that has been signed, and dated by the subject, or the – by the patient or the patient's LAR is brought back to the facility. That is not, a course, an optimal situation. And so then there's other options that can be used. For one, number two is VA DocuSign.

Number three, which is what we're going to discuss is a digital image of each page, can be sent back either by it using video technology, and having the the treating provider, or their team take a picture of each page of those documents. Or when the patient or their LAR takes pictures of each page and sends them back. And we're going to go a little bit into the, some of the mechanics of that.

And then, of course, VA iMED, we are indeed looking at a January appointment. And I'll discuss that in just a few minutes. So in reference to DocuSign, again, in our last meeting in this, in September, we discussed that we had developed a guidance document that goes step by step on how sites can seek approval, or seek permission from ORD, and the IAM office, which is the identity and access management office, which manages VA DocuSign, to be able to have access to the templates. You're now approved.

This is how you're processed. This is what you expect to have, and it goes step by step on how to seek approval, and how to – what will happen during that process in the timeframe. But what we found after the last meeting, and as a result of again, the deployment of VA DocuSign, and attempt in using this, is that there were lots, and lots, and lots of questions, and good questions about how do you do this?

Especially by our treating clinicians in terms of how do you physically do it and give it to me in a step by step way, so that I can understand it? And so, again, we cannot express enough from the Office of Research and Development, our appreciation to the IAM team, and team, and the Office of Information Technology. That they developed a step by step guide using PowerPoint, that literally takes you, if you were, each of you have that downloaded right now, accessed it.

That goes from how you log into VA DocuSign to how do you use each step in terms of how to access the forms? How do you fill out the forms? How does a patient complete the sign, the the signatures? What comes back to you? How do you retrieve it at that level? And what we did a couple of weeks ago is have a user group that the IAM team met with.

And these were sites that had requested already the use of VA DocuSign for this TPOXX program. And they went through it with them to go through the tool before we published it. This tool, which is called the VA DocuSign Job Aid, is on the ORPP&E website for this program, so all of you can access it. And again, when you – there is a place to give user feedback on this. Or if you're having issues with us, please let us know. Let IAM know.

Again, there's, if you're not able to use VA DocuSign for this, that's a problem. So we want, and we're listening to what you need in order to do this. But also, we, and since the last time we met, we wanted to get some clarifications as a result of an incident that happened, actually. When, when ORD went to the CDC IRB and said, "Okay we want approval for VA facilities to be able to use remote consent." And that includes iMED, that includes VA DocuSign.

And we also are requesting approval from the CDC IRB to use digital images, whether those be taken by the treating clinician, or those who were taken by the patient. And the CDC IRB approved it, fantastic. And this also applies to the VA Form 10-5345. So we, we have three methos we can do that. But what happened is, we got into a question, and this was just a result of actually a patient, a VA patient who was being asked to be in the protocol.

When he contacted ORD, and myself, specifically, and said, "I'm a little concerned here." Is the only way that I can do this to send my information on securely? I really didn't understand that well. So there is where we're going to talk a little bit here about what can, and cannot be done, and what are the options?

Okay. So first of all when we're looking at digital images in terms of the treating clinician, \_\_\_\_\_ [00:26:27] images, using a video technology utilized by the agency; so, in that type of situation, the the patient or the LAR has the consent form, and the 10-5345. And what happens is that each page of that that, that document that they have signed, that includes all pages, every single page not just the signature page itself, they're held up using…. This works with, and that's, of course, with one of our technologies rather than trying to do it with a phone, is, is the picture is taken care of. They, they do a screenshot of each page, which is downloaded.

Now, again, when they're using a phone, if the training provider or other team does it, they can indeed use a phone, but it has to be government furnished equipment. It can't be a personal cell phone. So that's one way to do it when the treating clinician – I should say the VA facility is the initiator of taking the images.

But so that, that has not, that's, that's one option, but what about when the patient wants to send the consent form and the HIPAA authorization? When they are the initiator of the digital images? Now, your optimal situation, and again, we want to reinforce that we work with multiple offices before we discuss this.

This includes VHA privacy, the information Access Law Group [PH]. We have vetted this when we discussed this with the Office of Research and Oversight. We discussed this with Ethics. And, of course, the CDC had already approved this.

