Seong Kim: All right, well my name is Seong Kim, and I will be your administrator today. I would like to go over a few reminders and housekeeping items. First, today’s session is being presented in lecture only mode and therefore the audience is muted. This presentation is being recorded. And hand outs should be sent to you in the next couple minutes.

Please reference the Q&A box for any questions you may have. Each question will be answered at the end of the call. Now, to find the Q&A box, please navigate to the lower right-hand side of your screen and click on the bottom with three dots and click on the blue Q&A text. When submitting these questions, please send to all panelists. The WebEx platform does not automatically attendees to see comments submitted by others. However, we will share submissions with the entire audience by responding to each submission with the phrase “Thank you for your question.”

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Now, with that said, I will pass it along to Karen Jeans, Director of Regulatory Affairs at ORPP.

Karen Jeans: Thank you. So, hi, everybody. My name is Karen Jeans, and I am the Director of Regulatory Affairs, as Seong said. And today is a very focused one-hour webinar on the implementation of the CDC’s IND program for TPOXX with emphasis on the Reliance. That is our primary focus today. I am joined here by other representatives of the Office of Research and Development and the Office of Research Oversight. And so, we will have sufficient time at the end of this presentation for your questions.

And so, the primary focus is we’re going to do a very brief, very brief discussion of you know, why we’re using tecovirimat in this expanded access program and why does it mean we use those words, but the majority of this presentation is going to be on how to do the steps in order for your VA facility to rely upon the CDC, Centers of Disease Control and Prevention IRB for this expanded access program using this drug, which is commonly called TPOXX for the treatment of monkeypox. And then, as part of in human subject protections, we are not going to be going into prescribing and into the implementation of the protocol in terms of the actual protocol itself. We are centering today on, again, primarily on the Reliance Agreement. We are going to describe some of the institutional possibilities and in particular informed consent and HIPAA authorization requirements.

So, with that said, again very briefly, want to emphasize, you know, so many of us, you know, we’ve all dealt with COVID-19. And monkeypox is not in the same league as COVID-19 in terms of its severity. It is a rare disease. It is in the same family of smallpox, but it is not smallpox, and it does not have that type of severity of symptoms. It is associated with a rash.

In terms of its origin, it was first discovered in 1958, when there were two outbreaks of a monkey like disease that occurred in colonies of monkeys. And that’s how it got the name associated with it of monkeypox. But that does not monkeys were the cause of it. Is that we still don’t know to this day here in 2022 what is the source of the disease. But again, you know, these animals, like primates like monkeys may, indeed, harbor the virus.

And again, it is one of the most common symptoms of course, is the rash. And so that is, as you’ll see on your slide here, our examples of different pictures of the rash that you’ll see with some patients who have monkeypox.

Now, the numbers have, of course, risen as this outbreak has been evolving. And what you’ll say, you know, two days ago, I did just part as another webinar series, you know, a bimonthly update in human subject protection issues. And we talk very high level about this. I was showing this map. And we were in the 3,000’s two days ago. So, as of the 28th, now, I’ve bought this slide in this morning, there were 4,907 cases across the country. And again, one of the cool things about this from the Center for Disease Control and Preventions website, the link that you’ll see at the bottom of the slide is that when you go to that link, you can see, and it’s updated daily, how many cases per state that CDC has had reported to them. And again, I want to emphasize over and over again, monkeypox is not COVID-19. It does not have that same pathway. It does not have that same severity.

Now, again, we are going to sit around today talking about the CDC IRB Reliance treatment that utilizes tecovirimat for the treatment of monkeypox. And this is a countermeasure for the treatment. It is an approved drug. It is approved by the Food and Drug Administration for the treatment of smallpox in adults and children. But it is not approved by the Food and Drug Administration for the treatment of monkeypox. And so, you know, there has been some data in animals that seem to indicate efficacy. And so, that is how it is being done across for the treatment of this monkeypox outbreak through this expanded access protocol. It allows the use through this medical countermeasure declaration for the stockpiles to be used to treat monkeypox during an outbreak. And while you will see a pill on the picture of the slide, it's given either as a pill or an injection. But most commonly, it’s given orally by mouth.

Now, I we’re going to jump straight into one of the order of businesses today. That is, indeed, you know, why are we doing this, what is the structure in terms of the human subject protection issues for the utilization. And we keep using the words expanded access program. So, the Center for Disease Control and Prevention has something, and it’s called an Intermediate Size Expanded Access Investigational New Drug Application for the use of this drug for monkeypox. And what this type of IND, investigational new drug application, which is approved by the Food and Drug Administration allows is for this drug which is indeed considered investigational in its use in monkeypox, to be used outside of a clinical trial for multiple patients who meet the criteria for inclusion in this program without every single individual clinician having to be an investigator seeking their own IND. And that is the advantage of this, this program and how CDC has, has obtained this IND to allow hundreds, thousands of institutions to participate in this without having their own individual IND’s.

