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Pharmaceutical R&D and the Evolving Market for Prescription Drugs

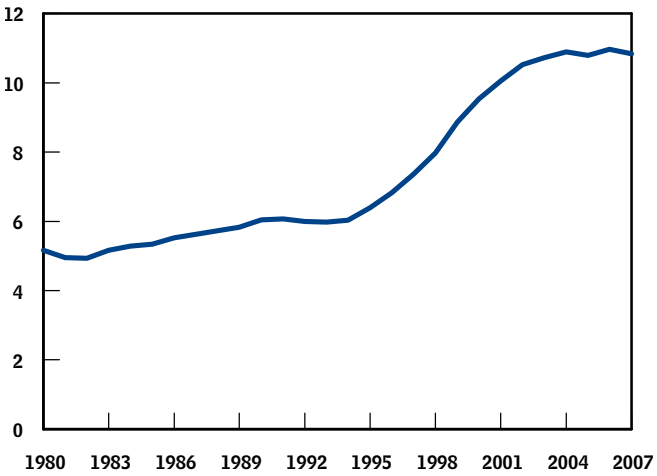
Investment in research and development (R&D) over the past several decades has produced a wealth of valuable new drug therapies that have made it possible to treat major illnesses that were not treated previously or were not treated as effectively. As the scope of available drug therapies expanded, spending on prescription drugs became the fastest-growing category of total spending on health care in the United States. Between 1994 and 2004, real (inflation-adjusted) spending on prescription drugs rose at an average annual rate of 11.1 percent, compared with 3.5 percent for hospital care and 4.3 percent for physicians' services. More recently, however, that growth has slowed: From 2004 to 2007, drug expenditures grew by an average of just 3.2 percent per year, slightly less than the rate of growth in overall health care spending. As a fraction of total spending on health care, spending on prescription drugs rose from 6 percent in 1994 to around 11 percent in 2004, where it has remained (see Figure 1).

That slowdown in the rate of growth in spending reflects changes in both the supply of and the demand for prescription drugs. On the supply side, the patents for many top-selling drugs have expired, subjecting them to competition from cheaper generic compounds. The resulting decline in spending on those drugs has not been fully offset by added spending on new brand-name drugs because, at the same time, the rate at which new drugs are being introduced has slowed substantially. On the demand side, many health plans have sought to control the growth in their expenditures by creating stronger incentives for their enrollees to choose generic drugs or cheaper brand-name drugs.

Decisions regarding pharmaceutical R&D depend largely on drug manufacturers' expectations about future revenues. Expectations about revenues are shaped by the conditions affecting the potential demand for each drug, such as the size of its market, its price, and the amount of competition expected from other drugs. The greater the expected revenue from a prospective new drug, the more willing a drugmaker will be to invest to develop it. Those decisions will help determine which drug therapies become available in the future and thus will affect future growth in health care costs. This brief describes the current state of investment in drug R&D and the factors that influence it. It also examines how various policy options to control the growth in health care costs or to expand insurance coverage could affect R&D spending.

Figure 1.

Spending on Prescription Drugs as a Percentage of Total Spending on Health Services and Supplies, 1980 to 2007

