Karen Jeans: My name is Karen Jeans, and I’m the director for Regulatory Affairs here in ORPP&E within the Office of Research and Development. And welcome to our webinar today.

 This is part of a bi-monthly series that we started a few months ago, 60 minutes long, where we take some topics and we do a discussion of those. And also, leave plenty of time for questions. So we are going to be talking about the expanded access use of tecovirimat. I’m going to call it TPOXX. It’s a lot simpler for monkeypox. But this is not—I want to say it right now. This is not the detailed webinar that we will be having on Friday to go into a lot of specifics. Now, I’ll reference that again later on.

We’re going to talk about the NCI. The NCI IRB communicates regularly with the Office of Research and Development and the Office of Research Oversight. And they had some issues that they would like to convey, and then also some problem-solving. And this is what this is about. So that’s the topic we’re going to discuss. And also, something that’s a continuing series we started with every one of these, and that’s commercial IRB issues and resolutions. And these are questions that Dr. Workman and I receive, are from you, from Advera, from WCG, from Sterling, or that Sterling is receiving. And our goal is that we share those with you all. And so that if you have a question, it’s probably everybody else is having the same thing, too. So these are ways to convey this to you, in this type of 1-hour format.

 So I’m going to jump right in and start in with our section, which is, again, not the specifics of getting into the detailed seminar. We will on Friday. But to go into our discussion of, basically a high-level discussion, of TPOXX and what we’re doing here. And this is an expanded access program involving a use of a drug called TPOXX. That’s the generic name for monkeypox.

Everybody has been like, what is monkeypox? So very briefly, it’s not so far a high disease, a disease like COVID. It’s a rare disease. It’s caused by infection with monkeypox. And this monkeypox virus—and I am not a poxologist, by the way. That’s a specialist who specializes in this field of medicine, which is amazing. But this virus is in the same family of viruses, like your variolas, which is the virus that causes smallpox. And that’s important here, because of why we’re using TPOXX.

Now, when you think, I just said “smallpox,” doesn’t mean you’re going to have the same symptoms as smallpox. They’re milder symptoms, generally. It's rarely fatal, and it is not related to chickenpox. And this information is from the CDC, Centers for Disease Control.

 So in terms of when this started—what was the origin of monkeypox—it was actually discovered in 1958. That’s how it got its name, when two outbreaks of a pox-like disease started in these colonies of monkeys. And that’s how it was nicknamed, the tradename monkeypox. But even though it’s called monkeypox, we really don’t know how did it really start. But this is how it all began in terms of our origin of that name. And on here, again from the CDC, Centers of Disease Control and Prevention, these are some examples of the rash that is associated with monkeypox. And again, the symptoms usually last for about 2 to 4 weeks. That’s its progression. And that’s what we’re dealing with here after seeing this situation happen.

 Now, monkeypox—and I’m sharing this very interesting location here in terms of the website at the bottom. The CDC, on their website, maintains a map of the incidences across the entire United States, state by state. And so as of yesterday, our total count was 3,591 across the country. I promise you that has changed, even as of today. And if you go to that website, you can go state by state and see the state incidences, the number, and it is updated on a daily basis.

 So now, we’re going to do a discussion, a little bit about what is TPOXX. It’s tradename—and I am pronouncing it badly—is tecovirimat. And it’s a medical treatment measure for the treatment of monkeypox. Now, again, it’s tradename is TPOXX RST246. Now, TPOXX is an approved medication. It’s approved by the Food and Drug Administration for the treatment of smallpox in adults and children. Now, we know that it has efficacy with smallpox. We really do not have the data at this point to know how effective it is for monkeypox. But based upon studies with animals, we—FDA I should say—is seeing efficacy.

 And so because of this, Centers for Disease Control, in conjunction with FDA, have obtained what’s called expanded access protocol. And a lot of times you’ll hear the word, “compassionate use.” That allows us the use of this drug, TPOXX, to treat monkeypox during an outbreak. And that’s exactly what is happening right now. And TPOXX is available as a pill, as you’ll see it in this picture here, but it’s also intravenously available.

Now, again, for the purpose of today’s discussion, again, we’re high level here. And one thing, you’ll see me, when we’re using the word, “expanded access.” And we use the word, “IND.” Well, it’s approved for smallpox. Again, TPOXX is not approved for the treatment of monkeypox. So for those purposes, it’s considered to be investigational.

