Cyberseminar Transcript

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Session: A Conversation about Human Subject Research in the VHA

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Dr. Molly Klote: Hi and welcome. I'm Dr. Molly Klote. I'm the Director of the Office of Research Protections, Policy and Education within the Office of Research Development at the Veterans Health Administration. Today's topic is a conversation about human subjects research in the VHA.

I'm the new director of the office as of October 29th, 2018, and upon arriving I asked if I could change the name of the office. We are the office formerly known as PRIDE which was the Program for Research Integrity, Development, and Education. And research integrity means something in research and it really actually means misconduct investigations is what is signals to people. And so I asked if we could change the name to something that reflected more what we actually do which is research protections through policy and education. Our office also oversees the VA Central IRB. So with this name change, I wanted to go ahead and signal a change in our mission and our vision.

So we had pretty lengthy mission and vision statements built for the office and wanted to really reduce those down to something simple that we could set our focus on. And so with the mission, and I chose these three words very carefully. We want to focus on effective, compliant and efficient protections policy, education and ethical review. And that's in that order really. The policies have to be effective in order to protect the human subjects. We've got to be compliant with all the rules and regulations that happen within research. But we want to also focus on efficiency and look for where we can gain efficiencies. And this is why I actually have been on this listening tour across the VA; to ensure that I can hear back from all of you where we can further improve our efficiencies within our policy and education.

The vision for the office is to create the model within the United States of effective, compliant and efficient research protections, policy, education, and multi-site review.

So where are we now? It is now February the eighth that I'm giving this presentation. We are past the compliance date of January 21st, 2019 which we had all been anticipating for a very long time. So there's one more shoe however that's going to drop out of the new common rule that was released and that is the cooperative research provision which is the single IRB review mandate for the country which comes into effect on January 20th, 2020. And I'll talk a little bit later about how we are approaching getting the VA ready for that other shoe to drop. So 1200.05, as of the date of this presentation was released just about a month ago. We did a lot of prep work before it was released in preparing you for what those changes were going to be. But now you've got it. You've had it for a little over a month on the day of this presentation. And really the focus of why it was written the way it was written was to better harmonize the way the VA aligns itself with all the other people within the United States who are doing human subjects research. There were things that were in the old 1200.05 that set us apart and it made it harder to do cooperative studies with us. So the goal of the 1200.05 was to better streamline what we were doing. It also incorporates into it the VHA Handbook 1058.06 which really doesn't effect anybody in the field, but does effect people within the staff here at the Office of Research and Development who conduct research studies.

So the changes that I want to talk about today that happened in 1200.05 and the new directive 1200.01 is not an all-inclusive list, but hits pretty much on the highlights of what happened. So in 1200.05, I think one of the biggest changes is our ability to now rely on an IRB from a non-affiliated medical or dental school for multi-site research. How exactly to go about that is a process that we are working on with the Office of Research Oversight. We've already met with them. We're developing a guidance document and hopefully soon we'll also have some additional staffing support to process what we think is going to be an onslaught of applications. What's really critical for you as investigators, if you're investigators watching, is that it is an institution's responsibility to submit to us a request to rely. Investigators cannot submit those requests to us because really the agreement that gets made is between your institution and the institution with the IRB on which you're going to rely. The process will still require ORO to review and approve these, but we really worked with them to try to develop a streamlined non-redundant process.

The second thing that actually supports the first item, is that there's no longer a requirement to place VA members onto an external IRB. And this includes your affiliate IRB. You may however continue to allow members to participate where it makes sense. But where it might not make sense is if all of a sudden you want to rely on the Duke Medical Center IRB, or medical school IRB for one study, trying to figure out how to get two VA members onto that IRB is no longer a consideration you have to make.

Now with your affiliate, you are probably going to want to keep some sort of relationship with them and continue to support the IRB especially if you rely on them solely you're going to want to continue to support that relationship. And they are most likely going to want you to continue to support that relationship. So this is not a prohibition on supporting, it's just giving everybody a little more flexibility.