But in terms of the, the patient takes the pictures of their, their consent form and their VA Form 10-5345 And they send that back to the VA provider, but they send it using My HealtheVet. Because my My HealtheVet has a secure messaging system. That's one of the, the beauties of My HealtheVet.

However, as many of us know, my My HealtheVet is not used by all VA patients. And many patients do not want to use My HealtheVet, just a preference. They were saying, "No I have my first personal phone here. I want to use it all." I want to use it so I can send it back to you that way.

Okay. It's very important to, to know, and this is a really key point here. That this agency cannot state that the only way you can participate in a study or – and I'm, again – you're ORD. We're the Office of Research and Development. So I use the word study. But, like, in this program the only way you can do it is if you do this in a non-secure manner, and you don't have a choice.

So you can't demand that the only way that you can participate is to send it non-secure. That is not an option. You have to be able to say, okay, here is another alternative. However, there are, again, many patients want to do this. So does that mean that they cannot send their information non-securely? No. It does not mean that.

It means they, actually, they can. But the patient must be told prior to sending, sending the images that by the way, you do realize when you're sending these type of documents using your personal cell phone to VA provider, that there is a risk that of loss of control of the documents. It could be intercepted. It could be received by a non-VA system, especially if you're sending the wrong numbers, the wrong e-mail.

And so that is an important issue that we wanted to make sure and reinforce. To make sure that happens. Now, the CDC did not want to alter the informed consent. They said that's something that is your agency specific. You make sure and you tell them that's fine. But we wanted to make sure you knew that that's something that you need to be doing.

When, when patients are being, for this protocol, are being asked to send the digital images back using their personal cell phone to let them know, by the way, there is a risk if you send it non-securely. But in terms of there had been a rumor out there; again, this is one of the reasons we're addressing it, that VA doesn't accept the images.

That is not true. They will indeed accept the images. And what's important again to reinforce is that every single page for purposes of this protocol, this program, must go in as well as every page of the HIPAA authorization.

Now, the reason that I'm bringing this up is that this is not just unique to this program, CDC's IRB expanded access program for TPOXX. This method can be used for VA research studies. It's not unique to this program. But there have been issues with who allows it, or how do I get it done? And I want to reinforce that, again, as part of the Common Rule, and FDA regulations as well; but again, I'm going to speak to Common Rule.

The IRB is responsible for process and documentation. That is part of the approval process of an IRB for a non-exempt study. So what that means is that once the IRB approves that, the – if we're talking research, again, study teams, this is why, again, ORD sought approval for the CDC IRB for this.

The study investigator in a non-incident study cannot just decide, or the, their coordinator, or research team, "By the way, we can't do it this way. We're going to use digital images because ORD talked about it on, on a on a conference call." Again, it cannot be just an act of, "This is what we're going to do with our multiple choices."

The IRB is responsible for approval, of process and documentation, process included. So that is why we wanted to reinforce, again, when you're looking at studies, and you're submitting these to IRBs, and you're talking about how you're going to obtain informed consent, and receive that documentation, if your study team is planning on doing this, it must be approved by an IRB, the IRB of record for the study.

It is something that is done prospectively. We've had a number of incidences here that it's done after the fact. It's, well, we did it, and now we're going to seek IRB approval. As we all know, and if IRB specialists who were in this, you cannot expect, obtain retrospective IRB approval.

In reference to iMED, again, this is a complicated consent document with lots of signatures. And, of course, we are not allowed to adulterate the consent form and that means we cannot change the fields. There is an entire section on exception from informed consent in the CDCs IRB approved consent form.

So, therefore, we have, with working with the the VA iMED team, who is again amazing, they have developed the template for the iMED consent for this program. They have also developed the fields and filled in the fields for the VA Form 10-5345, which is the HIPAA authorization for this program.

We will be deploying this in January. In January we will have a webinar solely dedicated to going through that consent form and HIPAA authorization in terms of going through it. How to access it. It will be a national deployment similar to what was done for the Mayo Clinic's national deployment of their consent form when we did that, I think, it was two, two years ago.

So again, that is coming in January. I wanted to make sure each of you knew about this prior to that deployment. Again, your iMED coordinators will receive an e-mail about the pending deployment of this, and again, the webinar will be planned. I don't have a date for that yet, but I'll be able to tell you that after the holidays.