Now, we’re not doing a clinical trial here. But the CDC has an IND, an Investigational New Drug application, under the expanded access use, that allows for the use of this TPOXX for this monkeypox infection in adults and children through a protocol that they have designed. That allows multiple other institutions, health care providers, to be able to administer this under the expanded access regulations. And these regulations are from the Food and Drug Administration. One doesn’t just get to access it and start treating it. It is subject to FDA regulations. And the name of the CDC protocol, that this is being done under their IND, is Use of TPOXX for Treatment of Human Non-Variola Orthopox Virus Infections in Adult and Children.

 Now, when we use this word, “expanded access,” it’s one of the pathways for use of drugs and biologics. We have ways to approve drugs and investigational drugs. Investigational drugs is exactly what TPOXX is for the treatment of monkeypox. And again, for the purpose of this, you have a slide that shows the different ways we do this. And under the investigational drugs and biologics not approved, when you see this commercial and non-commercial, those are your clinical trials, or your comparative effectiveness studies. That’s not what this is.

 This is called expanded access. And it is, again, a pathway for getting access to investigational drugs or biologics for treatment outside of clinical trials. The CDC protocol is not a clinical trial. But it does require IRB approval. And again, when you look at these four different pathways—a great example of each is your traditional clinical trial, your commercial and non-commercial INDs, your expanded access IND—that includes convalescent plasma for COVID-19, remdesivir was under expanded access. But a lot of times these move, just like convalescent plasma, to something called an EUA, an Emergency Use Authorization. That’s also still investigational, but it doesn’t require IRB approval. It’s a different type of situation, again, controlled by FDA, approved by FDA—a different scenario. And then right to try is a different type of category that is unique.

 Again, we’re focusing today only on one category for purposes of this discussion, which is expanded access IND. And when you use that term, again, there’s so many types of expanded accesses. All of these are under the Food and Drug Administration. There are specific regulations in 21CFR at 3-12 that covers these. And this is, again, from the Food and Drug Administration’s website. If you want to read a detailed discussion of each of these by FDA, again, there’s a reference at the bottom of the slide that you can link to.

But this is an intermediate size population IND. And what that means is that, with each person, each treating clinician who uses this TPOXX for monkeypox, they don’t have to apply to FDA for their own separate IND application, their own separate application to be able to use it. It’s all coming under the CDC’s investigational new drug application that they obtained from the Food and Drug Administration as part of this national response of this monkeypox outbreak.

 Now, again, Friday we’re going to be going through this much more in depth. But there is a lot of confusion, especially when we look at what happened with COVID. And a lot of times, the confusion is trying to extrapolate that to what you’re dealing with today. Again, when we started with the COVID-19—and this is why this is a good reference for thought. When the first drugs that were available under emergency expanded access was remdesivir. And in that, when we first started with remdesivir, it was under emergency access, again, an IND, individual. Any treating physician who ordered it had their own separate IND from FDA. Because it was emergency, COVID life-threatening, it was authorized under that type of IND, did not require prospective IRB approval. The VA did not require R&D committee approval. The reporting goes after it’s given. It was seen, as required by the IRB, to be notification to occur from the clinician who’s administering the drug within five days after the beginning of the initiation. But that’s emergency.

 What we’re talking about today with TPOXX is an expanded access IND, but expanded access for treatment, intermediate size. And this type of IND program, prospective IRB approval is always, always required—no exceptions, because it’s not emergency. In terms of VA, R&D committee, approval is required. It can be done by designated review, but it is indeed required. So that is in terms of the basics of the regulatory structure. And again, we’ll go much more into detail on Friday. That is the biggest difference between emergency and non-emergency expanded access use. For the purposes of the IRB structure and the IRB committee structure.

Now, specifically on monkeypox. We established very quickly—we’ve been negotiating with CDC, and everything fell into place last Thursday. The Centers for Disease Control IRB has agreed to be the IRB of record for VA facilities who wish to rely upon them for this specific expanded access protocol. Now, a lot of confusion here. And what’s already caused confusion is, again, expanded access is not research under the common rule. It is a treatment protocol. It is designed to give an investigational drug under FDA’s expanded access regulations outside of a clinical trial for this treatment purposes of a specific disease, in this case monkeypox. And the reason, again, it’s not research under the common rule, it is not designed to develop or contribute to generalizable knowledge about monkeypox. It doesn’t have real strict inclusion criteria. There’s not a lot of data collection. This is about treatment of patients, to get them access to this investigational drug. But there are specific regulations in line with it, because it is investigational.