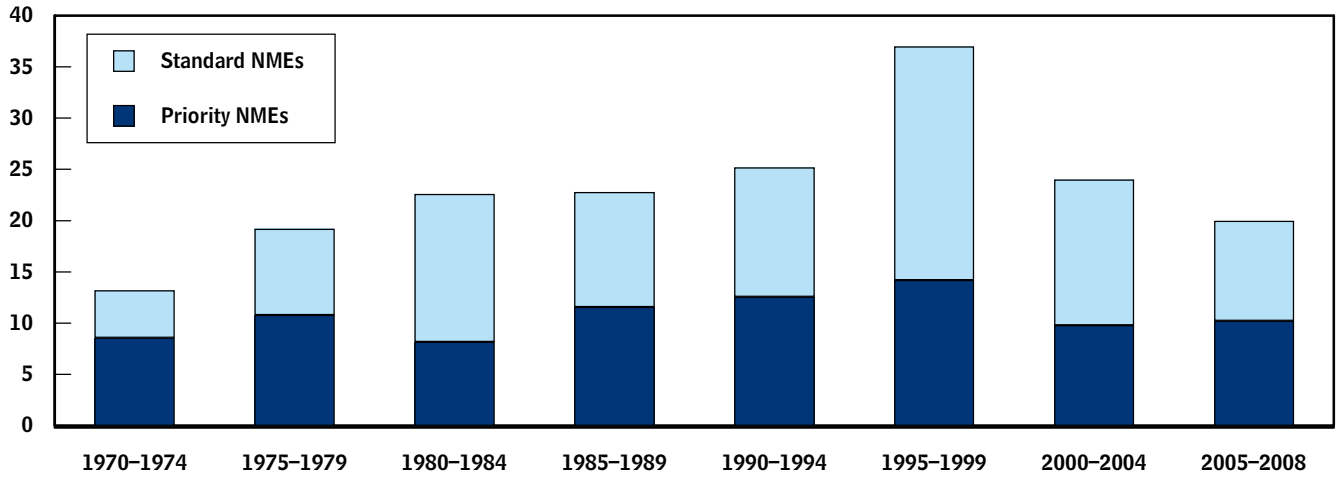


Source: Congressional Budget Office based on data on spending for health services and supplies, as defined in the national health expenditure accounts, maintained by the Centers for Medicare and Medicaid Services.

Figure 2.

Average Annual Approvals of New Drugs by the Food and Drug Administration, 1970 to 2008

(Number)



Source: Congressional Budget Office based on data from the Food and Drug Administration.

Notes: The data, which are for new molecular entities (NMEs) only, exclude extensions and new approved uses of existing drugs. New molecular entities are drugs based on a molecule not used before in any pharmaceutical product. Priority drugs are those that, according to the Food and Drug Administration, provide a "significant therapeutic or public health advance."

Beginning in 2004, approvals include those for biologics (large-molecule drugs such as monoclonal antibodies, growth factors, and recombinant proteins). The Food and Drug Administration approved five such drugs in 2004 (four given priority status); two in 2005 (both priority drugs); four in 2006 (all priority drugs); two in 2007 (one priority drug); and three in 2008 (two priority drugs). See www.fda.gov/cder/rdmt/default.htm.

The Rate of New-Drug Development

The rising-then-slowing pattern of growth in prescription drug spending (shown in Figure 1) is related to the evolving pace of new-drug introductions and patent expirations over the past two decades. Many of the new drugs introduced in the 1990s enabled physicians to treat previously untreated or undertreated conditions, and growth in spending on prescription drugs naturally accelerated. Drug introductions spiked in the mid- to late 1990s but have declined since 2000—in most years, back to levels not seen since the 1980s. The introduction of priority drugs—drugs that, according to the Food and Drug Administration (FDA), provide a "significant therapeutic or public health advance"—has also slowed, from an average of more than 13 a year in the 1990s to about 10 a year in the 2000s (see Figure 2).

With the decline in priority-drug approvals, a key source of rising drug expenditures—a rise in the number of top-selling drugs—has subsided. Between 1996 and 2006, the number of drugs with annual sales of $1 billion or more (in 2000 dollars) increased from 6 to more than 50, and the share of industry revenues produced by those "blockbuster" drugs rose from around 12 percent to nearly 50 percent. Since then, patent expirations and the arrival of competition from generic drugs have apparently reduced the revenue from brand-name drugs more quickly than it is being replaced by revenue from the introduction of new drugs. The number of drugs reaching $1 billion in annual sales, for example, has started to decline.[1] For the pharmaceutical industry as a whole, slower revenue growth could continue until sales of new drugs once again outpace revenue losses from expiring patents.

1. Data on the number and revenue share of drugs with billion-dollar sales are from Murray Aitken, Ernst R. Berndt, and David M. Cutler, "Prescription Drug Spending Trends in the United States: Looking Beyond the Turning Point," *Health Affairs*, Web Exclusive (December 16, 2008), pp. W151–W160.

Table 1.

Changes in Components of Demand for Prescription Drugs, Selected Years, 2000 to 2008

Year	Prescriptions Filled[a] (Billions)	Market Share of Generic Drugs (Percent)	Real Expenditures[b] Average per Prescription[c] (Dollars)	Real Expenditures[b] Total (Billions of dollars)	Real Expenditures[b] Average Annual Increase in Total (Percent)
2000	2.9	42	56	178	n.a.
2002	3.1	42	65	215	10.4
2004	3.3	48	70	246	7.2
2006	3.4	53	70	263	3.5
2008	3.5	58 [d]	72	265 [d]	0.8

Source: Congressional Budget Office based on data from U.S. Census Bureau, www.census.gov/prod/2008pubs/09statab/health.pdf; and National Association of Chain Drug Stores (2008 data are from www.nacds.org/pdfs/Pharmacy/2008CommunityPharmacyResults.pdf).

a. Includes chain drug stores, independents, mass merchants, supermarkets, and mail-order pharmacies; excludes in-patient prescriptions.

b. Adjusted for inflation using the gross domestic product implicit price deflator.

c. Excludes mail order.

d. Value for 2007.

