HEALTH TRACKING

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 devel-

opment 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

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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

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

| Testing phase | Survey | | Entry probability | | Expected cost[a] | | Total[a] | |
	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

Testing phase	Duration (months)			Mean cost[a]		Expected cost[a]		Total[a]	
	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

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EXHIBIT 3
Capitalized Preclinical, Clinical, And Total Cost Per New Drug, In Millions Of 2000 Dollars
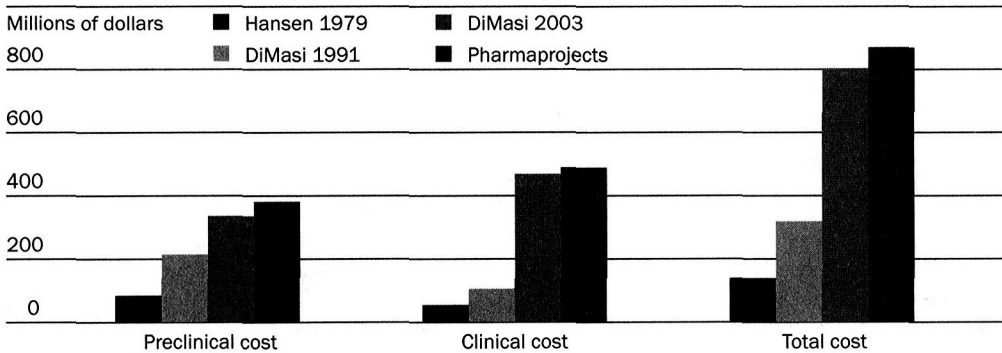
SOURCES: R.W. Hansen, "The Pharmaceutical Development Process: Estimates of Current Development Costs and Times and the Effects of Regulatory Changes," in *Issues in Pharmaceutical Economics*, ed. R.I. Chien (Lexington, Mass.: Lexington Books, 1979), 151–187; J.A. DiMasi et al., "Cost of Innovation in 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.

EXHIBIT 4
Probability Of Market Entry, Durations, And Costs For New Drugs By Firm

Firm	N	Entry probability (%)			Duration (months)			
		Phase II	Phase III	Approval	Phase I	Phase II	Phase III	Cost ($)
Top 10 by 2001 income	679	70	54	29	17	19	25	687
Top 20 by *Fortune* rank	549	61	43	20	21	23	29	942
Top 10 by drug count	1,055	61	44	19	18	27	28	992
Firm A	52	56	47	23	20	20	19	751
Firm B	53	64	27	16	17	29	35	1,032
Firm C	92	47	31	7	20	21	33	2,119
Firm D	60	62	53	20	24	22	21	977
Firm E	34	88	78	58	27	26	35	521
Firm F	62	76	59	32	17	31	30	734
Firm G	74	71	38	25	15	22	31	712
Firm H	83	50	43	15	31	28	31	1,260
Firm I	53	82	38	23	26	19	35	853
Firm J	62	81	30	16	22	39	36	1,240
Firm K	58	65	46	25	18	19	33	768

SOURCE: Authors' calculations.
NOTES: Phases are for human clinical trials. New drug application (NDA) durations are as for the average drug. Cost is the total expected capitalized cost per new drug (in millions of 2000 dollars).

post measure of size (Top 10 by 2001 income) is used, the average drug from a large firm has a cost much lower than the overall average. However, when ex ante measures of size are used, the cost of the average drug from a large firm is larger than the cost for the overall average drug. These results do not support the claim that larger firms tend to produce lower-cost drugs. Drugs from firms that had the largest number of drugs in development had an average capitalized cost of $992 million—some $124 million more than the average drug.