 So indeed, it requires—it is a non-emergency—prospective IRB approval. And as part of that, IRB-approved informed consent. And the CDC is the IRB of record for this. When you’re relying upon the CDC IRB, which we expect a large number of VAs to, that IRB informed consent is the informed consent that must be used.

Now, this is evolving as we speak. Again, we’ve very rapidly, as we’ve established this alliance—you’ve seen two emails from me across the VA research community already just this week, and today’s only Wednesday. You’ll see probably another one very soon. Yesterday, we went through, here are the steps. And again, we’re still trying to develop some of the things that need to be done to support this. Just like with convalescent plasma, just like with remdesivir for COVID-19, these programs evolve rapidly. And steps will happen rapidly.

 Yesterday evening, I put an announcement out that we would be establishing a web page. That website is already up and running. And literally, as soon as this is over, I’ll be putting up multiple forms that are populating this. So I did want to let this group know, it’s already up.

Again, the details of all the specifics in terms of different issues related to this alliance agreement, we are working with different program offices, especially pharmacy and iMed management. We hope to be able to put this all together in terms of procurement issues. But also, more details into the specifics of the informed consent. Our progress on different aspects are in that description of the steps required to rely, support where we are with DocuSign, iMedConsent—a lot of different components. That will all be discussed on Friday. I’ve included on this slide, if you have not seen it before, the registration link. It will be from 2 to 3 o’clock Eastern this Friday. Just like with our other types of expanded access protocols, we’re getting way too good at this in terms of seeing a lot of these.

We will indeed be having numerous guidance documents to support this, FAQs. We are grateful to the Office of Research Oversight. We could not be doing what we’re doing right now with the CDC IRB alliance without them. And we are grateful to them. And so again, our objective today is not to go into a full discussion for this. But this is to give this audience—this is a general overview of where we are. Please come and dial in on Friday. It will be taped, just like this one. But again, the website, we will be putting everything on there to support this as we can. And that is where we are with this broad overview of this reliance that we are seeking, as we are hearing more cases come across the system for monkeypox. And we indeed are striving to give the best possible we can, care we can, to our veterans.

And this is, this slide, a picture of the website page and the location. You’ll also see this in the references. I do plan to send probably another email out to the research community, again, to let people know the website is up and running earlier than we expected. And we’re grateful for that as well.

Again, this is an update. And so we take different topics, short bursts, so that if you don’t want to hear that part in your NCI. We have over 40 sites in VA that rely upon the NCI CIRB. This is not a small number, and we hope to get a lot more VA facilities relying upon the NCI CIRB. We are fortunate to have such really wonderful individuals, who are basically our concierge there. And this year alone, we have gotten some really wonderful people, who not just say, OK, there’s some issues. Let’s see how to solve them. And so this is a follow-up. And we will include in this bi-monthly webinar information about the NCI CIRB as we need to, since we do have a large number of VA facilities relying upon this.

 Now, with the NCI CIRB staff contacted the Office of Research and Development, they are not tattling. They are not saying, hey, whoa, whoa. They’re saying, you know, we’ve got a problem. Or we have some issues. We never use the word “problem,” by the way. But we are having issues with more than a few VA facilities that are having issues with two different things.

 Number one, is completion or revision or updating of their annual signatory institution worksheets. And also, their updating other boiler plate informed consent language.

And so I and the NCI CIRB discussed different strategies. And there’s just some general points that we want to emphasize, because we don’t want it going back and forth. Your time is valuable. And so if we can do something to help facilitate this, we are. And so as part of your handouts today, again, is a copy of the annual signatory institution worksheet. So even if you’re not a VA facility yet using the NCI CIRB, you will indeed know what we’re talking about here.

 And it’s not a long form, as you can see. But it has specific questions. And there is just a continuing issue with the completion. And it’s not all, but it’s more than a few, of these worksheets being rejected not just once, twice, three times—maybe up to eight, as was conveyed to me recently, for different reasons—involving content or just the pure technical aspects of it. And so as part of this webinar today, again, we wanted to reinforce, when you look at these questions that are on the signatory institution worksheet, that these are the most four common issues that the NCI CIRB administrative staff are seeing as causing delays or them to be rejected.

 If a question on the signatory worksheet requires a response, it needs a response. It can’t be left blank. A big one also is that responses must be relevant to the question. You’ll see an example of what I mean by that in the next slide that’s going to be associated with this.