Again, very briefly, to set the stage for why this requires IRB approval. You always hear the words expanded access and it’s commonly also referred to you won’t see the word under the drug regulations in FDA. It’s compassionate use. But it is a method for drugs that are investigation to be made available outside of the clinical trial when certain criteria are met. Again, this all falls under the Food and Drug Administration’s regulations.

Now, there are different pathways for use of investigational drugs and biologics. And again, you most commonly and most of us on the call who were involved, again, patient care, research and administration. We had a wide room, a scope of individuals on this call, you know, pharmacy. I mean the entire VA population. We see what we’re dealing with one of drugs that are investigational, we think clinical trials. And indeed, that’s the majority of the IND we deal with.

But then we get this special class called the expanded access. And that’s what we’re dealing with today. Now, with COVID-19, you know, one of the things we dealt with, many of us who are on this call today with convalescent plasma for COVID-19. That started out as an expanded access IND. Then it went to an emergency use authorization, which is another way to give it, but it's a different regulatory structure. So, there is a big difference. A lot of people use the terms interchangeably. They are not. They are nowhere near the same in terms of the regulatory structure.

So, that’s why it’s very important to use this word expanded access IND as what we’re talking about today. And again, in terms of what this drug is, there’s multiple different types of expanded access. And if not the scope of this call, not the focus of this call to go through every one of these. But I’ve got an arrow here to show this is an intermediate sized population IND. And that is, again, that, it helps multiple institutions be able to sign onto this protocol.

Okay, so now, now, we’re getting into what I call the meat of the presentation. It’s actually getting to reliance and why we have to have IRB approval. But as you probably heard, expanded access in terms of an IND is not research. What do we mean by that? VA is a common rule agency. We follow the federal, the federal policy for the protection of human subjects. And in that regulation, research is defined as a systematic investigation including research development, testing, and evaluation. It’s designed to develop or contribute to generalizable knowledge.

That is not what an expanded access program is about. It is about treatment. So, this expanded access program, even though it involves an investigational new drug application, it is absolutely under FDA regulations in 21CFR312.315. It requires IRB approval, this type of expanded access. And IRB continue to be. And we will be talking about it informed consent later on. But it’s a different type compared to the common rule definition of research, a different type of program activity.

But let me emphasize, in this program, again \_\_\_\_\_ [00:12:30] requires prospective \_\_\_\_\_ [00:12:30] approval. It requires informed consent that must be done unless there is a session from informed consent which this protocol has and can be used in specific circumstances, specific situations. But when that situation is used, it must be documented as required by the IRB. So, don’t get, do not use, you know, VA’s policies for clinical consent when it comes to this type of activity. It falls under the IRB approved methods and type and documentation of informed consent. And again, for the purposes of this program, this intermediated sized ID expanded access program from CDC for tecovirimat for monkeypox, the Center of Disease Control, they hold the investigational new drug application for this entire program, and they are considered the sponsor. And Dr. Peterson at CDC is the official sponsor principal investigator. And this is the protocol that CDC has made available.

Now, again, before we get into the actual Reliance in terms of just setting, again, the stage for why we’re doing what we’re doing, and why this is set up the way it is, and how it falls in the scope of expanded access, there is emergency and non-emergency. Again, going back to our experiences with COVID-19 remdesivir is a great example. When remdesivir was first made available for the treatment of COVID-19, it was on emergency expanded access IND. And that’s where each individual treating clinician who wanted to treat remdesivir, use remdesivir for the treatment of a patient with COVID-19 had to have their own individual IND. COVID is life threatening. So, in that situation, there was no prospective IRB approval required. There is no R&D committee approval required. But FDA regulations require the IRB to be notified in writing five working days after beginning administration.

Now, that’s not what we’re dealing with here. With this type of expanded access ID, it’s called a non-emergency expanded access. And so that’s why prospective IRB approval is required. In terms of VA, we’re going to paint prospective R&D committee approval that can be done by designated review.

And again, you’ll see a slide later on going a little more into detail, but in terms of the R&D committee approval, it is not the same as with your traditional research in terms of research as defined under the common rule. And so, in terms of what the R&D committee’s principal responsibility is, is indeed verifying that there is an IRB approval in place and a reliance was set up. And then I’ll go into a little bit later about the Central Privacy Office reviews and Information Security reviews that have been done centrally so that each facility participating in this program does not have to do this. And of course, most importantly, from the R&D’s role, is to make sure that there are the resources that are available in the pharmacy to support the program. There is no looking at reviewing this protocol that was published and is under Dr. Peterson to evaluate the scientific merit because that’s not what expanded access is about. And the FDA itself, in order to grant this expanded IND has already looked at the merits of this to decide whether or not this expanded access can begin. So, that is not done by an R&D committee. There is no evaluation of hypothesis is not applicable. Tt’s a treatment protocol.

