A Proposal For Financing Postmarketing Drug Safety Studies By Augmenting FDA User Fees

An incremental policy reform that would enable the FDA and others to exit the current dilemma regarding drug safety and public trust.

by Daniel Carpenter

**ABSTRACT:** I propose to raise funds for postapproval studies of long-term drug safety by augmenting the existing “user-fee” system. Fees would be raised by an amount deemed optimal for revenue collection, and the U.S. Food and Drug Administration (FDA) would direct the incremental funds to a combination of randomized controlled trials, epidemiological studies, and postmarketing surveillance. User-fee augmentation is an achievable, incremental reform that would subsidize information that is now undersupplied in the U.S. health care system; spread the burden of funding postmarketing safety studies among pharmaceutical sponsors; and help restore public, scientific, and professional confidence in the FDA and its user-fee system.

**Recent events have exposed** several problems in U.S. pharmaceutical regulation. Critics have pointed to insufficient regulatory attention to safety issues, an emphasis on quick approvals over safety, an undue dependence on pharmaceutical companies by the U.S. Food and Drug Administration’s (FDA’s) drug review branch (Center for Drug Evaluation and Research, or CDER), the role of drug user fees in promoting such dependence, the severe undersupply of information on long-term safety, the failure of the FDA to compel (and of pharmaceutical companies to complete) Phase IV studies, and others. There is no consensus on the existence, nature, and severity of these problems. Yet the trust of citizens, professionals, and health care providers in pharmaceutical regulation has been damaged. The very appearance of regulatory failure is a source of public and professional worry.

Rightly so. Perhaps the most important benefit of FDA regulation is not that it keeps unsafe drugs from U.S. citizens, but that patients and their physicians can enter the pharmaceutical marketplace confident that the nation’s drug supply is

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safe and effective. In other words, the value of sound FDA regulation lies not just in the fact of safety but in the beliefs it conveys. There is reason to believe that doctors, patients, and drug companies have all benefited enormously from this aggregate confidence over the past half-century, as I suggest below. In the absence of trustworthy regulation and science-based drug development, the market for prescription drugs might look more like that for herbal supplements or the snake-oily patent medicines that federal regulation long ago stamped out. In other words, a healthy society; a successful health care system; and a profitable, innovative world for pharmaceuticals all depend acutely on the actual and perceived safety of drugs. Yet Americans’ belief in the safety and efficacy of drugs depends heavily on their belief in the safety and efficacy of the FDA and the pharmaceutical industry.

At the moment, those beliefs have taken something of a hit. Recent polling reports by the Henry J. Kaiser Family Foundation and Harris Interactive point to an appreciable decline in public confidence in the pharmaceutical industry over the past few years. By a three-to-one margin, Americans feel that drug companies “put profits ahead of people,” and in terms of “favorability” ratings and reputation for “customer care,” the industry now ranks near the bottom of the U.S. economy, ahead only of tobacco and (slightly) of oil, and well behind airlines, banks, life insurance, and other industries. More troubling is the fact that this image battering is a recent development. In 1997, when asked whether the pharmaceutical industry did a good job or a bad job of serving its customers, fully 79 percent of respondents reported that pharmaceutical companies had done a “good job,” with only 19 percent reporting a “bad job”; as recently as May 2002 the good/bad ratio was 59 percent to 22 percent. Yet in April 2004 the percentage of “bad job” respondents outnumbered “good job” respondents by 48 percent to 44 percent.

The FDA’s esteem appears to have suffered less damage, yet here, too, there are warning signs. Politicians from both major parties have worried about an erosion of “public confidence” in the FDA, and a “lack of trust” appears to characterize the FDA’s image in the eyes of professional associations, providers, and many other health care stakeholders. Moreover, in a recent Gallup poll, 37 percent of respondents said that their confidence in the FDA has declined in the past few years, while only 8 percent said that it has risen. Significantly, these declines in trust have not affected other sectors of the health care system, such as doctors, hospitals, or even insurance companies and third-party providers.

