The FDA And Regulation Of Cost-Effectiveness Claims

How should the Food and Drug Administration regulate drug companies' claims that their products are "cost-effective"?

by Peter Neumann, Darren E. Zinner, and A. David Paltiel

PROLOGUE: As the channels through which drugs are sold change from individual physicians to far fewer managed care plans, value becomes increasingly important. In response, drug manufacturers have begun to make greater promotional use of cost-effectiveness information, which has prompted the Food and Drug Administration (FDA) to promulgate draft guidelines to restrict such practices. Peter Neumann and colleagues urge caution here. They contend not only that the FDA lacks the expertise and the historical mandate to regulate in this area, but that the agency's proposal could impede the flow of useful information. They suggest that existing and emerging institutions and incentives, along with only modest regulation, would impose sufficient discipline on the use of pharmacoeconomic claims as promotional tools.

The authors bring a wealth of experience to bear on this challenging topic. Neumann, who holds advanced degrees in economics and in health policy and management, has extensive experience in the economic evaluation of medical technology and has served in a number of high-level posts both in and out of government. He is deputy director of the Harvard School of Public Health's Program on the Economic Evaluation of Medical Technology. Darren Zinner holds a master of science degree from the Technology and Policy program at the Massachusetts Institute of Technology and is a research associate at the Harvard medical technology program. David Paltiel holds multiple advanced degrees from Yale University, where he is now assistant professor of health policy with joint appointments at the Schools of Public Health and Management.
ABSTRACT: The Food and Drug Administration (FDA) has issued draft guidelines that would require more rigorous standards for making pharmacoeconomic claims. This paper critiques the guidelines and explores the objectives of market regulation for health-related cost and effectiveness information on pharmaceutical products. It argues that the FDA should proceed with caution and flexibility. In particular, regulations should recognize the potential usefulness of pharmacoeconomic information in helping health care decisionmakers make better-informed choices. They also should acknowledge the enhanced ability of those using the information to evaluate pharmacoeconomic studies and the degree to which the various players in the market can impose their own regulatory discipline.

As competitive pressures mount in the U.S. healthcare system, pharmaceutical companies are increasingly conducting and disseminating pharmacoeconomic studies to provide evidence that their products are cost-effective. The studies, which assess the costs and health benefits associated with the use of drug therapies, offer a potentially valuable tool for health care decisionmakers. However, some observers have complained about the poor quality of studies, the lack of regulatory standards, and the potential for biased results, given the sponsorship of many analyses by the pharmaceutical industry.¹ The issue has concerned the Food and Drug Administration (FDA) because of the agency’s authority to ensure that promotional materials involving pharmaceuticals are not inaccurate or misleading.

The emergence of pharmacoeconomics forces the FDA, which historically has been concerned with the safety and clinical effectiveness of new drugs and devices, into new territory: judging the merits of economic evaluations. The agency has issued draft guidelines, enumerating the principles it will use in reviewing such pharmacoeconomic claims for promotional purposes. The guidelines raise important questions about the nature of the risks that the FDA is attempting to regulate and the ability of those who use the information-increasingly managed care plans-to evaluate pharmacoeconomic analyses. In this paper we explore the issues involved in regulating and evaluating cost-effectiveness information in health care. In particular, we discuss the actual and potential oversight of pharmacoeconomic claims by the FDA and the role of the private sector in evaluating pharmacoeconomic information.

The FDA And Promotional Claims

The rise of pharmacoeconomics. The increased popularity of pharmacoeconomic studies has been well documented.² By 1994 an average of twenty-four such studies were being conducted per pharmaceutical manufacturer, compared with fewer than two per com-
pany just six years earlier. The studies are designed to assess the efficiency with which a pharmaceutical intervention uses limited resources to produce favorable health outcomes. The basic approach is to compare one pharmaceutical therapy's incremental costs and health benefits with those of alternative interventions.