Now, in relation to this to get to try again to make sure that we try to get the best possible way to be able to administer this program, across the VA sites, just like with the Mayo Clinic protocol that was done where the Mayo Clinic held the protocol. They held the IND, again expanded access IND, and the Mayo Clinic IRB was the IRB of record, and that’s again where VA sites, they relied on the CDC IRB. Same thing here except this is a different type of disease, different type of drug, different type of protocol.

The Office of Research Development and the Office of Research Oversight have been working with the Center for Disease Control IRB to establish a way for VA facilities to rely upon their IRB to participate in this expanded access program. Again, we are committed to using the one IRB whenever possible. And clearly, as you’ll see, it makes sense. It would be, it’s very difficult. You would not want to have a 107 VA’s or, you know, even 15, 20, 30 doing this separately. And the reason is, we’re going to talk about this very quickly to explain why. Now, we are aware that some VA facilities have already obtained IRB approvals for their own facilities or own a university RB that already has, you know, decided to do their own review of this CDC IND protocol. But that does not mean that you know, there’s maybe other protocols involving this drug that are not the CDC’s. And I want to emphasize that right now. So, just because it involves this drug, TPOXX, does not mean its automatically CDC’s. There may be other studies that are going on with it. But in terms of the CDC protocol, we are aware there are more than one.

There are several VA’s that went ahead and obtained their own approvals. Just because you obtained your own IRB approval does not mean that you cannot transition your IRB oversight of record to the CDC. But there is also no requirement you have to do it, you have to transition as well. But the primary reason that you want to rely upon a single IRB for a protocol like this is many times changes happen very quickly. And if you are not using, for example, in this protocol, the CDC IRB, when the CDC changes its protocol, changes its informed consent, mainly changing the protocols \_\_\_\_\_ [00:18:59] they are changing the protocol as an IRB and approving it does not mean that if you’re using somebody else’s IRB that you are automatically have approval. It must review and approve that amendment such as what occurred last week when the CDC issued version six of the protocol. So, that’s why in terms of you know, being able to facilitate implementation, incorporation of any changes in this type of protocol, it is always preferred to use a single IRB.

And again, if you’re a VA that has your own IRB or has relied on another IRB to do this, if you do want to transition, you just can’t decide that you want to do it. Your current IRB of record has to agree the transition and so, and please, again, if you have questions about this, you know, I’ve given, there is a bot of IRB reliance in single exceptions VA box. I put that on the address. Dr. Don Workman is also on this panel today and we can work with you and help you if you wish to transition to the CDC.

So, now we’re going to go through the steps because this is what you have to do in order to rely on the CDC IRB. This is not a complicated process. And I want to say that up front. This, as you’ll se in a slide later, can take hours. We literally did it in hours last week with a certain VA facility because, you know, we had, you know, we got door to drug, patient presented, and received drug, less than 24 hours. So, please know this is not complicated and I want to allay those fears right now.

Also, I want to make sure you know up front that we’ve established a web page describing the steps that we’re talking today, current forms that will continually be updated supporting implementation of this program. If you go to this website right now, you’re going to see all the documentation, all the forms that I’m referring right now in terms of documents that are being used within VA to support this such as Privacy Office reviews, Information Security reviews. So, with that said, I am going to jump straight into the steps. And this is a picture of the website.

Now, there are basically four. I’ve broken this down into four categories, four steps. It does not mean that, for example, step two must be completed before proceeding to step three. And so, with this is really a snapshot of what must happen and as I’ve put and emphasized this can occur in hours. It does not take weeks. It’s a different type situation. And one of the reasons that this can happen so fast now is that we have negotiated as part of this ability for VA facilities to rely a master agreement. So, the CDC, ORD, and ORL work with CDC to get a national agreement that was signed by CDC directors and our chief research and development officer, Dr. Moroni. And that basically establishes the terms and the relationship between the VA and the CDC for our ability to rely upon the CDC IRB so that each individual VA facility is not entering into their, in terms of having to negotiate an agreement. And so, on the web page, you will see a copy of that agreement that has been signed by both parties.