In this paper I propose an incremental policy reform that would enable the FDA, citizens, doctors, health care providers, health plans and insurers, and pharmaceutical companies to exit the current dilemma. The basic idea is to increase user fees and use the incremental monies to fund improvements in postmarketing safety regulation. Specifically, the monies could fund epidemiological studies, randomized controlled trials (RCTs) to assess and compare the long-term safety profiles of widely used drugs for chronic conditions, and administrative and technological improvements to FDA postmarketing surveillance.
My proposal is simple; it would require amending the current user-fee law to increase the annual per application user fee by a percentage to be decided by Congress. For illustration, let us say that the user fee is hiked by 25 percent. Under a linear projection, a 25 percent increase in user fees would generate $42 million in additional revenue for fiscal year 2005. Readers can imagine less money or more, depending on their preferences. Exhibit 1 lists the different aggregate revenues that could be raised from various percentage increases in FDA user fees.

**Spending The Amounts Collected**

**Allocation.** How could $42 million from a 25 percent user-fee augmentation be allocated to improve postapproval safety regulation? I propose three ways.

*Fund RCTs of widely used drugs for chronic conditions.* One lesson of recent years is that Americans know too little about the long-term safety of drugs, particularly those for chronic conditions. This is something of a system failure and certainly a market failure. There exists no financial incentive, and insufficient reputational incentive, for long-term drug safety to be studied. It would appear that adequate experimental studies of long-term safety would cost $3–$7 million per trial. If perhaps half of the increment from our 25 percent increase—that is, $21 million—were devoted to RCTs of this sort, we could launch three to seven high-quality, long-term safety studies (all of them randomized and fully controlled clinical trials) per year. These studies could be conducted by the FDA or the National Institutes of Health (NIH) or by academic medical centers (AMCs) with strong biostatistics centers, using grants from the FDA. Ideally, such studies would be guided by well-defined and defensible criteria for the evaluation of medical technologies.

One question is whether so few studies could address the U.S. deficit in information about long-term drug safety. This is a reasonable concern, but I offer two responses. First, FDA officials and health care providers probably have their hunches about which drugs on the market present the greatest long-term safety risks. Well before Merck withdrew Vioxx, concern was expressed about its safety among physicians at Cleveland Clinic (Eric Topol) and FDA epidemiologists (David Graham), among others. So it is not hard to imagine that given proper funding,

**Exhibit 1**

<table>
<thead>
<tr>
<th>Fee increase</th>
<th>Amount per application ($)</th>
<th>Fraction of current development cost</th>
<th>Total annual revenue augmentation ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10%</td>
<td>67,200</td>
<td>0.000084</td>
<td>16,800,000</td>
</tr>
<tr>
<td>25%</td>
<td>168,000</td>
<td>0.000210</td>
<td>42,000,000</td>
</tr>
<tr>
<td>50%</td>
<td>336,000</td>
<td>0.000420</td>
<td>84,000,000</td>
</tr>
<tr>
<td>60%</td>
<td>403,200</td>
<td>0.000504</td>
<td>100,800,000</td>
</tr>
</tbody>
</table>

**SOURCE:** Author’s calculations.
“FDA epidemiologists need access to more data, including studies 
comparing long-term safety profiles across drugs.”

the FDA and its advisory committees would be inclined to target funds toward 
drugs presenting the greatest (subjectively perceived) risks.

Second, one lesson from the experience with Vioxx is that we should look hard 
at widely used drugs for chronic conditions: those prescribed to millions of pa-
tients over many years. Among other classes, these would now include COX-2 in-
hibitors, selective serotonin reuptake inhibitors (SSRIs) and atypical antipsycho-
tics, statins, prescription sleeping aids, and drugs for erectile dysfunction. The 
medical and public health rationale for this targeting would be to focus on drugs 
whose risks are not easily detected under current regulatory programs but whose 
risks (conditional upon utilization patterns) can aggregate into high total morbid-
ity and mortality (or, if you will, high aggregate quality-adjusted life years, or 
QALYs, forfeited). When drugs have this Vioxx-like market, even small changes in 
the relative risk of adverse events can add up to staggering numbers of deaths and 
injuries. With utilization data from the public and private sectors, combined with 
information technology (IT) advances, FDA scientists should be able to identify 
drugs in need of regulatory attention.6

Fund epidemiological studies of postmarketing safety in the long run. RCTs provide a 
better, more reliable take on whether a causal relationship exists between a drug 
and adverse safety risks, but they are often poor at helping translate that informa-
tion into what people need to know: How safe and effective are drugs when they 
are prescribed in actual clinical practice and taken under nonexperimental condi-
tions? For this reason, a nontrivial fraction of the user-fee augmentation ought to 
be devoted to epidemiological studies. Although purchasing and partnership in 
data sharing should be encouraged, FDA epidemiologists need access to much 
more data than they have now, including studies comparing long-term safety pro-iles across drugs.7

