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Report on Research Compliance Volume 22, Number 8. July 24, 2025 Klote's Termination Disrupts Major Efforts Launched to 'Fix' OHRP, the Common Rule

By Theresa Defino

Molly Klote, M.D., was director of the HHS Office for Human Research Protections (OHRP) for only six months before she was terminated, effective July 18, as part of the governmentwide purge of employees—an action she believes is a mistake and one she fought for months to reverse.[1]

But during her short OHRP tenure, Klote, a retired Army colonel with 26 years' experience as a researcher and leader overseeing federally supported human subjects research, brokered an agreement with the Department of Veterans Affairs (VA) to fund a new staff member to study various provisions in the 2018 revised Common Rule that she believes are not "evidence-based." Many of the changes were based on expert opinion, Klote told *RRC.*

These include requirements to revise consent forms to encompass "key information" and to use a single institutional review board (sIRB) of record in cooperative research. "No one has collected data on any of these to see if they are really working," she said.

Creating the evidence-based coordinator position is just one of a multitude of projects Klote initiated during her unexpectedly short stint at OHRP. Her exclusive interview with *RRC* provides members of the research compliance community a sobering account of projects she launched to help them that might never come to fruition.

"I had such high hopes when I came in. The saddest part is, I wanted to do exactly what this administration wants. I want to deregulate. I want to streamline," Klote told *RRC.* Among her goals in coming to OHRP were to "fix" some of the Common Rule's impractical and unnecessary mandates, harmonize requirements among the Common Rule agencies and repair deficits she said led OHRP to sometimes issue ill-considered policies.

Of course, should OHRP gain a new director and adequate resources, these projects could find their way back on the agency's to-do list. But this is unlikely to happen anytime soon, if at all, in light of the White House's continuing focus on cutting expenditures—particularly related to research—and reducing the federal workforce.

VA had agreed to fund the coordinator position for five years, Klote said. Based in OHRP, the individual was to "coordinate some experimentation" in collaboration with health care systems, such as VA and the Department of Defense's Military Health System, and organizations, such as The Consortium to Advance Effective Research Ethics Oversight, known as AEREO, based at the University of Pennsylvania Perelman School of Medicine.

SIRB Challenges Were Many

Klote noted that agencies can "waive elements of the Common Rule…to test and to do some randomized trials of some of these innovative things. We could then take the data and actually do some evidence-based rulemaking for the Common Rule."

The memorandum of understanding (MOU) had been written and was awaiting signatures by VA officials, who had already agreed to it verbally. "I have no idea what's going on with it, but frankly, I'm not sure that with the current level of staffing there that OHRP has the ability to put any attention toward new initiatives," Klote said.

Klote experienced problems with the sIRB requirement when she was at VA. For example, VA couldn't allow some university research partners to serve as the reviewing IRB because their systems don't comply with federal electronic security regulations, meaning VA couldn't even "transmit data to them," she recalled.

"People thought [sIRB review] was a good idea; they thought it would help. In theory, it is a good idea," Klote said. But her experience at VA showed complying with the sIRB requirement was "incredibly difficult," and the agency had to grant multiple waivers of the mandate, Klote said. She also knew that the Food and Drug Administration (FDA) had not adopted the sIRB requirement; in 2022, it published a proposed rule that has yet to be finalized.

Klote: Limited IRB Review Doesn't Work

Limited IRB review is another area that needs study, as it is not clear that this "is achieving what OHRP hoped it would achieve," she said.

"In my heart, I didn't think it worked, but I didn't have any data and I wasn't about to change something [without study and data]. Because anytime OHRP changes something, the ripple effects through the community are so profound," she said, as they are when FDA makes changes.

Klote's agenda for other possible revisions to the Common Rule included "adding new exemptions for implementation science and changing our rules on engagement to deal with decentralized clinical trials," she said.

Implementation science is the study of the best ways to encourage health systems and providers to adopt evidence-based practices, particularly focused on closing the "gap"—sometimes as long as 17 years, Klote said—between when findings are made and when health care changes as a result and patients see the benefits.

Some specialties—oncology, for example—are more adept at updating therapies and adapting to findings because they are "heavily research-focused," Klote said. But for others, "it takes a lot to change the way people have been trained and what they are doing."

Given that a randomized clinical trial is "not the real world," providers need workable strategies to incorporate changes from such research into practice. Studies that test these require more regulatory "flexibility," Klote said; implementation science studies shouldn't necessarily need full IRB review and may be able to be done under an exemption.

The Common Rule is silent on implementation science—in fact, "it's silent on a lot of particular methodologies," Klote said, noting the rule "doesn't talk about randomized clinical trials, either."

Instead, it's a "framework" that includes exemptions, she said. The revised rule included, for example, a new definition of research that excludes oral history projects and certain authorized operational activities.

