



Health Care Law Today

Health Care Law Today Podcast Episode 9: Clinical Trials in the Time of COVID-19

Please note that the interview copy below is not verbatim. We do our best to provide you with a summary of what is covered during the show. Thank you for your consideration, and enjoy the show!

In this episode, Foley Partner [Monica Chmielewski](#) and Of Counsel [Kyle Faget](#) sit down with [Laurie Halloran](#) (Chief Executive Officer and Chairwoman of the Board of Halloran Consulting Group) to discuss how conducting clinical trials has changed within the Health Care Industry in the face of COVID-19.

Monica Chmielewski

Thank you very much, Judy. Hi, my name is Monica Chmielewski and I am a partner in Foley's Chicago office. I am the Vice Chair of the Health Care Practice Group and Co-Chair of the Life Sciences Industry Team. I have spent the last 20 years representing pharmaceutical and medical technology device companies, and biopharmaceutical companies along with hospitals and health systems in all areas related to clinical research and FDA.

We're really excited to have everybody join us today to discuss what is a very timely and interesting topic: the conduct of clinical trials in the world we know today that has been impacted by the COVID-19 pandemic, and unfortunately, it really seems that no one and no industry has been spared from its impact. This includes the pharmaceutical and medical device companies, and the biopharma companies that have been conducting clinical research.

Prior to COVID-19, there have been many discussions and some thought about how it may be possible to conduct clinical trials in a virtual setting, using technology and innovative

measures, and while that technology has arguably been available and present, it really had not been embraced, it really had not been utilized in a widespread manner. Now that has all changed. COVID-19 has forced this issue to the forefront, and indeed, the FDA is focusing on this as well.

In March, the FDA urged industries and CROs to take a virtual approach to the conduct of clinical trials in reaction to COVID-19, and really, they wanted a virtual clinical trial platform to try and attempt to slow the spread of COVID-19. But what does this mean and how was it possible to take a virtual approach to the conduct of clinical trials? That's what we're going to look at today.

In this podcast, we are going to explore what are the major impacts that we've been seeing on the conduct of clinical trials in relation to the COVID-19 pandemic, what are certain regulatory implications associated with that and where do we see this going, and what is going to be the potential future impact of COVID-19 on clinical trials in relation to the use of technology? Trying to look into the crystal ball.

With that, I'm very pleased to have both Kyle Faget and Laurie Halloran here to discuss this with us. Kyle Faget is Of Counsel at Foley in our Boston office. She is a dedicated member of both the Health Care Practice Group and our Life Sciences Industry Team, and has devoted the majority of her practice to representing industry pharmaceutical companies, medical device companies, and biopharma companies in all areas related to R&D and clinical trials. She's also a core member of Foley's Digital Health and Telemedicine Industry Team.

Laurie Halloran is one of our special guests, and Laurie founded the Halloran Consulting Group in 1998, originally operating out of her unfinished bathroom. Laurie's time as a pediatric ICU nurse has inspired her to start a company that helps move new therapies through the FDA processes to get them into the hands of patients that are desperately in need. By providing a strategic development team, innovative startup companies could have access to world-class expertise at a fraction of the cost. Since its humble beginnings, Halloran has grown into a successful consultancy of like-minded experts who are dedicated to improving human health by making life sciences companies better at what they do.

I am pleased to have both Laurie and Kyle on this podcast to discuss virtual clinical trials with us.

Kyle Faget

I think first and foremost, it makes sense for us to start with what we're seeing right now. Laurie, since the beginning of the COVID-19 pandemic, what are the major impacts you've seen to clinical trials?

Laurie Halloran

It's been drastic and catastrophic. There were some data that came out last week on one of the major central IRBs was reporting that only 14% of the research sites are right now open to enrollment. There have been a staggering 100+ non-COVID-19 trials that were put on hold last month, and 60 new U.S. clinical trials for COVID-19. What we're seeing across the board is a huge drop in new patients, and if there have been studies that are existing, about 25% of those patients have dropped or their visits have been interrupted.

