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**Announcer:** The BioWorld Insider podcast.

**Lynn:** This is the BioWorld Insider podcast, and I'm Lynn Yoffee. Not long after the start of the COVID-19 pandemic, disruptions to clinical trials began piling up, recruiting slowed or was suspended for some while others grappled with changes to protocols and procedures. Trial sites raced to minimize potential COVID-19 exposure for study participants in part by adopting new ways to interact with them with a big focus on telemedicine. Meanwhile, regulators also looked for new ways to adapt.

As COVID-19 continues to shape how trials are run throughout the world both regulators and clinical experts are responding with new ideas to meet today's challenges. One of those experts is today's guest Laurie Halloran. She's president and CEO of Boston-based Halloran Consulting. While working as a pediatric ICU nurse, Ms. Halloran was inspired to help move new therapies into the hands of patients desperately in need leading her to start a consultancy to help life sciences companies do just that.

Today, we're glad to have her as our guest with world managing editor, Michael Fitzhugh. Welcome, Laurie.

**Laurie:** Hi, it's nice to be here today,

**Lynn:** Michael, all yours.

**Michael:** Thanks, Lynn. Thanks for being with us today, Laurie. Halloran Consulting offers a huge array of services, including advice on regulatory clinical and quality-focused work, just to name a few areas. Just to maybe ground us a bit as we get started, could you tell us a little bit about what's keeping you and your team busiest these days?

**Laurie:** Well, all the things that we were already doing are keeping us busy and there's been an unprecedented amount of investment in life science companies, and there's a really tight talent market. A lot of our past, present, and future clients turn to us but in addition to that, we really jumped into the whole decentralized clinical trial space because what we're trying to do is help our early-stage and small biotechs navigate and be able to act with the innovation of a large pharma. That's been a very, very big focus of the last year and a half.

**Michael:** Decentralized trials. Tell me just a little bit about what you mean when you say that.

**Laurie:** Well, it's everything that's been developed over the last year and a half, or I should say it was already developed, but nobody was really using it. That's really the big journey that we've been on over the past year and a half. If you didn't have a 20 person innovation team, you didn't have any way to get it implemented. That's the biggest thing that we've been doing. That's been an expansion of the work that we were doing into the space. It's a great topic for me.

**Michael:** There were all these disruptions during COVID-19, especially at the start of the pandemic and you have all of these innovations that are kind of, there in the tool kit, I guess, to be used. What were the risks that people were most worried about and how did they take up those tools as they tried to address them?

**Laurie:** Well, the biggest thing that happened in mid-March of 2020 was everything just came to a screeching halt. The worries that we saw and the anxiety we saw fit into three, and sometimes more than one of those three categories. First, sponsors who were developing potential treatments for life-threatening diseases when patients had no other alternatives, especially if the trials were being conducted in a hospital or in an infusion center, the top priority was continuity of care.

In these situations, many of the companies tried to have procedures and visits conducted remotely from visiting nurses who would go and see the patients at home to labs that could be drawn closer to home, but not necessarily in the original medical center to televisits. Everyone was simultaneously trying to adapt. Next, if the company had a single product with a major milestone that was coming up and even worse, if the next round of funding was dependent on that milestone. There was a huge challenge with meeting a deadline that was absolutely going to be impacted by the delays.

Then the third real aspect of anxiety was how to capture the massive business interruption in their trials so they could look back and be able to reference it later on. In some way or other, everyone experienced some level of disruption, but some experience a lot more than others when there really wasn't a good adaptation for those elements that I mentioned a minute ago. Probably the two biggest things that we saw shifted the mindset toward adopting novel ways to conduct the trials where the shift to reimbursement for televisits by the insurance companies and the new FDA guidances that came out.

**Michael:** I want to ask you about the FDA guidances but actually first I wanted to see, and can you give me an example of one of those types of disruption? Obviously, you covered a gamut of them, but is there one type of disruption that was most frequent or highest profile among them?

