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‘You Shall Not Pass:' Former Surgeon General on Why US Government Should Push Trial Diversity

by Sarah Karlin-Smith

A push for government-driven accountability in clinical trial diversity is coming from a right-of-center figure, but could it nudge the FDA to be tougher on industry? The *Pink Sheet* spoke with Jerome Adams about his more than 30 years of work on the topic.

Jerome Adams, former US President Donald Trump’s surgeon general, said that now is the time for smart, thoughtful regulation that will hold industry accountable for clinical trial diversity.

Adams has come to realize that without clear accountability and impactful consequences, the drug industry has little incentive to invest in improved trial composition.

The sentiment and Adams’ reasoning, which he outlined in detail in an exclusive *Pink Sheet* interview, is notable because it is coming from a person associated with Republicans, a party that typically prides itself on limited government interference in private industry.

The comments also emerge as FDA leadership repeatedly attempts to reassure drug sponsors they do not want

Key Takeaways

- Former Surgeon General Jerome Adams is skeptical clinical trial diversity will improve in the US without stronger government requirements.
- Addressing diversity early in development can mitigate industry fears that it will slow the approval process, he said.
- Adams said the current political environment, where Republicans in

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to delay applications because of a failure to meet diversity goals, despite suggestions that drug developers will only change their behavior when the FDA makes the consequences painful enough.

particular are pushing back against diversity, equity and inclusion work, is harming the trial diversity space.

Adams has substantial professional and personal experience with trial diversity. He has a history of asthma, which disproportionately impacts people of color. Yet the diagnostic equipment and medications used to treat the disease were not properly tested on people with diverse backgrounds and belatedly determined to work differently in those patients, he said.

An anesthesiologist, Adams was hired by Eli Lilly and Company about 30 years ago as a clinical research associate tasked with trying to increase diversity in trials. He is keenly aware of how little progress has been made in the area since he took that job.

But his recent experience successfully improving the diversity of Moderna, Inc.'s pivotal studies of its COVID-19 vaccine as part of the US government's Operation Warp Speed (OWS) showed him that government leverage can push companies to do the right thing.

His post-surgeon general experience working with Total Diversity, a full-service clinical research organization that specializes in improving trial diversity, illustrated that diversity in studies is achievable and can even be cost-saving if addressed upfront.

Federal might proved it could be done

"A watershed moment" was how Adams described former National Institutes of Health (NIH) Director Francis Collins and former National Institute of Allergy and Infectious Disease Director Anthony Fauci's' "challenging" decision to tell the companies in Operation Warp Speed that the government was not going to move forward with their products and approve them if they did not increase the diversity of their clinical trials.

During the height of the pandemic, the trio worked directly with the impacted sponsors, holding weekly Saturday morning calls to check enrollment status, and sometimes adding additional meetings throughout the week.

"We were able to go from single-digit diversity in Operation Warp Speed trials to ultimately, in the Moderna trial they were over 30% from diverse backgrounds by the time their [emergency use authorization] came out just three to four months later," Adams said.

“And that’s important, because it was the first time really in history that you had federal authorities saying, we’re not going to let you move forward unless you have diversity in these trials,” he added. “And we’re willing to accept the risk that these drugs will not be available for the broader public because diversity is important enough to us.”

“The other important part of that watershed moment is that we also proved that it could be done,” Adams said. “Because no one in the past had been willing to use their federal might to say, ‘You have to do it.’ And so it was jut kind of accepted that, hey, you try your best, but we understand that this is just not possible to get over this hump, and so we’re gonna go ahead and approve the drugs.”

Be like Gandalf

Adams said the government accountability made the difference in Moderna’s vaccine trials.

“Like Gandalf, we literally said, you shall not pass if you don’t show progress in this area,” he said. “Without accountability companies are just going to be like ‘Eh, we don’t really have to do this. So why should we do this?’ I think that was big for me to recognize.”

Of course, every clinical trial can’t have the surgeon general and top NIH leaders involved.

“But what you can do is have a clear directive from the FDA,” he said. “Now is the time for smart thoughtful regulation. We know it can be done. We know that we’re going to continue to see disparities increase if it’s not done.”

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Early intentionality prevents trial slowdown

Adams cited four reasons why trial diversity has not improved much over the years, despite plenty of recognition that there are gaps in equitable research.

The first obstacle has been financial.

"Drugs are big money, Adams said. "And if you delay a drug coming to market by even a few months on one of these big new blockbuster drugs … you're talking billions of dollars for an industry. So there's a monetary disincentive to slowing down a clinical trial for any reason."

The flip side is that trusted drug developers should be able to increase their market share by producing data in all relevant populations.

"Our belief is that if you're intentional about thinking about it from the very beginning then it doesn't slow down your trial," Adams said. "It slows down your trial when you wait until you're 80%, 90% done with your trial and go 'Oh crap, we're not even close to hitting our diversity enrollment targets,'" and then have to change your enrollment strategy to hit diversity numbers.

As to concerns that a less homogeneous study population could negatively impact trial results and hinder approvability, Adams said that while "science 101" says to try to eliminate extraneous variables that may impact a study outcome, developing drugs "for the average," person leaves many out. "There actually is a market, again to go back to the money issue," for drugs that are more directed at specific populations, he said.

Adams also said that not testing a drug in key populations likely to use the product and then determining postmarket that it does not work in that group or there are negative outcomes can be a bigger disaster.