"Implementation science wasn't called out and probably shouldn't necessarily be excluded as [not] research," Klote said, adding, "I think a lot of implementation scientists feel very strongly that what they're doing is research, but could it be its own exempt category, therefore, be able to be approved in an easier way?"

What Does 'Engaged' Mean?

When it comes to engagement related to decentralized clinical trials, Klote said clarity is needed. In a decentralized clinical trial, the "central, coordinating" institution receives IRB approval and coordinates with other study sites that are seeing research participants, collecting data, administering treatments, ensuring delivery of medications, etc. "It's a model that allows for a much broader patient base and much faster stand-up of studies because each site doesn't have to get IRB review," Klote explained.

"Right now, there's a lot of consternation [in the field] over what constitutes engagement; there is no clear, defined guidance about what being engaged means. When I was at VA, I met with OHRP on a number of occasions, and I got specific guidelines established within the VA for what constituted engagement." This was only possible because VA is "not required to follow OHRP guidance as HHS agencies are required to do."

OHRP issued guidance on engagement in 2008, but it has not been updated. The situation is further complicated by the fact that FDA "doesn't use the term 'engagement,'" Klote said. Instead, it requires investigators to complete the Statement of Investigator (FDA form 1572), that among other things, outlines their compliance with FDA regulations. The current 1572 "causes a lot of angst out in the field, as well," Klote told *RRC.* FDA published guidance on decentralized clinical trials in 2024.

Help From NIH; New Subpart F?

Other activities Klote undertook were trying to move forward HHS' own implementation of the revised Common Rule and ascertaining where the other agencies stood. "We were having interviews with all of the Common Rule agencies and all the HHS components to try to find out" their implementation status, Klote said. "We were writing a component implementation plan for HHS of the Common Rule, which every other federal agency had."

In addition to obtaining resources from VA, Klote got NIH to agree to provide OHRP funds to conduct not-for-cause audits of NIH extramural research. But then the NIH official who verbally agreed to the funding was among a wave of agency leaders who announced sudden and immediate retirements, so the plan stopped.

Another area of new OHRP activity under Klote was consideration of adding a Subpart F for classified human subjects research; with her top-secret clearance granted during her time with the Department of Defense and maintained throughout her VA and OHRP tenures, "I was able to start to work on Subpart F and have some meetings with some of the agencies that were interested," Klote recounted. Such an addition to the Common Rule would require rulemaking, and the idea was to involve all the relevant agencies and produce a single, harmonized policy or regulation.

No one at OHRP other than Klote had a security clearance, so she requested security clearances for then-deputy Julie Kaneshiro and a division director. But both of these individuals have left OHRP through early retirement.

Clearance isn't needed for broad policy discussions, but it is when conversations address specific research projects, Klote said, and when regulations or policies are drafted.

Effort to Ease Determinations 'Stopped'

The coordinator position isn't the only project Klote launched with VA. Another is adapting and expanding the VA Electronic Determination Aid (VAEDA) to make it available for use with HHS-funded studies. Klote developed VAEDA in her prior role as a deputy director of VA's Office of Research and Development before coming to OHRP. As the website explains, VAEDA is an online decision support tool utilizing "branching, logic-based questions to determine if their project falls under research or non-research categories. It helps route projects for appropriate approvals and provides next steps based on the determination outcome."

OHRP "had an MOU that we were working on with the VA" to have VA host an HHS-specific application and make it widely available, Klote explained. Standardizing determinations would alleviate the "huge administrative headache" of deciding whether "a project somebody's working on is research or not research, and if it's research, does it meet one of the exemptions? Does it need limited IRB review?" she asked.

'I Was the Logic'

Creating the tool—which has been operational at VA for two years—involved working with VA quality management officials to ensure they would be overseeing the "not-research" projects. "The research offices shouldn't have been approving not-research projects within their institutions. So, we separated it back out and got the not-research activities pushed over to the quality management offices so that they had visibility of what was going on. That decreased the burden on the research offices and both streamlined and harmonized how these determinations were being made," Klote said.

Prior to VEADA, determination decisions might have been based on checklists or someone reviewing a protocol and saying, "Oh, I think it looks exempt," she said.

"We brought the logic over to HHS; we were taking all the VA specific things out of it. We were retooling the branching logic so that we could then send it back over to the VA to have them reprogram it," Klote said. "We knew from some of our initial meetings with the components within HHS that this was something they would be very happy to have. But all of that work stopped because there's no one to do it. I was the branching logic."

1 Theresa Defino, "Amid Seeming Error, HHS Finalizes Klote's Termination as Director of Crippled OHRP; She Issues a Warning," *Report on Research Compliance* 22, no. 8 (August 2025).