Another, something that was written into 1200.05 which was sort of a self-inflicted wound was that expedited review had to be reported at the next convened IRB meeting. So if an expedited reviewer who was an IRB member was doing a review and the IRB meeting happened to be the next day, I think we all know that IRB agendas get made ten to fourteen days in advance of the meeting. And if you're doing a review the day before the convened meeting is happening, you're not going to get that action onto the convened IRB. So it just set everybody up for failure or delayed expedited reviewers from bothering to do a review because they knew they we're going to make it and it was just going to set the institution up for a problem. So that has been removed. Expedited reviewers of course still have to report their issues to the IRB, but you will establish those timelines in your IRB SOP.

I think something everyone knew but had never been codified in policy was that if ORD is funding a project, it has the right to suspend or terminate that project. I don't think there's a lot that needs to be said about that.

Let's talk a little bit through about broad consent. Broad consent is a new idea that was introduced within the new Common Rule. However the issue of using data and specimens for future research is not a new concept. This regulatory broad consent does not have to be used in lieu of writing into a current consent form the ability to ask a research participant for their permission for future use of their data and specimens in future somewhat unspecified research projects. Broad consent has some advantages when you are using or setting up a repository type protocol and those should be explored if you're doing that kind of a project. Within the VA however, and you will find that there are many VAs across the United States who are not allowing broad consent at all until it becomes a little more mature. But broad consent within the VA is going to be limited solely to data that are collected for the purposes of research. So if you intend to touch the medical record, the CPRS in any way related to your research study, or go and get data out of the CPRS for the purposes of your research study, that is not going to be allowed to be done under broad consent. And the reason for that is that if someone says no, a study participant says no to broad consent, the data and specimens that they have said no to can never be used in research again. The IRB will not have the ability to waive consent or HIPAA authorization for the use of those data or specimens. And in our current electronic health record, we have no way to track when someone says yes or no and be able to dice that out within the electronic health record. So VA has made the decision not to say no completely to broad consent, but to say it can only be used when all of the data and specimens are obtained for research only.

On the next item. Because of the changing population within the VA and changing services that are offered, in vitro fertilization research will now be allowed.

To better align us with what the rest of the country is doing, both stem cell and fetal tissue research is now allowed. However, for embryonic stem cell research or fetal tissue research, you have to follow the NIH guidelines and you have to look at what restrictions there are on the NIH website on almost an ongoing basis to track how the use of these types of tissue can be used for research purposes. There are prohibitions put on this type of research all the time and there are considerations from an institutional perspective about whether or not you want to allow these types of research to happen within your institution.

The next topic is pregnant women research. So historically if you even wanted to survey a pregnant woman under the old 1200.05, you had to get facility center director certification that you could handle that kind of research within your facility. That has been rolled back to only needing facility center director certification if it's going to be an international study with pregnant women or there's going to be invasive monitoring with pregnant women.

For neonatal research, if your facility does that, that does still require facility center director certification.

Let's talk about impaired decision making policies. So the VA historically had some additional hoops you had to jump through in order to have impaired decision making participants to have all the regulatory things match up with the VA regulations. We've removed those additional things that the VA had in place in order to better align. This does not mean that we don't care about subjects with impaired decision making capability. What it means is that we feel that the protections that are in place through the common rule and through the regular policies of IRBs take all of that into account. There are legal requirements based in states. There are both privacy and HIPAA issues to deal with when you're dealing with legally authorized representatives and personal representatives, so you need to account for all of that. But we took out the specific VA requirements.

