

## ORPP&E Webinar

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Session: VA ORD/Operation Warp Speed/NIAID Collaboration: ACTIV-2 Study Overview, Registration and Activation

Presenter: Victoria Davey, PhD, MPH; H. Clifford Lane, MD; Janet Woodcock, MD; David (Davey) M. Smith, MD, MAS, FACP, FIDSA; Donna Kostandy; Cristin Harrington; Rhonda Henry

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<http://www.research.va.gov/programs/orppe/education/webinars/archives.cfm>

Dr. Victoria Davey: Hello everyone and thank you for joining this Webinar on our collaboration with Operation Warp Speed in National Institute of Allergy and Infectious Diseases on the ACTIV-2 study. Next slide please.

This is just a list of acronyms for you to refer to when you look back at this slide. Next slide?

So we have a great list of presenters today, and I want to thank everyone in advance for taking the time today to be available to talk to us about the ACTIV-2 study. Next slide please.

So since the beginning of the pandemic VA has stood up to contribute to national and international studies on COVID-19. We've been working with ACTIV and Operation Warp Speed which are US Government initiatives to enable the development of diagnostics, therapeutics, and vaccines. Really since they came into being. Getting these protocols started at VA is the highest priority in our COVID-19 portfolio. And of course providing Veterans with access to these studies is a critical priority as well. Next slide please.

I'm really happy to introduce that we have two leaders in ACTIV and Operation Warp Speed to speak to us and welcome to this Webinar today. The first person that I'll call on is Dr. Janet Woodcock who is the lead for therapeutics for Operation Warp Speed. You may know Dr. Woodcock as Director for the Center of Drug Evaluation and Research at the FDA. But she is right now wearing an Operation Warp Speed hat and doing much to get us these trials going and enrolling and analyzing. Dr. Woodcock.

Dr. Janet Woodcock: Thank you very much Dr. Davey. I'm really happy to be able to talk to this audience and give a little bit of an overview about Operation Warp Speed. As everyone knows, one of the major goals of Operation Warp Speed is getting vaccines out there for our public. But there also is an effort on therapeutics, which I'm leading. And by getting therapeutics out there quickly one thing we are doing is subsidizing financially at risk, the scale up of manufacturing and production of these investigational products before we know whether they work or not. And that's sort of the acceleration that we're talking about. On the other side, we're not cutting corners on clinical evaluation. These trials are registration quality trials that are done to the

highest standards. And we're really pleased to have VA as partners on getting studies done. Part of the acceleration of clinical evaluation is, if we can add a large number of sites, and have a lot of people in this country, a lot of Americans and even people around the world participate in these trials, so that we can conduct the evaluation quickly and get answers about whether these products are going to help or not. One of the conundrums we have today with COVID-19 disease is we don't have outpatient therapies to keep people out of the hospital. And so ACTIV-2 is our outpatient Master protocols that is really intended to see if we can find interventions that could prevent hospitalization and actually get people back on their feet quicker in the outpatient setting. So we're going to go over that today. The conduct of that trial. And we'll really be interested in having the VA as a partner and participant with us. I believe that outpatient therapy is going to be really critical even as we move in, hopefully into the vaccine era and we do have effective vaccines available. So we look forward to you joining us in this endeavor. Thanks very much.

Dr. Victoria Davey: Thanks so much Dr. Woodcock. And now let me introduce Dr. H. Clifford Lane. Dr. Lane is representing the ACTIV trials which are led by Dr. Francis Collins of NIH and Dr. Lane is representing NIH today. He is the National Institute of Allergy and Infectious Diseases deputy director for clinical research and special operations. And Dr. Lane, thank you so much for taking time today to speak with us.

Dr. H. Clifford Lane: Thank you Dr. Davey. I wish I had the capacity of special operations, but actually it's just special projects.

Dr. Victoria Davey: Oh, I'm sorry.

