FORMER FDAER DEFENDS FDA DECISION TO WITHDRAW DATA FALSIFICATION RULE

FDA Week

August 16, 2019

Length: 1323 words

Body

A former FDA policy adviser believes a recent letter from senators, including two presidential hopefuls, calling for the agency to defend the withdrawal of its data falsification reporting rule, and possibly even revive the rule, is politically motivated, as FDA already determined the rule itself would not result in any practical benefit for public health.

One public health advocate, however, argued that had the rule been revised and finalized rather than withdrawn, it could have prevented the recent scandal surrounding spinal muscular atrophy drug Zolgensma.

Debate around FDA's "Reporting Information Regarding Falsification of Data" proposed rule was revived when five senators, including 2020 Democratic presidential hopefuls Elizabeth Warren (D-MA) and Bernie Sanders (I-VT), demanded FDA explain why it withdrew the proposed rule in September. Their concerns were sparked by the highly publicized revelation that Novartis' AveXis manipulated data on Zolgensma, which was approved in May.

The proposed rule, which was introduced in 2010, would have required sponsors to report information about study data falsification. According to the Federal Register, it would have required sponsors to report information indicating that any person has engaged in data falsification in the course of conducting or reporting study results. Sponsors would have been required to report to the FDA within 45 days of becoming aware of the information.

FDA withdrew the rule in September, saying it wasn't needed to protect research subjects or to help ensure the integrity of clinical trial data submitted to FDA to support marketing applications.

"Existing regulations require study sponsors to notify FDA when they end an investigator's participation in an investigation (21 CFR 312.56(b)), and institutional review boards must notify us when they suspend or terminate their approval of research (21 CFR 56.113)," FDA said in its withdrawal notice. "Based on our review of recent data, we conclude that we are receiving adequate notice of falsification of data, and we do not believe that adopting the proposed requirements would provide us with substantial additional information."

Aaron Josephson, senior director at ML Strategies and a former senior policy advisor at FDA's device center, believes senators' calls for the agency to explain the withdrawal decision is likely politically-motivated, and just another reason to "attack" the Trump administration.

"My impression is that the rule does not need to be finalized, since it would not have changed anything for the better, but it's an easy way for Democrats to attack a Republican administration for being too lax when there is a problem," he told Inside Health Policy.

The former FDA staffer said he was asked to weigh in on the proposed rule on behalf of the device center in 2017, as part of a larger regulatory reform initiative associated with President Donald Trump's two-for-one executive order aimed at scaling back regulations. Josephson said he and the device center presented four reasons that factored into the agency's decision not to finalize the rule.

The rule was intended to clarify the reporting process for sponsors, ensure the validity of data and to protect research subjects. However, Josephson said that when he and other staffers evaluated the rule, they determined that the rule actually would not have achieved any of those objectives.

The first reason for withdrawal: The rule was redundant, as it is already illegal for sponsors to present false information to the government, Josephson explained. The rule would have been similar to requiring witnesses in a courtroom trial to swear an oath to tell the truth before testifying, then swearing that they had told the truth again afterwards, he said.

Though the rule was also meant to protect human or animal subjects, Josephson said he and other staffers determined that sponsors would likely report data falsification only after studies of the product had already taken place, so the rule would not offer any additional protection for the human and animal subjects who participated in the studies.

"The rule really wasn't adding anything in terms of protecting human subjects," he said. "Based on conversations I had with our clinical trials experts, data falsification almost always happens after a study is completed and the results are not what the sponsor or investigator was hoping for."

FDA also determined the rule would not have led to an increase in falsification reports from sponsors, Josephson said. In its Federal Register notice, FDA estimated it would receive 73 reports per year, because that was how many reports the agency received per year at the time it proposed the rule.

The estimate means that the FDA itself forecasted "the new rule would not do anything to increase or decrease the number of reports they receive," Josephson explained. "If you're not expecting any change in the number of reports, what new information do you expect to receive that justified promulgating a regulation?"

The agency also was uncertain what actions it would take once it received reports of falsification, Josephson added.

"All it said was that FDA would conduct further investigation and take enforcement when needed," he said.

If the number of reports had gone up, there also would have been a question of whether the agency would have the resources to pursue investigations of those reports.

"Assuming the volume of reports goes up, are there resources to act on data falsification in a way that would be meaningful?" Josephson asked. "Nobody could answer that question because they hadn't done a proper analysis, but having worked in government where resources are perpetually scarce, the answer is probably no."

Finally, the former staffer said it was unclear what FDA's obligations would be to disclose falsification reports once it received them. The Zolgensma scandal illustrated the problem, he said, because FDA announced the falsification even though it would have approved the drug anyway. Based on public reactions to the announcement, it seemed to have eroded confidence in Zolgensma and drug-maker AveXis.

"Because FDA considers the totality of evidence in approving a medical product, an expectation that the agency would share information about data falsification could create tension between public health, patient safety, and transparency," Josephson said.

In their 2010 response to the proposed rule, the medical products industry attacked the rule for being too ambiguous. They said the rule was harmfully unspecific and would create an "atmosphere of suspicion among regulated industry because of its requirement to report even suspected falsification."

Despite the ambiguities, Michael Carome, director of Public Citizen's health research group, questioned why FDA would withdraw the rule, rather than revise it.

"If there were concerns that the ruling in the proposed rule was vague, a better approach rather than withdraw it would be to revise the rule," said the advocate, who threw his support behind Senate Democrats' requests for an explanation on the withdrawal.

Carome believes the 45-day limit for reporting a falsification would have prevented the Zolgensma scandal. He said the rule would have improved the data of medical products by closing a loophole where sponsors can choose to withhold reports of falsified information to avoid outright lying to FDA.

Carome argued Josephson's critiques clash with FDA's original intentions for proposing the rule.

At the time, Carome recalled the agency saying sponsors were sometimes uncertain about what and when they needed to report data falsification to the agency.

"That seemed like an important argument for why the rule was important," Carome said. "I agree it is currently illegal to submit false information to the government, but the rule would have required sponsors to report falsification to the agency. -- David Roza (*droza@iwpnews.com*)

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