Letters

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Vouchers For FDA Priority Reviews

David Ridley and colleagues (Mar/Apr 06) deserve praise for seeking market-based mechanisms to encourage the development of medicines and vaccines for diseases primarily affecting the poorest nations, but their prescription—a transferable voucher for priority review by the U.S. Food and Drug Administration (FDA)—is built on faulty assumptions.

They come to the value of an FDA priority review on the basis of an estimate that a standard review takes 18.4 months and a priority review takes 6.4 months. According to the FDA, in fiscal year 2003 the actual times for standard reviews were 13.8 months and 6.4 months, respectively. More important, under the Prescription Drug User Fee Act (PDUFA), the FDA has committed to delivering action on 90 percent of applications for standard reviews within ten months and for priority reviews within six months. A better estimate of time saved, then, is four to seven months, which would change the paper’s estimate of the value of the proposed incentive.

In addition, the proposal depends on the FDA’s doing priority reviews for drugs and vaccines that it otherwise would not deem as meriting the required resources. Although the authors propose requiring drug companies to pay an additional user fee for this, it is not obvious that the fees would be enough to ensure that the FDA would have the expert human resources to do so without taking away from reviewing medicines and vaccines that it believes need priority review.

Market mechanisms are the key to creating incentives for drug companies to increase research and development (R&D) commitments to meet the needs of the developing world. Strong advance purchase commitment (APC) proposals, which are advancing rapidly, are the most direct way to create these incentives.

Ian D. Spatz
Merck and Co. Inc.
Whitehouse Station, New Jersey

Vouchers: The Authors Respond

Ian Spatz raises important, informed questions about our proposal. First, how much faster is approval for priority-review drugs compared to approval for standard-review drugs? Spatz reports a difference of seven months in 2003 for new drug applications (NDAs). We use data on new molecular entities (NMEs), not NDAs. In 2005 the difference in median total approval time between priority review and standard review for NMEs was seventeen months, longer than our twelve-month estimate. Even assuming Spatz’s timing of seven months, the voucher value would be $180 million for a top-decile drug or $430 million with orphan-drug tax credits, which would motivate salvaging promising projects.

Second, will the voucher drug slow other FDA reviews, despite its additional $1 million user fee? If this amount is insufficient, it could be increased, as priority review is potentially worth millions of dollars to drug companies.

Third, are APCs better incentive mechanisms? We agree with Spatz that these are promising, but to our knowledge no one is proposing a $3 billion APC for leishmaniasis, Chagas disease, or dengue fever. Hence, as we wrote in our paper, “If the APC were directed at malaria, tuberculosis, and HIV/AIDS, then the voucher could be applied to other diseases.”

David B. Ridley for the authors
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DOI 10.1377/hlthaff.25.4.1184 ©2006 Project HOPE–The People-to-People Health Foundation, Inc.
Drugs Down Under

Steven Morgan and colleagues’ recent paper about the centralized drug review process of four Commonwealth countries (Mar/Apr 06) raises interesting issues about tough evidence-based coverage decisions. It is important to examine whether the differences in these review processes have different effects on drug coverage, and the authors’ first exhibit shows that they do. Unfortunately, it contains errors about the data for Australia and New Zealand because the authors analyzed brands rather than drugs.

First, Seretide is not a drug; it is a combination product (fluticasone plus salmeterol). The analysis should have considered the use of the individual drugs that are used together but supplied as separate items. In 2003 fluticasone (Flixotide) and salmeterol (Serevent) were reimbursed in Australia and New Zealand.

Second, paroxetine hydrochloride (Seroxat) has, in fact, been reimbursed in Australia and New Zealand for many years as Aropax. Venlafaxine hydrochloride (Effexor) was first listed on the Australian Pharmaceutical Benefits Scheme (PBS) on 1 August 1996 as Efexor. The reimbursement of venlafaxine hydrochloride (as Efexor XR) in New Zealand began on 1 January 2004.

Third, the analysis is correct that omeprazole (Losec) was reimbursed in Australia and New Zealand in 2003. Nonetheless, it was out of patent in Australia in 2003, with several lower-cost generic brands listed on the PBS. The analysis failed to consider their use and cost.