 Something also that we wanted to point out is that a lot of times the notes, they’re being overlooked. And it’s not because of anything bad. It’s just that they’re being overlooked. There may be numerous notes. Four of these notes that are being reviewed, but not the other two. And so it’s a simple matter of, OK, I thought I—I missed one. I missed two. I missed three. But that is happening. And the NCI CIRB has informed ORD that they also send them by email to try to basically double cover the ability for these things to be seen, but they can get overlooked. But that is an issue that is happening repeatedly that is causing issues, resulting in rejection of these signatory institution worksheets.

And then also what I call more technical issues, and that’s the last bullet on this slide. Where the reviewer rejects it, but they have notes saying, OK. We need more information regarding this. And another note is being added instead of putting the response in the original note. And so that is, again, a more technical issue that the NCI CIRB wanted to convey that’s causing issues. And again, everybody is wanting to do the same thing. Let’s get these done. But these are problems that are causing issues.

 And on this one, this is an example that was provided to me. Where on the annual signatory worksheet it asks: What is the age of majority in your state? And these are three example responses. One was, “Refer to the VHA publications.” One was, “We’re a federal institution.” And one is, “It’s going to be up to the NCI CIRB.” The question is, “What’s the age?” That means a numerical response is required. And this is an example where the responses don’t answer the question. And so it is indeed important to see, what is the question asking?

And also, then, on a related issue is not only the signatory institution worksheets, but this is something, an issue, that, again, we brought up in the first of this seminar series. And it's about the boiler plate language. This is the issue that continues to be an issue for the NCI CIRB. The NCI CIRB and VA have worked together to develop the boiler plate, the language that is to be included in VA consent forms. And we put this into a table. But again, more than a few sites, instead of changing the actual consent, the boiler plate, they’re just uploading the guidance document—the table that was developed with the NCI and VA. That’s not an option. That’s not what’s supposed to be happening. And then, of course, the NCI CIRB reviewers send it back. So again, the guidance document does not get uploaded. It’s the information in the guidance document that is to be used.

Another very, very common example that was conveyed to ORD by NCI is that the required fields are completed on the boiler plate itself. And so at the bottom of the slide, it has places to insert the VA facility name or insert a phone number. And when they’re coming back for review through the NCI CIRB, they’re not present. Those lines are still blank. And so those indeed require filling in.

 And so again, as part of this discussion, we want to reinforce, do not upload that form as your NCI CIRB VA facility boiler plate. That is not the way to do this. So I put a big red X there. Don’t do it. Resist the temptation.

 But also, this is again where the NCI and VA—again, it’s not just saying don’t do something. Well, let’s figure out a way to make it work. So as part of documents that were uploaded to the ORO, ORD, NCI, SharePoint slide that is used by you, the NCI CIRB gave us a template, a VA boiler plate language sample template, that you can use, again, to facilitate. And we greatly appreciate them for doing that. Word of warning, though. As was conveyed by the NCI CIRB, we don’t have an issue with using the language in this template, but do take the comment boxes out. And you’ll see this comment box on your slide. This is an example of VA template. Don’t send this with any comment boxes. And indeed, to make sure you include your specific site information.

 So we think this is—again, anything we can do to help is going to make things easier. And so this is, again, available on the SharePoint site. And these were uploaded. And if you go to it today, you will find them both on there. And on this slide, you will also see where it is located, not only the SharePoint, but also how to find it on ORD and NCI CIRB web page.

So now, moving to the third part of this webinar, we’ll end before question and answer period with actually questions and answers related to use of commercial IRB by VA. These are questions coming from sites. Questions coming to ORD from other sources. But also, questions coming from the commercial IRBs themselves. So we have six questions today. And again, this is actually a really good question. Because it does cause confusion. And the question is: Are the VA consent forms approved by the commercial IRBs required to be on the VA form 10-1086? And the answer is no.

But the reason I really appreciate this question being conveyed today is that there are many perceptions that ORD requires use of 10-1086. It doesn’t. We do not require that whatsoever. Now, your VA facility, Human Research Protection Program, may require it. But again, when it comes to—let’s say your facility is relying upon let’s say Avera. Does that mean Avera has to use the 10-1086, because your VA facility policy requires it? The answer is no. So while your local policy may require it, part of the master agreement between the Office of Research and Development and the commercial IRBs is that they must follow VA national requirements. But they are not required to follow local facility policies that exceed those of national requirements. Otherwise, it would be—they can’t follow 107 different—107 I think we are right now—different local specific requirements. So that is why they don’t follow your local-specific requirement for use of a VA 10-1086 if you indeed, as a local facility, require it for yours.