So now, we're gonna switch gears, and we are going to talk about commercial IRB issues. And again, on the slide are currently three already approved commercial IRBs. That's WCG, Sterling IRB and Advarra. So in the last couple of months there have been a number of issues concerning the master protocol. And all three of ORD's approved commercial IRBs have come back to ORD asking questions, asking questions about whether or not this is acceptable? Why is this happening, and wanting to understand, how can we fix this?

And so I wanted to, again, discuss this because a lot of the changes that are being requested in the master protocol, and this is the protocol – again, what we're talking about is within our commercial IRBs, and, of course, reviewing our, some of our industry-sponsored clinical trials. Not all of them, but those have, that meet the criteria. And they are getting a lot of comments, questions sent back stating that in order to approve the protocol, that these changes must be made in the master protocol, the protocol that goes to all participating sites.

And so these were examples that had been supplied to us by the different commercial IRBs. Please to include language in the protocol that written HIPAA authorization will be obtained from the subjects. Make a statement that VA will maintain records in accordance with our record control schedule. If there's non-Veterans, they have to be given a Notice of Privacy Practice. And these are given examples; in certain protocol, the location of the records to be maintained for the particular VA facility.

Now, these are, none of these changes can be made in a master protocol. That, that's just not an option. Again, these are specific to VA as an agency. They are specific to, and some of these specific to the facility. That doesn't mean that you don't do them. Again, VA is a covered entity. And so, we are going to obtain for example in these clinical trials, written HIPAA authorization from every single subject, but industry is not a covered entity.

And it's very rare in an industry-sponsored clinical trial that you're going to see the language that is required, or that you would expect to see in a VA initiated protocol, or a collaborative protocol between the university and the VA facility. And so that is an issue. And so, again, we wanted to reinforce, you cannot change the master protocols.

But this is another issue, and this is an issue that is a result of, again, it's not a bad thing, but it's it's why there's issues with this. When you look at the application forms that are used by our respective commercial IRBs that are currently approved. And you compare those forms with your own, for those of you who use an internal IRB, or even the VA Central IRB, as wel, are you even use – compare it to your affiliate IRBs, if you're using your affiliate IRBs?

Those applications do not contain the same level of detail, and they're not going to. But that creates unintended consequences. And that is part of the reasons why there is an issue. Because the privacy officers review using the VA Form 10-250. That is required by policy. And so the only way to remediate these issues is to have communication with the study team, the facility privacy officers. So that's why it's, there's, there is issues with this.

And what we're trying to do is figure out a way to create a supplemental sheet, a supplemental worksheet that would be used for these studies requiring utilizing commercial IRB, so that information can be obtained by the privacy officers. Because that is going to indeed be different than when you're using an internal IRB, the Central IRB, or an academic affiliated IRB.

So that is something that we do recognize here, and that we are working on it. Again, Michelle Christiano is ORD's privacy officer. And what, we are also now speaking directly to the privacy officers at this point. And then one of the things we recognize, your tremendous amount of work you do. And again this is a different process than utilize, utilization of internal VA IRBs or of the academic affiliate IRBs.

And so what we are working here on ORD is having a workshop just solely for privacy officers to specifically discuss commercial IRB applications, and issues. Solutions, more importantly, it's not just about, okay, here's the problem. Let's see how we can fix it, and and coming up with ways to make this better so that it makes your job easier.

And again, on some of these industry-sponsored clinical trials, they require, they do utilize the central, central privacy review, but many of them don't. And so this is an issue that we recognize, and that we are working to resolve. And so I wanted you to know, we hear you out there. And we understand the complexity of this and the frustration. And we're all working together to try to make this work.

And so this is an issue which we are working on actively to resolve. Now, what I want to talk about, I'm gonna switch, because that was the major issue I wanted to talk about with commercial IRBs. Is a selection of some questions from our regulatory mailbox that we wanted to share questions and our responses. And again, this is, this is, again, it's something that we think is very beneficial.

