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A Proposal to Increase Value and Equity in the Development and Distribution of New Pharmaceuticals

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Abstract

The process of developing and marketing new pharmaceuticals in the United States is driven by a need to maximize returns to shareholders. This results all too often in the production of new medications that are expensive and of marginal value to patients and society. In line with our heightened awareness of the importance of social justice and public health—and in light of our government's alliance with private companies in bringing us COVID-19 vaccines—we need to reconsider how new pharmaceuticals are developed and distributed. Accordingly, we propose the creation of a new agency of the Food and Drug Administration (FDA) that would direct the whole process. This agency would fund the research and development of high-value medications, closely monitor the clinical studies of these new drugs, and manage their distribution at prices that are value-based, fair, and equitable.

Keywords

drug development, drug industry, costs and cost analysis, health equity, United States food and drug administration

Impetus for Transformation

Health care goods and services, including prescription medications, are simply not equivalent to most marketed products. First, patients' choices are directed by the advice of their physicians, who order the medications, tests, and procedures expected to provide greatest benefit. Yet, most monetary costs in the United States are covered by private or public insurances—that is, they are borne not by patients but collectively by others in insurance pools or by taxpayers. Second, health care is ultimately a *social* as well as an individual good. Healthy citizens are happier, more productive, and less burdensome. The public has a major interest in preserving and improving the health of its members while controlling costs. However, like an iceberg, the problems created by the current way medications are developed and marketed in the United States are enormous and often hidden.

Current Problems

These problems result in large part from the need of private pharmaceutical companies to cover costs and maximize returns to shareholders. They obtain lengthy, government-sanctioned monopolies in the form of 20-year patents granted during drug development by the U.S. Patent and Trademark Office and by awards, at the time of Food and Drug Administration (FDA) approval, of five-year market exclusivity (12 for biologics) before a generic can be sold. These companies are also incentivized to take out a series of patents, make minor changes to prolong patents, and even pay generic manufacturers to delay market entry.[1–6] Many new pharmaceuticals with promising market potential are either close copies or high-priced specialty drugs rather than innovations with wide benefit.[3] Competition incites expensive efforts to influence prescribers directly through office interactions (including providing samples), payments to private physicians involved in drug trials, and financing of medical meetings, as well as indirectly through direct-to-consumer marketing, especially over television.[7–10]

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The involvement of pharmaceutical companies in drug studies can result in distortions of good science,[7,8,11,12] even though journals are making efforts to prevent this.[13,14] Trials may be allowed to use interim measures not closely linked to desired outcomes,[15] as in the case of aducanumab.[16] Conflicts of interest occur when academic leaders sit on the boards of for-profit companies [17] and when peer reviewers for medical journals have received grants from sponsors of the research.[13] The result may be FDA approval of, and an increase in expenditures for, medications of uncertain value,[18–20] especially in oncology[21]; this can be aggravated by FDA-accelerated approval.[22,23] Pharmaceutical companies also engage in expensive U.S. lobbying—estimated at $306,230,000 in 2020[24]—to influence the federal government's oversight or lack thereof.[25,26] The lack of central coordination of the development of new drugs can lead to a redundancy of efforts, a waste of resources, and a further increase in costs.[27]

While other wealthy countries face similar problems, their governments have taken actions to control drug prices.[28–30] The prices of pharmaceuticals in the United States are the highest in the world and are rapidly increasing.[4,31–33] This increases the financial burden on U.S. patients—especially with their high out-of-pocket payments for prescription drugs[34]—and decreases their use of prescribed medications.[35] Indeed, in January 2021, Americans rated lowering drug prices as their second highest priority for President Biden and the new Congress.[36,37]

The Long-Term Solution

Congress should authorize the creation within the FDA of a New Pharmaceuticals Agency, with the current Center for Drug Evaluation and Research as a branch. The Agency would have broad powers (expanding on proposals by Dennis Kucinich[38] and by Adam Gaffney and Joel Lexchin[7]). It would be composed of scientific experts in basic research, clinical medicine, clinical trials, and marketing and advised by representatives from key stakeholders, including pharmaceutical companies, clinicians, pharmacists, and patients. It would work to ensure a more equitable and value-driven process at each stage of drug development and distribution (similar to the goals of Ezekiel Emanuel and Richard Frank[39,40]). It would institute, in all its details, the plan outlined here. To wit:

