Karen: I am the Director of Regulatory Affairs here in ORPP&E. I would like to welcome you to our August HRPP bimonthly webinar. This was a webinar series that we started last April in which instead of doing a lengthy webinar on a single topic, our purpose is to give some snapshots basically of different topics of interest to the VA research community. Our topics come from you and are dealing with events that have happened since our previous one. Today, we are going to be giving you an update on the TPOXX Expanded Access Program, including some content that again VA has been asked to convey by the CDC Regulatory Affairs Office.

We are going to talk about humanitarian use devices, including some helpful tips with VAERS. I am very pleased to say that I have Ms. Amy Lauer [PH] who is going to be joining me for that part of this presentation. We are going to talk about the technical amendment to VHA 1200.05, which is the wonderful exclusion of VHA research from the Requirements of the Paperwork Reduction Act, commercial IRB issues including something that I think you will be very intrigued about. Again, these slides will be available to you after the conference after the webinar today.

Again, some situational awareness about the release of new final FDA guidance, I should say, on informed consent. The information for you is about VA’s participation in the upcoming Premier Annual Conference in December, which will be held in Washington D.C. As part of these questions and answers from you, some of those have been embedded through the content of today, but also as Parker has said, we will have some time at the end of this webinar for your questions about any of the topics that we are presenting today.

Again, we have a lot of content today, so we are just going to jump right in. The first topic we are going to talk about is an update about the CDC’s Expanded Access IND Program for Tecovirimat for MPOX. This is including my appreciation at the very beginning of this for your sites, your expertise, and your participation in data calls. It seems like recently, VA has and my office in particular, has been doing a lot of data calls. We know this is not easy. Again, I want to express my appreciation upfront for your participation.

What is interesting is that we had 81 sites that originally were approved by ORD to participate in this program. All but two are using the CDC’s Institutional Review Board as the IRB of record for this expanded access activity. MPOX, thank goodness, was not a pandemic and does not have the incidence that we had with Covid-19. As part of Regulatory Affairs CDC getting a handle on all the hundreds of sites across the country that are participating in this, CDC Regulatory Affairs reached out to ORD. we have been working together to basically get a handle on the VA sites. Again, we want to share the information. What is the use of doing a data call if we do not share it with everybody?

In terms of our current status as of today, we have 68 of our original 81 that are currently active, and 13 that are closed. We have others that we know that are going to be closing shortly. The CDC, again so that everybody is on the same page, the current IRB-approved protocol is version 6.3. It is also the same version for the informed consent document. These were approved on May 5, 2023.

CDC does a very good job of publishing their documents that can be accessed on their CDC website. We include that information not only on this slide set, but we also have our own webpage. We have a link to their webpage. There were a lot of questions about whether or not the CDC IRB would continue this protocol. The answer is yes. The IRB did indeed approve the continuing review application for this program activity on June 22, 2023. There is a continuing review approval letter that is posted on CDC’s website. Please know that ORD has sent a query to CDC’s Regulatory Affair Department. If you look at the letter, it says it approved it at a convened CDC IRB meeting on June 22, 2023. It states the expiration occurs in July. There is no doubt. Yes, it has IRB approval. That is not an issue. We have sent a query to CDC Regulatory Affairs asking about the time period that is listed as the expiration of the CDC IRB Expanded Access Protocol for 2024. Once we have that information, as always, we will update you.

Again, we participate in a lot of communications with the CDC Regulatory Affairs Department. CDC knows if they communicate with us, then we can disseminate that information to you in addition to communications that CDC sends itself out. That is the advantage of this relationship we have.

One of the issues that CDC was very concerned about was making sure the information they have on each of the sites that are active is indeed accurate. Specifically, it is whether or not all the clinicians that are participating in the program are listed in their registry. To that end, two months ago we started a data call. Sending letters to each of the sites that were registered, unless we knew they were closed, and asked for some specific information using a survey tool. Many of you have participated in this survey. It is very fast. It only takes a few minutes to do. We send it not only to the clinicians that that we had listed, to the research offices, but also to the individuals who were listed as the contact person if your site was one of the sites that were being approved by the CDC IRB.

