Study examines gap in federal oversight of clinical trials

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An analysis of nearly 24,000 active human research clinical trials found that between 5 percent and 16 percent fall into a regulatory gap and are not covered by two major federal regulations, according to a study in the March 5 issue of *JAMA*. These trials studied interventions other than drugs or devices (e.g., behavioral, surgical).

The primary federal human subjects protections (HSP) policies in the United States, including requirements for institutional review board review and informed consent, are the U.S. Food and Drug Administration (FDA) HSP regulations and the Common Rule. "The first covers FDA-regulated clinical investigations of drugs, biologics, and devices, regardless of funding source, whereas the second applies to human studies funded or conducted by 17 federal entities, regardless of the type of intervention studied. These regulations are largely consistent but contain differences. Concerns have been raised about burdens and inefficiencies for studies covered by both regulations (overlap trials), and about some studies that are covered by neither (gap trials).

Deborah A. Zarin, M.D., of the National Institutes of Health, Bethesda, Md., and colleagues conducted a study to estimate the number of active U.S.-based clinical trials subject to these regulations. From ClinicalTrials.gov records of active trials listing at least 1 U.S.-based facility as of September 2013, the researchers extracted the intervention type, investigational new drug application or investigational device exemption status, sponsor, and collaborators and approximated the number of trials subject to each regulation, using narrow and broad

criteria.

Of the 23,936 sampled trials, the authors estimate that 13,165 (55 percent) to 15,576 (65 percent) trials were covered only by FDA-HSP regulations; 1,442 (6 percent) to 2,497 (10 percent) trials were subject only to the Common Rule; 4,578 (19 percent) to 5,633 (24 percent) were overlap trials that studied drugs and devices and have some federal funding; and 5 percent to 16 percent were gap trials that studied interventions other than drugs or devices (e.g., behavioral, surgical) and had no federal funding. The characteristics of gap trials varied widely, but included research in vulnerable populations (e.g., pregnant women, people with major mental illness, children) with primary outcomes that reflected potentially consequential risk (e.g., organ failure, depression relapse, seizure frequency, hospitalization).

The authors write that their analysis provides the first quantitative estimate of the size of the gap in regulatory coverage, and also documents a large number of studies that are subject to both sets of regulations.

"Our data are not precise measures of the current scope of different regulatory categories. Rather, they represent the best current estimates [based on clinical trial registrations], and this analysis is intended to inform ongoing discussions about potential regulatory reforms."

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