What this turns into is that there are delays in enrollment and missed study visits. Basically, the patients just can't get to the research sites or the research sites don't want them there. Some of the things that we are also seeing is any new studies are just being, more or less, put on hold. There can be a lot of activities that can be done to get them to the point where they're just about ready to start enrolling, but the research sites don't have staff. Their nursing staff, in some situations, have either been laid off or they've been deployed to the frontlines in treatment of COVID-19, so we can get them right up to the brink of being able to enroll the patients, but no one wants to do any moving—which I couldn't blame them—to actually go and visit.

That cascades into protocol adherence issues, or potential protocol adherence issues, if they cannot comply with the procedures and schedules of the visits. Many of these procedures are designed to collect important data on both the safety and efficacy of the drug. They may not be able to get the drug, and then there can't be activities post those visits to clean up the data and get it ready for submission.

In another way, we're also seeing the actual material, the clinical trials material themselves, the drug, can't get to the sites. There's limited import and exports, there's limited distribution of the other types of equipment that are typically used and travel bans, so it's pretty much across the board that we're seeing these types of delays.

Kyle Faget

In advance of COVID-19, we saw a real reluctance on the part of the industry to adopt what may be better known as telemedicine or virtual clinical trials, for example, whereby visits with an investigator or a research nurse for example were conducted via Zoom, or something like that, to have these visits done virtually. Have you seen any shifts? Are there protocols being rewritten to incorporate the use of technology that we're seeing all across the board in terms of medicine, or are we hitting a standstill for clinical trials?

Laurie Halloran

No, there are people starting to break out and find work-arounds. A lot of this goes to the level of risk that the company is willing to assume, and that I would say is probably the biggest thing that has shifted drastically. The industry as a whole is very risk-averse, but

given this absolute standstill, there have been creative ways to try to have telemedicine visits or remote laboratory assessments where the patient goes to the lab, it's not affiliated with an academic medical center, and they have their bloods drawn or they have a visiting nurse come in and do some assessments. A lot of what goes into a clinical trial is not actually necessary to be face to face.

Here's a really simple example that, when you take it and you unpack it a little bit, illustrates the challenge. There's something called a six-minute walk test, and for years we have been having patients drive or fly hundreds to thousands of miles so that someone who is quote-unquote qualified to watch them walk for six minutes across a straight line, 20 meters, is doing that in order to define that the product is making the patient better. It's not an objective assessment, it's subjective. But we have put ourselves into the situation where we've mandated that without actually really knowing why, and people are starting to think more creatively about how could they do that and have it be videoed or watched remotely. There's a lot of creativity because of the necessity to do this.

Most of what can be done can be done with some level of remoteness. What we're also seeing people do is define what is a critical safety, or efficacy, measure and trying to figure out what they can do without having face to face contact to get that done. Anything that isn't a critical or safety or efficacy measure actually really shouldn't be part of the protocol because protocols are over-engineered a lot to ask for data that no one actually knows what they're going to do with. They just might want to have it someday. So I think there's a very strong focus on what is absolutely necessary, and they're whittling it down.

Now, one of the things that is required in doing clinical trials is you have to have an ethics committee, or an IRB, take a look at what's been changed, but if you're making the decisions on changing things in a study with the patient's safety in mind, those are often things that can be reported after the fact. They don't actually have to have extensive reviews and approvals. And because COVID-19 travel is patient safety-compromising, that kind of opens the door to a lot of creativity. Most of the time people don't think creativity is good in a clinical trial, but in this case I think it is.

Kyle Faget

That's a completely fair point. So just tackling this issue of creativity because I think it's a really important one, and I absolutely agree that researchers are going to have to think outside the box, the industry is going to have to think outside the box to tackle today's issues amidst COVID-19. And you know the good news about being forced to change is that some of the changes I think could be very long lasting, having said that though, what are some of the regulatory and compliance implications that go along with these forced changes?

Laurie Halloran

Ultimately the challenge will be is the data set that has been defined as critical to demonstrate safety and effectiveness—has that been met? That's the biggest risk of all, because if you've cut out so many procedures and tests, or the patients have skipped visits or not shown up, that could ultimately impact the ability to determine whether or not the study met its endpoints. So that's the highest risk for the company.