However, there are a few sites that have still not responded. Again, we appreciate your cooperation. We will be sending it out. Again, it is not a mean email. It is just, hey, if you could, could you fill out this and update this information for the CDC Regulatory Affairs Department. You will be getting an email if your site has not responded in the next week asking you to please do this. By the way, if you do not respond, it does not mean you are going to get in trouble. It just means this is something that the CDC wants and needs and is asking for assistance.

In terms of, again, what CDC has on their website, you will see on the slide this is the location of where they include the information that they post. We also, again as part of our commitment to this program, developed our own website which links to there, but includes VA-specific information. Again, we do not put their protocol and their informed consent document on our site. We include the link for it. All the information that you have about the TPOXX program for VA’s implementation specific to VA is located on ORD’s webpage.

Since the last time that we talked in our last webinar, again the CDC’s Regulatory Affairs Department is trying to make sure that while this is not a research activity, it is an FDA-regulated activity. CDC holds the investigational new drug application, the IND approved by FDA for this program. One has to do what is required by this program. That means adhering to the program.

On August 28th, which again was just a few days ago, CDC Regulatory Affairs sent a communication, a letter, to all the relying registered institutions that are participating in this program and also the IRB points of contact. For us and VA, it was who we sent them from your facility. Your facility supplied a name. They basically sent a letter reinforcing, you have to follow the protocol. You have to follow the program. It listed nine different things to reinforce. By the way, please be reminded. You have to do this. Again, if you would like a copy of that correspondence, if you did not receive it, if your site did not receive it, or if you on the call would like to see it, you can indeed just email the ORD Regulatory Affairs box. The contact is at the end of this presentation. Of course, many of you already know it. Or you can put a query into Find Pro. I will send you a copy of that correspondence.

It was indeed a reminder that sites that are participating in this program, you have to follow what the IRB tells you to do. That includes making sure that if you are doing informed consent, which you have to do, that you do it. There is some type of mechanism that is going on to make sure that you do indeed comply with the protocol. In terms of local context considerations, that is not an issue for VA. When VA entered into this agreement with CDC for VA facilities to rely upon it, we informed them of the VA requirements. That is a non-issue for our sites. CDC is reinforcing this communication. There is required reporting of adverse events or unanticipated problems involving risk to subjects or others that must occur if it occurs.

If you were a VA facility participating in this, you have to report using the mechanisms as required by this program. Again, CDC is also reinforcing as part of its communication that as the IND holder, they also have reporting responsibilities to FDA. If FDA asked them questions in terms of, by the way, here is this unanticipated problem involving risk to subjects for others, and if they need to come back to your site and say, could you give us some additional information, that is again part of the responsibility to participating in this program. CDC wanted to again reinforce, yes, it is not research. This is an FDA regulated activity. You have to keep records, including records of the informed consent.

These are critical points that had to be covered. Again, I have this picture to basically summate exactly what the bottom line is. Follow the protocol. Follow the protocol program to the letter. Do not deviate. If you do deviate, if you do need to deviate or you foresee a need, you must ask permission first. That means going to the CDC IRB if it is the IRB of record for this protocol unless you are one of the other two sites. They are sending queries to the CDC Regulatory Affairs Office. In terms, it is not going forth and asking for forgiveness later. It is asking prospectively if you are going to deviate from the program as required by the CDC. That is the information that we wanted to reinforce as part of this update in this group.

The next topic we are going to jump to as part of our topics that we are covering in this hour. It is about humanitarian use devices. The picture that you are seeing on your slide presentation is something called the PK Papyrus. It is a stent. The reason I chose that is because many of your VA facilities who are participating in this call today are indeed involved in the HUD for this device. It is being used at your VA facility.

In terms of just doing some basic background, an HUD is a medical device. It is for a small number of people. It comes under the orphan drug program, and it is a special designation that is given by FDA. In order to qualify to be a Humanitarian Use Device, it has to be that it affects individuals, not more than 8000 in the United States per year. It is not something that is a mainstream device. It is a very specialty niche.

This went back to 1990 when Congress established this device designation and the Humanitarian Device Exemption Mechanism which allows the HUD to be used so that companies would be able to develop these devices for these rare diseases. Yes, it is not throughout the United States, but it is a critical need. They established this mechanism to make it easier for products like the PK Papyrus to be developed. Try to say that three times in a row. Unlike other medical devices that go through the formal IDE process, Investigational Device Exemption, and the marketing approval application, this is not synonymous. Under the HUD HDE pathway, this Humanitarian Use Device mechanism, all that has to be approved is that the device is safe, and it provides a probable benefit in relation to the risk of using it.