The use of pharmacoeconomics in the United States has been propelled by the rise of managed care organizations, which has concentrated purchasing power in large plans so that they have greater leverage with which to negotiate drug prices. The consequence has been an increase in competition in the pharmaceutical industry, especially within therapeutic classes. Manufacturers face pressure to demonstrate that their products offer greater value-in terms of price and quality-than their competitors' products. Pharmaceutical companies have shifted emphasis away from traditional marketing campaigns directed to physicians to campaigns aimed at health plan purchasing managers. The pharmacoeconomic study is an important instrument in the new promotional toolbox.

As noted, the rapid growth in pharmacoeconomic studies also has caused concern. FDA officials themselves have expressed concern about promotional materials containing unsubstantiated claims about a drug's cost-effectiveness.

### The FDA and regulation of promotional claims

The Drug Amendments of 1962 grant the FDA jurisdiction to regulate and prohibit the misuse of drug labeling and advertising. The agency has interpreted this statute to include "virtually all information, disseminating activities by or on behalf of a prescription drug manufacturer." According to FDA regulations, labeling and advertising of pharmaceuticals must conform to several specific requirements. First, no labeling or advertisement may recommend a product for any indication that is not approved by the FDA; second, advertisements may not be false or misleading and must present a "fair balance" of "all clinically relevant information-the risks and the benefits-that can affect a physician's prescribing decision;" and third, any claims of superiority or comparability must be based on substantial evidence taken from well-controlled studies.

The FDA has never codified precisely what these provisions mean for pharmacoeconomic studies. One important area of contention involves the distinction between scientific exchange and promotional activities. In general, the FDA does not restrict the free exchange of scientific information concerning a drug, including dissemination of study results in scientific or lay media. This means that a pharmacoeconomic study published in a scientific journal is not considered promotion, but circulation of that study for promotional purposes would be. As a result, pharmaceutical companies...
have been sponsoring studies in abundance, encouraging the publication of (favorable) results in journals, but treading cautiously in using pharmacoeconomic studies for promotional purposes.

A second area involves new arrangements and forms of communication between pharmaceutical companies and managed care plans, including activities such as the presentation of outcomes research or decision analytic models to demonstrate the value of a drug firms products. The FDA convened a hearing in fall 1995 on the nature of the new organizational structures and information dissemination channels and continues to debate the issue internally.

**Draft Guidelines On Pharmacoeconomic Claims**

In spring 1995 the FDA's Division of Drug Marketing, Advertising, and Communications (DDMAC) issued draft guidelines, enumerating the principles it will use in reviewing pharmacoeconomic claims. In releasing the guidelines, FDA officials emphasized the agency's social responsibility in overseeing pharmacoeconomic studies and the important public health implications of doing so. The DDMAC director maintained that the pharmaceutical industry had a history of doing pharmacoeconomic studies without any scrutiny of their validity, that the FDA was well equipped to oversee the use of pharmacoeconomic claims, and that the risk in failing to ensure accuracy in pharmacoeconomics was an increase in healthcare costs and a deterioration of care.

The guidelines themselves state that pharmacoeconomic studies fall under the FDA's existing statutory authority and that the agency's approach is rooted in its general policy on the labeling and advertising of effectiveness claims. The guidelines stipulate that pharmacoeconomic claims should be compatible with existing rules prohibiting "false and misleading promotion" and must be "consistent with, and not contrary to, approved product labeling." All comparative claims would be required to provide "substantial evidence," typically demonstrated "by two adequate and well-controlled studies." Moreover, pharmacoeconomic studies would be required to produce "an adequate level of precision, scientific rigor, and validity (both internal and external) to support the resulting claims and take into account both the positive and negative effects of the drug."

A number of guideline statements delineate what constitutes a valid pharmacoeconomic study. For example, the guidelines state that studies must contain appropriate physical and monetary units and clearly state the perspective (for example, patient, payer, or societal) assumed in the study. Other statements note that computer and mathematical models will be acceptable only when well-controlled trials cannot be performed; intermediate health outcome...
“One must ask not whether any need exists to regulate pharmaco-economic claims but, rather, to what extent the need exists.”

comes and quality-of-life measurements can be used only with evidence of the scientific association; sources should be referenced; costs and discount rates should be explicitly cited; sensitivity analyses should always accompany studies; standards using overseas data must be applicable to the United States; and when quality-of-life information is presented, studies should show evidence of the validity of instrument and assume the patient’s perspective.