 The second question is really a good one concerning non-profit corporations. And I think a very—and this came from one of the commercial IRBs. And so a VA facility was conducting an industry-sponsored clinical trial with funds administered by the VA non-profit. Yeah, industry funds—major industry company. OK, and of course, the IRBs and ORD approved commercial IRB. And so the question came up, because of some other stuff that was going on, in terms of, hey. Do we need to put the approval letter that the VA non-profit corporation is also covered by this IRB approval? They’re administering the funds. Well, the answer is, no.

 Again, this goes back to the VA being a common rule agency. Now, under the common rule, and the way VA implements the common rule, is if an entity is receiving or administrating federal funds—such as an NIH grant, DoD grant, Department of Defense, Department of Energy—then that entity, such as a VA non-profit who is administrating the funds for a non-exempt human subject study that, again, requires IRB approval, then it is also considered engaged according to the common rule. But when it comes to a VA non-profit who’s administrating industry funds, that’s not the same thing. It's not subject to the common rule. And VA non-profits do not conduct research. They support us, thank goodness. But they actually don’t conduct the research itself. It’s the VA facility that conducts the research. So that is why, in this example, in this query, for an industry-sponsored clinical trial, the non-profit is not covered by IRB approval, because it doesn’t need it. They’re not conducting research. They’re not administrating federal funds. So therefore, that is why they are not required to be covered by an IRB.

Next question, number 3 of 6. This is about—oh. See, I did not get the titles right in this. So I apologize. In the set that will be posted, the titles will be correct. So I apologize in advance. So this is about the facility wants to amend the protocol. Again, you have a multisite industry-sponsored clinical trial being overseen by one of the ORD-approved commercial IRBs. So they’re looking at the protocol very well, very good. And they’re going, you know what? We’re going to do this, and we’re going to do this. We’re going to change our recruitment strategy. We’re going to do a little more than this, but we’re not covered in this. But we want to change the master protocol. So we want to amend the master protocol to put our site-specific request in there, because we’re going to do a recruitment strategy. And we’ve got to have IRB approval for it, because it’s not covered. But we think it should go in there.

 And so the question becomes, can you, as a VA facility, change the master protocol? And the answer is, no. You have two choices in a master protocol. You either join it or not.

Now, you can do a local site amendment. That’s possible, and that’s what’s commonly done. You’ll have a protocol that’s, for example, don’t by industry. And you’ll have a site-specific change that you want. So the entire protocol doesn’t change. And think about it this way. You have a protocol that’s being done by 200 sites. So if you had 200 sites that were putting in each of their specific—let’s say each of their specific ways they are going to do information security, or how each of them are indeed going to do different recruitment strategies. That would be impossible to keep as a master protocol. You would be changing that master protocol probably every week. And that’s why the master protocol doesn’t change, unless it changes for all sites. When it comes to site-specific amendments, again, those are specific to a participating site.

 So that’s why this is the way it happens. Because if you change the master, it affects everybody. So that is why this—and this was a very good question and something that we wanted to make sure we cover this month, because it’s a common question. And so that is why this question is being asked.

 Now, this next question is a variation on that. Now, again, it’s about the way master protocols, these, again, multisite clinical trials are approved. And again, we are a VA. We’re primarily adults. But many of these protocols—such as TPOXX even. TPOXX, that expanded access protocol, is for adults and children. Now, in VA, it will not be for children. We do not have a children’s population. But many institutions that will join onto that will have children.

 So there was a study that, again, commercial IRB had approved a multisite clinical trial. And as part of their approval, they go ahead and do a subpart B and D determinations for children and pregnancy. And so they came to several VA facilities. And the VA facilities came back to the commercial IRB and said, we have the approval letter. We have the approval letter for our site saying, you have been added to the protocol, IRB approval obtained. But we’re looking at the master letter, the letter for the approval of the protocol. And it says that it’s approved for subpart B and D determinations for inclusion of pregnant subjects and children. We're not doing that. So we need our letter to be amended.

And so is the commercial IRB required to remove that? And the answer is, no. Well, it is indeed your site may not be doing that. This IRB determination in terms of its approval of the protocol itself for all sites that are participating is, again, at the protocol level. It’s not the specific site level. They approve your site, but that protocol is also approved at that level. So it is indeed appropriate to keep that letter for the protocol content in it with a determination regarding subpart B and D. Again, I will correct the typos in this in the slide set that is posted.