■ **Comparisons with previous work.** These results contrast somewhat with previous work that found that drugs from small firms tend to have higher costs than drugs from larger firms.[13] DiMasi and Henry Grabowski found in 1995 that this difference was the result of high preclinical spending and longer durations for drugs from small firms. One difference is that we did not account for the mixture of drugs by therapeutic category among firms. Nor did we account for differences in actual spending by firm group. Another explanation is that our study is more recent, and contract research organizations might have leveled the playing field between large and small firms.[14]

■ **Variation within drug groups.** Exhibit 4 also presents average costs for drugs owned by one of eleven large drug firms. The results suggest that there is much variation in development costs even within the group of drugs from large firms. For example, Firm C had ninety-two drugs in development during this period, with an average expected capitalized cost of $2,119 million, while Firm E had thirty-four drugs in development, with an average cost of $521 million—close to one-quarter of the cost of drugs developed by Firm C. Note that the probability that a drug from Firm C goes from Phase I to market is only 7 percent, whereas that probability for a drug from Firm E is 58 percent. As stated above, Firms A and B have almost the same number of drugs in development, yet their costs are $751 million and $1,032 million, respectively.

■ **Role of strategic choice.** This variation highlights an important issue in interpreting cost data. These costs are not completely exogenously determined; rather, these cost estimates are based on data that are the result of strategic behavior by the firms themselves. Therefore, although some of this variation is the result of luck or specialization in particular therapeutic categories, some might be the re-

sult of strategic choice. Firms may choose a high-risk (high-cost)/high-return strategy or a low-risk (low-cost)/low-return strategy.[15]

Development Costs By Therapy

Exhibit 5 presents the capitalized cost per drug by primary disorder for all of the major disorders and for the primary indication for some of the major indications.[16] Again, the observed difference in development costs between disorders is attributable to observed differences in success rates and durations. We did not observe differences in actual spending by disorder or primary indication.[17] Correlation between actual spending and observed success rates and durations by disorder can either exacerbate or reduce the variation in development costs across therapies.[18]

The exhibit shows that there is much variation in phase transitions and success rates. Note that although low transition probabilities reduce the expected cost of a drug, low success rates increase its cost. A little algebra shows that the second effect always outweighs

the first.[19] We see that drugs in development for respiratory disorders such as asthma have very low success rates (16 percent), whereas drugs in development for genitourinary disorders, which include drugs such as Viagra, have much higher success rates.

Exhibit 5 also shows much variation across major indications. Drugs designed to treat respiratory disorders such as asthma or chronic obstructive pulmonary disease (COPD) have an expected capitalized cost per approved drug of $1,134 million, while drugs designed to treat genitourinary disorders have an expected capitalized cost per approved drug of $635 million. Some of this variation could be attributable in part to decisions by the drug firm based on the drug's likely revenue. For example, rheumatoid arthritis drugs have a very high cost of development and also have been quite successful.[20]

The results also give some indication that regulatory policy can help to reduce development costs. Exhibit 5 shows that the short Phase III durations for HIV/AIDS drugs are as-

EXHIBIT 5
Probability Of Market Entry, Durations, And Costs For New Drugs, By Disorder And Primary Indication

Disorder	N	Entry probability (%)			Duration (months)			Cost ($)
		Phase II	Phase III	Approval	Phase I	Phase II	Phase III	
Blood	163	60	57	25	18	32	33	906
Cardiovascular	280	69	42	22	14	35	30	887
Dermatological	122	84	44	29	13	29	24	677
Genitourinary	120	92	58	37	21	28	25	635
HIV/AIDS	108	75	50	36	19	23	19	540
Cancer	681	78	46	20	21	30	29	1,042
Musculoskeletal	134	73	41	22	19	39	30	946
Neurological	192	73	47	22	20	39	32	1,016
Antiparasitic	20	100	67	53	18	33	13	454
Respiratory	165	68	31	16	18	30	36	1,134
Sensory	53	88	60	40	11	44	30	648
Primary indication								
Alzheimer's disease	46	65	46	25	17	37	18	903
Rheumatoid arthritis	51	91	33	23	18	36	39	936
Asthma	74	81	36	26	18	33	31	740
Breast cancer	54	96	58	44	17	37	37	610
HIV/AIDS	89	83	56	44	22	22	19	479

