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Califf Laments Shift To Ex-US Clinical Trials – As Well As Pace Of Reforms At Home

by Jessica Merrill

US FDA commissioner tells J.P. Morgan conference that the agency, industry, and the entire healthcare system need to change 'at the same time' in order for clinical trials to improve.

US Food and Drug Administration commissioner Robert Califf was the keynote speaker to open the second morning of the J.P. Morgan Healthcare Conference in San Francisco – and he took the opportunity to get a point across to industry about relying on clinical trials that are run outside the US for drugs intended for the US population.

"I'm 100% in favor of globalization. I'm 100% opposed to offshoring as a financial arbitrage," he said during his 10 January talk. "We're seeing much more of the clinical trial enrollment coming from low-income countries."

Clinical trials run outside the US have become a hot button regulatory issue after the FDA pushed back on approving drugs tested in populations that aren't representative of the US last year. The agency declined to approve *Eli Lilly and Company*/*Innovent Biologics, Inc.*'s PD-1 inhibitor sintilimab because the application was based primarily on data from China, a decision that had implications for several other drug makers that are investing in Chinese-developed drugs. (Also see "*Foreign Data: Sintilimab's Development Shows What Not To Do When Pursuing US Approval*" - Pink Sheet, 16 Feb, 2022.)

"The reasons I emphasize I'm in favor of globalization … [is] we're only 4% of the world's population, so China, India, Africa, those people should all be doing clinical trials," Califf said. "But the idea that we're offshoring as a financial arbitrage, and the money is being made by selling the products here in the US, where the trials are not being done. I don't think that's a good way to do things."

“It’s not good for our economy,” he said. “We’re also seeing it in supply chains. It’s not good for our national security.”

The omnibus spending package that passed Congress at the end of 2022 contained several provisions aimed at boosting US pharmaceutical manufacturing. (Also see "*Advanced Manufacturing Centers Of Excellence Measure Finally Clears US Congress*" - Pink Sheet, 6 Jan, 2023.)

As for collective action that could spur reforms in clinical trials, Califf did not appear overly optimistic. “Among the experts in clinical trials, there’s almost complete agreement on what needs to be done. … The practice, I feel like is decades behind the theory at this point.”

The current state of research often puts FDA in a bind, the commissioner said. “By law and by convention, we often have to make decisions even if we wish a different set of studies had been done and there was much more robust evidence. And then it’s easy to have controversy about that because it’s more a matter of opinion than a clear cut-depiction of the risk and benefit empirically driven by well-done clinical trials.”

Califf called for a number of changes to clinical trials, from streamlined consent forms to increased use of electronic medical records.

“I think it’s not hard to imagine that the combination of the patient’s medical record and the use of digital technologies at home would give a much better portrait of what’s going on with a human being than going to a research clinic once every three months and having a study coordinator try to figure out what happened during that intervening period,” he said.

Unfortunately, “It’s not in any individual company’s interest to do all the work that’s needed to validate the technologies themselves,” Califf lamented.

Technology itself is not a panacea, he cautioned. Citing his five-year stint at the Google health subsidiary *Verily*, Califf said that “people trained in engineering, they know a lot about quality systems. But there's often an assumption that in human clinical studies, you can ignore things like missing data. … When often, for example, in human clinical trials, the most important data is almost always in the people who are missing. The reasons that people are missing, they are informative.”

Verily itself appears to be struggling, perhaps a symptom of challenges facing anyone who wants to change the nature of clinical trials in the US. The company reportedly is laying off 15% of its staff, and former FDA principal deputy commissioner Amy Abernethy is being elevated to chief medical officer as part of the restructuring.

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Califf acknowledged that FDA must rise to reform challenge as well. “There’s work to do inside of FDA, I would argue, because there’s a lot of comfort in FDA in the old methods. It’s hard to argue they haven't worked.”

Industry, academia and FDA “we've really got to work together on the culture, simplifying where we can, using digital technologies where they are effective,” he said.

Regardless of what reforms are undertaken, “it’s asking a lot of the clinical research system to overcome structural failures of our healthcare delivery system,” Califf said.

Califf has said before that improving health disparities would fix the lack of diversity in clinical trials. (Also see "*Clinical Trial Diversity Campaign Distracting From Health Equity Problems, Califf Says*" - Pink Sheet, 26 Jul, 2022.)

The commissioner did not use the term, or mention *FDA’s recently enhanced powers* on diversity, but that may have been what he was alluding to when he said “we’re all concerned about the populations enrolled in clinical trials.”

Califf squeezed in a mention of rural broadband before noting “I’ve listed for you about 10 things. They all have to happen at the same time.”

[*Editor’s note: Our Scrip colleagues are providing a daily I.P. Morgan conference notebook covering business development strategy and the commercial outlook for 2023.*]