 Question five. I’ll say it’s no, no, no, no, no. Well, here’s another no. Can a VA facility rely—this was, again, asked of one of our commercial IRBs—upon one of the ORD approved commercial IRBs, and its primary IRB of record, and cover all of its stays? Not just multisite studies. The facility had a great idea. They know the process. They liked working with this particular commercial IRB. And they think it’s a really good idea. And it’s no for several reasons.

 Number one, our policy doesn’t allow it. It’s only to be used for multisite research. But commercial, independent IRBs, there is money involved. Now we, as part of our alliance agreements and our master agreements with them, again, we do this when someone else is paying. But this is not something that—they’re not going to review 70 student research projects. And so this isn’t an option. So that is why, again, the commercial IRB contacted ORD, because the facility had contacted their marketing firm and contract group about looking at that option. And they knew they had to contact the Office of Research and Development. So just to clarify, no, the commercial IRB cannot be your primary IRB of record for all research. Only that which is cooperative research in which another party is providing the payment for the services for the use.

 And then our last question, before we go to questions and answers. And this is a yes, by the way. So I said no up till now. So this is a yes. And I really wanted to include this as the last one to make several points. So there was a clinical trial. And these are actual questions by the way. So these aren’t made up. And that’s why they’re even more important. Because these represent what is actually being asked.

So a clinical trial was being done in a VA facility. It received approval from one of the commercial IRBs. And the investigator was looking at the approval letter. And he was looking at it. And he looked at it. And he looked at it several times. And he said, I cannot find in that approval letter where it states that they approved the VA informed consent that is supposed to go with this. And he asked some people. And he was asking his office, and he did not go to the research office. He was just asking people around him. And some people were telling him, well, you know, it’s a commercial IRB. You know they do it right. Don’t bother. Oh, it’s fine. I’m sure it’s OK.

And so he wrote an email directly to Dr. Workman and I. And he says, if it’s OK, can I contact the commercial IRB? Because I’m not sure this is OK. And some people were telling me not to worry, but I think it may be a problem. And I said, of course.

Now, we do ask that you copy the ORD and your liaison to let them know that you’re querying. But it is OK to ask. There is some—and I’ve noticed this in the last few months. A belief that, well, they’re a commercial IRB. So they must do everything right. None of us are infallible, not a single one of us. And so I tell people, if you can’t find something—and in this situation, he could not find the documentation that it was approved—yes, query. Because at the end of the day, it’s the investigator who is going to be held accountable under FDA regulations for not obtaining IRB approved informed consent. And in this situation—so you will know the aftermath of that—he was right on. He was correct. When he went back and queried, again, professionally, he said, hey. I can’t find this. Indeed, they went back, looked at it. It had been missed.

Again, that’s an electronic system. It shows you nothing is failsafe. We produce all these quality checks we can. Things are going to happen every now and then. And then, we do something to prevent it from happening again. But again, the point of the story here is, it’s OK to ask. It is all right to query. And again, we do want you to indeed include your liaison so they will know that you’re contacting them, and what the kind of questions are. And then also feel free to contact Dr. Workman and myself if you have questions. We’ve answered a lot of questions in the last month alone about processes, and many are related to the questions we are here today asking. Can we do this? And why are we doing this, particularly when it comes to the issues involving the 10-1086, local policies? Again, as I said before, VA is truly leading the way when it comes to federal agencies and utilization of commercial IRBs, but it is a growing pains issue. It is learning each other. And we do indeed, when we see something, go right back and say, this is not OK. Or this is not right. Or this is a way we could improve communication. Or this is information that needs to be conveyed. So your questions help us and help them, because they do want to always do things right. It helps everybody.

 So in terms of what we’re looking at here, you absolutely—again, we’re the webinar on monkeypox that ORD is sponsoring will be held on Friday. But even the website is up. And even more updates will happen on a rapid basis, as we do anticipate that just like with the COVID-19 therapies under expanded access. And again, we will continue to work with our different IRBs—with the commercial IRBs and the NCI CIRB—to improve communication. It is about getting things out there, not just saying we have an issue, of how we fix things and how we can make it better.

 Again, as with all of our cyber seminars, we will have these posted. On this page, you will have a number of different references you will have available, including the location of the newly posted ORD web page on the CDC’s IND program for TPOXX. And so with that, I thank you. And I’m going to stop sharing my screen, Parker. And so Dr. Workman is joining me today on the panel. Thank you. And we will get your questions.

