Implications of FDA's Decision to Issue Fines for Failing to Submit Clinical Trial Data

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Transcript

Darshan Kulkarni: Hello, this is Darshan Kulkarni, Vice President of Regulatory Strategy and Policy at Synchrogenix, here with Nirpal Virdee. Nirpal, what is your role at Synchrogenix?

Nirpal Virdee: So, I'm the Director of Client Services. So, I'm typically involved in a lot of the transparency and disclosure space, some of the regulations, how can we apply technology and service to our sponsors.

Darshan: Yeah and Nirpal, we're actually here because we're discussing something that's new, that's innovative, that's just shown up and we're talking about the FDA's recent guidance on disclosure and the fines they're going to put out. What do you think about it?

Nirpal: Well, it's interesting that it's come out right now. We've all known it's a problem and there has been publications by many interested parties around the poor compliance. It is good to see something a little bit more tangible coming out and some of the data behind this is mind blowing, right? Just realizing how out of compliance a lot of institutions are and also I'm sure we'll get to talk about this in a little bit more detail but there are very specific institutions that are a little bit worse than others, right? So, again, that's a very interesting dynamic. Now, the true test is are we really going to make this situation better and are folks like the FDA going to start imposing these fines? Because it's not small change, right? It's $10,000 per day. So, it is relatively significant and if you look at some of the stats they've got behind the current compliance rate, this could be a huge impact to these institutions and also quite a bit of a generator for the FDA to try to get folks compliant. It's shy just over half? That might be in compliance. So, yeah, a big problem and interesting to see not only that the FDA is trying to do something about it but this rare coordination, right?

We're seeing some very interesting facts coming out from the EMA around the similar topic on these postings and they're also putting out these stats. So, what you feel Darshan, whether it's just a coincidence or whether there is some sort of coordinated effort to try and tackle this? And again, we'll have a conversation about what it means for the industry, for patients, for academia to be out of compliance with this and why does it really matter?

Darshan: I think it really comes down to the fact that at least industry has done a better job in understanding that they need to be patient-centric and those words mean a lot of things to a lot of different people but what we're seeing is that the FDA has been taking various steps to be quote unquote “patient-centric” and that's included having patient groups, that's included putting patients into, involving them in the impact of drug and development pathway and I expect that this engagement with patients is making them realize that these patients are effectively acting as guinea pigs, which is not okay for obvious reasons. They're going in there, they're giving their data, they're giving, literally, their blood, sweat and tears and they aren't even finding out what actually happened as a result of their participation and the FDA is coming back and saying, "Well, we have this authority. The NIH have this authority and didn't do much with it. FDA has this authority and we're going to actually enforce the $10,000 per day." Here's the first question to ask, number one, who will it affect? Because I imagine that a lot of people are saying, "We don't really have a problem."

I know, Nirpal, you and I both work with sponsors who really do try to be diligent. So, who is this really going to affect more often than others?

Nirpal: I mean, really interesting question. If you think about, I'm sure it's going to impact a lot of folks in different ways, right? In different dimensions but just looking at a lot of the data behind this, of course, anecdotally we've known there's been an issue and we've obviously partnered with sponsors to try and get them in a very good place but not to say that these sponsors have not got an issue, of course they have, but it's some of the academic institutions that really seem to be very poor at pulling this data together. Their compliance rate is in single digit figures. It's a huge issue and also, they don't potentially have the same level of funding, right? As sponsors do. So, if you think about impact, these fines will impact those academic institutions in a significant way, right? And it's in their vested interest to try and work through this and try and get in a position where they can get this data out, get it out in a compliant way and have robust process that is sustainable so that we don't have the same issue a year down the line and just have the one off activities because fundamentally, a lot of the research they do could be completely hindered by the level of fines the FDA are suggesting.

So, I think that's one of the big impacts, but you mentioned the patient-centric movement and we were seeing it all the way across the transparency space, right? A lot of the things aren't coming from the big regulators across the globe, is really trying to focus on that patient advocacy, the patient really having a voice and they've got the most to lose, right? If you think about, you mentioned, participation in a trial, trying to understand what does it mean for me in participating in it? That has many dimensions, right? We've talked about some of the obvious ones around providing them summary information and all those things but at the core of it, if you can't research in the studies that are out there, positive and negative, if it's an interest to you of particular disease state that you or your family are potentially suffering from and you want to know as much as you can and be informed, we've got a huge issue here. We've got a big gap and I think that's maybe a lot of the driver behind regulators getting a little bit more robust in what they're trying to do but it's interesting because from my perspective, the publication of a lot of this data is as much to learn from things that haven't gone so well to the negative outcomes as it is the positive, right?