As a result of our ability to use that master agreement, part of the agreement is that VA facilities that wish to rely upon the CDC IRB must sign a concurrence agreement, a concurrence form. And on the slide in front of you, you will see it’s a two-page form. And it refers to the master agreement. And it can only be completed by the institution official which is the facility director in which the facility director is affirming, yes, we are, we will enter into this reliance agreement with the CDC for this specific activity, not any others. It does not mean you can rely on the CDC IRB for almost any study, of any other study. And then it refers back to the master agreement. It’s a fillable form. It, again, it’s two pages. I’ve put here you fill in your VA facility name and on page two, you put in the name of your facility director, and you, then it can be signed electronically. This form has already been seen by OGC STAR and it does not need legal review. If your director wants to affirm that with and I know some directors have sent it through. I’ve received correspondence from OGC STAR. You know, it’s fine. You know, this is a reliance agreement that’s already been agreed upon. But please not, it does not need another additional legal review. If you have to send it, that’s for your investor, that’s your process.

In terms of what happens after you get that concurrence agreement signed by the medical center director, you take that, you send a copy to the four email addresses, Ms. Craig, Ms. Clark form the Office of Research Oversight, Dr. Workman, and then there is a general box, a general shared mailbox for IRB reliance in the Office of Research and Development. You do not need and please do not submit this concurrence form directly to the CDC IRB. We have already worked out a process with the CDC IRB on how we are giving them information regarding every single VA facility that is entering into this agreement. And if I am correct, I think right now, and Dr. Workman and Ms. Fark and Ms. \_\_\_\_\_ [00:25:09] correct me at the end of this when we get to the question and answer, but I think we have 14 right now that have already implemented reliance.

When you send that form back and you being research office, it should not be the investigator. I mean it should not be a treating clinician. It should be someone from the research office. Include in your email to ORD and ORO the name and position of the primary point of contact. And this is again, so the CDC knows who to contact if there is an administrative issue. You can include more than one person. Please don’t include more than two. And if you do send two, tell us which one is the primary point of contact. And so, we want your name, position, your email, and your phone number. And what happens when we get that information is that Dr. Workman will be sending that information forward to the CDC IRB administration.

Also, you will not, now, CDC is changing their process literally as we speak. What they did last week is not the same as what they’re doing this week. For example, now they implemented a process to allow, to do reliance agreements with individual sites. Now, this does not apply to VA. The process that has been agreed upon VA must be followed. But again, they’re evolving as would be expected with this rapidly developing program. But you will get acknowledgement, correspondence from Dr. Workman, acknowledging receipt and that indeed, you know, verifying you may rely upon the CDC IRB. But I want to emphasize something here. You do not have to wait upon that correspondence. Let’s say you’re doing it on a Saturday night, 3:00 in the morning, whatever. You know, you, as soon as you send back that concurrence form that has been signed and dated, you know, electronic signature or any signature of the medical center director, that is once it’s sent to the Office of Research and Oversight and the Office of Research Development, now executed.

So, you’ve now done the reliance. This is a little different than other types of reliance agreements because normally what happens is you must have SOP which are done prior to the reliance being executed. This is again a different type situation. Now, that does not mean that you do not get, you must not do SOP. That is required. That is required under federal regulations. It’s required by ORD. And so, again, with tremendous thanks to the Office of Research Oversight, an SOP, a standardized SOP has been developed for us for all VA facilities that rely upon the CDC IRB for this program and therefore a small amount of customization for the implementation of your facility. So, when using your concurrence form back, Dr. Workman, our, the Office of Research and Oversight, I think it’s primarily Dr. Workman, will send back the SOP. And we’re not posting that on the web because it literally changes as we update it. And so that’s why it’s being given to you instead of being publicly available. You’ll get it as soon as you can and as you send it back, and you do not have to wait to you know, to rely, you know, to get going on this until after the SOP is finalized. Now, with that said, we’re going to make sure you follow up and you complete it, but again, patient treatment can begin prior to the SOP being reviewed by the Office of Research Oversight. And again, when you start working on your SOP, you’ll send those to your oral contacts when you do the fill ins and modify it.

Step three in this four process, parts of this presentation is obtaining R&D committee approval. It can be done by designated review or convened R&D committee, again understanding that, you know, this is not your research as defined under the common rule. So, also emphasizing it, for this, purposes of this protocol, R&D committee does not keep issuing approval for it, with every patient that is entered in this protocol at the facility. Once you approve it, as an R&D committee, that’s it. That’s all there is. Subsequent uses do not require separate R&D committee approvals.

And the role again, this goes back to an earlier slide, and I put it here again, is that the primary role of the R&D committee is to verify that a reliance exists and that it has been executed and that is we talked about it, that’s why we have emphasized how, how you verify is. Once you send that concurrence form, if you’re using the CDC IRB, that is reliance, also, to ensure the privacy and information security reviews have been done. Now, we have done central reviews for these and throughout the life of this program, including any amendments that are done to this program, central reviews will be done in terms of privacy by ORD’s privacy officer, for information security by ROTCD. And we are coordinating that here in the Office of Research and Development. These reviews regardless if you are relying on the CDC IRB or if you’re relying on another IRB, we are making those reviews publicly available so that you can have them. These are currently posted on the ORD webpage that is supporting this program with, you’ll see a link at the end of the presentation. There are other links in the presentation. And so, even right now, right after this call, you’ll be able to download those and have those. And again, they will be updated with any amendments to the protocol. So, that’s again, a way to try to facilitate the execution of this program. Again, as we said before, you know. R&D committee make sure you have the resources and there is no evaluation of hypothesis.

