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# Problem FDA inspection findings in trials seldom reflected in medical literature

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When the U.S. Food and Drug Administration (FDA) identifies problems in its inspections of clinical sites where biomedical research is performed on human subjects, those findings seldom are reflected in peer-reviewed literature later written about the research, according to an article published online by *JAMA Internal Medicine*.

The FDA classifies its inspections based on the severity of the violations that are found and the most severe is "official action indicated (OAI)," which means objectionable conditions or practices were found that warrant regulatory action. During the 2013 fiscal year, about 2 percent of the 644 inspections the FDA carried out at trial sites were classified as OAI, according to background information in the study.

Charles Seife, M.S., a professor at the Arthur L. Carter Institute of Journalism at New York University, and his students identified published clinical trials where an FDA inspection found significant problems and determined whether there was mention of it in peer-reviewed medical literature.

A total of 57 published clinical trials were identified where an FDA inspection found one or more of the following problems: falsification or submission of false information, 22 trials (39 percent); problems with adverse events reporting, 14 trials (25 percent); protocol violations, 42 trials, (74 percent); inadequate or inaccurate recordkeeping, 35 trials (61 percent); failure to protect the safety of patients and/or issues with oversight or informed consent, 30 trials (53 percent); and violations that

were not otherwise characterized, 20 trials (35 percent). Only 3 of the 78 publications (4 percent) that resulted from the trials where the FDA found significant violations mentioned the objectionable conditions or practices.

"The FDA does not typically notify journals when a site participating in a published clinical trial receives an OAI inspection, nor does it generally make any announcement intended to alert the public about the research misconduct that it finds. The documents the agency discloses tend to be heavily redacted. As a result, it is usually very difficult, or even impossible, to determine which published clinical trials are implicated by the FDA's allegations of research misconduct," the study concludes.

In a related commentary, Robert Steinbrook, M.D., of the Yale School of Medicine, New Haven, Conn., and editor at large at *JAMA Internal Medicine*, and Rita F. Redberg, M.D., M.Sc., of the University of California, San Francisco, and *JAMA Internal Medicine* editor-in-chief, write: "In this issue of *JAMA Internal Medicine*, we publish a report that highlights an important area for improved public reporting of clinical trials and enhanced transparency at the U.S. Food and Drug Administration (FDA)."

"A central responsibility of medical journals is maintaining and improving trust in the medical literature. Journals should expect that investigators and sponsors of clinical trials would promptly notify them of substantial findings from FDA and other regulatory agency inspections and modify their reports of clinical trials as needed, either before or after publication. ... We look forward to continued progress on transparency from the FDA, investigators and sponsors to better protect research subjects and to better inform the medical and research communities, journals readers, and the public," they conclude.

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