Dr. H. Clifford Lane: And given that this is a VA audience that they have that distinction. It's a real pleasure I think for NIH to be able to partner with the VA on this study. As was mentioned both by Dr. Davey and Dr. Woodcock, the ACTIV initiative is something that came out of a desire by NIH, and Dr. Collins in particular to be sure that there was some degree of prioritization and focus on those studies that were thought to be most important for moving the field. Most important for getting the most promising therapies, vaccines, diagnostics to the public as quickly as possible. So in that regard ACTIV was stood up a bit before Operation Warp Speed, but is nicely dovetailed with it, and obviously has gotten a power boost from being tightly linked with Operation Warp Speed. And this regard for ACTIV-2 NIAID through our division of AIDS is very happy to be working as the sponsor for the study and holding the IND and providing a variety of different support in terms of subject matter expertise, administration, and funding in addition to what's coming from Operation Warp Speed. I would just say on a personal note for me, it's great to be able to see this type of partnership developing. In this instance, being a bit parochial between NIAID and the VA, because I think there are things that we might be able to do in the context of this study that actually would allow us to do additional things in the future together even beyond the COVID-19 outbreak. Because this will end. And I think we're going to learn a lot about how we can do clinical research better, what partnerships are key for doing studies quickly, efficiently, and as Dr. Woodcock said, to a degree that allows for registration of new products. So again, thank you to

the VA for your interest in being part of ACTIV-2, and we look forward to working with you. Thank you.

Dr. Victoria Davey: Thank you so much Dr. Lane, and we look forward to working with NIAID as well. And I agree, we're learning a lot about getting trials together quickly and moving out quickly while rigorously. So moving on. Next slide please.

So the objectives for today's call is to provide you all with key information about ACTIV-2. And we'll also go over the other ACTIV studies to bring you up to date on where they are. We've also hoped that we've clarified the Office of Research and Development Operation Warp Speed NIAID collaboration structure government and communication processes. And importantly, we'll go over some of the logistics of registration and study activation and then of course provide some opportunity for your questions and comments. Next slide please.

So just to talk about the ACTIV studies with regard to their position in VA. There are five. ACTIV-1 is an inpatient Master protocol to study immune modulators in COVID positive patients. We have been invited into ACTIV-1 and have made the corporate sort of decision not to support it centrally out of the Office of Research and Development because it competes heavily with both ACTIV-3 and with our own VA funded national studies on convalescent plasma CURES-1 and the HITCH trial. Certainly, VA sites are independent, and they may choose to join the study. Just be aware that the ORD support will have to be limited mainly to doing things like answering questions. The study is enrolling as of yesterday as I understand it. And ACTIV-2 which is the subject of today's talk is the opportunity Master protocol to study monoclonal antibodies. The first monoclonal in is a Lilly product. And you will be hearing more about that. We are doing central coordination between the division of AIDS at the National Institute of Allergy and Infectious Diseases. And the clinical research organization PPD. And ACTIV-2 is enrolling with about 95 people on as of yesterday. With a number of VA sites either in registration or wanting to start registration. ACTIV-3 is the inpatient Master protocol to study monoclonal antibodies. Again starting with the Lilly monoclonal product. Does have extensive VA coordination. It is enrolling. Currently on pause for evaluation of a potential safety concern. ACTIV-4 is an interesting design, really a three-part protocol to study antithrombotic therapies in COVID positive patients. Again, we don't have a central ORD coordination effort here. I know there are a number of VA sites interested in ACTIV-4 and of course VA sites are welcome to join ACTIV-4. We will be publicizing the contact information to talk with the ACTIV-4 registration staff for all of you. ACTIV-5 was announced earlier this week. It will be studying immune modulators, antivirals, and others for early large effects in COVID positive patients. I understand the first product to be studied is to inhibit cytokine storm. As I understand it, that study is in development. VA has not been approached yet, but I imagine with its inpatient design we probably will not have the bandwidth to support it centrally either. Next slide please.

So now I'm going to turn over the talk to Dr. Davey Smith, the protocol chair for ACTIV-2. Who's going to describe the protocol for us. Dr. Smith.