Now, because again, this is not research under the common rule, but it is indeed subject to 21CFR312, and indeed FDA’s regulations for informed consent, and IRB approval are in effect. So, again, there is training that is needed to be done, minimal training. But there has to be something. And so, what we did, just like what we did with the Mayo Clinic is make a very concise slide set. It is just a, it’s around 25 slides. It is now available. It again is posted on the ORD website for this CDC program. And at the end of the slide presentation, there is a certificate of completion. And there are two places that the person, the learner who is completing this, that training, and there is no test by the way, let me emphasize that, they put their name in and the date. And then it can be uploaded. It can be sent to the research office. Whatever your research office wishes to do, but this is a very easy and fast way, and it serves the purpose. Again, many treating clinicians who are going to be doing this, this is, they’re not doing research under the common rule. They’re not doing all these other protocols. They are doing this treatment protocol and that’s it. So, we are not going to do the normal requirements that ORD has for the CITI modules. And this is, again, practical, and realistic. This should take, you know, give a few minutes if, to do this and then a certificate.

Again, and in terms of the next part of this, again and we’re not talking about procurement. We’re not talking about the full implementation of the program. I’m really centering in on two, two primary issues concerning informed consent and the HIPAA authorization. Now, this is an infectious disease. Now, so, again, we’re going to have similar issues that we had with written paper. And I’ll start that up front. Now, the CDC IRB has approved the CDC IRB approved this form. And that form is located on the website on their program website that they have put, that they have the link that you have in this slide. Now, the CDC IRB has approved three methods of obtaining informed consent and it’s not multiple choice. And you can’t skip to one. They are in order in terms of first and always is to get consent from the patient, written informed consent. The second, if the patient cannot consent and they have a legally authorized representative, is to get consent from the legally authorized representative. The third is an exception from informed consent. And that requires a signature and certification of both the treating physician and a second physician who is not associated with the patient’s care for that bit for this program.

So, in terms of again, talking about the first two, for the written informed consent, there are no alterations allowed. It is not an option. And again, VA absolutely agreed to that. This is similar to the same thing that happened with the Mayo Clinic convalescent plasma was that was overseen by the Mayo Clinic IRB.

Now, we are going to require a VA informed consent addendum, but it has to be again, approved by the CDC IRB. And the reason we are requiring it is because the CDC IRB approved consent form has statements that, you know, insurance will pay. Patient could be billed. That will not happen in VA for anything that is not associated, that is associated with this program. And so, until the CDC IRB approves the VA informed consent addendum, we are indeed asking for the treating, the person obtaining consent, the treating clinician to convey to the patient you know, by the way, your insurance is not going to be billed as a result of you being in this. You are VA. So, that’s not going to happen. And also, you do not have to be worrying about treatment for research related injury. It’s going to be paid for. Now, this is under the prep act as well. And so, this is going to be, this would be covered regardless. But because the consent has language that infers that the patient could be billed, it is also unclear in some places, you know, who would provide it. That’s why the R&D are asking for those two elements of informed consent to be conveyed to the subjects or the patients.

Now, the third option in terms of this consent is the exception from informed consent. And this is where, indeed, you have a scenario where you cannot treating physician get consent from the patient who needs this therapy because they can’t respond. And there is no one around, a legally authorized representative or next of kin to be able to get next, get consent of legal authority. Now, the issue with this, there is a lot of confusion in this when this term is used, because sometimes it’s interpreted that an exception from informed consent means no IRB approval. That’s not true. So, that’s why you know, we emphasize they are not analogous.

In terms of the requirements for an exception from informed consent in this third scenario of where informed consent is approved by the IRB by the CDC, that it basically requires that, you know, these conditions are met and that there is documentation not only from the treating physician, but also again a second physician who is not associated with the patient’s treatment that is being administered under this program. The CDC has made this to ensure that the requirements are met. This is under FDA regulations under 21CFR.50.23. Okay, on the actual informed consent form, if you’re not getting consent from the subject, from the patient in this situation, because this third condition is met, they have made it where there is checkmarks to make sure that the treating physician goes through the process, have you done the documentation in the medical record, what is the name and signature of the treating physician and the second physician who are indeed the second physician certifying that the conditions are met. And then within three working days of this happening, the treating physician who is overseeing that patient has to notify regulatory affairs at CDC.gov within three working days that indeed an exception from informed consent was applied to a patient who received TPOXX under this program.