Slower revenue growth for drugmakers does not mean that consumers are using fewer prescription drugs. In fact, the number of prescriptions continues to increase, albeit more slowly since 2004 (see Table 1). But generic drugs, which cost less than their brand-name counterparts, now comprise a greater share of prescriptions, having increased from 42 percent in 2000 to 58 percent in 2007.

Investment in R&D

According to Pharmaceutical Research and Manufacturers of America (PhRMA), the industry's trade association, member firms spent $50 billion on pharmaceutical R&D in 2008, a 2.6 percent real increase over the amount the previous year (see Figure 3).[2] That increase is unusually small; over the past 30 years, PhRMA has seldom reported less than a 5 percent real annual increase in R&D spending, and the average has been almost 9 percent. Because global drug R&D spending is not estimated consistently over time, it is difficult to know exactly how it has changed. However, PhRMA's estimates account for a majority of that spending.

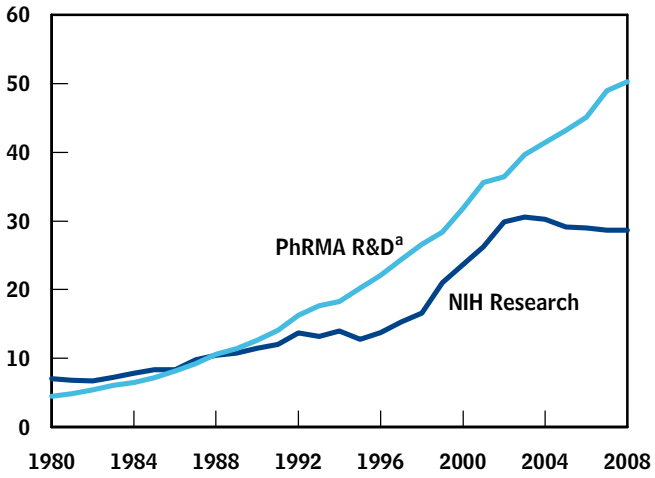
Pharmaceutical R&D in the private sector is complemented by health-related research funded by the public sector—most of it through the National Institutes of Health (NIH). Much of that funding is for basic research on the mechanisms of disease, which ultimately supports the discovery of new drug therapies. Public funding has tended to grow more slowly than private drug R&D except from 1998 to 2004, when NIH's research funding doubled in real terms (see Figure 3). It subsequently declined by 6 percent over the next four years. However, including the one-time increase of $10.4 billion in stimulus funding provided by the American Recovery and Reinvestment Act of 2009 (ARRA, Public Law 111-5), which remains available through September 2010, real growth in NIH's research funding will nearly equal that in private R&D over the 1998–2010 period.

2. See Pharmaceutical Research and Manufacturers of America, *Pharmaceutical Industry Profile 2009* (Washington, D.C.: PhRMA, April 2009), Table 1, p. 50; Table 2, p. 51; Figure 9, p. 32. About three-quarters of total R&D spending consists of all spending by U.S.-owned companies and U.S. spending by foreign-owned companies; the remaining one-fourth reflects overseas R&D spending by U.S. subsidiaries of foreign-owned firms. The total excludes non-U.S. R&D spending by non-U.S. companies. (In addition, other pharmaceutical firms based in the United States but not belonging to PhRMA spent $15 billion.)

Figure 3.

Annual Spending on R&D by Drug Companies and on Research by the National Institutes of Health, 1980 to 2008

(Billions of 2008 dollars)



Source: Congressional Budget Office based on data from Pharmaceutical Research and Manufacturers of America, *Pharmaceutical Industry Profile 2009* (Washington, D.C.: PhRMA, April 2009); and National Science Foundation, *Federal Funds for Research and Development* (various years), www.nsf.gov/statistics/fedfunds. Data from PhRMA members are self-reported.

Notes: Spending amounts are adjusted for inflation using the gross domestic product implicit price deflator.