If the company is able to take a critical approach to looking at the actual study design and determine things that can be pushed off, or eliminated, or done in a more creative way, the likelihood of the data integrity being maintained will get higher over the course. One thing that is an increasingly important aspect of doing, conducting, monitoring, analyzing, and saving a study, or reporting that study, is the regulatory agencies, especially in the U.S. and Europe are increasingly looking closely at what the pharma company, the sponsor company, has done to mitigate risk and to manage oversight, and oversight is the main role of the sponsor company, the pharma company. They have to oversee the research sites. They have to oversee the conduct of the trial. They have to oversee a variety of different vendors that they need to hire to perform the various thousands of activities. When things are changing so quickly in this type of an environment, if you're not proactively defining the risks that you have in front of you and documenting what you did to mitigate, or manage, or decrease those risks, you end up losing the plot.

What we're seeing a lot of is a heightened level of concern around a real time approach to that documentation. And what ends up happening at the end of a study, or an end of a program where a drug is going to be approved, is the regulators send in inspectors to take a look at what was done to verify that it was done according to the regulations, and the things that they look at are how all of the activities were defined, managed, and documented. So in this type of environment where there's so much happening at any given time, if you're not documenting the risks that you reprioritized and the ways you dealt with making decisions to put mitigations in place, you're going to lose it.

So a lot of our clients and a lot of our colleagues are pulling out tools and sharing them with each other so that they're basically creating storyboards and narrations as to what decisions they made, why they made them, and what the outcome was. That's actually a really good practice to do in a non-pandemic situation and often the thing that sponsors are dinged on in an inspection is that they didn't explain what they did and why they did it. So I see that as a positive.

Monica Chmielewski

I'm wondering as we're talking about this and these new, innovative ways to conduct the trials to reach the patients, to gather the data, all the while doing so in a compliant manner, what have you seen recently that these forced changes are bringing that are either enabling or inspiring industry to use technology in ways that we haven't seen before in relation to clinical trials?

We've seen a lot of—just in the general health care world—patients now interacting with providers on virtual visits, and one would assume that there may be aspects of a protocol that would lend itself to something similar. But then, as you were mentioning compliance and documentation, I wonder how does it monitor that to make sure everything is done correctly? But what have you seen in terms of this technology? What are your thoughts?

Laurie Halloran

What I've seen and what's actually in use there's a drastic divide between that. There's something like 0.04% trials that actually have brought in technology and adopted it in a meaningful way in clinical research, and that's really astounding. Basically, what could be occurring and it isn't yet because people are too busy just dealing with the now, but what could be occurring is a simultaneous evaluation of a subject for a trial as well as just doing a health history.

It could be that the physician is dictating the findings in the visit and there's an automatic, "behind the scenes" evaluation of whether or not that patient is eligible for a study that's going on. We're nowhere near that yet. What is happening is there are, like you said, tele-visits happening, there's home health aides coming, some sponsors are sending pinprick kits with a special surface that you put your drop of blood on instead of having it drawn at the research institution. That's not technology, but it's a little bit more evolved than making the patients go to the laboratory that's down the hall from the physician. It doesn't have to be super high tech to be effective and a lot of that is fairly easily implementable given the circumstances.

The things that aren't as easy to implement are remote. There are companies that basically bring all of the infrastructure and all of the expertise that you could have in place in a community-based physician's office and they will run your trial for you, or they will do most of it from a distance.

That hasn't really been widely adopted basically just because the time to get it up and running is not a matter of weeks, there has to be a little bit longer of a lead time. I see that a lot of those types of remote, supportive, or virtual opportunities will be tried out in this situation, and then might likely be thought of as much more feasible for future. So for the moment, I think a lot of studies are just trying to get by, but I think what this is doing is it's making people realize that they were caught very flat-footed and that they should be thinking about what they can do differently going forward.