So the informed consent HIPAA authorization. For anyone who has been around the VA long enough you know that at one time they were married. Then they were forced to be divorced and now they are getting remarried again with some caveats. So first of all, the reason the divorce had to happen was that people were changing the language of the HIPAA authorization text within the combined document and as a result we did not have legally effective HIPAA authorization. And so the privacy office cracked down on these practices and said, you know what? No more. You have to use VA Form 10-0493 and you cannot have the consent combined with it. As we have sort of grown up and gotten more used to the HIPAA authorization language, the privacy office is now giving us another opportunity to put these two documents back together. In the model document that we released on the website in anticipation of the new common rule and the new changes to 1200.05, there is highlighted green text within that document that cannot be changed if you intend to use that document as a combined consent and HIPAA authorization. You may remove the green highlighting however, but otherwise none of that text may be changed. There are times when you're not going to want to combine a HIPAA authorization and the consent form. And in those times, there's a prohibition on doing that, and that is if you're asking for future use of data and specimens you can't combine the two. But the other time you might not want to combine the two is when you're doing a longitudinal study and you intend to do re-consenting every five years and there are people in your study who may lose the capacity to consent for themselves. The HIPAA authorization that is done at the beginning of that study by the individual is going to be good for the entire duration of that study unless that person revokes that HIPAA authorization or their personal representative revokes that HIPAA authorization. The only thing that you would need to continue to do is to consent. And if you have them combined there, you can run into issues where the legally authorized representative is not in fact the personal representative. It's rare but it can happen and so avoid it. If you do intend to do a study where the HIPAA authorization is separate from the consent you must use the 10-0493. You may not create your own HIPAA authorization.

So now let's change gears a little bit and talk about 1200.01 which was released on January the 24th.

So the big change that you'll notice if you look at it is that the format was changed to match the format of 1200.05. And I think that is going to be reflected in all of the directives that start to come out, trying to align them. The responsibilities that are now outlined in this directive go all the way from the Under Secretary of Health all the way across to what the investigators responsibilities are. And there are lots of responsibilities. So everyone in his or her role should be looking to what those responsibilities are. For the Research and Development Committee, which is what this directive is primarily geared towards, it's re-looking at what is the role of the Research and Development Committee? There are new responsibilities for looking at agreements. There is a new requirement to establish a conflicts of interest committee and more information will be coming out on that. There are some things that were written into this directive that we are taking a hard look at right now with the potential for a rapid revision of some of these things. And that list will be coming out. The Office of Research Oversight has given everybody a 90-day, they're not going to enforce this policy for 90 days. So we have until May 1st to implement the policy at all of your sites. But within that time frame we are going to make it very clear to ORO what within this policy we intend to change. We're going to have a draft to them actually fairly soon so that they can see so that we don't have all of you standing up these massive conflict of interest committees when in fact we may end up with a financial conflict of interest coordinator. So more information will be coming soon.

Regarding voting membership of the R&D committee. The big change here is that without compensation employees can now be voting members. That's probably the biggest change with membership. It still requires a minimum of five voting members. There's no change in the R&D committee operations per say, other than they don't have to meet on a monthly basis anymore.

So in terms of oversight for the R&D committee, we're going to talk about how, when there is an IRB that is either external to the VA and your affiliate IRBs and how that relationship is going to work. And again, as part of the revision of the 1200.01 that's coming, this is going to be made a lot more clear.

What I want to focus on though is really the role of the R&D committee and what it's supposed to do for the institution. And a lot of that is looking at more strategic planning for the institution when it comes to how it's interacting with all the institutions around it. Who are the patient populations at the facility? Where could the R&D committee look to compare? Who are you seeing? What procedures are you doing? And what are you researching? And that's a focus that I think we need to push for the R&D committees.

There's still a requirement for an annual review of the subcommittees sent to the VA medical facility director. Again, we've eliminated the monthly requirement [for meetings]. It now will be an as needed requirement. I've been asked the question, is once a year adequate? No. I don't think that's going to meet the spirit of this, but there are times where monthly may be too many for some institutions.

What this directive puts into place is the requirement, although it was always a requirement by the ethics office, it just had not been put into policy [unintelligible 20:28] the OGE 450 Alt-VA be submitted by VA investigators. This is an eight-page PDF form that will need to be completed and submitted and the facility will have to review these OGE Form 450 Alternates, identify where conflicts are identified by the investigator and then those will have to be reviewed by trained ethics staff.