If we're not learning from things that we've done before and exposing them for others to use and not keeping them in the vaults of a sponsor, how do we progress, right? How do we make sure that we're being absolutely optimal in finding cures for diseases? There's a lot of valuable information there that I'm sure the regulators have been pitching but a lot of the institutions and some of these pressure groups and patient groups are really demanding that let's unlock this data because we want the best chance of getting cures to things that we might be suffering with.

Darshan: And I think those are all absolutely interesting and one of the things, I haven't talked about this as much on this podcast but I should probably introduce a little bit of my background, which is I'm an attorney but I'm also a pharmacist and I've practiced for, I'm dating myself, almost 20 years and one of the key pieces of working in a large, academic medical center is understanding what drives a lot of these institutions and a huge piece of what drives these institutions is this idea of publish or perish. If you aren't in the news, if you aren't breaking news, you aren't important. If you aren't important, you're less valuable to the academic community. So, I think that's actually becoming a huge piece and I think it's really interesting and I'm sure we'll link to the articles in our show notes but it's really interesting to look at what's been going on and I know there's a quote both you and I read, Nirpal, where one of the large, very reputable, academic medical centers basically came out and said, "We just don't have enough time to do this. It costs too much money to do this," but ignoring the impact on patients.

Ignoring how this changes the lives of patients and the fact that these patients have given so much to be part of this and they deserve it. It's not a question of this would be nice, they deserve and they should deserve the right to see this information. So, in your opinion, are we doing enough? Is this going to be enough to just fine these companies or do you think the FDA may look at more? Has the EMA looked at more? And is this just the first salvo in many more to come?

Nirpal Virdee: Well, first of all, let me just say you don't look a day over 21. So, it's how we feel, right? Going back to the question, is it far enough? You're citing some great examples there of different priorities, right? What does it mean for stakeholder groups and the folks who are actually generating the data? And a lot of the research, we know, we're part of the scientific community we work with, a lot of these folks, the importance is really on the writing and the publishing and maybe not so much about the education and the learning and the data behind it that can help others. It's always very specific to a cause. So, that's, I suppose, the way the priorities differ with different groups and there needs to continuously be work to remember that we have patients we are trying to serve here and there is some great value in everything we do and exposing that and being transparent about that is really fundamental for us to do, to have really quantum leaps in a lot of the things we're doing in medicine at the moment. So, can the regulations go any further? Well, if you think about the programs that are going on, some regulation bodies are progressing faster than others and maybe it's not just about posting results after the event, maybe there's something more.

Patients demanding different levels of this information from a transparency perspective. So, earlier in the process, things that maybe go well and don't go well and having some of that data exposed. The question is whether the regulators are going far enough and if this is just I'm sticking some

sticky tape over of a fundamental issue than just the current scope of these registry postings and trying to fix that. So, I don't know Darshan if you've got a perspective on that.

Darshan: So, I think it's going to really start depending on your perspective. I think, for example, the EMA has basically said that, "We consider disclosure to be a fundamental right," and they've taken that disclosure to be in various forms where they're doing a push around the disclosure of not just the results but the understandability of the results. So, doing lay summaries. You also have the EMA going out and saying that, "We want the actual data to be disclosed as well," and I know, for example, Nirpal, we do a lot of transparency and disclosure work where we help redact documents and help ensure that when the results are published, appropriate information is also not made available because company confidential information, for example has to be redacted so that companies retain a competitive advantage to the extent it's compliant. So, I think the FDA is going the other direction, which is instead of going for breadth, they're going for depth and they're saying that, "We're going to insist that we first fix the problem and the issues we already have and fine the companies and the institutions that are not compliant and then we'll look at the bigger issue we can go after."

I'm unaware and tell me if you've heard of anything but I'm unaware of the EMA going to academic medical institutions in Europe and saying, "If you're doing studies, we want to see the results," and maybe that's going to be something they look at in the future but at this moment, they're really looking more at a breadth issue as best as I can tell. Is that your perspective?