So some of these, again, and they're geared toward all levels. But this was, these, again, every question that comes to ORD is a good question. And I mean that by I, I think that, and I always tell people that, don't ever think you're asking…. That, I think Lynn Cates was here many years ago before Dr. Cloe [PH] came. And Dr. Cates, Lynn Cates, had a, had a phrase, "There's no such thing as a stupid question."

And that's indeed the philosophy of ORD. That's in the philosophy of Dr. Cloe. That's the philosophy of, of our CRADO, Dr. Ramoni, Dr. Ramoni, Dr. Rachel. So, here's a question. Our IRB voted on the study to, a study event to determine whether it was an unanticipated problem involving risk to subjects or others?

The vote was tied. How should the IRB handle a tied vote? Interesting, so our response was if a tie vote is not in the SOPs, and a lot of times you won't see that. You will not see, "Well, in the event of a tie, the following is going to occur." But what you do see in SOPs is how is majority defined?

Now, a lot of us use Robert's Rules of Order. And when there is a tie vote, and majority is defined as a simple majority, there is no majority vote. It's tie. That means the motion fails because in order for a motion to be approved, the majority must approve it. However, in many of those cases, what you will see an IRB do is, okay, we have the motion on the table that failed. Can we introduce another motion that will address the issue to see whether or not we can resolve the issue that's needing a vote on, resolve the topic at hand?

And so that is something that you will see a lot of time when you have a tie vote and the motion fails. And you either reintroduce a new motion, or indeed it doesn't get another vote again. It's just, okay, that's it. So that is how we responded to that question regarding a tie vote. And we appreciate the, the the VA facility that sent that question in so that we could share this today.

Now, a lot of questions ORD receives are about informed consent statements. Statements that are, are they acceptable or not? And again, when it comes to ORD required statements, there are very few statements that we put in policy that, this is the language you must use, or this must address a specific topic.

We defer to the Common Rule, and for FDA, FDA's regulations, basic, and elements, basic, and additional elements of informed consent. As again, VA is committed to harmonizing our, the use of single IRBs. So the more VA specific requirements are, the more inability it is for us to be able to, to facilitate that.

But this is a question involving banking, and data destruction for purposes of informed consent. So the question is, is it required to include the destruction date if the specimen banking is not included in the IRB approved consent form? If yes, what is the timeline or duration allowed?

And what I've included on the slide is the section of the consent form that was being asked for, ORD was being asked to consent for, and to comment on. And the sample language states, "Blood samples are being collected from you as part of this study. Future use of samples will be limited to analysis and testing necessary to support regulatory approval for the lung \_\_\_\_\_ [00:45:18] test as described in this consent form." The sponsor will keep his specimens until regulatory approval is obtained or not pursued.

So when you're looking at this section, you see a date. There's no date. There is no 1/2/2026. So is that a violation of the Common Rule, FDA regulations, ORD policy? And what you have to think about before you, when you're looking at this type of question is, what are, indeed, the applicable regulations that apply? Yet ORD policy is silent. Now, in terms of the Common Rule, it's really two key – and this doesn't mean there's not others, but two key Common Rules, Common Rule regulations that will apply when it comes to issues involving informed consent.

And that is, number one, that the subject or the legally authorized representative when they are giving consent, they had to provide you with the information that a reasonable person would want to have in order to make an informed decision. And that is a subjective call by the way. And then the second is involving a basic element of informed consent.

A statement that the study involves research, an explanation of the purpose of the research, and the expected duration of the subject's participation, a description of the procedure to be followed, and identification of any procedures that are experimental. Basically, what are you doing?

So when it came to this question as we evaluated with this within ORD, the answer is that, no. Neither the Common Rule nor ORD policy, require a specific data detection. You do not have to put in your consent form. You have to destroy this on 6/7/1992, or whatever.

But again, this is where, again, the subjectivity is involved. Individual IRBs have the discretion to decide whether or not they wish to convey that, or how they wish to convey it. A lot of times people will see in a consent form, "Your specimens will be destroyed after that date." But, or and they get, or most, they're usually silent on this. So again, dates of destruction are not specifically required.

And I very rarely see outside from the ORD level, date of destruction that is specified, just as usually you will not see on the data side, your data will be destroyed on this date. Again, that's an analogy to use. You don't see that in informed consent forms. Because, again, it actually sets you up for violating the consent form when you put a definite date in there, but you're really not sure whether or not you can adhere to that.