Insofar as Australia and New Zealand are the only two countries where data were cited on all of the seventeen selected drugs (products), making comparative statements on coverage is limited. Nonetheless, one can reasonably conclude that access to these drugs (and perhaps to drugs in general) appears to be poorer in New Zealand; in the end, all seventeen were reimbursed in Australia, whereas only nine were reimbursed in New Zealand.

Michael J. Wonder
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Debbie Wyber
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Drugs Down Under: The Authors Respond

We thank Michael Wonder and Debbie Wyber for pointing out errors in our paper: specifically, that the product Effexor (as Efexor) was listed as a restricted benefit and that Seroxat (as Aropax) was covered in Australia in 2003. When it comes to coverage of separate medicines that are equal to combination products or generic versions of brand-name products, however, our focus was on the brand-name drugs that make up global best sellers. The purpose of our exhibit (and, indeed, our paper) was not to assess access to medicines but to investigate differences in coverage decisions for particular products (that is, brand-name versions of particular compositions). To assess access would have required that we consider coverage in terms of products that produce comparable health outcomes—not merely chemically equivalent alternatives—and which portions of the populations have ready access to drugs that can produce the desired health outcomes.

Indeed, it is unreasonable for Wonder and Wyber to claim that access might be low in New Zealand or even Australia. Overall access to necessary medicines is undoubtedly greater in New Zealand and Australia than in, for example, the United States, Canada, or any other country not offering universal coverage of medicines of proven value.
Chile: The Author Responds

Victor Zarate and colleagues point out the tendency of economically advantaged countries in all parts of the world to lure physicians from poorer neighbors to take on the least desired medical jobs in the advantaged country. The Chilean experience replicates the well-documented tendency of anglophone countries to import large quantities of physician labor.

The optimal strategy to address this deleterious migration is for well-to-do countries to take seriously the issue of training their own physicians to create medical self-sufficiency. Otherwise, the laissez-faire education policies that led to insufficient medical training opportunities in the United States, as well as in Australia, Canada, and the United Kingdom, will continue to create major magnets for physician migration. Relying on the limited resources of poorer countries to train physicians for wealthier nations and creates permanent instability in the workforces of those countries. The Chilean example is an important case report of this global problem.

Fitzhugh Mullan
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Postapproval Drug Safety

No doubt it is helpful to have financial benchmarks for the biopharmaceutical industry, but the devil is in the details. The findings of David Ridley and colleagues on spending for postapproval drug safety (Mar/Apr 06) are incomplete if not misleading, and they might confound the public’s understanding of pharmacovigilance, regulatory mandates, and industry commitments.

The authors’ survey was limited to “postapproval safety activities.” To argue, as the paper’s title does, that these activities account for drug manufacturers’ spending on postapproval drug safety, misrepresents pharmacovigilance today. At best, the $56 million reflects only what is spent on complying with regulatory requirements, not on comprehensive pharmacovigilance programming globally.
Managing adverse-event information is a small part of pharmacovigilance; looking only at it ignores activities integrated into other postmarketing programs: trials, observational studies, registries, practice patterns/outcome surveys, claims databases and other electronic sources that respond to safety issues, regulatory filings, and legal analysis.

Postmarketing studies have been criticized as being driven by strategy, not safety. Bio-pharma is making a remarkable effort to mount integrated postapproval programs: clinically beneficial, scientifically defensible, transparent, accommodating to—but not compromised by—commercial priorities, and yielding data assets supporting pharmacovigilance. To exclude these activities disregards the true spending and underlying commitments, and it misinforms all stakeholders in drug safety. At best, the $56 million estimate is the reported spending by corporate headquarters on regulatory safety compliance, not on comprehensive postapproval pharmacovigilance programming, globally and locally. Yet the survey’s specifically stated goal was to assess what companies spend on overall safety activities, not just regulatory requirements. We included epidemiologic studies, registries, postapproval safety trials initiated by the company regardless of FDA mandate, and risk management activities.