- *Discovery and innovation*. Basic research—mostly performed by academic researchers—would continue to be grant-supported,[3] with Agency encouragement of creative freedom and of the investigation of novel mechanisms of action. Financial support of research and development (R&D) would shift the risk calculations of pharmaceutical companies and enable them to join researchers and the Agency in looking preferentially for drugs that would treat common, hitherto untreated illnesses or conditions or that would significantly advance current treatments, whether by increasing efficacy, reducing side effects, or including previously excluded patients.
- *Decision to proceed to development*. Researchers, pharmaceutical companies, and Agency members would collaborate to decide what potential new drugs merit further testing in light of their expected costs and their possible benefits to patients and society (including to patients at risk of or suffering from rare disorders). Companies would not be prohibited from developing new drugs on their own with completely private financing, including drugs of lesser benefit, even "me too" drugs. To obtain FDA approval, however, they would have to agree to Agency oversight of testing, production, and distribution (as described below).
- *Testing*. Clinical trials, whether performed by pharmaceutical companies or by academic institutions, would also be grant-supported (as advocated by John Ionannidis[41]). Going beyond the current use of Data and Safety Monitoring Boards[42] and building on Marcia Angell's proposal of an Institute for Prescription Drug Trials,[8] Agency members would provide scientific oversight from beginning to end: pre-approving protocols, monitoring progress, approving termination, and ensuring correct reporting of results. This insistence on sound evidence is consistent with the preliminary decision of the Centers for Medicare and Medicaid to pay for aducanumab only in the context of a clinical trial.[43] As further protection against "regulatory capture" of the Agency by pharmaceutical companies,[44] the Phase 3 trials would be run by independent bodies of experts in clinical trials, as proposed by Nortin Hadler and others.[45–47]
- *Production*. Extending the Operation Warp Speed model, pharmaceutical companies—usually those involved in developing the new drugs—would then produce these drugs under contract from the Agency, which would pay all costs, coordinate the supply of pharmaceutical inputs, and, by concentrating their purchase, generate a strong negotiating position with suppliers. Thereby the Agency would be able to lower costs and limit, although not eliminate, supply chain issues such as shortages, poor quality, or contamination of materials.[48]
- *Approval*. The FDA would continue its current premarketing approval process for new drugs, whether produced by U.S. or foreign companies. This would be facilitated for U.S. drugs by the Agency's involvement in testing. Their evidence-based development would reduce the risk from potential conflicts of interest within the FDA.[49]
- *Distribution and marketing*. The Agency would oversee the distribution of these FDA-approved pharmaceuticals to pharmacy chains, private pharmacies, hospitals, and other entities that distribute or administer them. To do this, it would establish its own supply networks or contract with private entities unrelated to pharmaceutical companies. Prices would be calculated both to cover the costs

of R&D and of distribution and to provide companies with fair profits that reflect the value to patients of each medication (as proposed by Emanuel[39]), the need to motivate companies, and prices in the international market (as in Germany[28]). The pharmaceutical companies would not be allowed to have patents on these medications (as has long been advocated by Dean Baker[1,50]). The importance of this is highlighted by the higher-than-necessary prices charged around the world, amid the pandemic, for vaccines against SARS-CoV-2 that were subsidized by public funds.[51,52]

- *Post-distribution surveillance* for effectiveness and side effects. This important but difficult task[53,54] is currently performed by FDA committees using data primarily collected "passively," that is, from adverse events reported by patients and clinicians and by manufacturers.[55,56] The FDA also started in 2008 a program of "active" safety surveillance, the Sentinel System, looking for specified adverse events in an increasingly large database of patient records in participating health care systems and insurers.[55,57–59] The Agency's increased role in development and distribution would enable it to expand on both types of surveillance, whether performed internally or contracted to outside researchers. Its centralized database detailing the development and clinical trials of new medications would not only provide key information to the Sentinel System's active surveillance program,[60] but could lead to artificial intelligence algorithms that identify reduced efficacy or serious harms in certain circumstances or populations.[61] The Agency could also increase transparency through public accessibility to the timely publication of the follow-up data on effectiveness and side effects.

The plan must take into account the international nature of the pharmaceutical market and of pharmaceutical companies. Only companies that are headquartered in (and, therefore, pay taxes in) the United States would be part of the plan, that is, would be both supported financially and regulated closely. All companies, however, would not only need FDA approval of their drugs for sale and use in the United States (as is required now), but also be subject to the Agency's control of prices and supervision of distribution.

Responses to Likely Objections

Opponents will allege that this plan would decrease incentives for innovation, not stop companies from focusing on high-profit drugs, delay patients' access to new medications and result in rationing, give the Agency the impossible task of determining "value," overexpand government's role, add enormously to the federal budget, use U.S. tax money to pay foreign pharmaceutical company workers, have no more impact than mere regulation of prices, lead to the expatriation of American companies,[62] have limited impact since foreign-based companies have (in total) higher sales than U.S.-based companies,[63] and alter but not reduce the influence of politicians and special interests.