You will hear the words HUD/HDE synonymously, but they are not synonymous. HUD is the device. The HDE, the device exemption, is the mechanism that allows that device to travel. It basically states that allows that it can be used without, what many of you see in VA facilities when we are dealing with medical device studies, the Investigational Device Exemption that is approved by FDA. Again, in order to have an HUD, it has to be found to be safe and provides probable benefits.

In terms of how this has happened and what does it decide today? By the way, I am going to do an HUD. I want it to have this special designation. The HUD process starts with the sponsor of the manufactured device. Now you submit an application to the FDA office, which is responsible for reviewing applications for an HUD. That office is called the Office of Orphan Products Development. What happens when this application comes in from a sponsor is that the FDA has 45 days to review it and give a decision. It does not mean that in 45 days if the FDA does not have the information it needs that it is going to say, you are either approved or disapproved.

It can indeed say, we do not have enough information to make a decision whether or not we can indeed make this an HUD. That is the determination that the group will make. Can it be approved? Is it going to be disapproved? Do we need more additional information in order to make that decision?

Again, the person that is responsible or the group that is responsible for making sure that the requirements are met for using an HUD under that HDE – that is where you get into these initials -- is the HDE holder. That is important. Amy is going to talk a little bit later about what needs to be uploaded into VAERS. You are always wanting to know, where is the letter? Who is the holder of the HDE? That is the critical issue. HUD cannot be used except at institutions where there is an IRB that is constituted and meets FDA requirement for review. That includes continuing review of the HUD use.

There is a lot of confusion. One of the reasons that we put this as one of our points of focus today is that HUDs are confusing. They are confusing because we do not use them every day. They are not something like what you see in exempt research where many of your research programs – I am speaking to the research offices right now – you do a lot of chart reviews. Okay, those are exempt category 43. All right.

Here we are. We have a clinical investigation involving an IND drug. Many of you do clinical investigations involving IND drugs. When it comes to HUDs, that is not something that you see a lot of in any facility, including our university counterparts. That is why there is a mystique about it and why it is not intuitive. Indeed, in terms of an HUD, it is not research. Because of the Safe Medical Act and the Food and Drug Cosmetic Act, it is required to be reviewed prospectively by a convened IRB prior to initial use. There is always an exception -- with the exception of emergency use. Emergency use is an entirely different situation where, again, the HDE holder will authorize that emergency use. Even then, it has to be reported to FDA. The bottom-line message that I want to get through to all of you today is, indeed, you have to have prospective IRB approval except in that rare emergency use.

While continuing review is required, continuing review can be done under expedited review. Again, that is allowed by FDA under the Food, Drug, and Cosmetic Act. However, you will have those rare situations in which you are using an HUD. A HUD’s normal use is for clinical care. That is why it has its designation under the Office of Orphan Products, but they are going to study it to see whether or not it is not only safe but is it effective. Get more data about it. When it is used in that manner, that becomes a clinical investigation under FDA. Then it becomes subject to the clinical investigation regulations and everything that goes with it.

It is not common to use an HUD in a clinical investigation, but it does sometimes occur. That is why it is important, when you are obtaining information about the HUD, that you do indeed confirm that it is for clinical care, and you are not doing an investigation about its use.

With that, I am now going to pass this off to Amy. Amy is going to talk about the VAERS component.

Amy: Hi, good afternoon. Let us just go ahead and dive in because we do have a bunch of slides to go over. In general, or really in all cases, there are two VAERS wizards that have to be completed in order to submit for HUD review by the IRB -- the VA project cover sheet and the IRB information sheet. Then there is required documentation that the IRB needs to see in order to conduct their review. There are three items or three types of documents: HDE approval documentation from the FDA provided by that holder that Karen talked about before, if available, product information and product labeling describing for what uses the device is indicated, and materials as applicable that will be shared with patients receiving the HUD. This could be an information packet for patients, or sometimes it is an informed consent document. Next slide.