Nirpal: Yeah, absolutely and EMA have also published their results and I think you're seeing the same patterns. I think you're seeing academic institutions are significantly behind with their compliance too. So, that hasn't different that much. The thing is EMA is striving to do, holistically looking at a different way of trying to do this, right? So, not necessarily trying to patch all of the holes within postings although they have a similar outreach as the FDA have just had, as we talked at the beginning, but they are trying to take a different perspective on it. Making data sets more widely available, trying to move away from their initial push to just get study reports out there with majority of the sponsors redacting them to a place in which there's much more data utility. So, trying to use different techniques to get these reports out there but also getting the actual raw data sets behind that as well. So, it'll be interesting to see whether FDA feels that it's not... is it just not about the depth of what they're trying to do but is there wider things that they can be thinking about that is going to ultimately give patients further data that they're asking for?

A lot of the groups like you've got all trials and many other patient groups really trying to force a lot of this information to get out there. Does it need to be more of a holistic look at how we collect this data? When should it become available? Is this the only mechanism in which we need to serve those groups, patients and really tackle this transparency? Because it is really the measure of transparency, right? And I think you mentioned it quite a lot of times that there is drive around transparency but where are you in the measure of transparency with all of these component parts? And it feels like there's been building blocks on things that the regulators started off with, which is fine, but you get to a point in which maybe you need to take a step up, maybe you need to look at how's our environment change? How's the patient's voice change and the way of accessing this information

changed? And therefore, what should be our strategy with all of this? These mechanisms to get that data out and then deciding how current stuff, like these registries still fit into that picture.

That would be the only difference I would see in this is not just about the here and now and not just about depth, not just about fines but fundamentally, looking at your overall strategy behind this and consistency between regulators, that's so important and we were joking, initially, on whether it was just a coincidence that the FDA and EMA have got some of this relatively similar data out at similar times but there is a, again, thinking about the measure, a real piece around the consistency of data because that could also be interpreted as not being as transparent as you could be, right? If you've got inconsistent data between these registries and generally with those regulators. So, trying to see a bit more harmony across some of those very large regulators, I think would provide a lot of benefit to ensure the right data is getting to the right folks and there's no misinterpretation of I'm producing one type of data in a certain way here and I'm doing something else there. I might try to hide something. Am I trying to not be as open and transparent as I could be?

Darshan: Any last comments before we switch off?

Nirpal: I would say this is important news. This is an important way to go by the regulators to really push on trying to get much more coverage of these registers and get the compliance up. It's a real issue and as you mentioned, the depth, if you've only got half of the potential scope of studies on these registers, then you're missing a huge amount of data for any further analysis, trying to inform the right types of groups. So, it's absolutely the right thing to do, the right steps. We're here to obviously, of course, support our sponsor, we already do and I'm sure we'll continue to widen our search a little bit to try and help some of these institutions, especially some of these very small academic institutions I think is going to be important to help them. We're trying to get out of the single digits and get them compliant. So, that's my closing remarks.

Darshan: Well done. Well, stay tuned. We're going to have a lot more of these talks as we continue but we're excited to have been able to have the first one today.

Nirpal: Thank you.

Darshan: I also reached out to Brenda Tiffin, Synchrogenix's Transparency and Disclosure Work Stream Lead for her thoughts.

Brenda Tiffin: Definitely one of the goals for Synchrogenix is to make sure that quality postings are written in CT.gov and are consistent with what might be written already out in the public, such as a journal or a manuscript or maybe a lay summary and also working on EudraCT to make sure that they're

being consistent as well as any potential international database that may include participant information.

Darshan: Now, Brenda, do we do summaries for all the different databases or is it only clinicaltrials.gov for us?

Brenda: We do have experience in all the databases. I'm sorry. We do have experience in writing postings in CT.gov, EudraCT and multiple international countries.

Darshan: Okay and have you found that there are some significant differences and this is finally getting us to where most countries are or are the U.S. requirements, should we say, more stringent than other countries? Or does it really depend?

Brenda: It depends. There's definitely some other countries that report data that is not included in CT.gov or EudraCT but then there's also some other countries that the data being reported on their database is minimal. It just really depends and so, you really need to have an understanding of the requirements for the specific country.

Darshan: Well, stay tuned. We'll probably have more of these conversations in the future. I look forward to talking to you Brenda about more of these, thank you.

Thanks for listening. For more information, visit us at Synchrogenix.com.