**Laurie:** It was really when there was a patient that needed to have a visit in a hospital where there was an infusion, or there was an MRI or an X-ray. There was a huge amount of fear on the part of the patients as well as the sponsors to expose the patient, especially if they were immunocompromised to what potentially could be COVID. A lot of people just were a little bit paralyzed as to what to do for the first few weeks. That's probably the best example I can give you.

**Michael:** With the dates that you talked about, all of these milestones that we're always hearing about a company is planning to have trial results in a particular quarter. The street is watching for public companies. There obviously must have been a lot of, I don't know, concern about figuring out how to best manage those risks when you talk to clients.

**Laurie:** Absolutely.

**Michael:** What was the tenor of those conversations?

**Laurie:** Well, I absolutely recall one CEO reaching out to me by text and then asking if she could talk to me like today. She said, "We are going to run out of money if we don't get our program up and running by the end of the third quarter. What can you do to help us do that?" There were situations like that, and obviously, they weren't across the board because plenty of companies weren't in that situation, but those tend to be are a lot of our clients. It was very much an emergency.

**Michael:** The FDA, obviously you referred to this before they were paying attention. In March, they came out with some guidance to try to address the landscape and they even came up with some further updates, just the other day at the end of August, how have those guidances and that update helped, how have they worked out in practice too?

**Laurie:** All along this journey, what we've been seeing and what we've been trying to manage is in our community, that the first people think of when they begin to sit, consider changing a trial by i.e. making it decentralized is fear. How's this going to be approved? The fact that FDA was supportive and releasing these relaxations of a lot of the protocol, the need to be 100% compliant with the protocol, was huge.

How the sponsor would make their trial decentralized, was what they were trying to help the sponsor do. They were very effective in that, but they had to-- The biotech companies had to be constantly reminded. FDA doesn't want you dead in the water, they want to help you get your product further along in this really, really challenging situation. What it did over the course of the six months at the end of 2020, was it really helped people start to think about how they could become more decentralized.

What they have done is in all of these experiences that we've had, where we've been involved, the FDA wants to hear about the sponsors' processes and use of technology so that they can obtain consent, collect data but what they really want to see is how you're going to work through the protocol to sort out the potential areas that might be a challenge. What the FDA will do, is look to the sponsor to defend their choices. That often is what a type C meeting request is, is to review the protocol, review the plan and justify why you've created the plan. In most situations, the FDA is supportive. It's been a real collaboration between the sponsors we encounter, we represent, and the FDA.

**Michael:** It's an interesting relationship between the FDA and company sponsors because on one hand, companies are paying all this money to you through PDUFA to support the system and they're reliant wholesale, at least in the US, of course, on the agency to make these life or death decisions for their programs. Sometimes, oftentimes it comes up that they maybe misperceived what the agency was saying, or they took a positive reading of what was said and the agency goes another way disagreeing with an Ad-comm for instance or some other surprising move. Was there trust in that relationship to leverage? I guess this is another what's the tenor of that like? What's that relationship evolving into?

**Laurie:** It really comes down to what the sponsor is considering as the top priority which is patient safety. If you've kept the safety assessments as your top priority, and you've gotten rid of some of the nice to have data that so many companies can't seem to let go of, and you have options for easing the patient journey through use of technology, the FDA has been collaborative and open to what your stated rationale is for doing that. If you thought through your execution and you have a solid rationale for your choices, it's not often that they are going to say an absolute no. They might ask some questions, but they often don't say no.

**Michael:** When you talk about nice to have data, what's an example of that?

**Laurie:** [chuckles] Probably about 30% to 40% of the data that's collected in a clinical trial is nice to have. When I've sat in protocol design sessions, often the clinical trial operations people recognize the challenges with collecting the data, but the medics and the scientists usually say, "Well, I'd really like to try and have that." It might be not safety assessments and not directly efficacy assessments, but they someday might figure out something they want to do with the data, so let's collect it.