Important to note, there are documents that we are used to submitting as clinical researchers that do not belong in your application for an HUD review. We are not submitting financial conflict of interest forms. There will not be a research privacy review. There will not be a research ISSO review. You will not be submitting a HIPAA authorization for research. These are not research subjects. These are patients receiving clinical care. Depending on what facility you work at, there may be documents required for R&D review. An HUD does not come under the oversight of the R&D. There is no R&D review, so there are no R&D committee submission documents submitted. Next slide.

Having worked in VAERS for a while, there are questions presented on our wizards for which there do not appear to be applicable answers. We walk through in the sandbox to take a look at how you actually would submit a HUD application using the wizards without getting stuck. You have to let yourself choose the most appropriate answer, so this should give you some guidance on what answers work. You create your new project and start the VA project cover sheet wizard. Next slide.

You are going to choose other. Your research topic is not reflected in this particular screen. We do want you to enter in a project summary and significance, again, pertaining to the use of this HUD and our veteran population. Tell us why it should be here and how you are going to be using it. Next slide.

This should not be a funded study because this is not a study, which is why we select no to “Is this study funded?” We are choosing yes for our response to contracts or agreements because, in general, when our facilities have to arrange for a device to be delivered, there are agreements in place. The way that you order an HUD follows the same clinical pathways that your facility orders devices in general. You may have a registration agreement. We ask you to select unsure as the type of agreement because none of the specific agreements we would expect to have for clinical purposes appears in VAERS. Next slide.

You are going to enter information about the VAPI and any additional providers who will use this device at your facility. This is so that we have a track of who is allowed to use the device. There are no FCOI disclosures required. There is not an answer that fits this particular scenario on the wizard, so select yes that there are no conflicts of interest. It is the best response that we have among the choices available. Next slide.

You are going to choose other for your project characteristics and describe the clinical use of a HUD. You are not asking for any kind of exemption or non-human subjects research determination with your form submission. That is the completion of the first of the two wizards involved for submitting. Next slide. Next, you return to the designer, and you start another wizard. You select the IRB information sheet. Next slide.

It is not going to be a multi-site study. You are not submitting to a non-VA site. You are going to select PI assessment of risk level greater than minimal risk. This is so that you are going to be headed toward full-board review, but it is not research. I could understand if you did not want to make a risk level determination. The right choice here is greater than minimal risk. Next slide.

You are going to be requesting IRB review. It is not a clinical trial. It is not international research. You are not using recruitment to recruit subjects. You do not recruit patients to treatment, which is why we choose other and describe our recruitment strategy as clinical care provision. Next slide.

There is no subject population. There are no intended participants. There is no interaction with the subject group. We do not pay people for receiving treatment. The only research procedure that should be selected is humanitarian use device. Next slide.

Under usual care, standard of care, and a clinical space we are going to select no because there is no element of research with usual care or standard care. There will not be a certificate of confidentiality, but you will fill out all of the information requested about humanitarian use devices. This helps us. We have to track the HDE number and the name of the device. As you know, these wizards inform our database. This is the kind of information that then ORD can use to pull reports on what kind of HUDs are being used across VA. After you finish this section, this wizard is also complete. Next slide.

You are almost finished. You are in the home stretch for submitting your HUD application for review. Remember, at the beginning of this section, there was a list of documents that needed to be provided to support the IRB review. You will upload your HDE approval documentation, product information, product labeling, and materials that will be shared with patients. That is all of the materials. Anything patient-facing, your IRB would like to see. An informed consent document if there is one or if your IRB requires it. The IRB can require that you have an informed consent reviewed by the IRB. I think that is as many slides as I am supposed to cover. If there is anything else, let me know.

Karen: Thank you, Amy. One of the things that Amy and I were talking about as we were preparing for this is in the VAERS library, there is an HUD application. One of the projects, again, that we are working on and by the next bimonthly webinar which will be in October, will be the release of a new HUD application form to make it easier to do this application. It is also to cover some of the material here. When you are reviewing as an IRB and HUD, you follow the FDA regulations that you would use for research, but it is not research. What we are doing is revising that application form supplement so that it is more user-friendly and more organic. Indeed, when it comes to how does an IRB review and HUD? Again, because it is not strictly in regulation, how do you actually do it? The FDA has issued of course recommendations. Again, ORD does not supersede FDA. We follow what FDA recommends when it comes to the review requirements and also what is required by regulation itself.

