MARKETWATCH

Estimating The Cost Of New Drug Development: Is It Really $802 Million?

Variations in cost estimates suggest that policymakers should not use a single number to characterize drug costs.

by Christopher P. Adams and Van V. Brantner

ABSTRACT: This paper replicates the drug development cost estimates of Joseph DiMasi and colleagues ("The Price of Innovation"), using their published cost estimates along with information on success rates and durations from a publicly available data set. For drugs entering human clinical trials for the first time between 1989 and 2002, the paper estimated the cost per new drug to be $868 million. However, our estimates vary from around $500 million to more than $2,000 million, depending on the therapy or the developing firm. [*Health Affairs* 25, no. 2 (2006): 420–428; 10.1377/hlthaff.25.2.420]

THE EXPECTED COST of developing an average drug was recently estimated by Joseph DiMasi and colleagues at $802 million per new molecular entity (in 2000 dollars).[1] The enormous cost of drug development is a key component of the current debates over prescription drug prices, importation of drugs from Canada, Food and Drug Administration (FDA) review policies, and barriers to generic entry. Given the central role of the $802 million estimate in these debates, it is important to ask two questions. First, is this number an accurate estimate of the expected cost of developing an average drug? Second, even if it is accurate, what does the estimate mean?

This paper independently verifies DiMasi and colleagues' estimate, in "The Price of Innovation" (hereafter, DHG), using a publicly available data set on drug development. Our analysis also raises several issues that must be accounted for in interpreting the $802 million as a meaningful measure of actual drug development costs: the meaning of "average drug," the impact of firms' strategic decisions, and regulatory policies' effects on development costs.

Study Methods

■ **DHG methodology.** DiMasi and colleagues took three steps to reach their $802 million estimate. First, they randomly selected sixty-eight drugs from the proprietary Tufts Center for the Study of Drug Development (CSDD) database of investigational compounds for ten multinational pharmaceutical firms participating in a confidential survey. These survey data provide the average cost of taking a drug through each step of the drug development process. This is the actual money that the drug companies spent on the process.

Second, they used the CSDD database to calculate the probability that the average drug will get to each phase. By multiplying the estimated average amount spent in each phase by the probability of getting to the phase, they calculated the expected cost of developing a

Christopher Adams (cadams@ftc.gov) is an economist and Van Brantner is a research analyst at the Bureau of Economics, Federal Trade Commission, in Washington, D.C.

drug for market. The authors then used the CSDD database to estimate the probability that a drug in Phase I would be approved and used this number to calculate the expected cost per approved drug.

Third, the authors used the CSDD database to estimate the average duration for each stage in the drug development process. These durations were then used to estimate the time cost or opportunity cost of developing a drug.

■ **Our methodology.** We estimated the expected cost of developing an approved drug in the same way. However, instead of using estimates from the proprietary CSDD database, we used estimates from the publicly available Pharmaprojects database. This allows others to verify our results. An important concern is that the data are likely to be less accurate than the survey data used to compile the CSDD database. The Pharmaprojects data are collected by the vendor (PJB Publications) based on press releases, academic presentations, and other public information about drugs in development. Because of this collection process, the data do not always include information on drugs in the earlier stages of human clinical trials. Although we have some concern about accuracy, we have no reason to believe that the data are biased.

To estimate the cost of developing drugs with different characteristics, we assumed that the average actual cost is the same across different drug characteristics. That is to say, the estimated variation in costs across drugs with different characteristics is attributable to differences in the estimated probability of success and in the estimated duration. It is important to also be aware that different drug types might have substantially different actual costs of clinical trials. Therefore, the estimated variation in drug costs could be higher or lower, depending on whether the correlation between actual costs, success probabilities, and durations is positive or negative. As discussed below, recent work suggests that HIV/AIDS drugs have high clinical costs, which may offset cost reductions reported in this paper.[2]

There is some controversy over how DiMasi and colleagues calculated their cost numbers, including the use of before-tax income and different discount rates. (See the authors' discussion of the issues and the references therein for more detail.) For this paper, we followed the DHG calculations.