Dr. David (Davey) M. Smith: Thank you Dr. Davey. So today I have the privilege to talk about Rise Above COVID ACTIV-2. Next slide please.

This is an adaptive platform treatment trial for outpatients with COVID, also known as outpatient monoclonal antibodies and other therapies. Also known as ACTIV-2, also known as A5401. Next slide.

So our objective is to rapidly and efficiently evaluate multiple potential therapeutics for COVID-19 in an outpatient setting. Next slide.

The trial design is a randomized blinded control platform that allows agents to be added and dropped during the study. Next slide. It begins with a phase 2 followed by a larger phase 3 for promising agents. Next slide. When two or more new agents are being tested concurrently the same placebo will be used if feasible. Next slide.

So our agent selection in the trial is prioritized based on activity against CoV-2 entry or replication. If pharmacokinetic and safety data, and the ability to expand to phase 3 if found effective. Next slide.

So here we have let's say an agent comes in in phase 2, we're going to enroll 110 participants with an agent A, and 110 people will also be in a placebo. If it doesn't show any promise we stop. Next slide.

So another agent might come in. It might actually come in at the same time while the original agent A is still ongoing. But there we put in 110 people with agent B, and it does show promise, then we go seamlessly into phase 3, where we'll enroll 890 people on ACTIV-2 agent and then 890 people on placebo. Next slide. We'll also have agent C that will come in, that may be even staggered at some point. And the same design follows through with that. And we're hoping to find better and then better and then better strategies to prevent, to help treat early COVID. Next slide.

So phase 2 primary objective is to look at the safety and efficacy of an agent to reduce the symptoms of COVID-19. The nasopharyngeal shedding of the virus through 28 days after study entry. Next slide.

So it's all about the graduation from phase 2 to phase 3. And there we're going to look at virology from nasal swabs. We're going to look at symptom diary that's going to be measured every day. And oxygen saturation. And then we're also going to look at safety, dynamics of the virology such as rebound et cetera. Comparing the investigational agent to the placebo arm. Next slide.

In phase 3, so if an agent graduates to phase 3, the primary objects are going to see whether or not the agent can prevent either hospitalization or death through 28 days after study entry. Next slide.

So study eligibility. These are adults with active CoV-2 infection, with a diagnosis within the previous seven days. And at least one COVID-19 symptom in the previous 10 days before study entry. And they must still continue to have symptoms within 48 hours of entry. And then we want to have a CoV-2 molecular test within the week, and at least one symptom within 48 hours of coming in. Next slide.

There is a stratification. Half the individuals will have a higher risk for COVID-19 progression being greater than 55 years old or a comorbidity and some of those listed here like hypertension, cardiovascular disease, diabetes, obesity. We're also going to look at half of the people having symptoms that started earlier than five days, and then the other half five days or later. Next slide.

We have a symptom diary for severity score, and these are COVID-19 symptoms like fever, cough, shortness of breath, fatigue, headaches, nausea, vomiting, et cetera. Next slide.

So here's the study visits. In phase 2 it's a much higher touch process. So they get an active drug or placebo, we see them what happens at day 0, we collect blood, saliva, nasal swabs. We teach them how to do a study diary, we also teach them how to do their own anterior nasal swab collections. We will call them every day after that. And then on days 3, 7, 14, 21, and 28 we have them come back in, we collect more blood, saliva, do more nasal swabs, collect pulse oxygenation et cetera. And then after 28 days we also see them on weeks 12 and 24 and follow-up to collect some blood. If we see graduation based on the day 28 data, we go into phase 3. Next slide.

And in that we do very similar evaluations. But it's a much lighter touch. So somebody comes in at day 0, they get the drug, we draw some blood, we do some nasal swab, pulse ox, study diary et cetera. But then we teach them how to do their nasal swabs, anterior nasal swabs at home, and they collect them and send those in before day 29 when they come back in and get some blood and some nasal swabs et cetera. So it's a much lighter touch in phase 3. Next slide.

And we've designed it so that the participants in phase 2 are also valuable for phase 3 which increases the efficiency of the trial. Next slide.