You want to have those same materials that Amy was talking about. In terms of the informed consent form, you will see one of two cases usually. Many times, for example, in the PK Papyrus, the manufacturer, the sponsor, the HDE holder is supplying, for example, a sample consent form. They want that consent form to be used by the institution that is indeed administering when to use that device. Then it of course includes specific information specific to the VA facility. It is with a person’s name, and what is the name of the facility. That is what is usually the norm.

Sometimes with an HUD, the sponsor, the HDE holder will not supply that sample. They will say this is the information you must convey. The IRB can either say, okay I want to use an IRB specific informed consent document to include that information. Or I may want that information to be included as part of the clinical consent. IRBs have discretion on this because, again, the FDA regulations do not indeed require an IRB to approve an informed consent document in relation to HUDs.

Again, one of the issues that we are dealing with in trying to address this and why we are talking about it today is that there are different types of information that can help an IRB understand what they are looking for. It depends upon the type of device that is used. The content that I have on these slides about, what are the post manufacturing modifications that are made to this? What is the provider training that is required prior to use of the device? It may not apply to every HUD. It depends upon the type of device. These are indeed types of considerations that an IRB may want to have or may need to have in order to figure out, okay, I need to approve this use of this device for this clinical care.

The big deal is, how is the device going to be used? What are going to be any requirements that this patient has to meet in order to get this device. Most importantly, what happens after the device is put in or used? What is post-safety monitoring? What are the tests that need to be done? Do they have to come back to clinic if we are talking about an outpatient procedure or an inpatient procedure. How many days do they have to stay in? What are the dangers to it? Of course, what is very important if you are an IRB that is reviewing this when you have a clinician who wants to use an HUD is whether or not you indeed have the facilities to support its use. That is where you get into the issue of if there is a specific lab or specific type of diagnostic or monitoring procedure that is required after the device is implanted, for example. Does your VA facility have that type of diagnostic test or have the ability to use it?

These are again different types of considerations, which you are not necessarily going to see. It is not in the regs themselves, but these are different types of considerations in Y&D ORD. We are working toward a 60-day deadline to revise the supplement for HUD that is in the VAERS library to indeed give the IRBs that are reviewing this the tools they need for considerations. My important reinforcement here is that it is not necessarily applicable to every HUD. It depends upon the type of HUD.

Again, in terms of how IRBs approve HUDs, it can be. You can approve it basically in total. We are going to approve the use of the device for this clinical care as at the VA facility. Any qualified provider that you list can indeed use this. Is it by groups of patients, or can it be under a specific type of protocol that the person that the provider provides? Do some IRBs – this is not common – but they will do it on a case-by-case basis. They want to know each time the HUD is used for its use. Please let the IRB know, and we will approve it for that specific patient. These are all allowed. It is all different options IRBs have. It is very flexible.

Regardless, one of the biggest things about use of an HUD is not just about putting it in. If there are adverse events, those are required to be reported as per FDA regulations, and of course to the IRB that approved the use of the HUD. With that in mind, I am going to move us along. Again, the other content is not as lengthy as the HUDs. It is about, again, a great notification to the research community about the technical amendment to 1200.05, which was exclusion of the Paperwork Reduction Act for VHA Research.

This was not originated originally by the technical amendment. Our technical amendments are based upon superseding law or regulation. In December of 2022, President Biden signed into law the Cleland Dole Act, which was part of a larger act called the Consolidated Appropriation Act. In it, it contained a wonderful section called Section 181. It is very important to read the exact wording. The Paperwork Reduction Act shall not apply to the voluntary collection of information during the conduct of research by the Veteran’s Health Administration, including the Office of Research and Development, or individuals or entities affiliated with the Veteran’s Health Administration.

It was signed into law, but unfortunately, we cannot implement it until we have policy. That is why there was a gap in time. The agency just cannot implement it without it having an implementing policy. This was a major event for the agency because the PRA – the Paperwork Reduction Act – can cause lengthy delays in our abilities to conduct VA research involving surveys, interviews in which you are asking identical questions to \_\_\_\_\_ [00:37:07] individuals who are members of the public. What we did to incorporate into policy is if we included a section in 1200.05 paragraph five which is talking about investigator responsibilities, indeed as part of an IRB review. If this is an exempt research project, many of these interview survey studies are now exempt research. You have to include the survey tool, and you have to send that to the appropriate research regulatory committee.