PhRMA = Pharmaceutical Research and Manufacturers of America; NIH = National Institutes of Health.

a. About three-quarters of total spending on research and development (R&D) consists of spending by U.S.-owned companies and U.S. spending by foreign-owned companies; the remaining one-fourth reflects overseas spending on R&D by U.S. subsidiaries of foreign-owned firms. The total excludes non-U.S. R&D spending by non-U.S. companies.

Analysts have found that increased public spending on basic (health-related) research stimulates additional private drug R&D.[3] Conversely, slower growth in public R&D spending could mean fewer new opportunities for drug development. Basic research can also help reduce the costs of R&D. For example, advances in biomedical science could provide ways to identify potential failure earlier in the development process, reducing the amount spent on failed drugs. In pharmaceutical research, the time and resources spent on drugs that ultimately fail in clinical trials account for a substantial fraction of total R&D spending.

Companies' R&D expenditures depend on the number of projects, their duration, the probability of failure, and financing costs. Scientific advances can reduce R&D costs for particular kinds of drugs but can also open up new areas of drug development that may be costly to pursue. R&D financing costs can be affected by revenue growth. Established drug companies—those with a variety of drug products on the market—can finance R&D using revenues from sales of existing drugs. If faced with slower revenue growth, however, some firms might turn to outside investors, who—because they know less about the firm's research progress and odds of success—would generally demand a higher return to compensate for that uncertainty, slightly raising R&D costs.

Real R&D spending per successful new drug has been rising for many years, largely because of growth in the size and length of clinical trials and an increased rate of failure. Those changes generally reflect drug companies' strategic choices about which kinds of drugs to pursue—choices that depend on anticipated demand and scientific opportunities. In particular, drug companies are devoting more resources to developing drugs for chronic illnesses.[4] In many cases, those drugs require prolonged use, so longer clinical trials are necessary.

Development times vary by type of drug but have been averaging about 12 years from discovery through clinical trials to approval by the FDA. Although private drug companies have been pursuing increasingly costly R&D projects, they would not do so if they did not expect to recoup their investment through sales of the resulting drug products.

3. Michael R. Ward and David Dranove, "The Vertical Chain of Research and Development in the Pharmaceutical Industry," *Economic Inquiry,* vol. 33, no. 1 (January 1995), pp. 70–87.

4. Joseph A. DiMasi, Ronald W. Hansen, and Henry G. Grabowski, "The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics,* vol. 22, no. 2 (March 2003), p. 181.

The Role of Health Insurance in the Demand for Prescription Drugs and Drug R&D

The scope of health insurance coverage of prescription drugs has been expanding for many years. From 1997 to 2007, the share of consumers' total drug expenses paid for by third parties (private health insurance plans and public programs) rose from 67 percent to 79 percent.[5] At least partly as a consequence, the number of prescriptions filled has risen substantially, increasing by 72 percent over the same period.[6]

Insurance plays a significant role in determining the demand for prescription drugs and, ultimately, drug R&D. By shielding individuals from the full costs of the drugs they use, insurance encourages higher spending on drugs. For example, spending can increase when insured individuals fill prescriptions that they would have forgone if they lacked insurance or when those individuals choose a more expensive drug than they would have if they faced the full cost.

Insurance plans have sought to control the growth in their drug expenditures by adjusting the cost-sharing provisions in their policies to encourage beneficiaries to make cost-effective choices. A typical policy now provides generic drugs to beneficiaries in exchange for a relatively small copayment but requires somewhat higher copayments for "preferred" brand-name drugs and still higher copayments for "nonpreferred" brand-name drugs. Some brand-name drugs may be placed in the preferred tier because of their unique therapeutic benefits; others are put in that tier because the manufacturer has offered the insurance plan a price concession. Copayments for brand-name drugs in the preferred and nonpreferred tiers have been rising more quickly than have those for generic drugs (see Figure 4), strengthening incentives to choose generics.

The creation of the Medicare Part D drug benefit in 2006 is a prominent example of how an expansion in coverage affects the demand for prescription drugs and alters incentives to undertake drug R&D. With Part D in place, the fraction of U.S. seniors who have drug coverage increased from about three-quarters before the program began to around 90 percent in early 2009, a gain of around 8 million covered individuals.[7] That coverage expansion almost certainly contributed to the growth in the number of prescriptions in recent years, although health plans participating in Part D often give their enrollees incentives to make cost-effective drug choices.

