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‘Do It Or We’re Not Going To Approve Your Drug:’ Industry Reps Ask FDA For Trial Diversity Sticks

by Sarah Karlin-Smith

FDA leadership has generally seemed apprehensive of going too hard on companies that don’t meet clinical trial diversity goals, but some industry insiders say a stronger FDA is needed to spark real change. Delayed guidance could indicate if the agency will change course.

Drug developers will change their behavior on clinical trial diversity if the US Food and Drug Administration makes the consequences painful enough, some industry insiders say, suggesting the agency needs to be more enforcement orientated than it likely has wanted.

“What will drive this most of all is the FDA saying either do it or we’re not going to approve your drug. Yeah, I mean that’s kind of what it comes down to,” Bob Zambon, VP of technology strategy and strategic partnerships at contract research organization *Syneos Health* said when asked what industry needs from the government to reach trial diversity goals.

Zambon and others were part of a 8 May Citeline Elevate panel discussion on disruptive clinical trial strategies moderated by the *Pink Sheet*’s Sarah Karlin-Smith.

As soon as the FDA starts rejecting applications or telling companies they will only get a label for a particular population due to diversity gaps, sponsor behavior will shift, Zambon said.

“Sponsors very quickly will pivot around and start doing whatever is needed there small and large, when there is a key risk to

Key Takeaways

- The FDA may need a stricter enforcement approach to revolutionize diversity in clinical trials.

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a business that they're operating in at the time," he said. "And until it's that point, there are still going to be conversations around, is this worth it from an investment perspective, do we have to do it? How much is it going to cost? How much do we have to go down that pathway? What will be the return?"

"Once it becomes regulatory mandated … that whole equation flips on its head," Zambon added.

- Diverse studies can help increase postmarket uptake of a drug.
- The FDA's diversity action plan guidance is more than five months delayed.
- Co-writing protocols with patients and investigators serving diverse populations, as well as building in more study support services like transportation and childcare, helped Genentech achieve big wins in trials diversity.

Diversity Is Good For Business

"It's a moral obligation, a scientific obligation, for us to know whether or not our therapies actually work in all patients," said *Genentech, Inc.* 's Georgia Dangel, a senior medical science liaison.

But even if you "just take a pure cynical view of the situation … it's good for business," said Matt Winton, the Chief Operating Officer of *Inozyme Pharma Inc.*, referencing Dangel's discussion of Genentech's CHIMES trial, which studied the company's Ocrevus (ocrelizumab) in exclusively black and Hispanic/Latinx multiple sclerosis patients.

"Right now, African-American, Hispanic patients with MS come to see their doctor and their doctors are actually able to show data in their population," Winton said. "The majority of the time that's the drug that they're going to say I want to be on."

"And I think the sooner as an industry we sort of associate that diversity and inclusion, both in the way we think and the way we do trials and develop drugs, is good for business," he added. "I think it should materialize into a seamless kind of approach."

Missing FDA Guidance May Answer Enforcement Questions

Since the 2022 Food and Drug Omnibus Reform Act (FDORA) implemented a requirement for sponsors to submit "diversity action plans" for Phase III or other pivotal studies, the FDA has generally tried to quell sponsor fears that their applications will be delayed due to failure to meet diversity goals, particularly for rare diseases. (Also see "*Cavazzoni Appeals For Pragmatic Approach To Clinic Trial Diversity Plans*" - Pink Sheet, 30 Oct, 2023.)

The one very notable case in recent years where sponsors faced adverse FDA action due to trial

makeup was *Innovent Biologics, Inc.*/*Eli Lilly and Company*'s cancer drug sintilimab, which was rejected in part due to its China-only data. However, the application also had other problems and the drug did not address an unmet medical need.

The FDA's potential reaction in more nuanced situations is less clear. Recent history suggests the agency would approve drugs even if significant portions of the US population who might need the medicine are underrepresented in the clinical trials. Case in point *Biogen, Inc.*'s Alzheimer's drug Aduhelm. (aducanumab-avwa) (Also see "*Medicare Alzheimer's Coverage Policy Advancing Clinical Trial Diversity Efforts*" - Pink Sheet, 21 Nov, 2022.)

More details on the agency's enforcement strategy should come in a mandated guidance on the FDORA-required clinical trial diversity plans. (Also see "*Clinical Trial Diversity Plans: Will US FDA Offer A Gentle Enforcement Hand?*" - Pink Sheet, 5 Oct, 2023.) That guidance was due in December 2023 but has not yet been published. The document went to the Office of Management and Budget for regulatory review in mid-April.

Genentech's Secrets Of Success

The drug industry still built up its diversity focus absent clear FDA sticks.

Genentech starts developing an inclusive research strategy before drugs enter the clinic. The company already voluntarily implemented diversity action plans and made them publicly available, Dangel said.

She highlighted the company's work recruiting and testing Actemra for COVID-19 in minority patients in the EMPACTA trial as the virus was disproportionately impacting minorities.

The study was for all comers, but 84% of patients enrolled were from minority groups. Dangel attributed the success to Genentech cowriting the protocol with the physician investigators who were seeing the targeted patient population in New York and New Jersey. A "simple" protocol was developed to pare down the study to the basics needed and minimize inclusion and exclusion criteria. A consent form summary also was created to communicate with patients and family members in advance of enrollment, along with other culturally sensitive materials.

"It was 15 days from when we had the idea to when we had the first patient in, which again is unheard of at least in our company," Dangel said.

Genentech built on the experience when designing the CHIMES study for MS. The company worked with MS patients, advocacy groups and site investigators with diverse patient populations to develop the protocol. Genentech also included support services in the study that in the past had been barriers to trial participation, such as transportation and childcare, and

went to non-traditional sites to increase enrollment.

Investigators enrolled 150 black and Hispanic patients two months sooner than anticipated.

“This trial helped debunk the myth that minority patients or communities of color won’t enroll in a trial,” Dangel said. “They do. They need to be asked.”

Indeed, data suggests minority patients are more likely to participate in clinical trials, but often are not asked. (Also see "*Clinical Trial Diversity: Data Points to Structural, Not Patient-Specific Solutions*" - Pink Sheet, 25 Aug, 2021.)