This does not mean case report forms. I want to reinforce that right now. Please do not confuse the use of case report forms with survey instruments. It includes that all-important note that the Paperwork Reduction Act does not apply to VHA research activities.

Since we have issued this, there have been a lot of questions. ORD issued a guidance document when we published the technical amendment which contains a variety of questions and answers related to this exclusion and how it applies. One of the biggest issues that we have already encountered that we wanted to relay today on this call is remember, while we are excluded – we being in VHA, Veteran’s Health Administration – from the PRA Act, it does not include our sister federal agencies that do not have an exclusion. The National Institute of Health has an exclusion from the PRA. DoD, for example, Department of Defense does not.

If you as a VA facility or a VA investigator are conducting a study that is funded by the Department of Defense, that is their study by the way. Even if we are conducting it, it is still their study. Do not be surprised. Again, when they say we have to apply the PRA, they are right. They did not get the exclusion. VA did. Even though we are doing the research, they still have to apply the PRA. That is a very important clarification that is not only presented today as part of this webinar. It is also included in this guidance document which has been published. It is available on ORD’s website and in Fine Pro.

Again, some points of information and clarification is we always include at least one topic related to our commercial IRBs as part of this bimonthly webinar. There are two issues that we wanted to talk about today. One is an update on our data call. Again, it is a very comprehensive data call. We had over 200 studies in May that we sent letters – we being ORPP&E – asking the study teams for those studies to do a self-assessment, to review their informed consent forms, and evaluate whether or not those consent forms that had been previously approved by the IRB contain the applicable VA-specific informed consent requirements as applicable. A few of the 2018 common rule requirements. This was being asked of our study teams because we were made aware that there had been a gap. The reviewing IRB had not consistently been reviewing informed consent forms for those two issues. It was not consistent.

We have had a tremendous amount of feedback. Again, ORPP&E cannot express our appreciation enough to the sites. We only have 11 studies as of now that have not yet responded. We are not going to be doing any more follow-up. Again, ORD wants to again reinforce that it is always the reviewing IRB’s responsibility to ensure that the IRB-approved informed consent document contains the required elements of a consent. That meets the VA policy requirements and is part of the reliance agreements that were executed between an IRB and your facility. In terms of our ORB-approved commercial IRBs, it is part of our requirements in the master service agreement. Again, it is not when sites did find issues. Again, this is an IRB issue. It is not the study team. Again, we are reinforcing that. Again, we are expressing our appreciation for the amount of work that the study teams did.

In terms of what has been happening in the last two months is another issue which I think you will be intrigued and excited about. We had three. We currently have three ORD-approved commercial IRBs. That is Sterling, Advara, and WCG. As more and more of our sponsors are finding out, the word was not out believe it or not. We have been using commercial IRBs for three years. Hey, by the way, we do use commercial IRBs. We have had a number of commercial IRBs that have reached out to Dr. Workman and would like to become an ORD-approved commercial IRB. That includes Brainy. Also, we have started talking to Castle.

Again, it is not as simple as here is a document. Sign and you are on board. Again, there is a careful vetting that occurs within our office. Again, it is ensuring that the requirements are met. Again, there is an ORD-approved commercial IRB. We have a master service agreement which we execute here at the national level between ORD, which is signed by our Credo, and the signatory official for that IRB. Then again, we develop. We have the reliance agreements that are executed by your individual VA facilities that wish to sign onto that specific IRB. We also develop standardized SOPs at your sites individualized for your individual use.

We are indeed working toward adding more commercial IRBs. What I think is very exciting to VA research is that more and more sponsors are realizing the advantages of conducting clinical trials with VA. This is a great time for us.

Again, in terms of the last two items which are informational before we open them up to questions, FDA has. In 1998, the FDA issued draft guidance on informed consent. It was around eight pages. This month, FDA issued a 66-page finalization of that informed consent guidance. It is quite comprehensive. FDA even prior to putting it in the federal registry for public comment, prior to finalization received input from multiple federal agencies, including VA to which we included a number of comments. This final guidance addresses many of the issues which were not even thought of in 1998. We all know even in the last five years research has evolved.

