New NIH/FDA Rules Will Bring Greater Transparency to Clinical Trials

The big stick is withholding grant funds

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By Melinda Young, Editor

The new rules published this fall by the NIH and FDA about reporting clinical trial results will expand transparency in research and give the world more knowledge about the effectiveness of investigational and new drugs and devices, FDA and NIH officials say.

Researchers and sponsors will have to submit their findings, whether or not they are going to be published, to ClinicalTrials.gov. Failing to provide findings could result in enforcement action, including the loss of federal grants, federal officials say.

“Clinical trials are vital for medical advancement, and increasing knowledge about clinical trials is good for trials, the patients, and for science,” said Francis S. Collins, MD, PhD, NIH director.

This requirement is important because of its focus on the people who volunteer to participate in clinical trials, said Robert Califf, MD, FDA commissioner of food and drugs.

“ClinicalTrials.gov contains information from thousands of people around the world,” Califf said. Califf and Collins were among a handful of government officials who spoke at a news teleconference in September about the change.

The NIH final rule, titled, Clinical Trials Registration and Results Information Submission, published in the Federal Register on Sept. 21, 2016, is effective Jan. 18, 2017. Organizations have 90 days after the deadline to come into compliance. The FDA is changing Section 801, also known as the FDAAA 801, and

NIH also has issued the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information with a Jan 18, 2017, deadline. (For more information, see article in this issue.)

“The new requirements outlined in the final rule are expected to provide greater transparency, not only of the information in clinical trials, but also about which trials are being done, what their designs are, and how they’re being analyzed,” Califf said. “The final rule expands and provides clarity to the statutes and requirements, allowing the FDA to ensure more efficient and effective compliance and enforcement activities related to the requirements for registration and reporting of certain clinical trial information.”

Rule Expands Results Information

While the NIH final rule expands submission of results information, it does not specify that such results need to be written in layperson language, which is what the European Union and many bioethicists promote. (See article on lay summaries in study results in the October 2016 issue of IRB Advisor.)

“The law said there could be lay summaries,” says Kathy Lynn Hudson, PhD, NIH deputy director for science, outreach, and policy.

Researchers and sponsors could add material to make their results more useful to participants, and ClinicalTrials.gov is being enhanced to make it easier to conduct searches, but what is required in the final rule is scientific information, Hudson says.

From a researcher’s perspective, a layperson mandate would set a very high bar, says Jennifer Grandis, MD, an American Cancer Society Clinical Research Professor, associate vice chancellor of clinical and translational research, director of the Clinical and Translational Science Institute, and a professor of otolaryngology at the University of California, San Francisco.

“Those are two different issues: One is making sure all data are available, and the second is making it understandable, in a format that everyone can understand,” Grandis says. “My instinct about what is lay language and what a true layperson thinks is lay language are not the same, and it’s not a trivial

difference.”

Researchers have to write a lay abstract for every NIH grant, so they’re accustomed to writing for nonscientists. However, even these lay abstracts do not go far enough, according to what Grandis has heard from lay cancer survivors. “They will say that the lay abstract is not intelligible.”

One Important Goal

The NIH final rule accomplishes one important goal, which is related to the spirit of making research data available to the public, but it’s not the complete answer for the public and research participants, she notes.

“Whether ClinicalTrials.gov changes from being a repository of information to a repository of information that is accessible to individuals who are not in science and medicine is an entirely different conversation,” Grandis says.

Part of the impetus for ClinicalTrials.gov and its recent change is to help the research community understand how well devices and drugs perform, Collins says.

“Even after licensed products are approved, clinical trials can help us learn of their effectiveness,” he says. “We can learn even more from clinical trials that indicate a product or device that is not effective or safe.”

ClinicalTrials.gov now has registration information for more than 224,000 studies that take place in all 50 states and 192 countries, Collins says.

“Not all of these are subject to the final rule,” he notes. “There are more than 50,000 unique visitors who access ClinicalTrials.gov every day, learning about trials open for recruitment, identifying new studies, new therapies, or looking for results of studies that have been completed.”

While the website has improved research transparency and accessibility, it hasn’t gone far enough because of the lack of study results, Collins says. “We in the research community have a disappointing track record in making those results accessible.”

For instance, a 2014 analysis of 400 clinical trials found that, within four years of completing the study, 30% had not shared results through publications or through reporting in ClinicalTrials.gov, Collins says.

“That’s clearly unacceptable,” he says. “A more recent study found that 51 of U.S. academic medical centers found that 43% of their studies were unpublished two years after the trials were completed.”

Key Elements

The final rule's key elements, according to Collins, include: providing a checklist of which elements are subject to the regulations and who is responsible for submitting the required information, expanding the scope of trials for which summary information must be submitted to include drug, biological, and device products that have not yet been approved, licensed, or cleared by the FDA, and requiring additional registration and summary information data elements to be submitted to ClinicalTrials.gov, including the rates, ethnicity, and the full protocol.

In order for a study to be registered on ClinicalTrials.gov, researchers will have to include information about whether the study has had IRB approval, says Deborah Zarin, MD, director of ClinicalTrials.gov.

"You're not allowed to go into recruiting status unless you tell whether or not you have IRB approval," Zarin says. "And you have to provide us with evidence of that."

The National Library of Medicine, which operates the clinical trials registry and results data bank, is gearing up for an increased volume of submissions, Collins says.

"The National Library of Medicine is continuously making improvements," he says. "All of our efforts are made at ensuring society gains from knowledge gained from participation."

Collins and Califf say they expect research organizations to comply with the new rule, both because they also care about greater transparency and because there are severe penalties, including withholding of grant funding for new projects to noncomplying institutions and publishing the names of noncompliant institutions.

"I really believe it won't take much to get people to comply with this once they realize how serious it is," Califf says. "I know the press will be on top of this."

While the agencies do not have extra resources for monitoring compliance of the rule, they expect the fear of taking a hit to one's reputation will do much of the job for them. "No one wants to be on the wall of shame," Collins says.

"We have a clear expectation of compliance with the appropriate clout behind it," Collins adds. "I don't think we'll have a very large challenge here with people out of compliance."

Research institutions and investigators will want to comply with the rule, but logistically it will be challenging, Grandis says.

"It's simply more things one has to do," she says. "Whose responsibility is it for doing it? How do they do it?"

Also, for studies that are published, it won't be as simple as linking the published report to the ClinicalTrials.gov website. All of the study information will have to be uploaded separately into each of the fields.

"It's really important to get the public the information, but there are so many consequences and requirements," Grandis says. "We'll comply and do the best we can, but it's not clearly obvious how one does this."