There's a huge disconnect between the people who have to execute the protocol and the people who've helped design the protocol on what makes sense.

**Michael:** Interesting.

**Laurie:** I can't give you an exact example, but, yes. It's very common.

**Michael:** Is that leading to some streamlining in which there's efficiency emerging or certain gains that weren't there before?

**Laurie:** It depends on the mindset. I'll do a little segue here. A few of the sponsors that we've been talking to are creating, a choose your own journey mindset, where if the patient really wants contact with the physician and wants to be seen live, they can elect to do that. The operations folks have to figure out how to collect consistent data so that if the patient is petrified of going into a research facility where that they might catch COVID, they have to figure out how to collect that data remotely.

There actually are a fair amount of both nice to haves and out-of-the-box thinking and how to do this, we've just never done it before. We didn't have any good reason to.

**Michael:** Now that people have that ability then to maybe choose that journey where they're at home, they're staying out of hospital because they're petrified, are there infrastructural challenges to that?

**Laurie:** Oh yes, absolutely, because what has to be done is the protocol needs to be written so that all of those potential options are laid out and then vetted with the ethics committees, the physicians that might participate as well as the FDA. It definitely makes it more complicated, but as an alternative to not being able to get done, it's a first step down the road to becoming more patient-centric.

**Michael:** Are there particular areas that are indications that have been more impacted than others? I guess you've mentioned really life-threatening diseases and perhaps rare diseases, is adoption of new technologies and new methods accelerated there?

**Laurie:** Yes, absolutely. What I will say as a caveat is what I have seen is that in many situations it absolutely depends on the buy-in from the C-suite. If the C-suite is absolutely on board and they're supportive of the protocol writers and the clinical development folks, then it's much more likely to get adopted. It's a little bit of an awakening across the board in all of the situations that I've been encountering where people say, "Oh wow, we can actually try to do this differently. Let's try it." The more support they have from the top, the more likely it is to be successful.

**Michael:** How much receptiveness is there in the C-suite to change?

**Laurie:** It absolutely depends on the executives. There are, it really is. Remember what the executives' biggest concerns are about is around the timelines that they've crafted and they've set as corporate expectations. They typically build the timeline off historical precedent. What we have been advising is that if you're trying to get your C-suite on board with decentralization, you have to build in the time on the front end and be very clear with needing longer to get started because on the backend you'll save time because often what you really need to do as a pilot to really establish what you're doing.

Then when you get to the end of the trial, your data collection, your data analyzation is much more rapid. You'll have the results much more quickly than you would if you did it the old way. That's the mindset change.

**Michael:** Interesting. Really it's an investing paradigm.

**Laurie:** Yes. It's a managing up paradigm.

**Michael:** It was interesting to me actually looking at the consulting side, it looks like you're doing some leadership coaching in your stock services as well, too. I would imagine to be engaged with that conversation and the need for that.

**Laurie:** Often, we're placed in the company where we're literally reporting to the CEO in a small company or the chief medical officer. There one of the techniques we use is to show our client that we have a real **[unintelligible 00:16:52]** with other companies, so that while we aren't necessarily going to reveal any science, we really know what people are doing that's ahead of the curve.

It's going to sound awful to say but if an executive sees that someone else is doing it and they've been the guinea pig, they're more likely to adopt something. Especially in a small company, if they think they're the first person to ever do this, they don't want to be the first. That's really one of the biggest things that's kept this industry behind the times is that there's a real lack of ability to think about you're not the first person to do it. You might be the first in your company but there are other people.

**Michael:** To shift gears a little bit there's another big important player in the clinical trial space in terms of clinical research organizations, how have these changes been affecting them?