Again, going back to biobanks, there's a lot of questions that ORD receives about banking. And one of the reasons is because of prior policy, or excuse me, prior guidance. So this is a question that not only our ORD receives from different facilities, but also even the Office of General Counsel, our STAR group.

So here's the question. If an IRB approves a human subject study that includes the industry-sponsored banking the biospecimens, does ORD or the Office of Research and Oversight accept the use of the VA, the non-VA biobank? Also, does the VA facility need to track the non-VA biobank?

The reason this question is asked a lot is because of history. And in the past, and this was for over a decade from, like, 2007 to 2017. ORD had this voluntary off-site biobanking waiver process. It was always voluntary, but it was treated by many VA facilities, they made it a requirement in their local standard operating policies and procedures.

And in those policies and procedures that were required under this waiver process, ORD had a, if you got a waiver, if you had a university, and your biospecimens were going over to the university, they can be kept for three years. And if more than three years, you had to come in again for another waiver. For industry, the most that biospecimens could be kept by industry was one year. And then if they wanted to keep it longer, like another vaccine study, again, there had to be a special application.

It was never policy. But that is where this question to this day has arisen from because of those issues, and and beliefs that VA does not allow non-VA biospecimen – I mean, VA biospecimens to be obtained by industry and kept. The issue is about informed consent. That is one thing ORD always wishes to reinforce. And one of the reasons why we, we took this program out as a voluntary program.

Again, if the subjects, the prospective subjects are given the sufficient information to decide, "This is what's going to be done with my biospecimens. If I'm participating in an industry-sponsored clinical trial," then that is up to the subject in terms of that issue. Now, whether or not it's a mandatory or optional biobanking issue is also something that the IRB has to look at.

Now, in the terms of the question in hand, in terms of when the IRB approves a human subject study that includes industry-sponsored banking, whether or not Central Office, ORD, and ORO, we're involved with that use. And that we have to approve it ahead of time, or we have to monitor it. The answer is no. Neither of our offices have a role in approving or accepting the use of these non-VA, these non-VA biobanks for industry-sponsored clinical trials. And your facility is not required to keep a record of those.

But I did want to point out that that does not mean there are not controls in place. It's not just about the IRB-approved protocol. It's not just about the informed consent and the HIPAA authorization. When we do industry-sponsored clinical trials, VA, the VA facility, and industry it execute a CRADA, Cooperative Research and Development Agreement.

Every single CRADA, when it involves biospecimens, also involving data, but always with biospecimens, always includes language that indeed binds the, the collaborator, and their contractors if contractors are involved with only using the biospecimens to the extent permitted in the protocol, and, or the informed consent document.

If they're identifiable, again, we go back to HIPAA. But that is something that, and again, we wanted to reinforce that, while there's no approval process at VACO, again, these, these activities are covered under CRADAs in terms of, there's legal language that binds them to indeed saying, "You can only do what's allowed in the protocol. You can only do what's allowed in the consent." And these are, again, binding legal agreements.

And so CRADA language is, is very important. And with many of our industry sponsors, we have executed model, we have master CRADAs, where the agency and the industry collaborator have negotiated. And sometimes these master CRADAs take a year or two to develop language that is locked in. This is what the two agencies agreed to in terms of binding language concerning these type of issues.

Now, this week is PRIM&R. For those of you who are registered for PRIM&R, ORD, and ORO taped in on-demand session that is available, basically summarizing, and discussing VAs implementation, or the Cooperative Research provision in relation to its use of commercial IRBs.

Yesterday we had office hours for, from 2:30 to 4:00. And there were some technological challenges with the use of the platform that PRIM&R was supplying. So again, we adapt. Everybody that was on that call, Dr. Workman sent up a, a Teams meeting, and we continued our session on the Microsoft Teams. So again, we did let PRIM&R know about the issues that we were having.

But, I think we had a very robust discussion yesterday during office hours. So in terms of, and I wanted to make sure we had 30 minutes to have any questions and answers for, for you to have time to talk to us about this. Again, there is a lot going on. And again, the issues that I haven't discussed here that we're working on. Again, we're going to be changing the format with the next bimonthly webinar.

