

FDA Drug Review Reforms: Faster Approvals and More Postlaunch Monitoring Could Save Lives

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THE HIGH COST OF CURRENT FDA DRUG REVIEW POLICIES

On average, it takes 466 days for a new drug to be approved for marketing by the US Food and Drug Administration (FDA). Pharmaceutical companies respond to the regulatory delay by bringing fewer new drugs to the market. A three-month delay in drug marketing is associated with one fewer drug in development for that disease category.¹ This phenomenon means not only that the public receives potentially life-saving treatments later, but also that, under current policies, some drugs are never going to be developed.

While the FDA performs an important social function of assessing new drugs' safety and efficacy, its lengthy review process is costing patient lives. This is only part of the story, though. It is not even clear that FDA review is a high-level guarantee of safety.

We outline these issues in more detail and present two politically feasible solutions: improving drug review transparency and implementing postlaunch monitoring.

DRUG APPROVAL PROCESS: BACKGROUND AND CHANGES

The modern era of pharmaceutical R&D regulation began in 1962 with the Kefauver-Harris Amendment to the Federal Food, Drug, and Cosmetic Act. The amendment required premarket approval of all drugs by the FDA, which was intended to ensure that new drugs met safety and efficacy standards.² The direct outcomes of the amendment were longer approval times and higher premarketing costs of drug development.

The drug development process is a costly endeavor. After discovering a new drug, the investor proceeds with required preclinical trials (animal testing that lasts up to six years). Following promising results from these trials, the manufacturer may submit an Investigational New Drug Application (INDA) to the FDA. Upon approval, the next phase of R&D involves clinical trials on humans, adding on average another decade to the process. After human trials, the drug producer may apply for approval by the FDA to sell the drug; even after more than a decade of R&D, the FDA takes on average more than a year to complete this approval process. Aside from the significant time costs associated with this process, it also involves over \$1.1 billion in monetary costs and the dynamic cost of fewer drugs being developed in the future owing to these obstacles.³

FACING TRADEOFFS

Balancing public health and safety with timely access to the benefits of innovation and R&D activity is a delicate task. If the FDA takes a strict stance on standards for approving new drugs, patients may be unnecessarily deprived of helpful treatments in the short run and receive fewer novel drugs in the future. On the other hand, if the FDA is not stringent enough, unsafe or ineffective drugs may enter the market and result in fatalities.

One only has to consider the lifespan of the drug Vioxx to understand the serious ramifications of the FDA drug approval process. Introduced in 1999 as a treatment for osteoarthritis pain,⁴ Vioxx was approved by the FDA. However, the drug was later found to significantly increase the risk for cardiovascular disease. Vioxx has since caused over 100,000 heart attacks and strokes in Americans.⁵ The prelaunch studies by Merck, the drug's producer, did little to evaluate the cardiovascular effects of the drug despite certain researchers' concerns over the issue. The magnitude of Vioxx's impact has led to it being described as the "single greatest drug safety catastrophe in the history of this country" by Dr. David Graham of the FDA.⁶ Merck eventually withdrew Vioxx from the market in 2004 and has since settled the 30,000 lawsuits it faced for \$4.85 billion.⁷ This issue demonstrates that FDA approval of new drugs does not automatically equate to safety, regardless of how long the review takes.

THE FDA REGULATORY PROCESS REDUCES WELFARE AND DRIVES UP COSTS

Over time, policies have changed. Studies have found that increased review time is costly and welfare reducing, while reductions in review time benefit consumers, producers, and society as a whole.⁸

Specifically, the Kefauver-Harris Amendment's efficacy standard reduced pharmaceutical innovation, and its cost to consumers is greater than the benefit they receive from FDA efforts to prevent ineffective drugs from entering the market. By contrast, the Prescription Drug User Fee Act (PDUFA) decreased review time. The benefits of decreased FDA review time are widespread. Studies find that net benefits to consumers increases.⁹ Patients have access to beneficial drugs

sooner. Since pharmaceutical companies also benefit, future R&D will be encouraged, leading to the production of even more new drugs, which then further increases benefits to consumers.

PROPOSED POLICY SOLUTIONS: POSTLAUNCH MONITORING AND IMPROVED TRANSPARENCY

The FDA approval process requires a significant investment by pharmaceutical companies to bring new drugs to market. The negative relationship between R&D by these companies and FDA approval time implies that firms are sensitive to the regulatory delay. It is important for the efficiency of the FDA approval process to be considered in policy discussions. Since 2009, FDA drug approval times have steadily decreased, but this decrease varies by drug category.¹⁰ Correspondingly, the number of new drugs submitted to the FDA has increased: in 2013, 5,400 new products were submitted, while 6,300 new products were submitted in 2016.¹¹

Shortening FDA review does not imply less review overall. Instead, an alternate approach to the current process would involve postlaunch monitoring, allowing the FDA to continue to monitor safety after approving new drugs. Preclinical trials are limited in that they necessarily involve relatively smaller populations, so postlaunch monitoring can reveal better information. In the age of big data, one could use a variety of medical records to detect even minor side effects promptly. This monitoring thus appears to be a crucial step to verify that safety and efficacy standards are met by all new drugs. It can also serve the purpose of enabling the FDA to reduce its premarket review time, leading to increased innovation by manufacturers and an increase in overall social welfare. This reduced premarket review time also results in people receiving potentially lifesaving treatment more quickly.

The recent shortening of review time can in part be attributed to an increased use of postlaunch monitoring by the FDA. There are already multiple postlaunch programs in use, such as the Sentinel Initiative, which has monitored “the safety of its regulated products” since 2008,¹² and MedWatch, which allows for users of FDA-approved products to report adverse effects to the FDA. Additionally, the FDA has postlaunch monitoring of drugs’ efficacy as well, such as through the Therapeutic Inequivalence Action Coordinating Committee (TIACC), which reviews reports of “drug products that fail to work in patients because the product simply has no effect or is toxic.”¹³ Products such as Vioxx reveal that postlaunch review is crucial in monitoring drug safety and efficacy, so why not incorporate this further into the review process?

In addition to using postlaunch monitoring to reduce review time, the FDA should improve transparency to the public. Specifically, the FDA should provide information on drugs that were not approved, instead of releasing information on only approved drugs. This is important because, although the agency is held accountable for approving drugs’ safety to prevent direct harm or death, it receives little public scrutiny for the indirect harm or death that occurs from patients

having to wait too long during the lengthy review process. This lack of transparency prevents both drug manufacturers and the public from truly understanding the dynamics behind closed doors.

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NOTES

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