We did not include what these authors refer to as “integrated postapproval programs… accommodating to…commercial priorities.” Such postapproval studies are usually designed to demonstrate advantages in effectiveness and are less thorough in identifying, collecting, and monitoring safety parameters. If studies specified a focus on safety outcomes, we instructed respondents to include them in our survey. Furthermore, we sought the global costs of companies with a U.S. presence. On the basis of valuable input from members of the Pharmaceutical Research and Manufacturers of America (PhRMA) Pharmacovigilance and Epidemiology Technical Group, we believe that we selected the appropriate scope.

We designed our study to provide an objective assessment of the costs of drug safety that could withstand scrutiny and be replicated in the future. We encourage debate about the nature and amount of spending by industry, government, and other partners in the drug safety system. Whether industry spending is too much, too little, or precisely the right amount should be decided following a focused debate on best strategies to accomplish the complex public health tasks at hand.

David B. Ridley and Judith M. Kramer
for the authors

Postapproval Drug Safety: The Authors Respond

The letter from Ivo Abraham and Karen MacDonald is helpful in highlighting the scope of activities included in assessing postapproval drug safety, but it suggests a misunderstanding about the scope of our study.

Abraham and MacDonald write that the $56 million figure we give for the costs of drug safety reflects spending on complying with regulatory requirements, not on comprehensive pharmacovigilance programming, globally and locally. Yet the survey’s specifically stated goal was to assess what companies spend on overall safety activities, not just regulatory requirements. We included epidemiologic studies, registries, postapproval safety trials initiated by the company regardless of FDA mandate, and risk management activities.

We did not include what these authors refer to as “integrated postapproval programs... accommodating to...commercial priorities.” Such postapproval studies are usually designed to demonstrate advantages in effectiveness and are less thorough in identifying, collecting, and monitoring safety parameters. If studies specified a focus on safety outcomes, we instructed respondents to include them in our survey. Furthermore, we sought the global costs of companies with a U.S. presence. On the basis of valuable input from members of the Pharmaceutical Research and Manufacturers of America (PhRMA) Pharmacovigilance and Epidemiology Technical Group, we believe that we selected the appropriate scope.

We designed our study to provide an objective assessment of the costs of drug safety that could withstand scrutiny and be replicated in the future. We encourage debate about the nature and amount of spending by industry, government, and other partners in the drug safety system. Whether industry spending is too much, too little, or precisely the right amount should be decided following a focused debate on best strategies to accomplish the complex public health tasks at hand.

David B. Ridley and Judith M. Kramer
for the authors
What’s Time Got To Do With It?

In their paper on trends in drug development times (Mar/Apr 06), Salomeh Keyhani and colleagues analyze clinical development and regulatory approval times for new drugs in the United States. They set out to examine the validity of what they assert is industry’s claim that recent increases in prescription drug prices are the result of increasing development times. The hypothesized connection links development times to R&D costs and then to drug prices.

The support offered for this claim about the “industry” view comes from several documents published by the drug industry’s U.S. trade association. The notion that these documents claim that rising development times are largely responsible for rising drug prices is, I think, tenuous at best; in any event, some industry leaders have explicitly refuted the view that there is a causal link between R&D costs and drug prices. At the time that drug prices are determined, the associated R&D spending for a drug is a sunk cost. Basic economic logic tells us that R&D costs do not determine prices. We do not need a study of development times to draw that conclusion.

If development times are not causally related to drug prices, then what is the significance of trends in drug development times? At least two fundamental reasons come to mind. First, if development times lengthen, then patients will get access to new therapies later than they otherwise would. Second, longer development times increase R&D costs and shorten the period during which drug companies can earn the returns they need to make investment financially viable. Other things being equal, longer development times reduce innovation incentives. As a consequence, fewer new therapies might be developed.

Joseph A. DiMasi
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Time: The Authors Respond

Our study examined trends in drug development times and found them to be decreasing. We agree that development times are important, as they affect R&D costs and potentially lengthen the time before there is access to effective and safe therapies.

We also agree that there is little direct evidence to link R&D costs and drug prices. Joseph DiMasi’s statement that the drug industry does not link drug prices to development times and R&D costs does, however, make light of industry lobbying on this issue. Indeed, DiMasi’s study that estimated an $802 million price tag for drug development is one of the most widely cited studies used to justify high drug prices.