Study Data

The data used in our study contain information updated monthly on drugs in a late stage of development, covering 1989 to the present, and include drugs now in development and those that have been discontinued or withdrawn from the process.[3] The recorded information includes the drug's current status, the original materials, the primary therapy, the primary indication and other indications, route of administration, and the name of the developing firm. It also includes major event dates in the life of the drug, such as entry dates in each of the phases, as well as exit and registration dates, when applicable. For this study, we limited our attention to all drugs that went into human clinical trials for the first time between 1989 and 2002 and for which we have an entry date and at least one additional piece of information after entry.

■ **Concern about dates.** There is some concern about the dates available from the Pharmaprojects database. In particular, the date is often only accurate to a particular month. We have discussed these issues with the vendor, and we are confident that every effort has been made to publish accurate dates. We know of no evidence that suggests that these dates are systematically misreported. In fact, we have found that statistics based on this database are consistent with other publicly reported statistics from other databases.

■ **CSDD versus Pharmaprojects.** Although both the CSDD and Pharmaprojects databases purport to include detailed information about each drug's development milestones, there are important differences.[4] The drugs used in the DHG analysis are all new molecular entities (NMEs). To obtain a sample of drugs that is closer to that used in the DHG analysis, we dropped drugs that were indicated in the database as being new formulations of previously approved drugs. The CSDD

sample is limited to self-originated drugs; unfortunately, the information in Pharmaprojects is not detailed enough to make the same restriction. The drugs used in the DHG analysis are drugs that first entered human clinical trials somewhere in the world after 1983. Again, unfortunately, the information in Pharmaprojects does not allow us to select on this criterion. The data set we used includes drugs that first entered one of the phases of human clinical development somewhere in the world after 1989—the first year for which Pharmaprojects provides detailed and easily accessible information on drug histories. The data selected for the DHG study were all first tested in humans prior to 1994. Because of the limitations of our data, we included drugs that entered any one of the three stages by 2002.

Using these criteria, our data set is much larger than the one selected from the CSDD data. Our sample includes information on 3,181 compounds, while the DHG sample has information on 538 compounds. It is not clear to us exactly which of these differences accounts for the discrepancy in sample sizes. Despite these apparent differences, the results presented here show that the two data sets provide a similar picture of success rates and durations for the average drug.

Replicating The DHG Results

■ **Development costs.** Success rates calculated from the two data sets give somewhat similar results (Exhibit 1). Note that the success rates for long-term animal testing are taken from the DHG study. The expected cost is the money that the firm expects to spend on the drug when it enters Phase I human clinical trials. This is calculated by multiplying the average amount spent on a drug in each phase by the probability that the drug enters that phase. All results use the same spending information (column 2), but the Pharmaprojects data set has higher probabilities of drugs entering Phase III and thus higher expected costs ($74 million, compared with $61 million). A drug's out-of-pocket expense is the amount of money that a company would expect to spend to get a drug approved for market. This number is calculated by dividing the expected cost by the probability that a drug in Phase I gets approved. Our estimated out-of-pocket costs are higher than those of DiMasi and colleagues—$310 million, compared with $282 million. This difference is attributable to the higher estimated expected costs.

There are a few things to note about our estimates. First, our phase transition probabilities were calculated by taking the drugs in

EXHIBIT 1
Average Out-Of-Pocket Clinical Costs For Investigational Compounds

	Survey		Entry probability		Expected cost[a]		Total[a]	
Testing phase	Mean cost[a]	N	DHG	Pharma-projects	DHG	Pharma-projects	DHG	Pharma-projects
Phase I	$15	66	100%	100%	$15	$15		
Phase II	24	53	71	74	17	17		
Phase III	86	33	31	46	27	40		
Animal	5	20	31	31	2	2		
Preclinical							$121	$133
Total			22	24	61	74	282	310

SOURCES: J.A. DiMasi, R.W. Hansen, and H.G. Grabowski, "The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics* 22, no. 2 (2003): 151–185 (DHG); and authors' calculations based on Pharmaprojects data.