Some tentative evidence suggests that, as a result of demographic shifts and increased demand from Medicare beneficiaries, drugmakers are devoting more R&D resources to developing drugs for conditions related to aging.[8] That finding is consistent with the more general results from a number of studies showing that spending on drug R&D is responsive to changes in demand: On average, R&D spending has been found to go up by an average of about 1 percent for every increase of 1 percent in potential sales.[9] The fraction of the population that is older than 65 is projected to rise from about 13 percent to about 20 percent during the next 20 years.[10] That demographic change, combined with the greater demand for drugs resulting from Part D, will continue to influence private R&D investment for some time.

Policy Options and Their Implications for R&D

The federal government finances a large and growing share of prescription drug sales—roughly 29 percent in 2007 compared with less than 15 percent five years

5. Congressional Budget Office calculation based on data on spending on prescription drugs, as defined in the national health expenditure accounts, maintained by the Centers for Medicare and Medicaid Services.

6. Kaiser Family Foundation, *Prescription Drug Trends* (September 2008), p. 2.

7. For pre-Part D coverage, see Congressional Budget Office, *Issues in Designing a Prescription Drug Benefit for Medicare* (October 2002), and Dana Gelb Safran and others, "Prescription Drug Coverage and Seniors: Findings from a 2003 National Survey," *Health Affairs*, Web Exclusive (April 19, 2005), pp. W5–W160. For coverage under Part D, see Kaiser Family Foundation, *The Medicare Prescription Drug Benefit* (March 2009).

8. See Margaret E. Blume-Kohout and Neerag Sood, *The Impact of Medicare Part D on Pharmaceutical Research and Development*, Working Paper 13857 (Cambridge, Mass.: National Bureau of Economic Research, 2009).

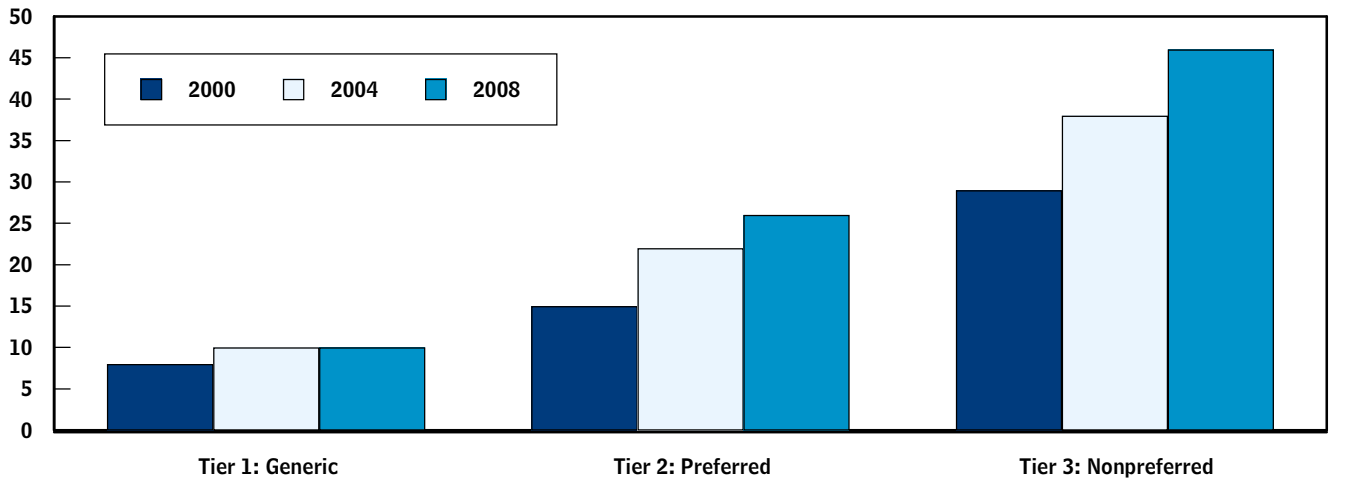
9. See, for example, F.M. Scherer, "Price Controls and Global Pharmaceutical Progress," *Health Affairs*, vol. 28, no. 1 (2009), pp. W161–W164.

10. Wan He and others, *65+ in the United States: 2005*, Current Population Reports, Series P23-209 (U.S. Census Bureau, December 2005), Figure 2-6, p. 12, www.census.gov/prod/2006pubs/p23-209.pdf.

