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A Systematic Evaluation of the Clinical Evidence on Drugs Receiving FDA Accelerated Approval

New York, New York, June 7, 2017—Therapeutic agents that treat serious conditions are eligible for the Food and Drug Administration (FDA) accelerated approval. A new study in the June issue of *The Milbank Quarterly* has found that these drugs often quickly become part of standard treatment, despite shortcomings in their evidence base. The study, the first to provide a systematic evaluation of all clinical studies conducted on drugs receiving this type of approval, assessed 37 novel therapeutic agents that received accelerated approval between 2000 and 2013.

Authors Huseyin Naci, Olivier J. Wouters of the London School of Economics and Political Science; Radhika Gupta of The Wharton School, University of Pennsylvania; and John P.A. Ioannidis of Stanford University, examined the timing and characteristics of 7,757 available studies. They assessed to what extent the objectives, nature, and timing of research activity were aimed at addressing the limitations of the data available.

"FDA's accelerated approval pathway allows potentially promising drugs to receive marketing authorization on the basis of surrogate measures that are easy to obtain, rather than clinically meaningful outcomes," said Huseyin Naci. "Surprisingly, the vast majority of clinical studies including these drugs after market entry are not designed to directly evaluate their benefits. Currently available evidence on drugs given accelerated approval has major flaws and is inadequate to address the information needs of patients and doctors."

Background

The aim of biopharmaceutical regulation within the FDA is to ensure that only effective and safe treatments reach patients. Over the past three decades, the FDA introduced flexibility to its evidence standards. Regulators created several programs aimed at expediting the approval of new therapies that address unmet needs. Drugs expected to provide a meaningful advantage over available therapies for serious conditions are eligible for accelerated approval on the basis of surrogate measures that are proxies for clinically meaningful outcomes and are "reasonably likely" to predict clinical benefit. The bar for market entry for these drugs is substantially lower than for those receiving regular approval.

Findings

Randomized trials—the gold standard of evaluating effectiveness—constituted only a small minority of existing evidence.

- One-third of randomized trials are in therapeutic areas outside of FDA approval and less than half evaluate the therapeutic benefit of these drugs, but use them instead as common backbone treatments.
- Drugs receiving accelerated approval were often tested in several therapeutic areas concurrently.

- For most drugs, no substantial lag time was apparent between the average start date of the randomized trial and their use as background therapy.

Taken together, the findings highlight the major flaws in the cumulative evidence base that exists on therapeutic agents given FDA accelerated approval. The authors conclude that the current research landscape is inefficient and fragmented with thousands of small and nonrandomized studies that provide questionable value on the effectiveness of drugs given accelerated approval.

About *The Milbank Quarterly*

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