Study examines expedited FDA drug approvals, safety questions remain

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Fewer patients were studied as part of expedited reviews of new drugs approved by the U.S. Food and Drug Administration (FDA) in 2008 and some safety questions remain unanswered, according to a study published by *JAMA Internal Medicine*.

The FDA is authorized to make new drugs available more quickly if they would be a significant therapeutic advancement and if they fulfill unmet therapeutic needs for serious illnesses, according to the study background.

Thomas J. Moore, A.B., of the Institute for Safe Medication Practices, Alexandria, Va., and Curt D. Furberg, M.D., Ph.D., of the Wake Forest School of Medicine, Winston-Salem, N.C., examined development times, clinical testing, post-market follow-up and safety risks for the new drugs approved by the FDA in 2008, when most provisions of current law, regulation and policies were in effect.

That year, the FDA approved 20 therapeutic drugs (eight under expedited review and 12 under standard review). The study findings indicate that expedited drugs took a median (midpoint) of 5.1 years of clinical development to get marketing approval compared with 7.5 years for the drugs that underwent standard review, according to the study results.

The expedited drugs were tested for efficacy in a median 104 patients compared with a median 580 patients for standard review. By 2013,

many postmarketing studies to gather additional evidence on the safety of expedited drugs had not been completed, according to researchers.

"The testing of new drugs has shifted from a situation in which most testing was conducted prior to initial approval to a situation in which many innovative drugs are more rapidly approved after a small trial in a narrower patient population with extensive additional testing conducted after approval," the authors conclude. "Our findings suggest that the shift has made it more difficult to balance the benefits and risks of new drugs. Further systematic assessment of the standards and procedures for testing new drugs is needed."

In a related commentary, Daniel Carpenter, Ph.D., of Harvard University, Boston, writes: "The findings of Moore and Furberg underscore the continuing importance of rigorous premarket studies of ample size. If the critical phrase 'serious or life-threatening conditions that would address an unmet medical need' is defined broadly enough (and there are lobbying efforts to define it as broadly as possible), the future of evidence for pharmaceuticals in the United States will look more like 100 patients for efficacy trials instead of 500 patients."

"If the FDA's requirements for new drugs, both premarket and postmarket, are weakened, trust in both the efficacy and safety of prescription drugs is likely to be weakened. The stakes of the current policy debates could not be higher. There is scarcely a feature of the American health care system that does not depend on evidence-based trust in prescription drugs, ratified and enforced by the FDA," Carpenter concludes.

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