NOTES: All survey costs were deflated using the gross domestic product (GDP) Implicit Price Deflator, and weighted values were used in calculating the survey means. Preclinical costs are calculated using DHG's preclinical to total research and development (R&D) expenditure ratio of 30 percent.

[a] Millions of 2000 dollars.

Phase II, for example, that successfully moved to Phase III and dividing that number by the same number plus the number of drugs in Phase II for which development was discontinued. We assumed that currently active drugs will experience the same probabilities of success and duration as drug candidates whose projects are completed.

Second, our estimate for successfully moving from Phase I to approval was calculated by simply multiplying the phase transition probabilities together. We did it this way because the data set has very few drugs with complete information for all three phases. This procedure is less efficient than using a duration model to estimate the success rates of these drugs (the approach taken by the DHG study). That approach relied on the assumption that the censored drugs will have the same probability of success, conditional on time in development, as the uncensored drugs. The approach we used in this paper does not rely on this assumption; however, the estimate could be biased if drugs with longer durations are more likely to either succeed or fail.[5]

■ **Opportunity costs.** Exhibit 2 presents a comparison of the capitalized expected costs from the two data sets. The capitalized cost is the opportunity cost of the money used to develop these drugs. It is calculated by taking the expected costs from the previous exhibit and spreading the spending uniformly over the length of the particular phase and then assuming that the money is all "paid back" when the drug is approved. Note that we followed the DHG approach and used an 11 percent discount rate.[6] The estimate for the capitalized expected phase costs from the Pharmaprojects data is higher than the CSDD estimate, around $116 million rather than $100 million.

The difference is due in part to the slightly different method of calculating the phase durations. The CSDD data include both start and end dates for the phases and show that there are some overlaps as well as some gaps between phases. Unfortunately, in the Pharmaprojects data, we have only phase start dates; we therefore assumed that the end date is equal to the start date of the next phase. The durations in these data were calculated for drugs that completed each phase.[7] The CSDD durations were calculated for self-originated drugs that were approved between 1992 and 1999. We estimated that the time from a new drug application (NDA) to approval is 15.8 months using data from the *Orange Book* matched to the Pharmaprojects database. This duration is less than the DHG estimate of 18.2

EXHIBIT 2
Average Phase Time And Clinical Capitalized Costs For Investigational Compounds

	Duration (months)			Mean cost[a]		Expected cost[a]		Total[a]	
Testing phase	DHG 1	DHG 2	Pharma-projects	DHG	Pharma-projects	DHG	Pharma-projects	DHG	Pharma-projects
Phase I	22	12	19	$ 31	$ 32	$ 31	$ 32		
Phase II	26	26	30	42	40	30	29		
Phase III	31	34	30	119	113	37	52		
Animal	37			10	10	3	3		
Preclinical								$335	$381
Clinical						100	116	467	487

SOURCES: J.A. DiMasi, R.W. Hansen, and H.G. Grabowski, "The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics* 22, no. 2 (2003): 151–185 (DHG); and authors' calculations based on Pharmaprojects data.

NOTES: DHG 1 is months to phase end; DHG 2 is months to start of next phase. The DHG new drug application (NDA) approval phase was estimated to be 18.2 months. Costs were capitalized at an 11 percent real discount rate. Pharmaprojects estimates used the DHG preclinical time of 52 months. The Pharmaprojects NDA approval phase was estimated to be 15.8 months.