In response, even if for-profit companies invest less in R&D if they expect lower profits,[3] much basic research is performed by academics, and innovation is proportionally as great in countries with government-restricted prices.[5,64] Government agencies already fund substantial basic research,[3,65] and Agency support even of R&D failures would foster more innovation and greater entrepreneurial risk-taking by private companies, including smaller firms and start-ups. Funds distributed to these companies would be designed to shield them from financial failure and keep them in the business of developing new drugs. These funds would incentivize companies to participate in the plan rather than develop drugs on their own, especially since they would still need to accept Agency oversight of clinical trials and distribution. Indeed, with Agency aid and oversight throughout, the process from basic research to distribution should go more smoothly and efficiently. The public would have increased and quicker access to beneficial medications. Other high-income countries use government regulations to restrain drug prices[28–30]—although far less than the regulations proposed here—without any apparent deleterious effects on patient outcomes, as compared to the United States.[66] Since the best way to determine "value" is indeed controversial,[67–71] the Agency would need to decide on an appropriate but flexible mix of patient and public benefit,[72,73] with help from the independent Institute for Clinical and Economic Review[70,74,75] (similar to the role of the National Institute of Health and Care Excellence in the United Kingdom).

While the Agency would indeed be large and have new responsibilities, its role would be mostly oversight and approval, with the major work performed by the academic researchers, pharmaceutical companies, and distribution enterprises with which it contracts. Already the FDA must approve all drugs produced here and abroad before marketing, and the Centers for Medicare and Medicaid Services plays an even larger role in health care. While the Agency would have a large staff and cover the high costs of R&D and distribution,[3,76,77] medication prices would be set to cover these costs, which would be lower because of reduced expenditures on pharmaceutical inputs, on utilization management,[78] on intermediaries[79]—especially pharmacy benefit managers,[80] on which the Republicans in Congress put primary blame for high drug prices[81]—and on marketing. Whether the drug R&D supported by taxes is performed here or abroad, taxpayers would benefit from the increased supply of better and affordable mediation and would, in particular, save money from the lower prices of new medications in government-run insurance plans, especially Medicare. Control of final prices alone, without support of R&D, would do little to stimulate the innovation that is of utmost benefit to patients' health.

U.S. companies would be unlikely to move their headquarters to foreign countries because they would lose the

Agency's financial support of R&D and production and its protection against the risk of failure. Foreign companies already face price controls in countries other than the United States; their drugs already must receive FDA approval; and the new price controls and regulation of sales in the United States would affect U.S. and foreign companies equally. The Agency's authority would enable it to negotiate fair but lower prices for those medications made only by companies headquartered abroad.

The choices of where to focus R&D would depend on what the Agency sees as beneficial to patients and society. Currently, for example, the National Institutes of Health HEAL project is funding research to deal with the opioid crisis.[82] The Agency would, therefore, surely face funding pressures from politicians and special interests (in line with Baker's warnings[1]), even if the pharmaceutical companies, with lower profits at stake, would have less reason to lobby Congress. These pressures can be resisted, to a large degree, by insisting on transparency (as the public also wants[83]) and by relying at all stages on the advice and judgments of independent experts.

Actions to Take Now

A wide variety of ways to reduce drug prices have recently been proposed[50,84–86]. These include allowing Medicare to negotiate prices for medications[4,87]; encouraging Medicare —and other insurance providers—to institute payment for value, providing less reward for "me too" drugs and those with limited benefits[2,39,87,88]; restricting maneuvers to extend patent protection[2,4,5,89,90]; limiting multimedia, direct-to-consumer advertising[7]; rewarding pharmaceutical companies that transform into "public benefit corporations[91]; setting up a "subscription model" to enable patients to obtain important medications at affordable prices[92,93]; allowing private not-for-profit companies to produce biosimilar products (such as insulin) and provide them directly to pharmacies at wholesale prices[94]; and using existing, but seldom applied, laws that enable the government to obtain drugs produced at public expense at affordable prices[95–97] and enable the FDA to switch a drug to over-the-counter status.[98,99] Recent suggestions to help patients deal with high prices have included patient assistance programs[100] and medication price guides.[101] Indeed, several bills to reduce high drug prices or mitigate their impact have been introduced in the current Congress.[102–104]

Our plan, however, would offer much greater benefits. With Agency oversight of the whole process and without the need to maximize profits, the newly developed pharmaceuticals would be innovative, more likely to benefit patients and society, priced fairly, and distributed equitably. More affordable medications would improve patients' health, decrease inequities in health care,[105] and lower costs. Central coordination would also enable greater availability of the data collected during the clinical trials and post-approval surveillance of medications,[106] in line with the National Institutes of Health's recent call for an expanded sharing of scientific value, citing its value in responding to the COVID-19 pandemic.[107]

The political barriers to change are, of course, enormous,[87,88] especially to the profound changes proposed here. Even if smaller pharmaceutical companies realize the benefits to them of risk-sharing by the government, the major companies will oppose these changes strenuously with large amounts of money. Nonetheless, is it not time to apply the lessons of our successes and failures in confronting COVID-19 to transforming how pharmaceuticals are developed, tested, and distributed? Is it not time to remind ourselves that health care's primary purpose is to improve the well-being of patients and society and, accordingly, to institute a process that yields a rational, high-quality, and affordable pipeline of safe, efficacious, and widely available medications? To us, it is past time.

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