The other big change though for the R&D committee is the allowance of a designated reviewer process. So designated review is a lot like an IRB expedited review. Right? Or an IACUC designated member review. You only need to have one member do it, you can assign two members to it, but only one member has to. And they may review on behalf of the full committee. The designated reviewer is allowed to require changes. They are like an expedited reviewer to the IRB. They must report what they review to the full R&D committee and the way this is currently written, it must be reported to the next convened R&D committee, which again we will take a look at as we revise this policy.

So below, on the same screen is examples when designated review is permitted. And just like with expedited review, we've put some parameters. These are not all inclusive, but just to give you a sense of when expedited review can be used. And it's really, it's about minor changes. It's about giving out a final approval when the privacy officer and information security officer review is pending. If you've got exempt protocols and expedited protocols, they can be approved by one member of the R&D committee.

So there's three different sections within 1200.01 and if you don't read carefully and identify which section you're in you can get confused as I did the first time I read it.

So the first section is when the R&D committee is reviewing when another subcommittee is primary and this subcommittee is an internal subcommittee to the VA, right? In these instances there's no need for the R&D committee to see amendments or to conduct continuing review of these protocols, okay? They do need to oversee the minutes from the subcommittee. They may still disapprove and they may still require changes to a study that was submitted or approved by a subcommittee. The second section is when the R&D committee is reviewing when there's been an external IRB involved. And an external IRB would include your affiliate IRB. So the role of the R&D committee is a little bit different here because an internal VA IRB or IACUC or other committee didn't review it. And so the R&D's function then is also to ensure that the research supports the VA mission, that's it's scientifically sound and feasible, and that it complies with all the privacy and security requirements in accordance with 1605.01 and 6500 because that outside institution is not going to do those things on behalf of the VA. These are institutional responsibilities and the R&D committee reflects those institutional responsibilities. And so that's the difference there, but it doesn't really change your relationship with your affiliate. And when this is done is really up to the institution. The final R&D approval has to occur after the IRB approval. But all of these things can be, and in my opinion, should be checked prior to sending something over to an IRB to avoid any unnecessary amendments that would happen or the worst case scenario where the R&D committee would say or would disapprove something after it has already gone all the way through the IRB process and been approved.

And then the final section is when an R&D committee is going to review when it's the only reviewing committee. So in these cases the R&D committee has more responsibilities because there isn't another committee doing the work of looking at amendments or looking at continuing reviews. Now the term continuing review with the R&D committee is something I hope to change in the new 1200.01 just because I think it evokes the spirit of an IRB and that's not what we're really doing. This is institutional oversight of these projects. Whether we really need to do it every 365 days for an exempt study or a bench lab study is something we need to take a look at especially when the IRB now is under the new common rule for low-risk things or not requiring continuing review, having that same level of continuing review for an R&D committee is something that we have to reconsider.

What the R&D committee is supposed to be looking at when it does continuing review or institutional oversight, or whatever we're going to end up calling it, are things that affect the institution. Are you making progress in your study? Are there any budgetary changes? Are there any changes to the study that are going to impact the institution in some way? Have there been an unanticipated problems that the institution needs to know about or any issue of noncompliance that could potentially affect the reputation of the investigator, the reputation of the institution, all those sorts of things.

So collaborative research is another area where we're working hard with the Office of General Counsel. One of the reasons why both 1200.01 and 1200.05 were held up for a while was actually on the topic of collaborative research and we are looking to streamline how to get this done with both of those offices. What was agreed upon as it came out of this was that if you're going to transfer biospecimens from an individual VA facility, even if you're transferring them to another VA facility, you have to have a Material Transfer Agreement in place. If you're transferring data along with those specimens, some form of a data sharing agreement will need to also accompany that. Now, if you already have a CRADA in place, now CRADAs are between federal and non-federal institutions. So if you have a CRADA in place that CRADA could cover both the material transfer aspect and the data sharing aspect and you wouldn't need to do all three different agreements, you could just have one overarching agreement. [Unintelligible 27:53] Office of General Counsel is leaning toward having CRADAs for projects when you deal with non-federal institutions, but the process of how that would work given the centralization of the STAR committee right now, which is the OGC reviewing body for these types of agreements, is something that we're working and negotiating with them on.

