Experts say ethical dilemmas contribute to 'critical weaknesses' in FDA postmarket oversight

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Ethical challenges are central to persistent "critical weaknesses" in the national system for ensuring drug safety, according to a commentary by former Institute of Medicine (IOM) committee members published today in the *New England Journal of Medicine*.

With a caution against "reactive policymaking," committee co-chairs Ruth Faden, Ph.D., M.P.H., and Steven Goodman, M.D., M.H.S., Ph.D., with fellow committee member Michelle Mello, J.D., Ph.D., revisit the controversy over the antidiabetic drug Avandia that led to the formation of their IOM committee on monitoring drug safety after approval.

The Avandia postmarket trial, halted in September 2010, was "a lesson in how our current approach to the oversight of drug-safety and postmarketing research can fail both the public and the research participants," the authors write. With those lessons in mind, their independent commentary follows the May 2012 IOM report with a focus on the ethical challenges ahead.

The authors detail the IOM report's recommendations for maintaining the delicate balance of drug innovation and drug safety. Increased "fast-tracking" of drug approval for medical conditions with no effective treatment necessitates a counterbalance of increased postmarket oversight, the authors argue. They echo the IOM report's call for an independent ethics advisory board to the Food and Drug Administration

(FDA), focused on postmarket research and safety surveillance.

"As the pace of the translation of discoveries from bench to bedside continues to intensify, so too does the imperative for thoughtful ethical governance throughout the lifecycle of a drug," the authors write.

The authors also amplify one of the IOM report's key ethics points Â– the responsibility of the FDA to participants in postmarket research, particularly in randomized trials that determine which treatment they receive. The FDA has a unique ethical obligation to the welfare of research participants when requiring a postmarket study, the authors assert, which "cannot be handed off to contractors or the industry sponsor."

"The FDA is uniquely positioned to ensure ethical postmarket research, including a proper informed consent process," says Faden, director of the Johns Hopkins Berman Institute of Bioethics. "Because some postmarket trials are required specifically to address mounting concerns that the drug's risks may outweigh its benefits, there are heightened obligations to ensure that potential research participants understand the risks of enrollment."

The authors also note that the volume of postmarket studies is increasing, due not only to FDA-ordered research but also the growing field of academic comparative-effectiveness research. The ethical issues involved can vary widely, the authors say, which makes clarity about the context for the research crucial. "Depending on who is initiating the research, for what reasons, and when, the same study design may have very different ramifications for the benefitÂ–risk balance of the study and what patients need to know in order to provide meaningful informed consent," the authors write.