Fund improvements to FDA surveillance infrastructure. Augmented user fees could also 
be used to increase the FDA’s organizational capacities by hiring more epidemiolo-
gists, purchasing more data, and upgrading IT, thereby allowing its scientists to 
better aggregate and analyze epidemiological and utilization data (including ad-
verse-event reports, or AERs).8

Institutions and criteria. Who should decide how augmented funds are allo-
cated across studies? And what criteria should guide these choices? Prudence might 
suggest separating the allocation function from the CDERs reviewing divisions, 
perhaps by involving a trustworthy FDA advisory committee. A statutory commit-
ment that a minimum proportion of the funds be spent on clinical trials and epide-
miological studies, a role for meaningful administrative discretion is preserved, an 
advisory committee role—all three of these mechanisms could increase the credibil-
ity of the program.

As for criteria, consider the recent recommendations of Jerry Avorn and the FDA’s own Robert Temple. Avorn’s mixed strategy of “generating new information” as well as “digging out the [existing] data on risk” focuses most heavily on comparative safety data, how one drug’s safety profile compares to those of other treatments for the targeted condition, or even with other treatments in the drug’s class. So some minimum proportion (perhaps 20 percent) of the funds should be devoted to comparative RCTs and case-control epidemiological studies of this sort. Temple has proposed a general conceptual scheme for what kinds of postmarketing studies are needed, under what circumstances. His rule of thumb is to begin by using existing surveillance (including AERs) to establish the existence of safety issues and to generate hypotheses. Where the hypothesized increase in risk is modest, and where utilization is broad, reliance on RCTs is called for. Where hypothesized or suspected increase in risk is manyfold (>2), then epidemiological studies using case-control methods are more appropriate. The data discussed here could supplement AER data, which should not be abandoned but used in conjunction with RCTs and epidemiological studies.

The value of bandwagoning. One way of investigating safety rigorously yet more cheaply is to use ongoing trials for supplemental new drug applications. Upon approval of a new molecular entity (NME), many companies continue studying the compound for potential use for other medical conditions. Much as the NIH and medical researchers do, the FDA can “jump aboard” these existing clinical studies for supplemental efficacy submissions and create trial arms for safety studies.

Advantages

Restoring confidence. Perhaps the most important benefit of a user-fee augmentation policy is the greater credibility and legitimacy it would lend to current and future drug regulation. With improved postmarketing safety regulation, the public’s confidence in the FDA could increase appreciably, and hence the public’s (and doctors’) confidence in the nation’s supply of pharmaceuticals could increase as well. Once the user-fee system is understood to support postmarketing safety studies as well as premarketing review, many physicians’ doubts about the perverse incentives and effects of the current user-fee system will be addressed and perhaps answered. And once the pharmaceutical industry is seen as making direct contributions to the funding of postmarketing safety studies as well as speedier premarketing review, its own public legitimacy would likely benefit.

Neither in science, nor in medicine, nor in government, nor in business do we rely heavily on markets to tell us how good drugs are. We rely instead upon large-scale statistical studies conducted prior to market entry. Given learning difficulties, physicians and patients face something of a lottery when they enter an unregulated pharmaceutical market—they can only guess at how good the products are. This can lead risk-averse consumers and physicians to forgo use of pharma-
ceuticals altogether. Yet if patients and doctors are persuaded that the worst drugs—bad both in efficacy and in safety—will not enter the market or be very unlikely to do so, greater confidence will result, to the benefit of all in the health care marketplace. Conversely, if confidence in the FDA’s ability to screen out the worst drugs dwindles, then doctors and patients might well avoid treatments that would otherwise benefit them.

Politicians, journalists, and policy analysts have spoken vaguely about this “confidence mechanism,” but they seem to recognize its potential. Although no empirical studies of these phenomena exist, there is suggestive evidence from the decades before and after the 1962 Kefauver-Harris Drug Amendments. Those amendments coincided with a decline in the introduction of NMEs to the marketplace, as the FDA began to sift good from bad products and as the costs of pharmaceutical research and development (R&D) increased. Yet other patterns also followed the amendments: The volatility of prescription patterns and their prices declined, per drug sales rose, and drug prices declined. It is plausible, then, that U.S. pharmaceutical markets were characterized by greater stability and certainty following stronger regulation.