Finally, the draft guidelines stipulate that claims that advertise a product’s unconditional “superiority” must be based on studies that investigate all relevant comparators; otherwise, the claim must be appropriately qualified. Claims that promote “equivalence” must be grounded in controlled clinical trials that not only show no statistical difference but possess the statistical power to detect such a difference. Price comparisons must be from the same (and referenced) source and compare equivalent doses or dosage forms. Promotional advertising also should include disclosures that discuss underlying assumptions, a description of the outcomes, the specific comparator used, and the overall limitations of the study.

Objectives Of The Guidelines

- Theoretical framework: balancing risks. In assessing the FDA draft guidelines, one must ask not whether any need exists to regulate pharmaco-economic claims but, rather, to what extent the need exists. The FDA has a legal obligation to protect society from the adverse consequences of misleading promotional material. At the same time, it has a responsibility not to impinge on the free and fair exchange of information that may improve the public’s health. At times, these goals are not mutually compatible; the challenge is to identify a policy that strikes an appropriate balance.

  Regulations often are promulgated in the hope that they will reduce the frequency and costs of unfavorable outcomes. Historically, an unfavorable event in the context of drug regulation has meant the use of an unsafe or ineffective product. In the context of pharmaco-economic claims, an unfavorable event means the use of a cost-ineffective product. That is, in the absence of regulation, users of cost-effectiveness information might select an inferior medication than they otherwise might choose.

  Unfavorable events also may include intangible losses attributable to an undermining of confidence in the integrity of the entire
drug regulation system. This phenomenon is a form of “Gresham’s Law,” which holds that bad information eventually drives out (or drowns out) good information. Allowing poorly substantiated information onto the market could unleash a torrent of lower-quality pharmacoeconomic claims, thus making it ever more difficult for consumers to distinguish between hard scientific information and marketing excesses.

Although regulations may reduce the costs and risks of unfavorable events, they inevitably impose adherence costs, which are borne by a variety of stakeholders. The government pays the administrative costs of enforcement. Manufacturers incur both the direct costs of complying with rules and the indirect costs of doing business in a more strictly supervised environment. Most adherence costs are passed on to individuals, either in the form of higher taxes or higher prices, or in less tangible forms such as delays in the development and approval of potentially useful products. In the case of the draft guidelines on pharmacoeconomics, the indirect costs likely would take the form of less cost-effectiveness information being produced and disseminated to consumers, because manufacturers would find it more expensive to conduct analyses in the more heavily regulated environment.

Less stringent regulation imposes low costs of adherence but increases the risk (and costs) associated with unfavorable outcomes; in contrast, greater regulatory oversight raises the costs of enforcement and adherence but lowers the chances (and costs) of unfavorable events. The challenge for society is to find the level of regulation that balances the costs of adherence against the competing costs of unfavorable consequences.

Analysis of the guidelines. In practice, it is difficult to know precisely the optimal level of regulation. The FDA faces a great challenge in attempting to ascertain the truthfulness of pharmacoeconomic claims. However, a number of observations lead us to speculate that the draft guidelines may propose too much regulation, thus imposing unnecessarily high adherence costs with little improvement in the FDA’s ability to curtail unfavorable outcomes.

First, the guidelines stipulate in too much detail the content and nature of information that will be needed to support pharmacoeconomic claims. Although many of the specifications are grounded in standard, well-known methodologies of cost-effectiveness analysis, there are dangers in having the FDA prescribe them.

Of particular concern is the guidelines’ predisposition toward randomized controlled trials. This is understandable: Such trials have long been the gold standard by which the FDA judges the safety and efficacy of new drugs. Moreover, use of economic analyses
“Since a drug has already been certified as safe and effective, the major risk to a consumer is an economic one: paying too much.”

alongside clinical trials may produce more reliable estimates.\textsuperscript{15} However, imposing such a requirement on cost-effectiveness analysis likely will create a higher standard of evidence than what is needed. The likely result will be fewer cost-effectiveness analyses conducted and thus a stifling of potentially useful information.