And here's an ad you might have seen. We have a very large press campaign going on right now. Maybe you've seen it on Facebook, it's going to go on Instagram soon or on the News. So let us know what you think. Next slide.

Here is also on the website, please check it out. It's one word, [riseabovecovid dot org](https://riseabovecovid.org) or [ACTIV-2, A-C-T-I-V no E dash 2 dot org](https://ACTIV-2.A-C-T-I-V.noEdash2.org). And here's the sites. At the moment you can see we're enrolling and activating more sites all across the country at the moment. And we'll have international sites soon. And it's very fast paced activation process. So this is changing every day. But please feel free to go on the website and check it out. A lot of what I talked about today including a Webinar on exactly what I just presented is on there as well. Next slide.

This is the study team. Next slide.

And here's more of the ads. Hopefully, you'll see those soon. So I will turn it over to Dr. Davey, thank you.

Dr. Victoria Davey: Thank you so much Dr. Smith for that very clear overview. Next slide please.

So now Cristin Harrington of our Perry Point Cooperative Study Center and Donna Kostandy from PPD the CRO for ACTIV-2 are going to go over requirements, registration and activation. Cristin, Donna.

Donna Kostandy: Hi, this is Donna. Next slide.

So I'm going to go over a couple of anticipated questions to help walk you through the beginning of the startup process. So what happens once your site wants to participate and find out more information? Please send an email to me, Donna Kostandy at PPD, that email is in this handout as well. And we will go ahead and get your site the feasibility questionnaire for you to walkthrough and evaluate. And then once the feasibility process is completed, we'll move you through the regular startup process. How long does it take to register? Once your site is active, you can register on the AIDS clinical trial group at ACTG Network dot org and I can send that link. But it's also in the manual of operations and the protocol specific webpage once your site is active. There's lots of resources there for you. And it takes about five to seven days for the registration to be complete. The primary point of contact, once your site is enrolling will be the PPD CRA or monitor. That monitor will be assigned through PPD and you will be in constant contact with that representative. The website that I mentioned earlier will allow you to track registrations and enrollments and ask questions. And as far as information, there are joint study coordinator and investigator calls every Thursday at 5 PM Eastern time. Of course that's subject to change or frequency as more sites are onboarded. You also can request to coauthor a paper. You will just need to get submission; you'll have to get approval by the AIDS clinical trials group. Next slide.

So this is the website that I mentioned. And links to help you walk through once your site is active. As I said, there will be lots of information here that you can walk through to help you get your sites moving forward in this study. Next slide.

I'm going to turn it over to Cristin to answer these questions.

Cristin Harrington: Thank you Donna. Hi, this is Cristin Harrington and I am the deputy director at the VA CSPCC in Perry Point, Maryland. But for the purposes of the ACTIV trials essentially, we're serving as the site coordinating center for the VA sites. So as Dr. Smith showed in his presentation, they are onboarding many sites all across the country, only some of which will be VA medical centers. And that kind of describes our role a little bit. We come at it from the VA perspective and we'll help you to kind of work out some of the nuances for VA sites that may