Monica Chmielewski

From a compliance standpoint, you mentioned the taking of an HMP at the same time perhaps a patient is evaluated for maybe meeting the inclusion, exclusion criteria in a

clinical trial, getting consent, and there's a whole myriad of different regulations on both the health care side and industry side that may implicate that. Using a lot of this technology, I know there's state-by-state regulations for obtaining consent from a patient when you're using a telemedicine technology versus when you're in person doing an HMP. And there could be some carryover for those state by state regulations of these telemedicine technologies that may potentially apply in the research setting.

Do you see that as something that maybe is deterring industry from really embracing this and jumping in with both feet as to how they can utilize novel technologies, or is it something that you think it's more, they've just always done things one way and now this will be more of a force shift.

Laurie Halloran

There are quite a few large companies that are embracing technology and they've started to blaze a path. The challenge is that most companies don't have the extra people to do that technology-blazing activities. A lot of pharma companies are thinly similarly resourced, so they don't have a clinical innovation department. With that being said, I think that to me the biggest impediment that I've seen between the current practice and the idea of doing something more innovatively, which usually translates into using technology, is a disconnect between the folks who run the development organization and the executives.

In a small company, the head of clinical development is going to, in some situations, report to a CEO or a chief medical officer, and there's a lack of interest in taking a chance—with air quotes around it—on doing something novel or different. I think that's always gone from the top down.

If someone wanted to try a new technology, the question would be, "Is this our pivotal program? Why would we want to make any changes to that? Let's just go and do it the old way." So I've been very interested in exploring for quite a while what those department heads define as their technology adoption strategy and what kind of business case they can create to take that strategy to reality and how they define the value that they get from taking the technology, using it, and actually bringing it in, getting it up to speed, having everyone on the program, working on it in a productive way, not just in a, "Oh, this is a brand new toy," way.

And really what it's always come down to is, "Well, let's not do it now, let's wait till someone else does it." And this pandemic has changed that and I hope it's changed it for the future. Because everyone realizes now that maybe they should have tried some of those things and they wouldn't be so stuck because it's too hard to change on a dime in a matter of weeks. I actually am very optimistically thinking that the mindset of everyone from now on

will be different and will be, "What can we possibly leverage technology to do more efficiently and more effectively?"

Monica Chmielewski

That's interesting and I really like what you had mentioned near the beginning of the conversation where this really is tied to patient safety. The more we can argue the use of technology is a benefit to patients and will help with patient safety, I think that the more it'd be adopted. And it even seems like with the FDA looking at this, it may be that when they have time look to maybe issue some guidance on this, which would help the industry embrace it even more.

Laurie Halloran

FDA has never been a huge impediment to this. I have never seen FDA say, "Don't try it, it's new." FDA has come out and put out risk-based approaches. What they want is for the sponsor organization to manage and mitigate the risk. They don't want every "i" dotted and every "t" crossed, and double checked and triple checked three times. They've never said that. It's just evolved into that practice and I don't know why, but it's gotten more and more complicated and less and less efficient in the 30 years that I've been doing it for no real good reason.

It still doesn't impact the ultimate outcome if an investigator is going to commit fraud. It doesn't change that. If there's a little bit of sloppiness in the handwritten transfer between a medical record and a report form, most of that is picked up by data analysis. So there's like 2% of serious issues that are picked up by the practice of doing site monitoring. And a lot of that, it isn't about safety, it's about detail. So it doesn't add value, but it sure adds cost and time.

Monica Chmielewski

At the end of the day, do you think that the triple checking, making sure all "i" dotted and every "t" crossed is really self-imposed by industry and FDA is more interested in the integrity of the data at the end?

Laurie Halloran

Absolutely, and the real challenge is if you're so focused on that minute detail, you don't actually see trends. You're too close to it. The trends are not seen during the monitoring phase. They're not seen until the analysis phase or until a data cut, so we're adding immense amounts of cost and time for really no value whatsoever, which makes me go back to the question that I ask heads of clinical development. What is the value that you want to get? What is the value proposition?