Also, randomized controlled trials provide only a part of the picture. Trials typically do not capture a drug’s longer-term clinical and economic effects, for example. Indeed, many of the consequences of interest (for example, the impact of the therapy on future hospital or nursing home admissions) are not realized until long after the completion of the trial. Randomized controlled trials, conducted under highly supervised conditions involving carefully selected patients, are not always generalizable to other populations.

Decisions must be made in the face of this uncertainty. These decisions may be usefully informed by “modeling” exercises, whereby the effects of drugs are simulated based on various data sources and assumptions. In their current form the guidelines appear to treat modeling unfavorably, giving grudging acceptance to its use “only if well-controlled trials are not available.” Similarly, other information not available in trials—including summary checklists and consumer surveys—also may prove useful in informing purchasing decisions, even though they may not satisfy the requirements of the guidelines.

Second, cost-effectiveness should not be held to the same standard as safety and efficacy are, because there are fewer reasons to worry about the adverse consequences of using a cost-ineffective drug. The FDA’s intervention into the pharmaceutical marketplace in particular, its prohibition of new drugs from the market until the agency has formally approved them—is generally justified on the grounds of protecting consumers from potentially harmful products.\textsuperscript{16} The agency’s oversight of inaccurate or misleading advertising and labeling can be seen as an extension of this authority. The danger to consumers, however, is likely much smaller when it comes to economic information. Since a drug has already been certified as safe and effective by the FDA, the major risk to a consumer is an economic one: paying too much for the benefits conferred.

Moreover, the chances of making unwise choices have diminished in recent years. The draft guidelines adhere to the FDA’s historical tendency to insulate individual decisionmakers, namely physicians,
from the predations of manufacturers. FDA regulations in the area of
drug promotion have been based on the model of the sales call and
journal advertisements targeted at independent physicians. However,
pharmaceuticals are increasingly sold to, and evaluated by,
large and more sophisticated purchasers—hospital and managed
care pharmacy and therapeutics committees and pharmaceutical
benefit managers—who have the leverage and expertise to negotiate
with manufacturers and are better positioned to evaluate
pharmacoeconomic claims. In fact, this is precisely why the use of
pharmacoeconomics is rising.

Finally, overly prescriptive guidelines are likely to be costly for
the FDA to administer. Costs of care and prices paid for drugs can
vary widely among different payers and can change dramatically. The
comparative therapy in the pharmacoeconomic analysis often is
unknown or changes over time. There are no standards for defining
costs or the appropriate length of follow-up time. Existing instru-
ments for assessing quality of life or for valuing health benefits are
imprecise. Whether a product is cost-effective depends on the per-
spective of the user. Moreover, the FDA traditionally has not dem-
onstrated expertise in this area. The agency likely will have a diffi-
cult time discerning whether a claim is valid in any particular

All of this does not suggest that no evaluation is needed. Indeed,
testimony presented at the recent FDA hearing on pharmaceutical
marketing and information exchange in managed care environments
indicated that many consumers of pharmaceuticals—including rep-
resentatives of institutional purchasers—are genuinely confused
about much of the pharmacoeconomic information targeted at them
and believe that more rigorous and independent evaluation is re-
quired. The arguments do suggest, however, that having established
the foundation for comparative analysis and dialogue, and
while maintaining its vigilance over the general accuracy of claims,
the FDA should allow information to flow as freely as possible. They
also suggest, as staff members from the Federal Trade Commission
(FTC) have stated in formal comments submitted to the FDA, that
the FDA might consider a more flexible substantiation for economic
claims for pharmaceutical products—for instance, “one requiring
‘competent and reliable evidence’ to support the claim that is made,
without an a priori specification as to the type of evidence re-
quired.” Finally, the arguments suggest that the focus of the debate
should be on promoting informed and reasoned decision making by
improving information and the means to evaluate it.