not be the same for other participating sites such as academic sites or private hospitals. So we are here for you as a resource. Obviously, registration in and of itself, Donna explained it very succinctly, and we all wish it was that succinct, but there's a lot of paperwork involved and a lot of multilayers of approvals. So there are a few efficiencies that we've put into play in the ACTIV-3 trial so far that we feel like could translate over to ACTIV-2 to help you navigate some of these reviews and approvals as well. So first and foremost. Looking at this slide. I'm going to talk to you about the reviews and approvals not necessarily of the protocol itself, but of the platforms to be used. So obviously information security and privacy are very serious issues within the VA. And before you can even submit to the IRB, which in this particular study, will be the commercial IRB Advarra, you'll need to submit for a preliminary information security officer review and privacy officer review at your site. So one of the efficiencies that we've built in on ACTIV-3 and we're happy to execute this for you as well on ACTIV-2 is that we've organized for a centralized ISO review by the research support division. This would satisfy that preliminary ISO review. It would help you get the endorsement letter. Which I'll talk about in just a second. It will not satisfy your privacy officer review. But essentially, we'd be collecting from you, your site informed consent forms, your HIPAA authorization, any other relevant documentation about how you intend to keep the data and secure the data. And we would submit that centrally to the RSD. They would execute the central review based on everything that they already know about the platforms being used. And by platforms, I mean your electronic data capture system, websites, you know where you'll be storing the data. If it's in or outside the VA firewall. And they'll issue a report that will list your site as having gone through this preliminary review. We would ask that before you start the protocol a final ISO and privacy officer review orchestrated at your site just to account for any changes that may have happened since you embarked on it. At the top of the slide, I have actually a link embedded there. So the requirement for a preliminary ISO and privacy officer review prior to the commercial IRB submission, is a relatively new kind of ORD guidance. And I've embedded the link in there to where you could go and just look at the ORD guidance yourself. I feel like that's a little safer than trying to repeat it and run the risk of not saying it correctly, but in essence what needs to happen is that the ACOS of research at your site needs to ensure that these considerations have been evaluated by your local ISO and privacy officer before you submit to the IRB. And he or she will need to author an endorsement letter. And also within that link there's a template endorsement letter that you can look at for reference. Next slide please.

So as I mentioned, Advarra is going to be your commercial IRB. They're the single IRB for this study. Which means there's no local IRB review that's needed. What does need to happen if your site does not already have a reliance agreement with Advarra, so you'll need to enter into one. If you don't have a reliance agreement with Advarra as a single IRB, again I've included a link here to the IRB reliance group VA email. And you can start there by reaching out. Sarah Rule is very responsive. She's helped to get a lot of our sites up and running with these. And we're seeing more and more reliance agreements being executed within the VA. Advarra is definitely adding an element of efficiency. Their average turnaround time at this point in time, at least on the ACTIV-3 trial is approximately three to five days. And they are even reviewing on Saturdays which is nice. Let's see. We do provide VA template informed consents. So I can reference ACTIV-3. We'll basically have established an informed consent template that meets

Advarra requirements and VA requirements. We pushed that out to sites. You would add your site-specific language, and then that's what you submit. And provided there are no sweeping changes on your part. Again the average turnaround time is approximately three to five days to approval. And then obviously you would need to go through your local research and development committee reviews. What we would ask, because a lot of the R&DC reviews are on a scheduled basis, is that if you can't allow for an ad hoc R&DC review at your site without a change to your SOPs, we'd ask for you to work with your ACOS of research or your medical center director to pursue a change of your SOPs so that you can allow for ad hoc reviews. What we would hate to see in Warp Speed is for you to get so far through the registration process and kind of do this furious paper chase only to sit around at the backend because you just missed an R&DC meeting cutoff. So the other thing that we think might be helpful in that, is if you kind of work with your R&DC and let them know that it's coming. Keep the line of communication open, let them know you're participating in ACTIV-2. When you might assume that you can be in a meeting. And then just that it's highly prioritized. If you have any great limiting factors, or anything coming up locally at your site that you think might be a hurdle or might add time to your bottom-line, please bring those back to us. Bring them back to Donna and her group at PPD and just make us aware. So the one thing I can say having struck out in ACTIV-3 months ago, is that there's so much support coming from all levels of government to get these trials done in as an efficient of manner as possible. So you don't have to be alone. If you've got a frustration or a hang-up, if there's some red tape that you just can't seem to clear on your own, sound the alarm, let us know. If there's some way that we can intervene or escalate for you, we most certainly will help to try to get you through that. Next slide.

And with that I believe I'm going to turn it back to you Donna, so that you can discuss some of the pharmacy requirements.

Donna Kostandy: Thanks Cristin. Next slide please.

So I want to make sure to let everyone know, these are the highlights of the pharmacy requirements. There are more detailed information in the feasibility questionnaire. But we do require that for the ACTIV-2 study the licensed pharmacist is available and ideally a backup pharmacist is recommended as well. There's a list here of the equipment for the investigational product. Also to ensure that you have the space requirements that are required of the investigational product that I'm listing here as well. So if you have any questions, please don't hesitate to reach out to me after this Webinar. I'll be happy to answer specific questions. Next slide.