[a] Millions of 2000 dollars.

months.[8]

■ **Cost comparisons.** Exhibit 3 presents a comparison between our results and previous estimates of drug development costs. To the extent that we were able to verify the estimate of $802 million per approved drug using publicly available data, we did that. Indeed, our estimates indicate that $802 million might be an underestimate. Our clinical cost estimate is $487 million, compared with the original estimate of $467 million. Our estimate for the total capitalized expected cost per approved drug is $868 million, which is higher than the DHG estimate. Note that for the preclinical cost estimate, we used DiMasi and colleagues' 2003 estimate of fifty-two months for preclinical development.

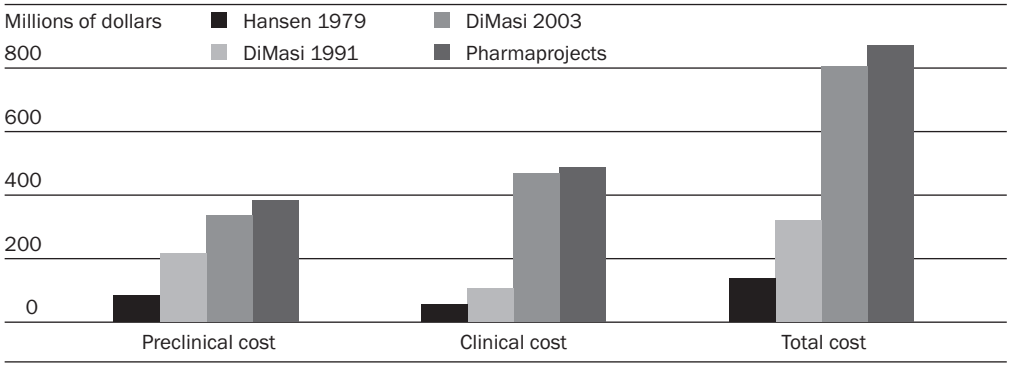
Drug Development Costs By Firm

Exhibit 4 presents cost estimates for different subgroups of drugs from large pharmaceutical firms. The variation reported in this exhibit is the result of variation in measured success rates and durations for these firms. We did not observe actual differences in spending on drugs by firm or firm group.[9] This could lead to an overestimation of the variation across firms if actual spending is correlated with success rates and durations.

The results suggest that there is little advantage from being large and that drug development costs vary greatly among large firms. Exhibit 4 presents results using three different measures of "large." "Top 10 by 2001 income" are the drugs being developed by public companies whose worldwide income for 2001 was in the top ten for drug firms. "Top 20 by *Fortune* rank" are the drugs that were being developed by a worldwide *Fortune* top twenty pharmaceutical firm at the start of the drug's development.[10] "Top 10 by drug count" are drugs that were in a firm ranked in the top ten for the largest number of drugs in development at the start of the drug's development. Also, the drugs included for each firm (A–K) are all of the drugs owned by that firm as of July 2002.

■ **Impact of size.** It has been argued that larger companies have economies of scale and scope in drug development that might be associated with lower development costs.[11] One difficulty in measuring such an effect is that large firms might be associated with successful (and lower-cost) drugs, either because such drugs tend to earn substantial revenues or because mergers and acquisitions lead to such drugs being in larger firms.[12] The results suggest that this could be a problem. When an ex

EXHIBIT 3
Capitalized Preclinical, Clinical, And Total Cost Per New Drug, In Millions Of 2000 Dollars



SOURCES: R.W. Hansen, "The Pharmaceutical Development Process: Estimates of Current Development Costs and Times and the Effects of Regulatory Changes," in *Issues in Pharmaceutical Economics,* ed. R.I. Chien (Lexington, Mass.: Lexington Books, 1979), 151–187; J.A. DiMasi et al., "Cost of Innovation in the Pharmaceutical Industry," *Journal of Health Economics* 10, no. 2 (1991): 107–142; J.A. DiMasi, R.W. Hansen, and H.G. Grabowski, "The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics* 22, no. 2 (2003): 151–185; and data from Pharmaprojects.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.