Parker Cunneen: It should be coming up momentarily. You guys can see the first question.

Karen Jeans: And I will read the questions out loud. So the question is about tecovirimat. I don’t understand the information provided by HIPAA authorization. Why is it up to the sites whether to get signed HIPAA or not?

Well, again, we’re dealing with recommendations. Again, HIPAA is, under this program, expanded access at the current time, it is not research under HIPAA. It is treatment. However, as we stated in the guidance, we did the same thing with the Mayo Clinic. It is strongly recommended—it is recommended to get that HIPAA authorization.

And so we want you to do that. But again, if you don’t do it, unlike for research, for an activity that is research under HIPAA, the covered entity, VA, is not in non-compliance with HIPAA. Because we are collected PHI using utilization, are disclosing PHI, without authority to do so, because the authority is under treatment. But again, as we have stated, VHA pricing recommends it. We are telling you, we really want you to do it. And therefore, that is why—and I know this kind of morphs into it a little bit—we are in the process of putting these documents in iMed. And again, also making these available through DocuSign so that, again, it facilitates the completion of these forms. Thank you.

Next question? Question about tecovirimat. We will cover this on Friday, because this would take the next—all the minutes.

Any guidance on how to get written consent? Again, this is why we’re using iMed. Without getting into iMed, also DocuSign, for COVID, this was difficult as far as carrying things out of the room. This is going to be very similar. This is an infectious disease.

Is the same going to be for getting paper consent from a person with monkeypox? Yes, we’re dealing with the same exact issue for those sites that have already had experience with it. This is indeed an issue, which is why we are mobilizing as quickly as possible to get these into an electronic format so that we will not have to deal with paper copies. But indeed, at this point, as described in the CDC protocol—we’ll discuss this more Friday—it is. Consent is required. There is an exception, which is a different issue. But when you’re getting informed consent, right now, for the case that I was involved with last week, we did a photograph of each page of the informed consent document and the HIPAA authorization. And that is the record that is being used.

Next question? Unrelated to tecovirimat, any information about availability of—oh, I can’t—genais vaccine for use in the VA? Or will VAs being using vaccine through its local jurisdiction? I have no information about that. That’s definitely not something within my authority. What I will do is convey this to pharmacy benefits management, as this will be a question that they can answer rather than the Office of Research and Development. Thank you.

Next question? Is it also the reason why NPC is not engaged in research, because VA requires NPC personnel to conduct research to have a VA walk or IPA appointment, making them a VA appointment? Yes, that’s exactly right. The NPC itself doesn’t conduct research. So when an NPC employee is indeed involved in the conduct or area of research, they are wearing their VA. They’re doing this under a VA appointment. So it is the VA that’s conducting the research. Again, I won’t emphasize how much we value the VA NPCs that support us in our research activities. But indeed, it’s the VA that is conducting the research. That is exactly correct. A NPC employee, who is conducting research, is doing that under a VA appointment. Thank you.

Next question? For question number 3, who reviews the local site-specific amendment? Assume it is still the commercial IRB that does the review. You are indeed correct. You cannot have two IRBs that have the regulatory oversight of the same protocol. So once an IRB, again, takes oversight, regulatory oversight of that protocol, it’s all of it. All the amendments. Great question. Thank you.

Next question? Question four. Can the R&D limit the recruitment to non-pregnant participants? Well, I mean, the R&D committee, it’s about the IRB approval. When you put in your—here’s the problem. Here’s the issue. Of course, you can say you’re not going to include individuals of child-bearing age. But accidents happen. It’s like when you have a clinical protocol that indeed excludes individuals of child-bearing potential, but perhaps, depending on the clinical trial, it may be that their partner becomes pregnant or something. I’m a trialist myself. I had an individual who was not supposed to be able to have children, and it happened. So yeah, again, you can say, as part of my protocol plan, investigator, I’m not going to include—I don’t plan to include—women of child-bearing potential. There will be methods to use. But there are things than can happen. So that’s why, in almost every clinical trial protocol, you’re going to see that, “if this happens.” VA is a predominantly male population.

Next question?

Parker Cunneen: Karen, give me just one moment. I wasn’t able to access the questions when I went into screen share mode. So let me just pull a couple more in here, and I will just be a minute.

Karen Jeans: OK, no problem, not at all.

Don Workman: While we’re waiting, I just wanted to add a comment to the question a couple slides ago about site-specific amendments. If you want to do a site-specific amendment on an industry-sponsored trial, you’ll need to provide the commercial IRB with documentation that the sponsor has approved the change you’re proposing. Because they have to evaluate whether it makes sense in terms of their larger protocol. Over.