So I wanted to also ensure that everyone is aware of the funding considerations for the ACTIV-2 protocol. Next slide.

It's just important to be aware that you'll be dealing with a revenue stream that's coming from industry. So you will need to be working with your NPC as far as your requirements for staffing for equipment and storage, that you are working with your NPC to ensure that you have all of the access that you need for industry funded revenue. Next slide.



So I think Cristin and I are going to tag team a little bit on this one. Cristin already outlined a little bit some of the challenges that she's experienced with the ACTIV-2. And these are some recommendations and some tips that we're suggesting that you think about when you're ready to go ahead and submit for the ACTIV-2 protocol. Is to really think about and create a project plan for how you will get through the approval process. To keep the line of communications open. Don't hesitate to reach out to myself, to Cristin, to Vicky, to all of us. If there are any questions or challenges or you're running into an unanticipated roadblock, we're here to help you, and help ensure that things go as smoothly as possible, as efficiently as possible through the startup process. You know designate a point of contact at your sites to be sure that we know who we can reach out to for any questions. And as I said, Cristin and I are also available as your points of contact to help you through this. Cristin is there\_

Cristin Harrington: Yes. If I could just add to that. If we don't know the answer to a question that you may have, chances are we can certainly find someone who does. The other thing really I think to point out is that we work with so many capable and individual coordinators and regulatory professionals who upon receipt of instructions and a mountain of paperwork, they just retreat into a corner and work their magic and turn things back in. But I really do want to make the point that if you think about these ACTIV studies as a whole and you think about Warp Speed as a whole it's really all built on collaboration and communication. No one agency can get it done by itself. And no one person can get this done by him or herself. So as you have questions please don't be afraid to ask them. Don't make assumptions if something is unclear. We've built a lot of infrastructure in a very brief period of time, so it goes without saying that there may be an instruction that isn't clear or a policy that's recently changed. And I'm finding as much education coming from the field my way as the opposite way. So I really can't stress enough that communication is going to help you get through I think a lot more efficiently and a lot more smoothly. And obviously that's what we're looking for here in order to get the Warp Speed that we're after.

Donna Kostandy: I think we can go to the next slide.

So I think the next slide after has a list of yeah, a list of resources. Also for you if you have questions, if you need help with a particular question about patient care and facilities, home health, there's a bunch of information on this slide and I think the next slide as well with points of contact to help you as you walk through and get you through. And some of these are PPD contacts, and some of them are Operation Warp Speed as well. So there's a lot of information here to help you get through the startup and enrollment process. Next slide.

So I'll just reiterate. If you are interested in participation, we would dearly love you to participate. Please contact me, my email is here. Please when you're doing that please have an investigator designated at your site so that we can quickly and efficiently get the feasibility process started, and get your site going on ACTIV-2.

Dr. Victoria Davey: Thank you Donna. This is Vicky Davey again. So if you have questions that we in the Office of Research and Development Central Office in Washington might answer, whether it's on the ACTIV studies, Operation Warp Speed, policy, local barriers, please email us at the email address you see there. Our people in that email answer very quickly and get your question to the right person. Next slide please.

So to summarize, why are we doing this? Why are we doing ACTIV-2? Of course there's a promise perhaps of treatment for COVID-19. This is a contribution to the global effort to fight this pandemic. Of course it provides access for Veterans to clinical trials, which is one of our constant goals. It's efficient the way the trials are designed, so we can look at multiple investigations in a single trial. This is a great opportunity for VA researchers to be on publications, to have access to data and biospecimens, and let me say that it's also a great opportunity for the non-VA investigators to have access to you all. We certainly have vast experience in multicenter clinical trials and are very capable. And these trials admittedly are challenging. And so it's a good exercise for our clinical research organization. Next slide please.