Figure 4.

Average Copayment for a Prescription Drug, by Tier, Selected Years, 2000 to 2008

(Dollars)



Source: Congressional Budget Office based on data from Kaiser Family Foundation and Health Research and Educational Trust, *Employer Health Benefits: 2009 Annual Survey* (Washington, D.C.: Kaiser/HRET, 2009), Exhibit 9.4.

Note: Tier 1 (generic) drugs are copies of brand-name drugs whose patents have expired and that therefore may be produced and distributed by multiple drug companies. Tier 2 (preferred) drugs are brand-name drugs that typically are still protected by patents and therefore have no generic substitute. Tier 3 (nonpreferred) drugs are brand-name drugs that typically have a generic substitute.

earlier—and it faces severe long-term budgetary pressures, with rising health care costs playing a key role. A number of policy options for reducing those costs or for expanding insurance coverage would affect the market for prescription drugs. This section presents a sampling of such options—some of them detailed in the Congressional Budget Office's December 2008 report *Budget Options, Volume 1: Health Care*. All of them have potential implications for the revenues that drug companies would expect to earn from new products and, therefore, for the incentives to invest in drug R&D. In general, policies that would lower expectations about revenues would discourage R&D investment, and those that would raise expectations would stimulate R&D. For some policies, the effects on expected revenues would vary by product or therapeutic area; total R&D investment might not be affected, but patterns of R&D resource allocations could be.

Expand Prescription Drug Coverage

The Congress is considering proposals that would increase the fraction of the population covered by health insurance. Depending on the breadth of the expansion and the provisions for drug coverage, such proposals would probably increase the quantity of prescription drugs purchased in the United States. A simple expansion in health insurance coverage—for example, broader eligibility criteria for Medicaid—would increase drugmakers' current and expected future revenues, making investing in R&D more attractive for drug companies. However, the impact of a major health care reform proposal on incentives to undertake R&D would depend not just on the number of newly covered individuals but also on other factors such as changes in payment policy.

Expand the Medicaid Rebate Paid by Manufacturers of Brand-Name Drugs

In the fee-for-service part of Medicaid, drugmakers pay a rebate to Medicaid for each drug that the program purchases on behalf of its beneficiaries. For brand-name drugs, that rebate has two components. The first part, known as the basic rebate, equals 15.1 percent of a drug's average manufacturer price (AMP—the price that the drugmaker receives from sales to retail and mail-order pharmacies) or, if it is greater, the difference between the AMP and the lowest transaction price (the "best price" that the drugmaker receives from sales to certain private buyers). The second part, the additional rebate, equals

the difference between a drug's current AMP and the AMP at the time it was originally marketed, adjusted for inflation using the consumer price index for urban consumers (CPI-U). (Drugmakers owe no additional rebate if growth in a drug's AMP does not exceed growth in the CPI-U.)

The President's 2010 budget proposes changes to both components of the rebate for brand-name drugs. For the basic rebate, the President's budget would raise the flat rebate percentage from 15.1 percent to 22.1 percent, yielding savings for the federal government and state governments.[11] A potential drawback is that drugmakers, faced with reduced revenues from Medicaid, might invest somewhat less to develop drugs whose sales would be concentrated in the Medicaid program.

The President's 2010 budget also includes a proposal to alter the additional rebate by treating many future modifications of existing drugs more like the original product in calculating rebate obligations. Under current law, a drugmaker can avoid the additional rebate by slightly modifying an existing product; doing so establishes a new AMP that can exceed the inflation-adjusted AMP of the old product without triggering an additional rebate. The proposed change would lead to savings for the federal and state governments because rebates would increase. That policy would make it somewhat less attractive for drugmakers to improve existing drugs, although if the clinical benefits of those improvements were sufficiently great, manufacturers would still find it worthwhile to develop them because of the higher prices they could command outside the Medicaid market.

Require Drugmakers to Pay a Minimum Rebate on Drugs Covered by Medicare Part D

Some proposals would require manufacturers of brand-name drugs to pay the federal government a rebate equal to 15 percent of the price they receive from sales of drugs for Part D beneficiaries to retail and mail-order pharmacies, plus an additional rebate if a drug's price grows faster than inflation. Such a policy would reduce, by the amount of those rebates, the manufacturers' expected revenues from sales for Medicare beneficiaries. That, in turn, would reduce manufacturers' incentives to invest in R&D on products that would be expected to have significant Medicare sales.