Again, it is guidance. That is the whole thing. What this guidance does is include lots of different practical examples that one can utilize and say, okay, let me look at this. How does it apply to my situation? What we are planning to do as part of the next HRPP webinar, which is in October, is to include a section on informed consent issues in VA where we will bring in some of the topics from this newly finalized FDA guidance on informed consent into our topic for discussion in October. That is one of the topics planned for October.

Also, as a point of information, Premier is coming up in DC December 3-6. ORD and the Office of Research Oversight will be doing a joint session called a Dialogue with Department of VA. It will be December 6th from 1:45 to 2:45 Eastern. Similar to not only the virtual, but also even prior to the virtual pre-Covid, when we had the in-person meetings there will be federal office hours. Representatives from ORD and ORO are going to do two of the office hours in the afternoon on December 3rd and December 5th. These are all times that we are going to be participating to support this conference. We are excited about having an in-person meeting again, another opportunity. We look forward to being in Washington in December.

With that said, this has been a lot of content we have talked about today. We wanted to allow at least ten minutes for questions. Again, we always have recordings of these sessions. There are no handouts that are associated with this. Again, you will get a copy of the slides, but they will be posted on the ORPP&E Cyber Seminar website. Again, there are two ways to ask questions. Number one, the regulatory mailbox. Also, we have an Ask ORD option in Fine Pro. Again, when it comes to asking questions, if they are policy questions, absolutely. If it is something that should be addressed by your research office first, we would ask that you go to them first before coming straight to ORD.

We have a number of references that are included today in this slide set which touch on all the areas that we discussed today. With that said, I am going to stop sharing, I think. I think now we are ready to go to questions and answers.

The first comment is extremely wise. Whoever wrote this, thank you. Note that some CDC TPOXX communications to our VA addresses go into the junk folder. People should remember to check that from time to time. Absolutely unequivocally agree. I do not have a lot of information on the spam folders, but there is a lot of information that is going into our spam folders that used to come straight to our focused mailboxes. Thank you. Thank you for that point of information. Next.

With the next FCOI wizard in IRB Net, our COI administrator had an instant where the PI completed the wizard, and a conflict was disclosed. The FCOI was sent to ODC and cleared. How do I upload that information for our ORDC review and documentation in IRB Net since we just have an email from OGC approving it. You cannot upload FCOIs into IRB Net itself.

Dr. Workman: Karen, do you want me to step in and try to provide that?

Karen: I would love that. Thank you, Dr. Workman.

Dr. Workman: I thought you might. I actually do not know the process. If you send an email to VAERS@va.gov, they do have. They should be able to answer that and at least inform you what the process is. I am aware there is a process. I believe that some of the central IRB staff assist with that process, but I do not know any of the details of it. If by chance you do not find that email address or I somehow misspoke it, please feel free to send me an email don.workman@va.gov. I would be happy to get the answer for you.

Karen: Thank you. I would also like to mark this as a question to add to Fine Pro. This is a very good implementation question, so we are going to mark that. Thank you. Next question. Oh, Dr. Workman, this is yours as well as you. Are AQD reviews, such as PK Papyrus, used at many VA sites appropriate for VA CIRB review rather than at each individual site?

Dr. Workman: The VA Central IRB does not review some of the device studies because they are being used as clinical interventions. That really requires oversight at the local site. It sometimes involves issues of storage and the handling of the devices. To this point, the VA Central IRB I am not aware has ever reviewed an HUD. Certainly, things like the compassionate use applications, again all of those really need to be done at a local site with local IRB oversight. Do not ever hesitate to send a question. We are happy to answer it.

Karen: Dr. Workman is absolutely correct. So many of the issues involving use of an HUD and the approval involves, can I do it at the local site? Do I have what I need? Those are decisions that are made locally. I am not aware, although I could be wrong, of any central or commercial IRB that does HUDs. That is something I will have to look at. That is indeed why it is not at the central IRB level. Next question.

Right. The reason we brought PK Papyrus is that it is used a lot. IT is a really incredible device. We are in the process of submitting the Papyrus HUD through our local IRB who would normally act as the PI. For Papyrus, we are planning on assigning our Cath lab director. It is interesting. From the world of the HUD, this goes back into what Amy was talking about with the VAERS forms. They are PIs, but they are not PIs.

