MEDICINE

Clinical-trial rules to improve access to results

Agencies propose expanded reporting of drug-test data.

BY SARA REARDON

The US website ClinicalTrials.gov is the world's largest repository of clinical-trial information, containing the results of more than 179,000 studies conducted in 187 countries. Yet the database represents only a fraction of the trials that are run. Despite US laws requiring that results be posted to the site, drug companies and academic researchers have found numerous ways to withhold data that show that a drug did not work or had serious side effects.

Now regulators are trying to close some of these loopholes. On 19 November, the US National Institutes of Health (NIH) and the Food and Drug Administration (FDA) proposed regulations that would tighten reporting requirements and expand financial penalties for violating them. "When a lot of dollars and time and volunteers are potentially putting themselves in a risk situation, we need to be sure the results of that are finding their way into view of the public," NIH director Francis Collins said at a press conference to announce the regulations.

Transparency is necessary, he said, to ensure that study volunteers can find out what is known about a treatment and its side effects when deciding whether to participate in a trial. Researchers benefit as well, because complete reporting of data allows them to build on the results and avoid repeating failed experiments.

But although some bioethicists praise the initiative, many worry that the new rules will not solve the underlying problem. "In a lot of ways, coming up with new regulations is really the easy part," says Christopher Jones, a physician at Rowan University in Camden, New Jersey. "The more difficult and more important phase is going to be making sure that the new regulations are enforced fairly and transparently."

The proposed rules would broaden a 2007 law known as the FDA Amendments Act (FDAAA), which requires researchers to post the results of studies involving FDA-approved drugs on ClinicalTrials.gov within 30 days of approval. But such results may never be posted if a drug is never approved. One new proposal from the government would require companies to post results for all drugs or therapies submitted for FDA approval.

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"It's a great step," says Jones. "Industry in general is pretty good at following regulations as long as regulations are clearly stated and enforced."

But Jennifer Miller, a bioethicist at Duke University in Durham, North Carolina, says that the majority of trial sponsors are not following the current law. Data she has compiled comparing the number of trials registered with the FDA to those reported on ClinicalTrials.gov suggest that many are not reported, even for drugs that have been approved. The FDA can levy a fine of US$10,000 a day for noncompliance, but has never done so. "If you were going to expand or enhance FDAAA, you would think there would be considerations around monitoring and enforcement of the existing law," Miller says.

PHASE TWO

A second proposal released by the government this week would go a step further by requiring federally funded researchers to post the results of phase I clinical trials, which focus on the safety of a drug or device rather than its efficacy. Researchers would also have to register and report the results of studies that evaluate surgical techniques or non-medical interventions, such as public-policy changes intended to curb smoking. The NIH says that it plans to enforce this rule among its own researchers, and could withdraw funding from external institutions that do not comply. The agency would first try to resolve the problem with an institution before taking this step, says Sally Rockey, NIH deputy director for extramural research.

"I think there's a lot of good here," says Kay Dickersin, director of the Center for Clinical Trials at Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. "This shows a much broader understanding of what a clinical trial is." Still, she and Jones say that they wish that studies sponsored by industry and private sources were also required to report results of phase I trials. Pharmaceutical companies often guard these results, because they can contain proprietary information. Jones says that even if a drug never makes it to market, revealing the results of early safety tests could save time and money for researchers trying to develop similar therapies in the future.

Dickersin worries that it will still be hard to find information about unwanted side effects and other adverse events under the proposed regulations. Trial sponsors are required only to report summary data about volunteers' reactions to a drug, not each person's results. But data on individuals allows outside researchers to do independent analyses that may yield different conclusions (M. A. Rodgers *et al. Br. Med. J.* **346,** f3981; 2013).

This may change, says Kathy Hudson, deputy director for science, outreach and policy at the NIH. The US Institute of Medicine is working on a report weighing the downsides of summaries against other concerns such as volunteers' privacy. That report is expected to be released in early 2015. For now, the public has 90 days to comment on the proposed clinical-trial regulations before they become law. ■

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