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Legal Expert Weighs In On New US Mandate To Diversify Clinical Trials

by Brian Bossetta

The omnibus spending bill passed at the end of 2022 requires clinical trial sponsors to submit a diversity action plan to the US Food and Drug Administration. Attorney Faraz Siddiqui, who coauthored a blog post on the new regulation, spoke to *Medtech Insight* about the requirement and the push to increase diversity.

Advocacy groups and other stakeholders argue that for too long, clinical trials have lacked participants from racial minorities and other socially disadvantaged groups. Last month, the US Congress passed a new law that could begin reversing this trend.

A provision in the omnibus spending package passed in December, "*The Food and Drug Omnibus Reform Act (FDORA)*," requires sponsors of most drug and device clinical studies to include a diversity action plan explaining how they propose to enroll more diverse participants when they submit key trial documents to the FDA.

The new requirement essentially follows the principles outlined by the FDA in an April guidance, which was aimed at boosting diversity in trials. (Also see "*FDA Draft Guidance Takes Aim At Racial, Ethnic Disparities In Clinical Trials*" - Medtech Insight, 13 Apr, 2022.)

The FDA can waive the diversity plan requirement if it determines that the prevalence or incidence of the disease or condition being studied makes it impracticable to conduct a clinical trial in accordance with a diversity action plan, or that a waiver is necessary to protect public health during a health emergency.

The FDA has been trying to chip away at this lack of diversity in trials for years, according to Faraz Siddiqui, an associate at DC-based law firm Hyman, Phelps & McNamara. In a recent *FDA Law Blog post*, Siddiqui references a 2013 FDA report that revealed the glaring disparity of certain

groups in trials, which "many in the industry and academia already knew."

But as Siddiqui told *Medtech Insight*, the FDA has been thinking about the lack of diversity in clinical trials long before that report.

A History of Exclusion

As far back as 1977, the FDA understood that its policy of excluding women of childbearing age from participation in certain clinical trials for safety reasons was "overly paternalistic," Siddiqui said. The agency didn't reverse that policy until 1993.

However, the US government focused on inclusion in federally funded clinical trials throughout the 1990s, Siddiqui pointed out. For example, the 1993 National Institutes of Health (NIH) Revitalization Act required the NIH to include women and members of minority groups in federally conducted or funded research. And in 1997, President Bill Clinton formally apologized for the government's role in the Tuskegee Experiment, in which hundreds of low-income Black men were used as test subjects without informed consent to observe the progression of syphilis – at the time an incurable disease. The trial continued until 1973, long after penicillin became widely available as a treatment for syphilis.

"Despite these efforts, researchers studying the adherence to NIH guidelines in 2004, 2009, and 2015 found that inclusion of women and racial minorities in NIH-funded clinical research was still lacking," Siddiqui said.

And though the NIH reported in 2009 – and again in 2015 – that it had succeeded in increasing representation of women and minorities in clinical research, the US Government Accountability Office (GAO) found that data on subgroups remained insufficient.

> ***"Even COVID-19 trials were reported to be insufficiently diverse, despite the fact that racial and ethnic minorities were disproportionately affected by the disease." – Faraz Siddiqui***

It wasn't until 2012 that Congress asked the FDA to collect data from industry-sponsored research, which resulted in the 2013 report Siddiqui referenced in his blog. Since that report, he noted, the FDA has undertaken numerous initiatives to encourage diversity, such as its 2014 action plan to enhance the collection of data from diverse demographics and declaring 2016 "the year of clinical trials diversity."

A few years later, the FDA Reauthorization Act of 2017 (FDARA), required the agency to publish guidance to enhance diversity in clinical trials – guidance the agency finalized in 2020.

Pandemic Impact

In his blog, Siddiqui says many clinical trials were put on hold because of the pandemic, which also halted the progress of trying to advance participation of minority groups. For example, he said it is unclear if the use of telehealth services and remote monitoring increased access to clinical trials for the elderly and disadvantaged.

"Even COVID-19 trials were reported to be insufficiently diverse, despite the fact that racial and ethnic minorities were disproportionately affected by the disease," he said.

FARAZ SIDDIQUI

For instance, according to a recent meta-analysis published in JAMA, Black and Asian people were underrepresented in COVID-19 vaccine trials, while women were underrepresented in trials for treating the virus.

Another example is kidney disease.

Despite renal disease disproportionately affecting Black Americans – 1 in 3, or 33% according to the American Kidney Fund – only 1 in 10 participants in kidney trials are Black. Similarly, Hispanics are nearly 1.5 times more likely to have kidney failure compared to non-Hispanics, but only about 1 in 10 clinical trial participants are Hispanic, while nearly 7 in 10 participants are non-Hispanic.

Why it Matters

The lack of diversity in trials goes well beyond optics, as the FDA made clear in its April guidance. Racial and ethnic minorities are often more likely to develop certain diseases despite being disproportionately left out of the trials that study those very diseases.

Variations in skin pigmentation, for example, can affect the performance of certain devices, such as pulse oximeters, which means different skin tones should be considered during trials.

And while inclusion for all subgroups for a given trial may not be necessary, Siddiqui said that in some cases safety concerns and efficacy in a particular subgroup may differ from the broader population.

“If the incidence and prevalence of the disease in the population is known, that can be used as a target for the minimum percentage of individuals from that subgroup,” he explained.

Siddiqui also noted that underrepresented groups can also include non-demographic groups, such as those with certain comorbidities.

Industry Response

Siddiqui expects clinical trial sponsors to embrace the new FDORA requirement, as they understand the need for more diverse research subjects and have already taken steps in that direction. For example, Siddiqui pointed to a set of principles for conducting clinical trials released in 2020 by PhRMA, which represents biopharmaceutical research companies. Those principles include a “commitment to enhancing diversity in clinical trial participation.”

“I think sponsors will appreciate that the statute and the guidance will hold sponsors accountable to their own recruitment goals,” he said, adding that it would be impractical for the FDA to hold all sponsors to a single standard due to the uniqueness of individual trials.

But moving the needle toward more diverse cohorts in trials is not just about recruiting more participants from traditionally underrepresented groups, Siddiqui said. There are larger issues at play, such as access to research institutions, socioeconomic and educational status, and stigma.

“After many years, NIH-funded research made some progress in increasing inclusion of subgroups in trials,” he said. “It remains to be seen if this guidance will help privately funded trials to make a difference.”