**Laurie:** Interesting. It's evolved over time. One of the main things that CROs do, is they by extension of being the sponsors' feet on the ground is they go to the research sites and they monitor. 10 years ago, the concept of risk-based monitoring was endorsed by FDA or I should say written as an acceptable new method of being efficient in clinical trials.

Most companies have not really ever adopted that in any meaningful way but the CROs were completely prevented from being able to go to the site. What they needed to do was figure out how to do it remotely.

That's complicated when the research site doesn't have or will not give the CRO access to the medical records, when they're electronic medical records, they often can't give access to it. In that situation, it was a huge disruption. I did another presentation where I looked at the good, the bad, and the ugly of how compliance was managed over the course of this. What sponsors do and CROs do is they dictate how frequently they're going to go and what they're going to look at. That's what they anticipate is going to be part of the inspection that comes along at the end when the program's being reviewed by FDA.

To start with an expectation of every six weeks, we're going to go and have it drastically changed to, we can't go for an indefinite period of time made the CROs need to think out of the box. One of the challenges with CROs and the bigger they are, the harder it is, is thinking out of the box. What CROs do is they do their standard procedures really well but thinking and acting differently on the fly is quite different.

To sum that up, I would say, CROs are needing to get on the truck. That's moving into the decentralized space, but what will change, is most of what they charge is based on people hours and technology is going to change a lot and how that's going to shake out yet, I don't yet know, but I have some guesses.

**Michael:** Tell me that. I want to hear about those guesses.

[laughter]

Where's this all going?

**Laurie:** I think if a CRO isn't embracing the use of technology to reduce or eliminate some of the very laborious activities that they were charging the sponsor for, if the folks who don't do that are going to ultimately find that the business model for their work has changed. Most of the big CROs are saying that they've embraced all of these things, but when you audit them before you select them, it often isn't what it has been built as when you dig deeper. They might be partnering with a third-party vendor who complicates the data custody, but they don't necessarily-- You can't choose your own journey, put it that way, as a sponsor.

They're fairly rigid in how they do things. I think if they don't get on the bandwagon with that, they're probably going to see their business erode over time. That's my projection. I might be wrong, but I still think it's something they really need to watch.

**Michael:** Further to the crystal ball, how durable do you think the changes, the pandemic type changes to trials that have occurred that have been adopted by sponsors and trialists how durable do you think those are? Are they going to last?

**Laurie:** Great question. I'll share two experiences that I had. One is when this first started, we started having town halls, and my goal was to not have to lay anybody off basically. Because everything was disrupted, we started pulling people together, and really quickly the town halls on Zoom grew to 250, 275, 300 people every week. Everyone was looking for answers as to how to make changes that they will ultimately be able to make last.

One of the things that came out of that, not the town halls but in a parallel way is something called the decentralized trials and research alliance. It has grown to several 100 companies who are working and volunteering to share their insights, their best practices. I think there are 20 working groups right now on how to change this so that it's broadly adopted. It's everything from standard nomenclature, to education and training, to how to adopt change, regulatory impacts. It's really huge effort, which I'm really happy to see.

I think that probably is the best thing that's come out of this because I think people see that there's the opportunity to make real change.

**Michael:** It sounds like some really strong momentum there. That's excellent. I think that's a good place to leave things today. Laurie, thank you so much for joining us on the podcast. It's a real pleasure to talk to you.

**Laurie:** You are welcome.

**Lynn:** Thank you, Laurie and Michael, the way the industry and FDA are evolving is certainly a reason for optimism as always, BioWorld we'll continue to keep you informed of all the most important scientific clinical, and business updates in this field. That's our show for today. If you need to track the development of drugs, turned to BioWorld.com, follow us on Twitter or email us @newsdeskatbioworld.com. If you're enjoying the podcast, don't forget to subscribe. Thanks for joining us.

**Announcer:** BioWorld published by Clarivate is a subscription-based news service, but all of our COVID 19 content, more than 5,000 articles, and data entries since the start of the pandemic are freely accessible.

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