

Adrian: [00:04](#) Hey, this is Adrian Hernandez, and welcome to the NIH Collaboratory Grand Rounds Podcast. We're here to give you some extra time with our speaker and ask them the tough and interesting questions you want to hear most. If you haven't already, we hope you'll watch the full grand rounds webinar recording to learn more. All of our grand rounds content can be found at rethinkingclinicaltrials.org. Thanks for joining.

Adrian: [00:28](#) Hi, this is Adrian Hernandez with the NIH Collaboratory, and today we're here with Rob Mentz, who will be reflecting on Good Clinical Practice Guidance and Pragmatic Trials: Balancing the Best of Both Worlds In the Learning Health System. So Rob, thanks for joining us after a great to grand rounds.

Rob: [00:46](#) Thanks so much, Adrian. It was really a privilege to be able to talk with a group.

Adrian: [00:50](#) So Rob, people often talk about a GCP, and something that we have to do, and I wonder if you could describe a little bit about what's been your thinking regarding GCP? Why would you even take a deeper dive in this?

Rob: [01:08](#) Great, Adrian. So as we think about what are some of the key values of GCP and the rationale of taking a deeper dive into this, I think it really is based on the context of GCP really does offer some key important benchmarks as we think about scientific standards trying to harmonize conduct of clinical trials. But over the years as the clinical trial landscape has changed so much, we felt that it would be so important to get a better understanding of how GCP applies to clinical research in the current environment.

Adrian: [01:40](#) And in your view what's been missing? What's been the challenges here?

Rob: [01:44](#) I think some of the key challenges as we reflect on GCP is that while it gives this construct of different checklists to try to make clinical research more precise, it misses some of the key details around actually the reliability of research and making sure that it's not just check boxes around documentation and monitoring, but really that we focus on key efforts that are the key measures for quality in an overall clinical trial.

Adrian: [02:13](#) One of the things that seemed like they came up here is that most people thought of GCP and traditional trials for pragmatic trials or embedded trials with health systems. What are the

different issues that come up in that setting versus traditional trials?

Rob: [02:36](#) In terms of some of the key issues that come up as we think of the application of historic GCP to either pragmatic trials, and in particular those embedded within the health system, some of the key areas focus around consent is is it really practical in this setting? Are there strategies that we can actually use opt out of consent, figuring out the nature of interventions where it can be very different from a historic clinical trial that might be patient level randomization, but if we're looking at cluster randomization or health system interventions. But also importantly thinking about some of the regulatory implications. If we're looking at off label uses of approved products, how do we explore the IRB context of looking at a central IRB versus a local IRB with a multitude of different perspectives. And then some other key measures are actually thinking about data monitoring. So if we're using a trial now embedded within a health system where we may be dependent upon EHR, electronic health record data from a data mart, we may not be able to have some of the historic measures in terms of frequent data checks for data put into a case report form in more traditional measures. So it's really getting at the central issues of as research has modernized, we really need to figure out whether or how we can best tailor a GCP criteria to support research quality and patient safety.

Adrian: [04:02](#) Well it certainly poses sort of different issues, and on this grand rounds we had the pleasure of a couple people who gave perspectives on the kind of regulatory as well as the IRB perspective, so the good Dr. Rob Califf on as well. What did you think about what he had to say about GCP?

Rob: [04:28](#) I thought some of the key things that Dr. Califf highlighted were around how we can best apply these principles to trials in different domains, and understanding some of the key measures of if we're looking at a comparative effectiveness trial of two therapies that are already a standard of care, that the monitoring and management of that trial really could be quite distinct from many respects in terms of how GCP was initially designed. So I thought he had some really important perspectives as both a trial and investigator in clinical trial leader, but also from a regulatory perspective around those pieces. And then I think there were also additional points made around the IRB perspective. We were fortunate to have a seasoned group of individuals that with different perspectives

on how the IRB landscape has changed and made some important points around monitoring and trials, this adverse event reporting. And I think those are some of the key areas as we think about making the GCP construct more modern is really understanding what is the optimal strategy around adverse event reporting in the context of clinical trials.

Adrian: [05:39](#) It sounds like the timing may be really important now to get people more involved and thinking about how to reform or reapproach GCP. What are your take home suggestions regarding how the community should try to address the evolution of GCP versus evolution of clinical trials right now?

Rob: [06:08](#) I think some of the key messages that were discussed were around much of the work that CTTI has done to really help give a perspective on investigator qualifications and quality by design. So this idea of really to optimize clinical trial quality, we need to identify these critical quality factors early on, be able to react over the course of the trial, mitigate these risks, and to be able to accommodate the changing landscape. There was some really good discussion around the lessons learned from some of the collaborative trials, including cluster randomized trials as new guidelines are coming out, or the landscape is changing and we now have increased focus on things like the opioid epidemic that may actually influence ongoing clinical trials. So I think the central take home message, we're figuring out how to best incorporate quality by design into clinical trial conduct in figuring out how to optimize this historic GCP perspective, but making it more modern in terms of investigator qualifications and overall optimizing quality and clinical trials, whether they're pragmatic, embedded within health systems, or even more traditional trials as well.

Adrian: [07:19](#) It sounds like one thing that comes up from this is that while a GCP, when it was first put together for the conduct of clinical trials, it was in a setting where there wasn't really anything to provide guidance regarding clinical trials and the good conduct of that. Now that things have evolved, I guess it's also clear that we should consider GCP as an evolving document, hopefully, as clinical trials also evolve. Hopefully both can be done in near simultaneous sequence, so we actually understand what these new approaches with clinical trials that so too new standards will be needed, and how we ensure good clinical practice and quality.

- Rob: [08:10](#) Adrian, I think that's really an excellent point. And a number of the individuals that joined the call highlighted that since the earliest GCP document there have been really important revisions focus on things such as risk-based monitoring, centralized monitoring. So these have been some incremental changes. But I think as Dr. Califf rightfully highlighted, while there's been progress, we really are not necessarily to the extent that we need and that a number of these ongoing efforts through CTTI, through collaborative efforts, that these will really help advance not only this document, but how we conduct clinical research.
- Adrian: [08:46](#) So Rob, any last minute predictions on GCP over the next five years?
- Rob: [08:55](#) Well, I think we concluded the discussion with an optimistic outlook that whether through measures such as quality by design and the CTTI efforts, but really getting all the different stakeholders at the table. And that's a critical piece, whether looking at important efforts through PCORI and PCORnet about making sure we're embedding patients voice and involvement in clinical trials from the onset. So I think that would be a key message as we move forward, thinking how we best change some of this guidance, but making sure that all the different stakeholders have a seat at the table.
- Adrian: [09:29](#) Terrific. So Rob, thanks for joining us on this podcast. And for everyone, thanks for listening to this podcast. And please join us for our next podcast as we continue to highlight fascinating and important changes in the research world.
- Adrian: [09:50](#) Thanks for joining today's NIH Collaboratory Grand Rounds Podcast. Let us know what you think by rating this interview on our website, and we hope to see you again on our next grand rounds, Fridays at 1:00 PM Eastern time.