Again, the focus of these first topics have always been \_\_\_\_\_ [00:54:35], since April has been TPOXX. So that no longer will be the lead topic in these upcoming ones because we're not seeing a lot of incidents of this. And so the focus has changed, and we will again deal with different topics that are important to the VA research community.

Again, the commercial IRB issues, we we work with them actively, and there are a number of different types of issues that we are working on to address, recognizing again, the issues that you're bringing forward to both the Office of Research and Development, and the Office of Research Oversight. And so again, we do work on those. We may not have a solution tomorrow. But please know that when when you bring these issues to us, we are working on them actively.

Again, we try to get these up as quickly as possible, but and for most of the time no longer than seven days. We get these posted to our Cyberseminar website. There is a Regulatory box, of course, that you can send regulatory questions to. We have a number of different references that are included today for purposes of this program today. Again, we always include the references to the CDC's webpage for the TPOXX expanded access program, as well as ORD's webpage supporting this program is well.

And so with that said, I wanted to make sure we were done by 4:00, so we'd have plenty of times. I'm going to stop sharing my screen, which I just did. And then, I am going to open this up for questions and answers from you.

Okay. The first question is as follows: is the VA DocuSign Job Aid applicable to any study, not just the Mpox expanded access program? If not, it seems worthwhile to create a general version that anyone in VA research could use for any VA approved study once the have VA DocuSign approval.

Absolutely, unequivocally agree, the VA DocuSign Job Aid that is posted on ORPP&E's, PP&E's website page for this program is indeed specific to the CDC program for TPOXX. However, what is important for all of you to know is that VA research is one of the biggest users of VA DocuSign. And as a result of that, they are very much wanting to work with research to help facilitate. So that's why the feedback we get on these tools are very important.

So we absolutely, that is phase two of this. We wanted to see how this worked. You're absolutely correct, there are a lot of technical issues involved with you, use of VA DocuSign. That is indeed a product that we are planning to release. It has to be generic, like you said, but that is indeed the second, the second version of this product which we are planning to have a release on. Thank you for your question.

Well, this is a great question. Thank you for that, whoever submitted this. So any IRB, even local can approve a photo of the ICF HIPAA being e-mailed back non-securely to the PII for any study. Okay. Again, it's the IRB, again is in charge of, by regulation for approval of the process, and documentation of informed consent. And again, one of the reasons we did discuss this today is to say this is an accepted method by the agency to allow this to happen; and again, what must be conveyed to the prospective subject when this occurs.

So is it unique to this protocol? No, it's not unique. It can be used for other studies. And that's indeed absolutely, this reinforces why we brought this up. It can be used in VA research, but again, it must be described, it must be prospectively approved by the IRB. The answer is, "Yes."

Don Workman: Karen, Karen, this is Don. If I could just add?

Karen Jeans: Please.

Don Workman: It has to be IRB that approved the study. So for instance, your local IRB cannot approve a deviation from the expanded access protocol that requires CDC IRB approval, over.

Karen Jeans: Thank you. That's a very important clarification. We want to make sure we're very explicit on this. Yes, the next question? A lot of logistics that Karen described for the TPOXX expanded access program can be overcome if patients want to go into the study. STOMP is setting out to allow patients to go into the study remotely. That is what we have, and ORD has heard. I am indeed waiting on more instructions on that, so that is true.

Can this be added to the VA facility endorsement letter as a checklist perhaps? I'm not. I apologize. I'm not. I'm not, I'm unclear what this is. If, if you can specify what this is, I will be more than happy to come back to the question. And, yes, we can always – we can redo those endorsement letters. We can revise those to meet the needs of of the sites. So give us a an, an indication what, 'this is,' and let's come back to this question. The next question?

For commercial IRBs, we have some issues with our local radiation safety review, and they wanting changes in the consent. How should we handle that? This is a really important question because if the radiation, your local Radiation Safety Committee wishes a change in the consent form, that, again, this is where it's an all or none. Is it absolutely appropriate to inform that the the, the applicable commercial IRB, that's the IRB of record for the study? Yes.