It is your lead clinician. Indeed, it is who is going to be the individual who is the lead for that use of the HUD. You can have multiple individuals who are using that. That is usually. For PK Papyrus, in particular, many times we see that the director of the Cath lab or the director of interventional cardiology is usually listed as the lead clinician for purposes of the submission. Thank you. Next question.

If there is a survey included in a DoD funded study, is the VA PI let us say? Is the PI informed of the PRA requirements by DoD so they can begin the process? This is actually a real-life scenario. The DoD initiates the process because it is the DoD that is responsible as the federal agency which is held accountable for the PRA. You are indeed correct. It is the DoD in that situation that would initiate, not VA. Next question.

Has the ACOS research at sites that did not respond to the check of commercial IRB informed consent documents? We only have a few sites that did not respond. We are very aware that there is a heavy load on all research offices and all investigators and study teams right now. We only had a few that did not have yet the opportunity to respond. In terms of the Advara data call, we are not going to go back and have any more contact with them. Again, we only had a few sites that did not respond. Next question.

This is a great question. What is the average turnaround time for a reliance agreement between the site and a commercial IRB? Actually, the question is, what is the? I am going to change the question to, what is the average turnaround time between when a commercial IRB wants to. There are two questions. If a new commercial IRB wanted to enter into a relationship with ORD to become an ORD-approved commercial IRB, we are probably looking anywhere from three to six months. It depends. If we are talking about, let us say you currently have an ORD-approved commercial IRB. Let us take Sterling. All right. Your VA facility wanted to enter into a relationship, and it does not have one, with Sterling IRB. That reliance agreement can be done in a matter of a day, two days, three days, or less than a week. Over and over again we have done that. We have it all streamlined to an art right now. It is days when a VA site is seeking to rely upon an ORD-approved commercial IRB. Dr. Workman, do you want to add anything to that?

Dr. Workman: I was going to say there are times when there are hiccups in that, but it is usually not more than a couple of days in terms of an average. There are times when there is a sense of urgency, and we have turned around a number in a two-day timeframe. It requires the local site to do a couple of things. You obviously need to circulate a standard reliance agreement for signatures by the facility director and the MPC director. Then we need an SOP supplement to be modified by the local site to fit for your location and your specific requirements of your HRPP.

Karen: Thank you. In a previous webinar, it was mentioned that VHA directive 1200.05 would be revised to allow VA IRB staff to be voting IRB members of a VA IRB. Is this still in the works? If so, when is the expected date of release? Would that then allow staff to sign off upon waivers of HIPAA authorizations and waivers of alterations of consent? ORD does indeed plan to issue a number of amendments to 1200.05. that is indeed one of the ones that we plan to do. It makes sense. It is efficient. It is just a matter of getting that process in and getting the technical amendment process done. For the PRA, for example, that took us six months. We hope to be able to streamline that process with the group that helps us with this, which is the OO Reg Department in VHA. I do not have a timeline. We are hoping to get that done. If we cannot get it done in this calendar year, it will be next year.

In terms of waivers of consent, there is no requirement for a voting member of the IRB to sign off on a wavier alteration of consent. In terms of a waiver of HIPAA authorization, if an IRB approves a waiver of HIPAA authorization for research, the HIPAA Privacy Rule requires that the approval be signed by either the chair or a voting member of the IRB. Again, if VA IRB staff member is a voting member of the IRB, they could then indeed sign off on that. We will take one more question because we are at the top of the hour.

Will the dialogue be available for those who are attending virtually? The webinar is taped, so all of this is indeed taped in part of the webinar which is placed on the ORPP&E Cyber Seminar website. All of this is indeed available. You will be able to not only hear the dialogue, but also see the video including the questions which I have been reading.

With that though, because I do want to respect everybody’s time, we are at the top of the hour. I want to thank my panelist today. I want to thank Amy. I want to thank Dr. Workman. Of course, thank all of you for attending. I hope everyone has a great rest of the day. Parker, if there are any other closing comments, I will yield to you now.

Parker: That is it. Thank you, Karen. I will just mention the last question. We do also typically put up a transcript on the archive, usually a week or so after the video is up just to give the transcript service time and to give our panelists time to review and make sure there were no errors. If for some reason you specifically need a transcript, that will be up just a little bit later. Thank you, everyone. Have a great afternoon.