It is quite likely that the proposed user-fee augmentation will improve public confidence in regulation. A large number of recent complaints about drug regulation are aimed at a perceived “imbalance” at the FDA. Prominent observers have lamented that the user-fee system is tilted too much toward the approval of new medicines and not enough toward their safety. If an augmentation proposal does nothing else, it will specifically, formally, and publicly commit tens of millions of dollars per year to safety-related studies and surveillance. And as the funded studies make their way into academic, public, and regulatory discussions, the public will increasingly recognize the contribution of augmented and safety-directed user fees.

**Funding scientific studies of long-term safety.** A user-fee augmentation would also help correct the rather severe deficiency we face in knowledge about drugs’ long-term safety. By financing three to seven large-scale, long-term clinical trials per year, just half of the augmented user fee could address a critical failure of the current pharmaceutical market and regulatory system. Large epidemiological data sets—of the sort that have assisted detection of associations between estrogen and endometrial cancer, between SSRIs and teenage/adolescent suicide, and between Vioxx and heart attacks—will also be required.

Our current policy of relying on Phase IV studies and postmarketing surveillance falls far short of addressing the public’s need for greater safety information, for several reasons. First, the completion rate and quality of data for Phase IV studies are quite poor. Recent data suggest that of the 1,191 Phase IV postmarketing commitments that had been made as of 30 September 2004, 68 percent had yet to be commenced, compared with the 30 percent that were either ongoing or already submitted. Drug companies lack incentives to complete these studies, and
the FDA lacks the legal authority and the political incentive to compel them once a drug is approved. In addition, the set of available punishments is brute. Faced with a firm that refuses to honor its Phase IV commitments, the FDA cannot issue fines, restrict advertising, or administer any administrative penalty save that of withdrawing approval of the company’s NDA. The political incentives weighing against withdrawal—as well as the punishment this delivers to patients and physicians—render Phase IV commitments essentially unenforceable.16

Second, many Phase IV studies are insufficiently powered or not designed to address long-term safety, which is the very issue raised by the Vioxx and SSRI debates. Finally, some critics believe that the FDA often requests Phase IV studies in the final days of a drug review, which leaves little time for sponsors to work with the agency in shaping trials that are feasible and informative. As an unfortunate result of this pattern, many Phase IV studies are poorly designed or conceived and are doomed to fail from their outset.17

**Political And Legal Obstacles To Reform**

There are real and nontrivial obstacles standing in the way of this policy proposal. Generally, one can imagine a proposal such as this “taking hits from both sides” (from the industry and consumer-safety advocates).

**Pharmaceutical industry.** As with the passage of the Prescription Drug User Fee Act (PDUFA) in 1992 and revisions in 1997 and 2002, industry assent will be required to change the user-fee law in Congress. For at least three reasons, the industry might be reluctant to embrace user-fee augmentation. First, it might dislike the additional tax imposed upon pharmaceutical submissions. Second, it might dislike the diversion of user-fee revenues to any purpose other than quicker approvals (in other words, it might fear that if funds are diverted, progress in accelerating approval times will decline). Third, pharmaceutical firms and their political representatives might view federal funding of more safety studies with suspicion, preferring instead to conduct such studies on their own, independent of government promotion or oversight.

These obstacles are real but not insurmountable. Consider the following three points.

1. **Precedent in existing law and proposals, and plausible support from industry.** PDUFA III, enacted in 2002, contains provisions for postmarketing surveillance. So industry has already agreed to postmarketing surveillance funding from user fees; the real question is whether the proposed hikes in these fees will be unpalatable. On this point, the benefits of the proposal and, most important, the specter of uncertain PDUFA reauthorization could induce industry to see an augmentation program as a good deal. Conservative commentators and industry supporters have all embraced the idea of more funding for the agency’s postmarketing safety program.18

2. **A political mechanism: establish user-fee augmentation and user-fee–funded safety studies as the political price for PDUFA reauthorization.** Although industry assent might be re-
“If the user-fee monies are seen as simply whitewashing drug-safety issues, then the money will have done only harm.”

quired for user-fee augmentation, industry enthusiasm might not be. PDUFA itself cannot live on past 2007 without congressional reauthorization, and that program has come under increasing attack. The industry’s assent is needed politically for PDUFA reauthorization, but so is the assent of Congress. In light of recent events, it would hardly be surprising if user-fee reauthorization in 2007 were the target of a broader backlash: scrutiny from members of both parties, obstruction from well-placed committee chairs in both chambers, or even a filibuster. PDUFA’s supporters, including many in industry, will soon realize this prospect, if indeed they do not fear it already.