Karen Jeans: Thank you. And I’m glad Dr. Workman just brought that up. Because all amendments are not going to get approved. There was a local site that wanted to eliminate some of the data collection. Well, that directly affected the data integrity of the study. That was not permitted.

On the topic of approval letters, why do the VA Central IRB approval letters no longer have any information on them other than approved for approved documents, reason for amendment? This was very hard for staff and RCOs to quickly understand what changes are made. I’ll pass that to Dr. Workman.

Don Workman: I spoke up too soon. So the reason in IRBNet is that we publish the board documents. And those are all the documents that are approved, along with the letter. So we no longer have to list them out. Because if you list them out and publish them, you introduce the possibility of error. You forget to list something in the letter, and it’s published. So for clarity, the documents that are approved are all published or documents and not listed again in the approval letter. Over.

Karen Jeans: The question is, I understand master protocol changes versus site-specific changes, but can you please explain why, if a change is approved for the overall study, why our VA site would need to submit an additional one to use such approved changes at your site? You wouldn’t need to. For example, let’s say that the master protocol has changed to say, we’re going to include an extra survey. So you don’t have to have a site-specific amendment that states, now we need an extra one just for the VA. If that is the question that’s being asked.

Don Workman: Karen, if I can just add—

Karen Jeans: Yeah, I’ll defer to you, Don. Am I getting this right?

Don Workman: Unless, of course, it changes the informed consent form. So if the change of the overall protocol means that you have to change information in the VA site-specific consent form. Then you do need to submit that change to the consent. Because, again, the Central IRB’s approving changes to the sponsor consent form and not the individual site consent forms.

Karen Jeans: But I also want to add, this question may be about the issue of amendments to protocols, amendments to the master protocols, requiring submission to the VA prior to the sponsor approving. The sponsor is not approving amendments to master protocols on our behalf. And that’s because many of these amendments involve information security and privacy reviews that need to be done to make sure that they are acceptable. So that’s the question that you’re asking. That is the reason why, when sponsors do amendments, that they do indeed have them go to the VA to say, please submit this amendment to your site. Because they know it requires a privacy and information security review if it involves the data in our information security transmissions. Thank you.

 Follow-up question on consent piece. Will there be something from national that can be uploaded to iMedConsent? Or do you recommend we do that one locally for now? This is already in progress. We have already been working with the National Center for Ethics, and they are fast-tracking this. So they are already working on this right now for both the informed consent and the HIPAA authorization. Thank you.

 Is an additional request required for the use of electronic consent for a protocol project that has already been approved and inclusive of a COVID population? The IRB approved the process, as well as the documentation of informed consent. So if you are changing the method of documentation of informed consent, that is a modification to the protocol. That is a modification that requires an amendment. That would require approval from the IRB. Thank you.

Parker Cunneen: And that is the last question I’m seeing on my end.

Karen Jeans: Excellent. We finished just in time. So, Don, do you have anything you want to say before I close this out?

Don Workman: Just thank you for all the information. It was a very informative webinar. And I hope it was helpful to the audience.

Karen Jeans: Thank you so much. This, again, is part of a bi-monthly series ORD has started on, again, sections of different topics of interest to the research community. And, again, Friday will be the detailed webinar, more descriptive, on the CDC IND TPOXX program. Parker, I will close it for you so you can close it out totally.

Parker Cunneen: Thanks, Karen. And I just want to share another webinar update. I’m not sure who on this call may be interested. But there were a couple changes to the monthly finance webinar series. We are still having the webinar tomorrow. There’s no changes to that one, our July event. The August one, which is August 25, the topic has changed. But it’s still going to be August 25 at 2:00PM—the typical time slot for that webinar series. And then September is going to be off, and then they will resume in October. So I just wanted to follow those emails up.

 And Karen, I think if we do have a minute, I am seeing just one quick question here. I don’t know if you want to address it.

Karen Jeans: Sure.

Parker Cunneen: Do the RCD approval dates at our site have to be the same as the NCI CIRB approval dates?

Karen Jeans: No.

Parker Cunneen: All right, quick answer. Thank you, Karen and Don, for hosting this webinar. And thank you, all the attendees, for joining us. As a reminder, there should be a survey appearing after this webinar closes. And we would appreciate if you could fill that out, and we will take your feedback.

 Thank you very much, and have a good afternoon.