Now, in the earlier emails I sent this week, and again, I will always say when I make a mistake. We conveyed, I conveyed that written HIPAA authorization was not required. That is not true. Unlike the Mayo Clinic, again comparing it to other expanded access informed consent, the CDC is not a covered entity. So, no authorization language is included in their consent form. And so, again, this is treatment. It does not meet the definition of research under common rule, but it is treatment. So, therefore, the patients are to sign a VA form 10-5345 which is request for and authorization to release health information. Now, this form is already present in iMed. And we are already working with DocuSign. I’ll talk about that in just a second. To be able to do that from the point of a legally authorized representative is needed.

But we’ve also, to facilitate this, a sample VA form 10-5345 in terms of how it should be completed is available as a guidance document. And it has been uploaded already onto ORD’s website for this program and you can view that also to facilitate, again, standardization and again, trying to make this as easy as possible.

Okay, in terms of other related information, again, this is expanded access. So, research compliance officers are not required and do not audit these programs. And so that, that is a given. And this again is not coming from ORD. This is coming from the Office of Research Oversight.

In terms of, again, the issue involving paper. We’ve already come up against this and we knew we would. So, trying, as soon as, you know, Tristar implemented this program, we have already contacted and they are in process fast tracking this for both iMed and DocuSign, putting the CDC IRB approved consent form into the translations to the electronic versions of this. And I see a typo I did, and I will correct in the slides that is posted, into these formats so they can be available. They are fast tracking, but it will be probably closer to ten, probably ten business days more before we can get this done. We have already sought permission. Again, this is a change in format, change in method in terms of how we are doing this. And so, we already sought approval from the CDC IRB to use these methods. Any change in format, CDC IRB has told they have to see it, as is correct. And so, as soon as we get these forms put in and we have CDC IRB approval, we will, of course, notify all of you of how to access them and that they are indeed approved.

Although we are not getting into, we are not parts of this presentation, our focus is on the reliance. We’ve already gotten a lot of questions about the form 15, Form FDA 1572. And there is only one form FDA 1572. There may be 30 people on it that is required to be completed by the VA facility. This, again, is an arrangement that the CDC made with FDA. So, there does need to be, if you have ten treating physicians who are doing this program in your ID service or in your ER, you do not need to have ten separate form FDA 1572’s, only one. Again, the, and that’s been a frequent question and not only by I was talking to CDC last night. And it’s a common question. It’s not VA. It’s everybody who is participating in this program because it’s a different type. And also, in terms of correspondence with the CDC IRB itself and not reporting, but in terms of if you have if you had a question about you know, something, again, they are, as you can imagine, you know, lots of institutions are relying upon them. But you can correspond with the CDC IRB for purposes other than reporting at the huma@cdc.gov address. Reporting on the OR, on their web page, they have a section in terms of if you’re reporting adverse events on specific method that are to be used. And so, those are separate and distinct than routine correspondence.

Again, this is a recorded session. It will be available shortly on this ORPBD cyber webinar webpage again, for references for your, for your access. The ORD webpage again is active with the documents that I have referenced today. The CDC webpage again is invaluable resource. They, we expect that to and as they continue to implement this program, frequent changes to that webpage. And so, with that said, that’s the end of my part. I am going to stop sharing my screen. And Seong, I think we’re ready for questions.

Seong Kim: Sounds great. Let me go ahead and share my screen.

Karen Jeans: Okay, the question is in the prevalence map, it was too small on the screen to read the legend. So, where the grey starts, so where the grey states where is present? Most of the map was blue.

Male: Karen if I could just add the grey states.

Karen Jeans: Please, yes.

Male: There were only a couple of grey states and those were the states where it doesn’t exist. Almost all of the states and there were only three states that were grey, oh, three let’s see, Puerto Rico, Hawaii both have the monkeypox. Alaska had none. So, there are four. I couldn’t think what the fourth one was. But there is a link there on the website and just an interesting map that gets updated every Wednesday. Over, Karen.

Karen Jeans: Thank you. Okay, can the prospective IRB be done expedited for EA-IND protocols? No, no, this is coming from the Food and Drug Administration. This is, this is under their regulation. IRB only meets once a month, and we have a hard time scheduling emergency meetings. Do amendments, SAE reports, and continuing reviews need to be submitted to IRB for EA-IND protocols? Can they be reviewed expedited, or do they need to be full board? Should pharmacy treat EA drugs like investigational drugs?

So, there are multiple questions here. But again, it’s this, this protocol requires prospective IRB review by convened IRB. Modifications to the protocol, these protocols will either be expedited or by convened meeting depending upon, again, whether or not they represent substantial changes to the approved protocol.