Many people don't even know how to do that. What are you going to save? And they can say what they might save in real dollars, but they can't save what's really meaningful to the executives, which is time to market or overall development costs. And that's where I see technology changing things.

Monica Chmielewski

In your mind, in your opinion, do you think it's going to continue to evolve? Do you think there's already a sufficient amount of breadth of technology there that is just waiting to be utilized? And where do you see this going in terms of the advantages or the disadvantages?

Laurie Halloran

So the challenge is, there are 9 million—I'm exaggerating a bit, but there are hundreds and hundreds and hundreds of different tools and enablers and technology-oriented things that are supposed to facilitate how you get things done. It's a little bit of a tsunami effect where you've got 15 different possible vendors for every single activity or step that you're going to do in a clinical trial. Where I see the disconnect, is in one unified stream where data is generated based on one touch entry or one touch dictation, and then it is managed through the entire process until it is visualized as part of final data set.

That's the opportunity, but I don't think we're there yet. There are a few companies that are on the leading edge of that, and that's what we're studying right now so that we can define how those disparate silos of vendors should be working together or creating some way of having the data move seamlessly from one place to another. That's where I see the value and the opportunity here in taking that to another place.

Monica Chmielewski

Yes. One would also think that use of certain technology and explain that would allow for expansion by industry to reach even more potential subjects, and to allow people who might otherwise not been able to access or participate in a clinical trial to be able to participate as well. You mentioned people having to travel thousands of miles to do the walk the line test. If conducting trials and using certain technologies for part of it, I mean, I would think that would open up access too.

Laurie Halloran

Absolutely, and the challenge is that your standard community-based physician is really stuck in a really tight place because they have to get reimbursement and they get pushed down by the insurance companies. So they're getting a percentage of what they would normally charge and they're fighting with the insurance companies, trying to get the payments that they should be due. They don't have time to start a clinical research program.

And what I usually tell—and I've told my own physician— is you don't have the staff. You'd need another whole set of redundant people to do that work. So you have to really be willing and open to making an investment in starting up a research practice. I see it as that it shouldn't be one or the other. It shouldn't be the enormous investment in order to have all the people to do all the procedures and do all the paperwork that really shouldn't be done because it's not ultimately benefiting the outcome for the patients and it's not creating better and safer data.

So, if you had a mechanism by which you could have a community-based physician participate in a large trial with a very light touch, and that touch could be facilitated by technology, then you would open up a lot more opportunities to get to the patients where they are, where they live, and make it less burdensome for them to participate.

Monica Chmielewski

And that makes perfect sense. What do you see though as some potential disadvantages? I mean I know you said starting up some of these practices takes extra time, it's a longer process, but what are the other potential disadvantages you see that might be hindering companies from embracing this?

Laurie Halloran

So there's a disadvantage if you're doing a large study and you have 100 different physicians as their principal investigators, you have a hundred people to keep on track. If you are doing broadly distributed decentralized model where any physician could be an investigator, you have a lot more people to keep track of. So that's a big disadvantage. That's something that we're now seeing glimpses of with the COVID-19 pandemic where the sites are being brought on remotely and they're having remote training done, and they're having telemonitoring visits to check in, which increases the complexity, but it's on the sponsor side, not on the site side or on the patient side.

So that's one thing that could be done if people want to go there. I think if they're able to save the time and money that I believe some of the integrated systems could bring, they might be more willing to add a lot more sites because it would actually speed up enrollment. So that's one area, which could be something that we embrace going forward. Companies that already have orphan diseases or ultra-rare diseases already have to do that, so they may have research sites all over the world who each have one patient.

Kyle Faget

It would seem to me that the use of technology, particularly in the ultra-rare space, would be a really good thing. I can't imagine why anyone in that space wouldn't want to move to a model where utilizing technology is almost a must because all of a sudden you can reach—via technology—patients that as Monica suggested you otherwise couldn't get to clinic or there's this huge barrier for travel or something else to get these subjects into the clinic. So

I think that virtual trials, to me, seems like one solution, but simultaneously, at least what I've seen over time in my own practice, and I'm curious what you've seen Laurie is that sponsors don't want to deal with what was, at least in advance of COVID-19, this sort of state-by-state patchwork of laws and regulations dictating how virtual visits can be done.