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A Private Sector Model For Pharmacoeconomic Oversight

Curiously, much of the debate over pharmacoeconomics thus far has ignored the actual use of the information. Instead, the debate has focused on developing appropriate methodological standards and suitable protocols to ensure the independence of researchers.22

The FDA draft guidelines are part of this trend. The notion underlying them is that the establishment of more exacting rules will by themselves legitimize the field of pharmacoeconomics and lead to proper uses of the technique. Robert Evans has called the guidelines a procedural solution to a structural problem.23 But guidelines can accomplish only so much. Even with the most prescriptive instructions for pharmacoeconomic claims, the FDA still would function as a policing and enforcing authority, attempting to ensure that promotional materials were not misleading. It would not, however, evaluate the value of the cost-effectiveness claims themselves. But such an evaluation is precisely what buyers need.

We suggest that the private market is in a comparatively strong position to develop this ability. Managed care plans or pharmaceutical benefit managers have the knowledge, size of operation, and economic incentive to determine for themselves the validity of pharmacoeconomic claims. Alternatively, private organizations could emerge to evaluate pharmacoeconomic information and package it in a useful form for consumers. Even without regulation, market forces would dictate the appropriate format and content of the information. The sole criterion would be the usefulness of the information in assisting decisionmakers. The structural problem would be addressed, not by rules, but by the more rigorous test of the market, which would impose its own quality control discipline. This model works well for a number of other industries.

Parallels to other Industries. Products marketed in the United States come under varying levels of government regulation, reflecting the degree to which consumers are believed to be able to make informed decisions about the products. The government establishes and enforces standards for manufacturers and ensures that promotional claims are not false or misleading. But a host of private organizations evaluate the products for consumers. Consider two examples: the securities and consumer products markets.

Parallels between the market for financial securities and that for pharmaceuticals include complexity of products; disagreement, even among experts, about appropriate performance measures; informational asymmetries between sellers and buyers; large institutional purchasers (such as mutual funds and health maintenance
organizations [HMOs]); and an array of public and private mechanisms to ensure the fairness and efficiency of the markets. The Securities and Exchange Commission (SEC) serves as a policing and enforcement agency, ensuring that the securities markets operate smoothly and fairly. It also maintains minimal reporting standards; for example, it requires investment firms to tell consumers that their products are not insured by the federal government. With regard to promotional claims, the SEC guards against fraud and regulates the format and dissemination of a bond issuer's prospectus.

The SEC does not, however, evaluate the quality of the securities themselves. That function is left to the private sector, which has evolved an efficient means of producing information in a useful form for consumers. Firms such as Moody’s and Standard and Poor’s (S&P) evaluate and rate the financial instruments—essentially conducting an economic analysis—for investors. The private market also produces a host of other informational products, from journals and magazines to investment outlook sheets and financial newsletters. Publications vary in their content, format, and level of sophistication, but each of them also conducts a cost-effectiveness analysis of sorts. Investment houses themselves are free to undertake research and produce their information for individual clients, as long as they meet minimal SEC reporting requirements.

A similar situation exists for consumer products, although with different institutional arrangements. The government establishes and enforces minimal safety standards. For example, the National Highway Traffic Safety Administration mandates and enforces airbag and side-impact standards for new cars and requires that automobile stickers list the vehicles’ gas mileage and the percentage of U.S.-manufactured components. The Consumer Products Safety Commission promulgates regulations on such areas as flammability standards for children’s sleepwear and warning labels for step-ladders. And the FTC oversees truth-in-advertising laws.

Private organizations have emerged to evaluate the quality of the products themselves. Examples include Underwriters Laboratories (UL) and MET Electrical Testing Laboratories, which evaluate a wide array of consumer products and disseminate information. A broad range of private publications, from Consumer Reports and Motor Trend magazines to various newsletters and guides, evaluate and rate the cost-effectiveness of products.

**Independence of the evaluator.** The integrity of these markets stems from three assumed conditions: (1) the presence of informed buyers and sellers; (2) the free exchange of information; and (3) the existence of a government entity establishing minimal standards and enforcing truth-in-advertising laws. Notably, if these con-
ditions are satisfied, the source of funding for the evaluator becomes secondary. In several of the examples noted above, funding is provided by consumers themselves, an arrangement that helps to foster the evaluator's reputation as a trusted source of information. Consumers Union, for example, a nonprofit organization that derives its income primarily from the sale of Consumer Reports and other publications, does not accept advertisements for its magazine, nor does it allow its ratings to be used in manufacturers' promotions.