The possible political conflict and uncertainty over the user-fee reauthorization might allow policymakers to extract some policy concessions from the pharmaceutical industry and (separately) from the FDA. The industry presumably wants the user-fee act to continue. Suppose, then, that a user-fee hike, combined with safety-related expenditures from user-fee revenues, were presented to the industry as the political price of PDUFA reauthorization. Indeed, thinking prospectively, pivotally positioned legislators might be in the best position to deliver such a message. In light of the specter of uncertain reauthorization of the entire user-fee program, an augmentation plan begins to look like a good deal for industry.

(3) Reputational and informational benefits of the proposal. In the aggregate, I think that it is possible to persuade drug companies that they would benefit from more and higher-quality information on safety—information that could be better distributed using improvements from the user-fee augmentation. Using an argument such as that advanced by Avorn, one could make the case that collective action problems prevent pharmaceutical firms from investing in data-gathering mechanisms that are in their interest.19 The industry’s public reputation, now quite weak, would also stand to benefit.

■ Consumer-safety advocates and patient groups. Fears of the conflict of interest created by user fees have led many observers to propose scrapping the system altogether; voices for a consumer-safety focus at the FDA might not readily agree to a hike in the fees that would perpetuate the system.20

These concerns are understandable and real. The key concern to address is the credibility of safety-related studies and analyses undertaken with monies from the user-fee augmentation. If the user-fee monies are seen as simply whitewashing the drug-safety issues in U.S. health care, then the money will have done only harm. Here the partial independence of the allocation authority is crucial; the user-fee monies should be allocated by decisionmakers from both within and outside of the FDA, whose responsibility and interest is not the approval of drugs, but their postmarketing regulation. Moreover, studies funded by the user-fee augmentation
should be fully revealed to the public, and any such disclosure commitment should be made before a study commences.

With the proper institutional protections, safety advocates will see an augmented user fee as a costly and real commitment by industry and the FDA to bolster the study and regulation of drugs after they have entered the marketplace. With these protections in mind, it warrants remark that there was genuine support in some quarters of the medical profession as little as five years ago for using user-fee monies in much the way I have proposed here.21

**Problems with other proposals.** Other proposals advanced to solve the problem have more daunting problems. Per prescription taxes are politically unpalatable and would require a costly new administrative apparatus to collect. FDA mandates for Phase IV studies are widely ignored now, and few if any of these studies are observational or directly compare therapies. As with any discretionary component of general revenues, FDA appropriations can always be cut in any fiscal crisis, which means that they are less stable on an annual basis.22

**Answers To Questions And Concerns**

**Isn't this a tax on pharmaceutical companies?** Will it discourage innovation? Prescription drug user fees are a per application tax on pharmaceutical producers. No analysis of the problem should sidestep that fact. Yet the benefits of a stronger user-fee system and a credible program for drug-safety analysis would outweigh the relatively small costs of a user-fee hike. If user-fee augmentation made it less likely that insurers and providers would remove approved products from their formularies for safety reasons (as recently occurred with COX-2 inhibitors), or that doctors and patients would shy away from new FDA-approved products, is it then not easily conceivable that these benefits would aggregate at least to tens of millions of dollars annually for the industry?

One might be concerned, still, that a user-fee hike would slow innovation. For most companies, this is arguably not an issue. Other determinants of development cost dwarf user fees by multiples of hundreds or thousands. From 1991 to 2003 the Tufts Center for the Study of Drug Development estimate of drug development cost rose from $291 million to $802 million. From 1994 to 2004, the nominal value of the per drug user fee rose from $208,000 to $672,000, or less than a half-million dollars. In other words, the increase in user fees can account at most for 0.12 percent of the increase in development costs over the past decade, and this calculation assumes that the user-fee system brings no offsetting benefits with it. Even if development costs are a nonlinear (convex) function of nominal user fees, the overwhelming share of the increase in drug development costs must be attributable to other factors. Another consideration comes from a second glance at Exhibit 1: For a 25 percent increase in the product user fee by itself to render drug development unprofitable, the present-value margin of the product at the date of regulatory submission must be at or below $168,000. This seems exceedingly unlikely for
any drug now under development.