So at this point we can take questions in the chat. And let me take the opportunity again to thank the presenters for being on and being quick to get this webinar together. And also to all of you for joining this webinar in the middle of the day on a Friday. Next slide.

And this as with all of our ORD and Office of Research Protection and Policy and Education Webinars, these are available, recorded, and available on the website listed. So Sarah, do we have any questions in the chat?

Erica: This is Erica, and I will walk you through those questions. Let me see, I'm about to share my screen. Whoa, let me make sure I'm sharing the right screen here. There we go. Okay. Do you see my list of questions in this Word document? Anybody?

Dr. Victoria Davey: Okay, the first question is, can VA employees that test positive for COVID-19 participate in the VA arm of ACTIV-2? You've probably seen the policy statement on VA employees enrolling in vaccine trials, which are quite a different animal than an outpatient trial for COVID-19. There are of course, if a Veteran employee is a Veteran enrolled in the VA healthcare system, probably certainly you can enroll in ACTIV-2. Other than that, it would be I believe up to your medical center site whether a non-Veteran VA employee could be enrolled in ACTIV-2 because medical center directors make a decision on providing clinical care to employees. I can research this further and get back to this group. But I believe it would be up to the medical center director. The next question is probably best for Donna. Could we be added to the call, the coordinator investigator calls that happen on Thursdays at 5 while working on the startup documents. Donna, could you answer that?

Donna Kostandy: Sure, yeah, this is Donna, yeah send me your contact details and I will be happy to get you included in those invites.

Dr. Victoria Davey: Thanks Donna.

Donna Kostandy: Sure.

Dr. Victoria Davey: Another question, does ORD have recommendations for our privacy officers on what they should be reviewing as preliminary review. Cristin, can you answer that?

Cristin Harrington: Yes, I think the best place to start is probably with the policy link that is embedded in the slides. If you read the policy on the need for an endorsement letter before submitting to the single IRB, the commercial IRB I believe there is essentially a list that describes what types of element needs to be included in both the privacy officers review and the information security officer's review. And again, just to reiterate, if you'd like to partake in the central information security officer review, we can include you in that, but we do not at this time have a central privacy officer review. There's a lot of local information that goes in there about how you're keeping, storing, and maintaining the data locally.

Dr. Victoria Davey: Thanks Cristin. And let me remind you that the slides are available as a file, a document in the window here so you can have a version that you can click on links and they'll work. Can we have a contact for Donna at PPD? Her email was provided in the slide presentation. And so you can see it there. If you have any questions of course, ORDCOVID19 at VA dot gov also can provide you with any links. Next question, it was my understanding that with the new ORD VHA directive 1058.03 that we wouldn't have to add external IRB's to the Federal wide assurance. Is this an exception to that directive?

Cristin Harrington: So I can answer that. And if Sarah is on the Webinar and wants to add to it or correct me, she can as well. This is Cristin. So I was just recently made aware of this. It made it into the slide, but whoever asked this question you're absolutely right. There is a change, this new directive, that means that external IRBs will not have to be added to your FWA.

Dr. Victoria Davey: Thank you.

Sarah Rule: Hi, this is Sarah Rule. And that is correct. I'm confirming that.

Dr. Karen Jeans: And this is Karen Jeans with the Office of Research and Development. I'd also like to provide a comment about the privacy reviews. In terms of the documents that the privacy officers need to do, and have for their preliminary reviews, that's going to be driven by the 10-250 which is a form that the investigator submits to the privacy officer. And that form includes comments about are you going to have a waiver of HIPAA authorization? Where is your data going to be stored? What is your PHI? So at a minimum the privacy officers are going to need the copy of the protocol, the informed consent document, if there is a request for a waiver of HIPAA authorization they're going to need that, and they're going to need the HIPAA authorization document itself. So those are the minimum documents that the privacy officers would need. Thank you.