In some cases (such as UL and S&P), evaluators derive funding from the industry they evaluate but retain powerful incentives to be independent and objective. Manufacturers of consumer products fund UL, which tests more than 70,000 products each year, because both consumers and insurers perceive the UL label as a sign of quality and safety. In the case of S&P and Moody’s, which are funded largely by bond issuers, the integrity of evaluations is further ensured because they compete with one another for business.

**Can it work for the pharmaceutical industry?** The question for the pharmaceutical market is whether an analogous structure might be expected-or encouraged-to blossom. The rise of more sophisticated managed care purchasers provides cause for optimism. The existence of informed buyers is a critical condition for ensuring that evaluators are independent and objective.

Various types of private organizations might emerge to evaluate the information and package it in a useful form for consumers. They may be private, nonprofit publications funded by consumers of the information-for example, members of formulary committees. Using methods similar to those of Consumer Reports, they might evaluate pharmacoeconomic information on a checklist of important dimensions, such as the reliability of the data, the uncertainty surrounding estimates, and the validity of the quality-of-life instruments used.

Alternatively, one or more private organizations may emerge to rate the quality of the pharmacoeconomic analysis, or provide a stamp of approval on studies that have met certain criteria (perhaps using established criteria based on the recently completed work of the U.S. Panel on Cost-Effectiveness in Health and Medicine). For example, a single organization could be funded by drug companies whose products are evaluated. There might even be competing evaluators, which would help to safeguard the independence of the assessment. But the particular form of the arrangement would be dictated by market demands. Private evaluators would rise and fall on their ability to produce credible and useful information.

A reasonable question, then, is why such private evaluations do not already exist. One explanation is that uncertainty about FDA policy has hindered their development. A second, less charitable
one, is that pharmacoeconomic analyses have not proved to be useful tools for managed care plans. Part of the problem may be that purchasers may not yet have gained the expertise necessary to appreciate the value of the new analytic techniques. Another obstacle may be that existing cost-effectiveness analyses are not being conducted in the most useful form for consumers. For example, many studies are conducted from a societal perspective, even though managed care plans are concerned with their own perspectives.

A fledgling evaluation industry is developing. A number of new publications either publish cost-effectiveness analyses (for example, *PharmacoEconomics*), or summarize the results of published studies (for example, Outcomes Research Digest or Drug Outcomes and Managed Care). Others (such as *Medical Letter*) evaluate drugs and may include information on cost, although they do not conduct evaluations on the quality of existing analyses. Private organizations (such as the Blue Cross and Blue Shield Association and the American Medical Association) publish newsletters that review the clinical literature and rate the effectiveness of various drugs, devices, and procedures.

The pharmaceutical industry has begun promoting its own set of standards. The Pharmaceutical Research and Manufacturers of America (PhRMA) has developed its own set of methodological and conduct principles for pharmacoeconomic analyses. A separate task force, funded by a coalition of drug companies, has developed guidelines to govern the independence of researchers in the field. Furthermore, medical journals’ peer review process has played, and will continue to play, an important quality assurance role for pharmacoeconomic analyses. The process serves as an important filter and means of independent evaluation. In one survey, consumers of cost-effectiveness information reported that peer-reviewed journals were among their most important sources. Studies have demonstrated wide variety in the quality of economic evaluations published in peer-reviewed literature. As cost-effectiveness analyses become more widely disseminated, journals should raise their standards and develop their own quality assurance policies.