Another section that was added to 1200.01 which at first when I read it I wasn't sure why the non-Veterans section was in 1200.01 when it's a human subjects protection issue I thought, and I thought it should have been in 1200.05, but it's really an institutional issue. Because when you enroll a non-Veteran, and non-Veteran is probably not the right term for this, because it's really any Veteran who is not eligible for care within our system, is really what we're talking about. These are active duty people. These are Veterans who don't qualify for care within the VHA system. If you're going to enroll them in a study where they potentially could get hurt, you're going to need the R&D committee to approve that because the R&D committee represents your institution and enrolling people who aren't eligible for benefits puts the institution at a little bit higher risk because of research-related injury costs potentially. Even for something as simple as a blood draw study. Someone's getting their blood drawn and they fall and they crack their head open and they've got now a traumatic brain injury as a result. The care for that research-related injury falls upon the VHA. If they're already a beneficiary it's not as big a deal as if they're not a beneficiary. The other big issue with this as raised to us from the privacy office is that all non-Veterans that are enrolled into research studies within the VHA must be given a copy of the VHA privacy practices.

So that's, I'm finishing up there with [unintelligible 30:02] directives that are new. And I'm going to switch for a moment to some strategic issues that are going on. And the first is Dr. Ramoni's signature initiative which is the ACT for Veterans initiative. And ACT stands for access to clinical trials. And so there was a meeting back in March of last year where a lot of stakeholders came together to try to figure out how we can better both bring clinical trials into the VA and where that's not possible, do like a match.com to send Veterans out to clinical trials if they would like to, to get them sort of the cutting edge drugs, devices if they're so inclined to enroll in a clinical trial. What, some of the subcommittees that came out of this looked at using electronic platforms. How do we engage [unintelligible 31:02-31:03] and small sites into things like this. What policy changes would we need to do to be able to do this? Also what came out of that meeting was something called the Research Support Division. And what that is, it's a group that's headed up by Dujuan Williams currently that's uniting all of the information security officer policy to try to get sort of a single voice when you're doing a multi-site study. I think anyone who is familiar with the VA Central IRB knows that there's just a single ISO review done and a single privacy officer review done when something is approved by the VA Central IRB. Those decisions are then communicated out to the field. So the goal for this Research Support Division is to be able to be a resource for any sort of multi-site studies that go on. Any sort of clinical trials that are being spread across the VA so that there is a single voice answer. I think this is a great start that they're doing for information security. I think something very similar is needed for privacy. We all know that even if you get an information security approval, your site may not have the IT infrastructure to go ahead and execute what they're saying. They may say, sure you can transfer the data through your local air gap connection. Well you may say, well we don't have an air gap connection at our site. So it's some of those issues where you're still, even though the central ISO is going to say sure, this can be done, you're still going to have to look at it from an institutional perspective to see if you have that IT infrastructure and if you don't, how you could potentially get that IT infrastructure.

For those who haven't seen yet, the Office of Research and Development now belongs to a new division headed by Dr. Carolyn Clancy called 10X. We used to be in 10P. We are now in 10X with all the academic affiliates and the innovation groups. It's really the first time that these groups have been put together. We think it's going to generate a lot more collaboration and make things a little bit easier to deal with in the VA in terms of our affiliates and collaborative studies.

So what are we doing in the Office of Research Protections, Policy and Education? For any of you involved in the transition to the new common rule, we posted more than 50 documents onto the ORD website in order to help support you in your transition. None of these forms had to be adopted. They were put up there as tools for you to pick and choose from and even pick certain questions out of to enhance your own local forms if you were so inclined, although you were welcome to adopt them. We are putting together a research regulatory support network where Dr. Karen Jeans is going to collaborate with a number of regulatory experts across the VA that are located at sites in order to create a network for our office as sort of outreach, a first stop shop for institutions that are put under their control. And part of that is to limit what is an unending number of questions coming directly into our office because we like to answer your questions. And we spend a lot of time answering your questions as you all well know. But we need some time, we need some cover, for us to be able to do more of the strategic planning, for us to be able to put together frequently asked questions and guidance documents and allow others to answer questions on behalf of our office with the support of our office. So as we create this network there will be weekly calls, we'll be looking at the questions they're getting, the answers they're giving and making sure that everyone is getting sort of a unified voice. And out of those questions will come FAQs that will be searchable and posted and hopefully at some point you'll be able to just go on our website, type in your question and have an answer pop up that is a standard answer for the VA.