Regulatory gaps, FDA fears

After monetary disincentives, Adams highlighted the missing regulatory sticks.

"We also know that people do what they have to do to get the drug to the finish line, to approval or EUA," Adams said. If trial diversity is not required, but costs resources, "whether it's money or time or effort or what have you, then these are for-profit companies, so without the regulation, the requirements, very few of them are going to do it as a matter of course."

Adams recognizes that industry often opposes regulations that could impact their bottom line and that the FDA operates in a political environment that constantly pushes for faster drug development. The FDA may worry about being seen as slowing approvals down, but the expected

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tradeoffs for improving diversity can be avoided, Adams argued.

“Total diversity has hit 100% of enrollment targets” on time, he said.

Trust

The third barrier to improved trial diversity is know-how and gaps in understanding best practices, including how to build trust in communities. The fourth is social drivers.

“You can’t go to a community that has barriers to literally being able to exist, I mean these folks are struggling just to make it through the day, and then say well, why don’t you want to carve time out of your day and come participate in our clinical trial?” Adams said.

He found that intentionality and relationships at the site and investigator level make a huge difference when dealing with populations with many barriers to enrollment.

Operation Warp Speed considered two different approaches after realizing it needed to up the vaccine trials’ diversity. One was a shotgun approach, where they would work to increase diversity at every site participating in the trials.

The second was a rifle approach, where it would work with a few key sites to increase the numbers. OWS thought about which sites it would focus on: communities that geographically look like they should be doing well or sites that were actually doing well.

“We learned that you can’t just go by geographic location and expect that just because that’s where Black people are from, that’s where the Native Americans are, and that’s where the Latinos are, that that’s where you’re going to be able to maximize your enrollment,” Adams said. “It all comes back to trust.”

Supportive sponsors are not enough

Adams is the chairman of the board for the Association of Diversity in Clinical Trials (AOD), an organization that started when Total Diversity realized it was important to bring all parts of the community responsible for trial enrollment together to help facilitate best practices and partnerships.

“Normally everyone looks at [diversity] through their own lens,” he said. “But we wanted to be a neutral place, a convening ground where people would come together,” to better understand each other and get multidisciplinary input into solutions.

AOD also exists in part because the trial diversity problem cannot be solved by drug sponsors alone.

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“Supportive sponsors are absolutely necessary but not at all sufficient,” Adams said.

One concrete example of conversations that AOD can facilitate is on the costs of dealing with the socioeconomic factors preventing trial participation.

Current rules and regulations prohibit sites from paying for certain items that could help someone participate in a trial out of fear of unethical inducements, Adams said. AOD can help sponsors understand sites' needs when negotiating contracts or advocating for regulatory changes.

“One thing I can tell you is that the federal government is often well meaning when it comes to regulation … but they don’t understand their blind spots,” he said. “And so I think it’s critical to have a place where people can come together who are doing the work on the ground” to give feedback.

AOD also is committed to research that can address knowledge gaps in the space, he added.

Backlash against DEI hurting effort

Adams said reaching consensus with AOD members has not been challenging.

“What has been challenging has been the broader political environment in which we’re having this discussion,” he said.

In 2020, there was a “racial reckoning” as the US grappled with the COVID-19 pandemic, which disproportionately harmed minorities, as well as the murder of George Floyd, a Black man, by police officers.

Companies started spending more money on diversity, equity and inclusion (DEI) efforts, including trial diversity. Some sponsors created teams with as many as 20 people to address the issue, Adams said.

That impacted AOD because after standing up the large teams, many companies wanted to address the issue internally.

That’s not necessarily a bad thing, but still makes it challenging to bring people together, Adams said.

He suggested some companies do not want to participate in AOD in addition to their internal efforts because they lack the bandwidth, rather than from concerns about sharing information they believe give them a competitive advantage.

At the same time, Adams believes sponsors are more competitive in the space than other entities.

“Not from the standpoint of they don’t want to share their trade secrets,” he said. “But that there is a belief when you’re a giant company that you’ve got this all figured out, you’ve got this under control. And it reflects a lot of the challenge that we’ve had over the last 30-plus years in this space, where these companies often don’t know and don’t want to admit what they don’t know, what they can’t do.”

Hence the need for regulatory intervention.

“Having some regulatory requirements behind this, to kind of force the issue, to kind of say to these big companies and to everyone, ‘hey this isn’t a nice to have anymore. This is a you’ve got it do it,’” he said.

Now, four years after Floyd’s murder and the reinvigorated DEI push, the environment is even more challenging.

“We went from a high of attention and resources to what we have now, which is a backlash in many communities on diversity, equity inclusions programs,” Adams said. “I mean we literally in two different states have made it illegal for academic institutions to have diversity equity and inclusion programs within their university systems.”

So now the same companies that “were flush with resources,” a few years ago are saying “Gosh are we putting a target on our back if we continue to talk about these things in this way?” Adams said.

This is the purpose of regulations, he said.

“If everyone just did the right thing all the time, you’d never need regulations,” he said. “You wouldn’t need a speed limit if everyone just drove like, like they have common sense, right?”

He urged the US government to capitalize on the COVID-19 trial lessons before it is too late.

“We have the largest drug trials in history to provide wind in our sails to talk about this issue, to make progress on this issue,” Adams said. “So shame on us if we don’t take advantage of this opportunity. I think we have a unique opportunity in US history to lean into this.”