**Public/private mixed models.** Various public/private mixed models also might serve to improve the manner in which pharmacoeconomic studies are conducted and evaluated. First, the federal government (specifically, the Agency for Health Care Policy and Research [AHCPR] or the National Institutes of Health [NIH]) could fund more research in the field and disseminate the results to private-sector decisionmakers without imposing requirements. This is essentially the role undertaken by the U.S. Department of Health and Human Services (DHHS) in convening the Panel on Cost-Effectiveness in Health and Medicine, which met during 1994
and 1995 and has recently published its report. The panel was charged with “assessing the current state of the science of the field, and with providing recommendations for the conduct of studies in order to improve their quality and encourage their comparability.”

Other models also might apply. The FDA might impose disclosure requirements for all disseminated pharmacoeconomic information. It could require, for example, that all communications, including those in the context of managed care, disclose the source of the data, including whether any information on the comparative effectiveness of two drugs was obtained from a randomized controlled clinical trial. Manufacturers still would have to substantiate a “reasonable basis” to support the truth of their claims. The FDA would appeal to the substantial body of evidence on these grounds, examining factors such as the type of claim made, the nature of the product, and the consequences of making a false claim.

Alternatively, Congress might compel the certification of pharmacoeconomic claims by an accredited organization before companies can make such claims. The certification would create the legal presumption of a lawful claim. The FDA could regulate the certification industry but not the claims themselves. The process could involve competitive bidding among certifiers, which would generate new ideas about appropriate pharmacoeconomic standards and uses of the information. It could in some ways mirror the arrangement by which the Health Care Financing Administration (HCFA) grants “deemed status” to the private Joint Commission on Accreditation of Healthcare Organizations (JCAHO) to determine that hospitals meet certain standards, thus making them eligible to receive government program payments. Funding for certifiers could come from the FDA, or even from manufacturers themselves, as JCAHO funding is derived from hospitals.

These types of arrangements could offer a more efficient process for reviewing and approving pharmacoeconomic claims, thus allowing quicker and more widespread diffusion of cost-effectiveness information. Moreover, regardless of the model employed, other system safeguards would still exist. First, as Jack Calfee and others have stressed, pharmaceutical firms always maintain strong incentives to be truthful, since consumers (particularly recipients of business-to-business advertising and promotional claims) are always skeptical of manufacturers’ incentives, and because consumers who detect deception can choose not to purchase the product again. Second, manufacturers of competing products as well as consumers would retain the right to sue over misrepresentative advertising. Third, because of the FDA’s authority to approve
their new drugs and devices, manufacturers would retain a strong
incentive to preserve a positive relationship with the agency.\textsuperscript{35}

\textbf{An Example}

Consider the example of thrombolytic therapy for patients with
acute myocardial infarction. Recent years have witnessed much de-
bate about the comparative benefits of one particular agent, tissue
plasminogen activator (TPA), compared with its competitor, streptoki-
nase. One large international study funded by Genentech (the
manufacturer of TPA), released in spring 1993, reported that TPA
was associated with a small but statistically significant reduction in
mortality compared with streptokinase.\textsuperscript{36} Although the fact that ear-
lier studies had failed to demonstrate a clear benefit from using TPA
versus streptokinase, the market share for TPA reportedly rose from
50 percent to almost 70 percent on the basis of the news.\textsuperscript{37}

Upon release of the 1993 study findings, Genentech petitioned
the FDA to change its product labeling to expand the target popu-
lation for TPA and to include data on the drug's lifesaving benefits.
The FDA reviewed the request and, more than two years after the
results were first announced, approved the labeling changes.

Now consider the issue of cost-effectiveness. TPA costs more
than $2,200 per dose, compared with approximately $270 per dose
for streptokinase. One recent cost-effectiveness analysis reported
that patients who received TPA had $2,845 more in total medical
expenses, on average, compared with patients who used streptoki-
nase, but have a slightly higher life expectancy (15.41 versus 15.27
years).\textsuperscript{38} The incremental cost-effectiveness ratio of TPA compared
with streptokinase is $32,000 saved per life year, on average. The
ratio varies considerably across patient subgroups and is lower for
older than for younger patients and for anterior compared with
inferior infarction.