Increase the Availability and Use of Follow-On Biologic Drug Products

Biologics—drug products derived from living organisms—constitute a small but growing share of health care spending. Some biologics face competition from other brand-name drugs that have similar therapeutic effects. For example, several competing brand-name biologics are used to treat rheumatoid arthritis. To date, however, brand-name biologics face no competition from follow-on imitators in the way that conventional brand-name drugs do (from generic compounds) when their patents expire. The absence of such competition makes it more difficult for private health plans to negotiate discounts for biologics.

The Congress is considering proposals that would establish an abbreviated regulatory pathway for approving follow-on biologics under the Public Health Service Act. (Such proposals aim to create a streamlined process analogous to the one for generic drugs under the Federal Food, Drug, and Cosmetic Act.) Also, the Medicare Payment Advisory Commission (MedPAC) has recommended changes to Medicare's payment incentives that would encourage the use of follow-on biologics as they become available.

The overall impact of such policy changes on R&D is difficult to predict. An abbreviated regulatory pathway and stronger incentives for doctors or patients to choose follow-on biologics would encourage investment in the development of those imitative products and reduce the expected returns to R&D from original, pioneering biologics. However, there would probably be fewer manufacturers of imitative biologics than there are of conventional generics because biologics are far more complex and more costly to develop than are conventional drugs. So the reduction in the returns to R&D from pioneering biologics—and therefore in the incentives to undertake that R&D—might not be great.

11. CBO previously analyzed a similar policy option, specifically, raising the basic rebate percentage from 15.1 percent to 23.1 percent while maintaining the best-price provision. That option would reduce the federal deficit by $7.2 billion over the 2010–2019 period. See Option 74 in Congressional Budget Office, *Budget Options, Volume 1: Health Care* (December 2008). For background on rebates, see Congressional Budget Office, "The Rebate Medicaid Receives on Brand-Name Prescription Drugs," letter to the Honorable Charles E. Grassley (June 21, 2005).

Incorporate Findings on Comparative Effectiveness into Decisions About Insurance Coverage

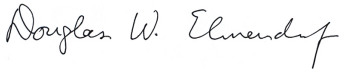
The Congress recently expanded government support for research on the comparative effectiveness of various medical treatments for patients with particular conditions.[12] Many medical experts suggest that creating more data on comparative effectiveness and providing appropriate financial incentives to encourage the use of those data could allow payers to slow the growth in health care costs and also improve the quality of care. If payers could do that, drug companies might invest less in the development of so-called me-too drugs—new products with effects similar to those of an existing class of drug—because they would anticipate earning less revenue from such products if a comparative effectiveness (CE) study showed that they were no better than existing drugs. Drug manufacturers' incentives to develop highly innovative, breakthrough products would not necessarily decline, however.

The effects of CE data on pharmaceutical revenues are difficult to predict because it is not possible to know beforehand what a CE study would find. (Nor is it possible to know exactly which therapies would be studied.) So it is not clear what effects increased support for CE studies would have on pharmaceutical R&D. Some CE studies might find that a newer, costlier brand-name drug confers few or no added benefits compared with those from cheaper compounds. If payers responded by discouraging the use of that drug, or if they limited its use to a restricted set of patients for whom substantial clinical benefits could be demonstrated, the revenues from that drug would be lower. Other CE studies might find that a particular drug confers benefits comparable with or superior to those from a costly medical procedure. Such a finding would lead to more widespread use of that drug and to higher revenues for its manufacturer.

Health plans could use findings from CE studies to negotiate more effectively with drug manufacturers over a drug's price and its placement within the plans' drug formularies. However, such studies can be costly: Because differences between drugs are likely to be narrower than those between a drug and a placebo, CE studies can—for statistical reasons—require larger, more costly clinical trials. Establishing criteria for deciding which treatments to compare could help ensure that resources are expended cost-effectively on CE studies, and public-sector sponsorship of those studies could contribute to greater objectivity in their findings.

12. For a discussion of research on comparative effectiveness and its possible effects on future health care spending, see Congressional Budget Office, *Research on the Comparative Effectiveness of Medical Treatments: Issues and Options for an Expanded Federal Role* (December 2007).

David Austin and Colin Baker prepared this brief. It and other CBO publications are available at the agency's Web site (www.cbo.gov).



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