Again, I think you know, again, my question on this one, you know, again, is you know, we would like to follow up about whether or not about seeking reliance upon the CDC IRB.

In terms of the pharmacy treat EA drugs like investigational drugs, the answer is yes. Under VHA handbook 11-804, this is indeed an investigational drug. It’s also investigational drug under Food and Drug Administration. And so, that’s why it need, it has an IND. So, great questions. Okay, let’s go to the next one.

Does the local R&D committee need to approve after CDC IRB approves?

Well, the CDC IRB has already approved protocol in terms of if we’re talking about the current one in place. So, it’s already done. As soon as the concurrence memo goes back to ORD and ORO, the reliance is complete. And so, there is no, there is, you’re added on as a site. So, there’s, you’re done. And so, the local R&D committee would indeed approve as soon as the concurrence memo has been sent back to ORD and ORO.

If we were, and in terms of amendments, the R&D committee does not review and approve amendments to this protocol. It is under the oversight of these, of an IRB regardless of if it’s a CDC IRB or another IRB. Thank you, next question.

Can the VA form 5345 be made fillable? Also, comment to the audience, VA form 5345 is different than the HIPAA authorization we are used to using for research projects.

Absolutely. I do believe that the 5345 and Michelle was unable to join us today, but if I am correct, it is fillable. It is in iMed. And so, it is already a fillable form. In terms of the issue involvement the HIPAA authorization, if they sign a VA form 10-493, you know, that’s fine. But on the 5345, is again authorization for treatment. It is much easier to complete. That is the one that we, we do wants you to do. That is one that needed to be done because it’s treatment purposes. And indeed, that’s why we want to give you one that was filled out so you could see how to fill it out for the patients that are under this protocol, this treatment protocol. Next question.

Really appreciate this question. Can we have a medical center director sign the concurrence agreement without a patient to treat yet, just to have it ready?

Absolutely, the answer is yes. We have, I, and I am going to ask, you know, Dr. Workman to jump in here because that’s exactly why we wanted to have this webinar today to, so that you can be ready. You may never use it. And we hope you don’t have to. But again, we want to have it ready for you in case you need to use it. And Dr. Workman.

Don Workman: Oh, absolutely, I couldn’t agree with you more that having the pieces in place where you have the IRB approval applying to your facility even if you never have a patient show up allows you to be ready to move. It’s just a lot of complicated pieces with getting pharmacy to procure the medication, and then you can focus on the patient care related issues. So, yeah, I couldn’t agree more.

Karen Jeans: Okay, next question. Is the addendum the ICF CDF approved yet?

 No. I will be honest here. We sent it for IRB approval and the CDC IRB reviewed it and had comments back. And so, they wanted some language changed and had some very good questions about you know, how do we document this for the third scenario in terms of when there is an exception from informed consent. So, we are responding to their questions. And so, it is not approved yet. Again, we do get it approved, we will make sure of course, to inform everybody. But no, the answer is no. Thank you. Next question.

Oh, really good question, you know, and I think we’ll change our instructions based on this really excellent question. If the clinician already has CITI human subjects up to date, is the abbreviated training certificate still required?

No, this can be used n lieu of. And we put that on the top side of the instructions that we have on our web page and also in our optional courses for ORD. But no, so, this is truly for those treating clinicians and we’ve encountered this lady where this is, this is the only thing they’re doing. They do not need to do all the CITI. They need to do this very quick training. So, the answer is no. This is not required training. It’s just in lieu of CITI. Thank you, next question.

For the informed consent, when you have physician, does that strictly mean M.D. or can be N.P., P.A., a licensed provider?

This is a question I am going to have to go back to FDA and CDC on. If you look at the language of the regulation it talks about the word physician, but it could be provider. And so, and that includes of course, A.P.N.’s, and P.A.’s, physician assistants. So, this is a question that we will need to go back to CDC and FDA for this specific project and seek clarification. So, we will get that clarification. We are noting that right now. And we will get that out. We are, indeed, everyone on this panel has been working on FAQ’s that we will get up onto that site. This will be one that we will get clarified. Thank you for this question. Next question.

Because this is not a clinical trial, we would not be required to be, as it is in California, a research subjects Bill of Rights?

I can’t answer on behalf of legal, but if a research subject Bill of Rights only applies to, to research as defined in the common rule, and does not apply to individual receiving investigational drugs in any context, then the answer would be, would probably be you’re correct, it wouldn’t be. We can go back, and we will check on that for you as well on that one. Again, I suspect you are correct, but I don’t like to suspect. I like to have a yes or no answer. So, we again, will follow up on that. Great question, thank you.