The drug industry, as well as others, now posits that drugs should be priced on the basis of value. We agree. More rigorous and robust cost-effectiveness analyses would help in assessing the value of new drugs.

Salomeh Keyhani for the authors
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NOTE


Editor’s Note: A longer eLetter version of this letter and the response are available online at http://content.healthaffairs.org/cgi/eletters/25/2/461.

Read And Decide

In his Perspective on physician-owned specialty hospitals (Jan/Feb 06), Charles N. Kahn III compliments the Centers for Medicare and Medicaid Services’ (CMS’s) May 2005 Report to Congress on Physician-Owned Specialty Hospitals for breaking new ground on quality and community benefit. Kahn also, however, criticizes the report’s methodology and analysis of emer-
Emergency department (ED) issues, as well as the nature of some purported conclusions.

The CMS report is both rigorous and unique in its use of specific hospital ownership and financial data. This approach enabled the CMS to quantify its analysis of referral patterns and community benefit, which no analysis has done to date. These data are not imputed, as Kahn suggests, but empirical.

Our analysis of community benefit found that the proportion of net revenue that specialty hospitals devoted to uncompensated care and taxes combined exceeded the proportion of net revenue that nonprofit community hospitals devoted to uncompensated care. In criticizing this finding, Kahn asserts that the CMS omitted for-profit hospitals that, in his view, are the “prevailing type of hospital in the markets studied.” In our six-market study, however, only two of the twenty-one competitor hospitals were for-profit hospitals, so omitting them due to lack of financial information did not substantively affect the results.

Kahn also states that “the CMS report glosses over…the current [ED] on-call crisis imposed by the Emergency Medical Treatment and Active Labor Act (EMTALA)” and physician call. These issues were not part of our congressional mandate; moreover, they are considerably more complex than Kahn suggests. For example, in providing emergency care, cardiac hospitals differ greatly from orthopedic and surgical hospitals.

Finally, I am puzzled by Kahn’s observation that the “CMS report, however, curiously suggests that specialty hospitals’ physician-owners are part of the solution, not the problem.” The CMS quite clearly did not draw this conclusion (or any other broad policy conclusions); instead, it presented findings in response to congressional inquiry. We invite Health Affairs readers to read the Report to Congress at http://www.cms.hhs.gov/reports/downloads/RTCPhysSpecHosp.pdf and draw their own conclusions.

**Timothy P. Love**  
Centers for Medicare and Medicaid Services  
Baltimore, Maryland

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**Come Look At Lafayette**

As a physician partner with MedCath Corporation in the Heart Hospital of Lafayette (Louisiana), I was disappointed in Kahn’s seemingly one-sided coverage of the debate on specialty hospitals (Jan/Feb 06). Our data, gathered and analyzed by the nationally respected Lewin Group, demonstrate that MedCath heart hospital facilities are great assets to their communities. In fact, the Lewin data illustrate that patients who are cared for in MedCath facilities have better outcomes, such as lower in-house mortality, shorter lengths-of-stay, and higher percentage of discharges to their homes, than do patients in other facilities.

Contrary to the claims made by Kahn, specialty hospitals exist to provide valuable additional resources to their communities—specifically, resources that were not provided before a hospital such as ours opened. As an example, in 2005 approximately 28.6 percent of our MedCath hospital patients came in through the ED; another 19.3 percent came from a nearby hospital that did not have the capabilities to treat cardiovascular patients.

Specialty hospitals create an environment of fair competition that improves options for patients. In fact, the Medicare Payment Advisory Commission (MedPAC) report Kahn mentions stated that physician-owned specialty hospitals often serve as a “wake-up call” for traditional hospitals to improve their services. In its study, the CMS found that specialty hospitals have superior quality outcomes and, when taking into account the taxes they pay, contribute more to the community than general acute care hospitals.

I invite Kahn to come here and spend time with my patients and me. He will then understand what goes on when health care is practiced within a community. He can see how specialty hospitals are market driven, thus ensuring that patients’ needs and care come first.

**Edgar L. Feinberg II**  
Heart Hospital of Lafayette  
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