- Didn’t PDUFA III (2002) already devote user-fee revenues to drug safety?

Not for the kind of information that everyone agrees is needed. PDUFA III allocates several million dollars per year to the collection and analysis of AERs. AER data are useful, and along with the FDA’s Temple, I envision them as allowing hypothesis generation and complementing observational and experimental studies. Yet AER data are far from sufficient for rigorous analysis of drug safety, and if the monies were used for surveillance only, the user-fee augmentation will have been a wasted policy opportunity.

- Couldn’t these studies be used against pharmaceutical manufacturers in court? We already have Phase IV trials and ongoing epidemiological studies that present this risk. Clearly, then, tort risk cannot be a prohibitive consideration here; otherwise, even the modest level of Phase IV clinical trials and epidemiological studies that we observe today would not be carried out. It is possible, though, that to expand postmarketing safety studies, some restrictions on the evidentiary use of federally funded studies in tort cases might be considered.

- Why rely on taxation rather than enforcement of existing policies? The FDA really has no enforcement authority. It cannot issue fines, cannot compel Phase IV studies, and cannot enforce Phase IV commitments. So the agency’s weaknesses leave it with a brutal trade-off: Let companies off the hook, or withdraw NDA approval altogether (a political disaster that hurts patients). Moreover, increased enforcement and the present proposal are not exclusive options. The funds from user-fee augmentation can be used to bolster enforcement and (just as important) to supplement the data gained from enforcement. The user-fee augmentation policy proposed here offers much more incremental, more achievable mechanisms for postmarketing analysis and regulation of drug safety.

As Avorn has recently written, “The initial FDA approval of a drug should be seen as the beginning of an intensive period of assessment, not the end.” For a decade, user fees have been used with great effect to accelerate “initial approval.” Let us now harness them for improving drug-safety activities as well, not just by increasing postmarketing surveillance but by funding scientifically sound studies (experimental and observational) of the drugs used most widely and durably in our health care system. User-fee augmentation might not solve all of the problems facing the FDA, the U.S. health care system, and the pharmaceutical industry. Yet an augmentation proposal would cost little, fund the revelation of health information that is now undersupplied, and offer a means for increasing public confidence in the current health care system, which seems perhaps the first place for policy reforms to start.
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NOTES
10. I thank an anonymous reviewer for many of the considerations in this section.
11. I thank an anonymous reviewer for this suggestion.

13. Note, for instance, the recent decision of Kaiser Permanente to remove Bextra from its formulary, even though the FDA has allowed the drug to remain on the market.

14. P. Hilts, Protecting America’s Health (New York: Knopf, 2003), 193–194, 214. When Health and Human Services (HHS) Secretary Michael Leavitt announced recent changes at the FDA, he stated that “the FDA is an icon of trust, a certifier of safety, an enabler of innovation, and a repository of information.” Whether the decline in new molecular entities in the 1960s is traceable to the 1962 Amendments is not clear; see Law, “History of Food and Drug Regulation.” For evidence on increasing per drug sales after the amendments, see M.B. Balter, “Coping with Illness: Choices, Alternatives, and Consequences,” in Drug Development and Marketing, ed. R.B. Helms (Washington: AEI Press, 1973), 37–43, and D. Schwartzmann, “Pharmaceutical R&D Expenditures and Rates of Return,” in ibid., 68–69. Per drug data on prescription patterns are unavailable, but the variance of prescription drug prices dropped heavily after the 1962 regulations. In the twelve years before the 1962 amendments, the variance of the pharmaceutical CPI was 18.7 CPI points, whereas the variance in the twelve years following the amendments was 6.1 points—less than one-third of its pre-1962 value. The level of the prescription drug CPI also fell continuously during the 1960s, from 51.4 in 1961 to 46.9 in 1970, and reached its pre-regulation peak only in 1976. All data are from Consumer Price Indices as calculated by the Bureau of Labor Statistics, U.S. Department of Labor.


17. I thank an anonymous reviewer for this suggestion and the language in which it was expressed.


19. Avorn, Powerful Medicines, 374–375.