There have been issues that our VA facilities have picked up. And so I want to make sure and reinforce that just because it's a commercial IRB study – excuse me, an industry-sponsored clinical trial, does not mean that there is not a point of questioning. So that should indeed, that that question, and that issue should indeed be sent back to the applicable IRB that's sought. And then depending upon it, whether or not that change will or will not be adopted for all sites is up to the IRB.

And here's the bottom line. If, if they don't change it and and your site feels that it is not something that your site can accept that this indeed is contrary to the Common Rule. This is contrary to patient safety. This is not consistent with the basic elements of informed consent. Then that is something which Dr. Workman and I would very much like to know about, so that we can indeed, follow-up with the commercial IRB.

It is not uncommon for us to go back to commercial IRBs and ask, "Okay, well, what was your thinking on this?" We don't. Again, they are the IRB of record, and we're not there to, quote, question their decisions that they have authority over. But at the same time, if there is an issue that's there, we want to raise it. So you always have the ability to go back to the commercial IRB and say, "Okay, we're seeing this. Why is this not there? Can you please address it?" And if you don't have an appropriate response, you can please feel free to contact Dr. Workman and myself. The next question?

And how do we deal with sponsors who submit to the commercial IRB, but we at the local site are unable to view the documents that have been submitted? This is an issue we have had with WCG-IRB.

I am going to need some…. So I think if you can e-mail Dr. Workman and myself with some specifics? Because we're gonna – I don't know if we're talking about amendments or not? But if you can let us know? One of the things that we do is if you \_\_\_\_\_ [01:03:53] these IRB s, and so this is an issue that we would, number one, if you're having issues with WCG, you are more than – we have liaisons at every one of these.

And ADVARRA, \_\_\_\_\_ [01:04:06] and Sterling who were assigned to deal with VA issues. And so, number one, if you're not, if you're not coming, if the WCG, and IRB has not given you a response, please let us know about it so we can try to figure out what's going on as well. And and Don, do you have anything to add on this?

Don Workman: No only that there are times when sponsors submit things like amendments, and they don't go through the VA first. And that can be problematic. But certainly when something gets approved by the commercial IRBs, the documents that are approved should be available. to the local VA site. Otherwise you can't implement. So, again, I, I'm happy to learn more the details about what the concern is. Over.

Karen Jeans: Thank you, the next question. Regarding the statement on the CDC website about using CDC IND only if a STOMP site is geographically unavailable. We are a CDC IND site, but there is a STOMP site approximately a mile from our VA. Should we treat patients here rather than refer them to STOMP? Again, this is an issue, why when this came out with the protocol revision, it was unclear to all sites that are not STOMP sites, what it meant by referring them?

And also, to prevent the, to be careful in terms of are we recruiting, are we referring? And also, if we're referring to a non-VA site, what happens if there is an injury? Which is, by the way, covered under the PREP Act. So, this is an issue when I last spoke to CDC about this, that it is, you can indeed tell them that there is a randomized clinical trial that's being conducted at, for example, let's say, university.

You can indeed tell them this. But if they wish to be in the expanded access protocol since it's not available at your site, you can still put them under the expanded access protocol at your site based upon the current \_\_\_\_\_ [01:06:31], the current information that ORD has received from the CDC. The next question?

Are clinical personnel who are performing clinical procedures in a patient care area required to be listed on an IRB/RDC application for a clinical trial. For example, blood draws by pathology lab personnel? The answer is, "No," because they are not conducting activity which would make them constitute being a study team member.

They're not, they're not involved in the conduct of the study. They are providing a service as part of their usual duties. But that is not being a member of a study team. The next question?

Okay the original, this is about can, could this be added? I appreciate the person writing back. Could this be added to the VA facility? Endorsement letter, as a checklist, perhaps, but this in my prior question. It was in reference to the statements that VA facilities asked to be added to the industry master protocols under commercial IRB oversight. I thought perhaps the supplemental sheet Karen proposed, and the facility endorsement letter could somehow be combined for efficiency.

This is an issue, this is in relation to the privacy. The privacy questions that we need to make sure that we can get when the applications don't contain enough in the commercial IRB materials for the privacy officers to conduct the reviews that are required under 10-250, the preliminary reviews.

This is an issue, again, that we are going to be focusing on. We will, we will indeed, look at all options. And again, I want to ensure that, if you're a privacy officer in the call, on the call, you're going to be part of the solution. We are not going to do this independent of you. So please know that we will be following up with you. Thank you, the next question?