We now have our own educational platform. I'm speaking to you on it today. That allows us a lot more flexibility in the number and types of classes and courses that we can offer.

We're revising our web presence. We know that we don't get a lot of hits on our website and we're working to make our web presence a little more interesting that people will come to it. Put more content on it that will be of value to you in the field.

We're working with the cooperative studies program SMART teams to try to get you FDA site inspection reports. We know that in 2019, nine VA sites are going to be visited and inspected by the FDA. We don't know what nine sites they are. We are working to try to risk stratify where the highest risk is within your institutions. People who have not had an FDA inspection recently or have not had a cooperative studies program SMART team come visit them and have a lot of FDA studies going on. You're the groups that we want to work with the cooperative studies program SMART teams, get them out to your site, have them do some education programs. We're also going to have them conduct a Cyberseminar or workshop on how to prepare for an FDA site inspection. There are things you can push back on with the FDA, you don't have to be afraid of them. And we want you guys to be ready for that.

As I've been out on my listening tour across the VA I've been looking for best practices. There will be a call coming for best practices. There's a lot of people out in the field who are reinventing the wheel and I've seen some of the great ways people are doing business and I think it's worth sharing that with all the other institutions.

The other thing we are working on is a workshop that's coming hopefully late this spring, early this summer on preparing us for the new single IRB review mandate. And part of that is going to be a little bit of a cultural change for the VA in looking at what are institutional responsibilities versus what are IRB responsibilities. Because as we move to rely more and more on IRBs that are outside of our comfort zone, places like commercial IRBs and non-affiliated IRBs, we're going to have to be very clear on what our institutional responsibilities are when we do that. We're not going to be able to just send every question we have to the IRB when something happens in a study. We're going to have to internally learn how to deal with some of that.

For a strategic plan of course our main concern is supporting you for common rule implementation. Here within the office we've made some personnel support gains. We've gotten approval to [unintelligible 38:38-38:39] research regulatory support network which is going to unburden, we hope, a lot of regulatory questions from us and allow us to do some things. We were given the ability to add additional time to IRB members within the VA Central IRB in order to help with that. We're working on a contract right now to try to get some additional staffing in for the VA Central IRB in order to sort of shore up their process right now. We've made an investment in education and communication. I've been out on a listening tour and gathering best practices and ultimately we're going to do some further policy revision.

So the big questions I have for the field are, how do our policies affect you? You've had a little bit of time now to look at 1200.05 and 01 and start to live with them a little bit. Love to hear your feedback on how those affect you, how we can better build community within the VA and what educational topics would you like to hear from our office? How can we better help you either within your day-to-day jobs or support even your investigators? If you need an investigator 101 course. If you need, like we talked about, the FDA course. If you need some good clinical practice training. I mean all of those things we can look to try to build into our strategic plan for education. And then really, I'm just open to hearing other issues. We know that within VA, and I've told this to Dr. Ramoni and Dr. Clancy, that I can fix all the research policy that we put out and it may not change anything for the researchers if we can't influence areas like privacy, information security, the Office of General Counsel, contracting and human resources. And I have collected up almost eight pages of comments from the field that I have sorted and broken out into things we can effect and things we need to influence and we're working on setting up meetings with those groups that we need to influence to bring back to them exactly how the policies in their offices are affecting the research community.

So I hope this has been helpful to all of you. I look forward to hopefully at some point getting out to your site and meeting with you. But wish you all the best and please know that we here in D.C. are rooting for your success in medical research. Thank you very much.

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