And what's interesting to me, at least, during the pandemic, is that a lot of these barriers to entry for telemedicine, which by extension are used in a clinical trial, are crumbling down and opening a pathway. If these laws and regulations that were barriers to entry remain at bay after the pandemic, this could be a real opportunity for sponsors to utilize telemedicine in a way that they may be—not that they couldn't before—but that there was a lot of background research and knowledge that might have been required to utilize technology in a compliant way.

Laurie Halloran

I couldn't agree more and I hope that that is one positive impact that comes out of this. What we really need to think about is does the patient know and do they care how their data's being used, if they're getting a lifesaving or life altering treatment. There's a growing movement for a very large ubiquitous department store to open up clinics within the store to bring in patients and do primary care.

Very good idea, but the way they get the patients is they ask people as they walk through the door if they'd like to see a primary care doctor. If so, click here, and the patient gives away all their rights to their protected health information with that click and doesn't even know. So I would say, why aren't we asking the patients what they want rather than making the states decide what's best for the patients and that could be an outcome of this.

Monica Chmielewski

It'll be definitely interesting to see where this takes us. As mentioned, COVID-19 has, and is, impacting the world, the economy on a global basis, and this type of industry is no different. In kind of wrapping this up and summarizing, Laurie, what would you say the big takeaways are that you're seeing? You've been in this industry for a number of years, you've assisted pharmaceutical companies, biopharma companies in the conduct of clinical trials. What would you say is one of the largest takeaways, one of the largest impacts that you've seen this pandemic have on the world of research?

Laurie Halloran

I think it's actually bigger than the world of research. I think it's on the world of health care and I think we're going to look back on this time as a pivotal point in time when we realized that we couldn't afford not to have people have access to health care. It will cascade to research because if people are in the system, they're almost always benefiting from participating in a clinical trial. They just don't know it exists. There's data and there have

been studies done that patients who are on a clinical trial feel really well cared for. It's seen as a positive thing when they have been part of a clinical trial.

So I actually think that there's huge potential if we have systemic change as an outcome of this, and it seems as though that's becoming more and more obvious to everyone that there has to be that outreach so that everyone has as an option. That's not a political comment, that's a human comment, and I think that will transfer to how we do our work. I just hope that we are embracing technology so that we're not wasting time and money, which could be saved in order to pass the savings along to the patients because I think that's another big thing that's going. It's gone quiet for now, but it will come back. The pharma industry really can't afford to be on a lower level of trust than used car salesman. We haven't gotten away with that. It's just been put off for now. It's a really big chance to do right and do what's right for the patients and still allow the pharma companies to have some level of profitability that makes sense.

Monica Chmielewski

Very well said, and I think that's absolutely right. At the end of the day, what everybody really needs to remember is that the focus is and should be on the patients and the welfare of the patients. Everything that pharma's doing, that we're doing, the FDA should be for the benefit of patients, including access to health care, access to these trials. Laurie I think that's very, very well said, and I agree completely with that.

Laurie Halloran

Well then everyone who works in clinical research doesn't work in clinical research because they're quote-unquote pharma. They are passionate about trying to make patients' lives better. And that's why they're as dedicated as they are. So I would see this as a huge opportunity to give a resounding pat on the back to those dedicated workers.

Monica Chmielewski

Absolutely. This has been, I think, very informative. I find it very interesting. I'm very curious and will be very poised to see where this goes and how this continues to evolve to shape the industry in the world. But with that, any last concluding thoughts, Laurie or Kyle?

Laurie Halloran

Stay positive.

Monica Chmielewski

Yes. Positive, safe, healthy. Thank you both for your time today. Laurie, your wealth of knowledge and behind the scenes expertise is just absolutely wonderful. We hope everybody enjoyed this and found this to be very informative and interesting, and I hope everybody stays healthy and safe in the wake of the COVID-19 pandemic and afterwards.