Brandon Alexander: I'm still waiting for some more questions to come in, so.

Karen Jeans: Okay. And again, we we wanted to make sure there's plenty of time. Again, if there is no questions, we'll, we will, we will end it early. But I will at this point say that just in terms of one of the common issues in terms of questions that I received probably 100 times a month is about DUAs and MTAs.

And when is ORD going to release the research specific data use agreements? We are, very soon you'll be seeing a posting for our agreement manager who will be working, of course, for us here in the Office of Research and Development to help us get this through the finish line. We're about 90% through with these, but we do need to… As you know, it's not just about issuing the templates. It's about issuing guidance, and coordinating with the other division, including OGC STAR.

And so that is coming very soon, again, and you will see that position posting. I am desperately hoping to see it within, like, days. So I did want to make sure and address that. It is a major issue. It is an issue that I work with many of your sites on data use agreements. And as we all know, in the last five years in particular, we've seen a proliferation in the use of data use agreements, as well as the MTAs.

Because I think there is a better understanding and increase the importance of the institution to be able to use these agreements to, to to do accountability. To state what is going to be done, and also what comes back to the agency when that's applicable?

So that is something that I wanted to make sure that you all are all aware of is in process. This is not just things will continue the way they are. So that is coming again to address this critical need for the research community. And Brandon is, there's not any more questions?

Brandon Alexander: Yeah and there's no more questions coming up.

Karen Jeans: Then, then I'm going to go ahead, and again, valuing your time, say thank you very much. I want to thank our panelists who have also joined today. And thank you very much for having, coming today to this webinar. I hope all of you have a wonderful holiday. And –

Unidentified Male: Karen, Karen –?

Karen Jeans: Yes.

Unidentified Male: – If I could just interrupt you for a second?

Karen Jeans: Ask away.

Unidentified Male: There's one more, one more question in the chat.

Brandon Alexander: Yep one more.

Unidentified Male: And it says a person with a dual appointment at VA and university wants to interview Veterans about satisfaction with the VA Whole Health Program. The research, the researcher hopes to record the conversation on VA Teams. There it is. I'll let you finish reading it.

Karen Jeans: Okay. So the question is, a person with \_\_\_\_\_ [01:11:51]at VA and the university wants to interview Veterans about satisfaction with the VA Whole Health Program. The researcher hopes to record the conversation on VA Teams and bring the recordings to the university to transcribe for qualitative analysis. Is this researcher QI?

Well, first of all, I want to see, there's, there's, there's some interesting words here because it's not a researcher. If it's QI, it's not, it's not a researcher. And that's one of the things, that just because we use the word, "research," doesn't mean it's research. But again, what is going to be done?

There is insufficient information based upon these sentences to, to say whether or not this is research or QI? The question I have is, okay, they want to interview Veterans about satisfaction with the VA Whole Health Program. Okay. How is that data going to be used? Is it to be used internally within the agency to look at the, again, to be used for internal purposes? Or is indeed, is this intended to be used for development of generalizable knowledge?

So at this point without more information, it's impossible to state whether or not this is research or QA based upon the information provided. If anyone else wants to add on the panel, I welcome their comments.

Don Workman: Hey, Karen, this is Don. I I just would add, I mean, I I would at least add, ask some more questions. Because the university is not engaged in quality improvement for the VA. So it, perhaps there's some group of people at the university, be it the quality improvement individual who wants to use, but again, like, there would need to be a real good reason for the data, the information coming over from the VA to the university for qualitative analysis. Over.

Karen Jeans: Agree, the question, of course, I have is, that it's talking about. Are they using them as a service? And is that where the transcriptionist is? So there's, as as Don has said, there's a, there's questions here that need to be answered. So where specifics are needed on this one? It's a really good question. It's a great example of where, this is, a lot of times, this is exactly what you're given. And there's not enough information but someone who wants an answer. Again, additional information is needed.

Okay so, again, unless something comes in in the next 15 seconds, I'm gonna, I'm gonna call it for today. And thank you all for joining. And thank you very much. And I hope you have – see, see everybody in the next New Year.

[END OF TAPE]