Before the informed consent addendum is approved does a treating physician need to convey the information verbally or in writing?

Orally is fine.

Does the patient need to sign it?

No, and the reason is there is no CDC IRB has not approved the addendum. So, for them to sign it, again, that’s, it does not meet the purpose. So, therefore, we are doing this please convey to subjects and to patients because the patients may say it says I’m going to be billed. And so, we want to make sure they know you’re not going to be billed when you sign this form. And so, oral conveying is fine. There is not, there is no requirement. And for the treating physician to say I told them this information. We are also not requiring that as well. We just want to make sure this, the patients know they are not going to get billed and that they don’t have to worry about any costs associated with any injuries as a result of participating in this program. Next question.

Can IRB’s that have already approved the TPOXX protocol used to combine ICF/HIPAA document?

There is an optional component to this program. And again, it’s not, again it doesn’t meet the definition of research under the common rule, I mean either HIPAA or the common rule. So, that is a question I am going to have to defer to, I am going to need consultation with Price to answer that question because it’s a different category. It’s not research under HIPAA. So, it’s treatment. So, I will, again, another question that I will have to check with Price because that is not something I can answer on the fly. Definitely we’ll check on that one. And would you also, would you, whoever asked this question, would you tag me in terms of just, just so I’ll know to reach out to you, okay. \_\_\_\_\_ [00:56:19] I can follow up as soon as I get an answer to you. And then also, we will make an FAQ on this. I want to commit and make sure you know we are committing to you know, getting FAQ’s out. These questions that you’re asking, everybody else is going to ask them. So, we appreciate this. Next question.

Yeah, okay, so the reliance agreement, again, we, we use a standard reliance agreement.

Are we responsible for providing reports?

The reliance agreements states that participating VHA medical centers are responsible for providing reports of institutions facilities research compliance reviews or audits with reportable findings for the protocol under CDC IRB’s oversight. Information proceeded by ORO indicates that RCL’s will not auditing the EAP. If RCL’s will not be auditing the EAP, what research compliance reviews or audits would there be to provide to the CDC IRB? What entity at the facility is monitoring compliance, if not the RCO?

I’m going to pass this to my colleagues.

Christina: Hi, this is Christina. There could be any number of organizations that could be monitoring the oversight of the study and although we don’t require the research compliance officers to audit this study, if they do, and they find issues, those will have to be reported under the reliance agreement. I don’t know if Priscilla and Elizabeth have anything to add.

Priscilla: This is Priscilla. Your R&D committee will be monitoring reports of adverse events but the RCO under 10-5801 is part of the reporting chain when IRB makes the determinations and reports are provided so the RCO’s do need to be informed. They should have copies of the SOP’s and reliance agreement for their reference.

Karen Jeans: Thank you, Christina, and Priscilla. I think we have time for one more question, Seong.

My experience with relying on other IRB’s or working with a central IRB is that local sites still have to submit an application to the IRB. What is the process here?

You don’t. That’s why this is very, very individual, now, we do want you enter this in \_\_\_\_\_ [00:58:59] we want you to have a project cover sheet and we want you to have the IRB information sheet. But again, the way this is designed is that you know, we’re giving the information to the CDC concerning, you know, your POC’s, but they are not requiring in terms of the CDC IRB process, you to submit an application. This is a very different type scenario. And so, the answer, that’s the process that is used.

Male: Karen, if I could just comment, this isn’t like the commercial IRB’s where the commercial IRB’s already approved the protocol and the model consent form sponsor. And that’s what the VA works with. We don’t submit the protocol. In fact, we take the approved informed consent form and add the VA language to it, which is what we’re doing in this case with the VA consent addendum. So, again, there is no need to submit the protocol itself. They’ve already approved it. Over.

Karen Jeans: Thank you. So, it being 3:00, I am going to for my part close out in terms of the before I turn this back to Seong, thank you so much for your participation. I want to thank our panelists today. Again, we are looking at all of these questions. As you can see, we’re working very rapidly to get the \_\_\_\_\_ [01:00:26] for everybody. There were follow up questions that we will be answering, but again, as we’re, you know, again starting to implement this process, we will work to get information out as quickly as we can, but accurate information as well. And so, I want to thank you for joining us on a Friday afternoon. Seong, I am going to turn it back over to you.

Seong Kim: Thank you so much, Karen, there is a lot of informative information, and it’s been certainly very helpful. And thank you to really all of our audience members as well for listening in and tuning in. As a reminder, the slides have already been sent to you at 2:10 p.m. Eastern Standard Time. The link is Laos located in the Webex registration email, and the recording of this webinar will be located there as well. And so, one way or another, you will receive links to the handouts and recording somewhere or another if you have not already. And so, that’s it. I hope you have a great weekend, everybody.

[End of audio]