Now consider the use of this information for promotional pur-
poses. Suppose Genentech claimed that, based on the study, its
product was cost-effective. How could such a claim be evaluated?
Under the FDA draft guidelines, the agency presumably would scru-
tinize the claim and supporting evidence and determine whether
the various principles enumerated in the guidelines had been satis-
fied. Under the "pure" private-sector model, the pharmaceutical
company could make its cost-effectiveness claim, as long as it met
minimal FDA standards and did not violate truth-in-advertising
laws. Private evaluation firms would judge the merits of the claim.
Presumably, they would review the trial data and publish whatever
criticisms or praise of the studies they believed were warranted.
They might note, for example, that certain study assumptions were
questionable, or that the study did not fully consider quality-of-life factors, or that the populations might not be representative. They might question the overall design of the trial (for example, that it was not double-blinded) and the data-gathering technique. They might ask researchers for additional data. They might consider results from earlier trials and conduct a formal meta-analysis. Upon completion of its review, the private entity would publish its findings. Just as Moody's rates a bond, the evaluator might attach a rating or score to the pharmacoeconomic claim. Alternatively, it might provide a Consumer Reports-type checklist or simply give a stamp of approval that the claim was reasonable.

Under a private/public mixed model, other arrangements would apply. AHCPR might fund its own study of the question, or the FDA might require any firm using the information for promotional purposes to provide appropriate disclosures. On the other hand, Genentech might be required to acquire approval from an FDA-accredited certifying organization before making its claims. The manufacturer could submit in advance its proposed promotional materials and supporting data. The certifier would have a specific period of time in which to state whether the claims were reasonable.

Ultimately, whether consumers are willing to pay $2,000 more to reduce their risk of mortality by 1 percent in the event of a heart attack is an open question that only individuals and those who act on their behalf can answer. In fact, there is some evidence that opinions are split on this issue. But private-sector evaluation promises a more efficient and effective process. In time, such evaluations may become commonplace. Just as investors would not buy bonds without a private bond rating, managed care plans might not accept pharmacoeconomic claims without a similar review.

**Summary And Conclusions**

Heretofore, economic information has never been considered explicitly by the FDA. But the growing use of pharmacoeconomics by drug manufacturers and the FDA's far-reaching mandate to oversee advertising and labeling have forced the agency to appraise economic information formally. Although the FDA has an obligation to protect society from misleading promotional material, it also has a responsibility not to impede the flow of potentially useful information. There is a need for caution and flexibility on the part of the agency. As is often the case, the right question is not whether regulations are necessary, but what level is reasonable.

FDA policy should recognize the usefulness of cost-effectiveness information—in a variety of forms—helping decisionmakers to make clinical and resource allocation choices. Since decisions will
(and must) be made, it makes sense to avail ourselves of as much information as possible, however imperfect. There are compelling reasons to believe that information about the cost-effectiveness of new pharmaceuticals should not be held to the same standards of evidence as are the safety and efficacy of pharmaceuticals. But there is also a need for more rigorous analysis. This might come from independent, private-sector evaluators who respond to market demands for prompt and reliable information.

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NOTES
7. Ibid.
11. Ibid.


17. Kuhlik, “The FDA’s Regulation of Pharmaceutical Communications.”


20. J. Lax and E. Moench, “Pharmacoeconomics and Managed Care: Understanding the Issues, Concerns, and the Environment,” and W. Zellmer, “Comments of the American Society of Health-System Pharmacists” (Presentations at the FDA public hearing, “Pharmaceutical Marketing and Information Exchange in Managed Care Environments,” Silver Spring, Maryland, 19 October 1995). In the survey of health system pharmacists by William Zellmer and colleagues, for example, only 60 percent of respondents believed that their managed care organization was “well equipped to critically analyze the comparative pharmacoeconomic claims of drug manufacturers,” and only 18 percent believed that “comparative pharmacoeconomic claims made by drug manufacturers generally meet high standards for reliability.”


23. Evans, “Manufacturing Consensus, Marketing Truth.”

24. Gold et al., Cost-Effectiveness in Health and Medicine.


32. A similar suggestion was made by Bryan Luce in testimony at the FDA hearing, “Pharmaceutical Marketing and Information Exchange.”


40. Siegel and Roberts, “Reforming FDA Policy.”