Dr. Victoria Davey: Thanks Karen. [inaudible 0:45:37] Any other comments about that question? Next question then is, how many patients need to be enrolled to cover the cost of the study coordinator? So interesting question. Of course it depends on how you need to use the administrative startup funds that come as a part of the budget for this study at sites. We are working actually on a calculator for that, or a modeling for that, for ACTIV-3 that we can probably convert to ACTIV-2. So I don't have an answer for you for that. But if we can work at this modeling and it's really a quick and dirty excel model, then we'll share that with all of you to help you do that calculation. Next question is, what is the timeline for the information security officer preliminary review? Cristin or someone?

Cristin Harrington: Sure, sure. This is Cristin. So I'm looking ahead, there are two questions down we have a similar question. So let me see if I can't kind of tackle both of those with one answer. So the timeline for the centralized information security office review, I'm ballparking this. This is a new process. It's certainly one that we've been taking advantage of in ACTIV-3. And we've probably gone about three rounds with a central ISO review by the research support division. So if I had the ballpark, I'm going to say about a five-day turnaround from the time that I provide Mr. Peters and his colleagues with your documents. Until the time that he turns around and provides me with his review, which would include the individual sites that submitted. So again, that's a ballpark. That's kind of give or take. It depends on how many sites I submit at once. But a lot of the work is done initially in the beginning. So as we speak, Donna and I spoke yesterday about kind of embarking on this background ISO review before we get any site-specific documents, so that the RSD has this sense of this study, the platforms used, the encryption, security. And then when the sites are ready to submit, really then they're just looking at the sites documents in context with all of the information security parameters that have already been established. So part of the five-day turnaround too is a little bit on us at Perry Point at this point in time. If I know that two sites are going to provide me with their site-specific consent forms, their HIPAA authorization et cetera within days of each other, I'll hold site A back for a day or two until I get sites B, C, and D, so that I can just submit en mass. So again about an average of five days. And then the secondary question is, what do you need to do if you want to take advantage of that preliminary, I'm assuming this is the central, ISO approval that you're asking about. And if you'd like to take advantage of that, really all we'll need from you, we have a series of questions that we ask, it's similar to the 10-250 that Dr. Jeans mentioned. So we will ask you these questions, you'll provide us with the answer to these information security questions, your site-specific informed consent form or forms, depending on the protocol, and your HIPAA authorization. We've turned that around and provided to the RSD for their review.

Dr. Victoria Davey: And Cristin, what sites have to do is contact you all in Perry Point?

Cristin Harrington: Yes, please contact me at Perry Point so that I can orchestrate that for you. And the other thing too I guess just to the timeline is, give or take five days, if you have a better turnaround time locally with your local ISO you can certainly go through your local ISO for that preliminary ISO review. There's no requirement that you go centrally. We just built it in in case your site needed or wanted that efficiency. So if it's a matter of getting a local turnaround in a

day or two days or waiting the five and you want to go with speed then certainly that's an option for you.

Dr. Victoria Davey: Thank you Cristin. Let me go back up to a question on study related specimens. If we participate as a site, would it be possible to access study related specimens? And will saliva be banked? Dr. Smith, are you still on?

Dr. David (Davey) M. Smith: I am on. Hi, yeah. We will have saliva banked. And we have a concept sheet process that allows other investigators to access those specimens.

Dr. Victoria Davey: Great, thank you. Erica, are there more questions?

Erica: That's it, you've hit them all. Oh, no. One just popped in. Okay, here it is. Our site has been in contact with the PPD outside this network, should we start all over to be registered through the VA? Or Donna, can retrieve all documents?

Dr. Victoria Davey: I'll start Donna. Of course we can work with you on what you've already done. And as long as we know your details, we'll merge everything and make sure that you're linked between Perry Point and ORD and PPD. So please get in contact with Donna and Cristin. And you can always copy me, Vicky Davey. Victoria dot Davey at VA dot gov.

Erica: Okay, I think for real this time the questions are done.

Dr. Victoria Davey: Okay. Well thank you again very much for your time and your attention. And thanks again to all the panelists. And we hope this has generate more interest in ACTIV-2 in the VA network and we hope to hear from you. Thanks again all.

[ END OF AUDIO ]