SOURCE: Authors' calculations.
NOTES: Phases are for human clinical trials. New drug application (NDA) durations are as for the average drug. Cost is the total expected capitalized cost per new drug (in millions of 2000 dollars).

sociated with lower capitalized costs for those drugs.[21] Almost all AIDS drugs were allowed to file NDAs without completing large-scale human clinical trials. Our results for these drugs contrast with the results presented in a recent extension of the DHG analysis.[22] That analysis found that HIV/AIDS drugs have quite high clinical costs and anti-infectives (of which HIV/AIDS drugs are a part) have somewhat higher-than-average expected capitalized clinical costs. Another issue is that a sizable proportion of HIV/AIDS drugs' development costs was moved from the preapproval clinical trials to the required postapproval studies.[23]

Discussion

■ **Variation by drug type.** The results presented here suggest that there is considerable variation in the estimated cost of developing different drugs. The estimated expected cost of developing an HIV/AIDS drug is $479 million, while the expected cost of developing a rheumatoid arthritis drug is $936 million. DiMasi and colleagues similarly found large variation in the estimated expected development costs.[24] Using the same data as in their original 1991 study, they found that capitalized clinical costs per approved drug were 25 percent below the average for anti-infectives (such as penicillin) and 75 percent above the average for nonsteroidal anti-inflammatory drugs (NSAIDs, such as Celebrex).[25] Their more recent work reports variations from 13 percent above the average to 20 percent below the average. These estimated differences imply that different therapies might have different costs. For example, anticancer drugs have much higher expected durations, implying higher development costs.

■ **Other factors affecting the estimates.** Another issue is that these estimates are based on observed success rates and durations of actual drugs. The concern is that these numbers are affected by many factors, including factors under the control of the firms developing the drugs. This fact makes it difficult to determine the extent to which these high measured costs really impede new drug development or reduce drug companies' incentives to develop new drugs or types of new drugs. The results show that for one large pharmaceutical firm, the expected cost of developing a drug is $521 million, while for another large firm, it is $2,119 million. This difference suggests that some of the estimated costs could be attributable to the strategic decisions of the drug firms themselves.

■ **Impact of regulatory policies.** The estimated cost of developing HIV/AIDS drugs suggests that regulatory policy can also have a substantive effect on the cost of drug development. In particular, the low cost estimates of developing HIV/AIDS drugs seem to be in some part the result of the short durations for these drugs, which is in part attributable to FDA policy regarding review of these drugs.[26] However, as discussed above, there may be reasons to be cautious about this explanation.

RECENT ESTIMATES on the cost of drug development play an important role in the current debates on drug prices, regulatory policy, generic entry, and drug importation. This paper attempts to verify the accuracy of the DHG estimate that the expected capitalized cost per approved drug is $802 million. Our estimate of $868 million suggests, if anything, that $802 million is an underestimate. However, we also found substantial variation in estimated drug costs, which suggests that policymakers should take care in using a single number to characterize drug costs and that these cost numbers are determined by a series of factors including the strategic decision making of the drug firms themselves.

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NOTES

1. 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.

2. J.A. DiMasi et al., "Research and Development Costs for New Drugs by Therapeutic Category: A Study of the U.S. Pharmaceutical Industry," *PharmacoEconomics* 7, no. 2 (1995): 152–169; and J.A. DiMasi, H.G. Grabowski, and J. Vernon, "R&D Costs and Returns by Therapeutic Category," *Drug Information Journal* 38, no. 3 (2004): 211–223.

3. See C.P. Adams and V.V. Brantner, "New Drug Development: Estimating Entry from Human Clinical Trials," FTC Working Paper no. 262 (Washington: Federal Trade Commission, 2003).

4. Pharmaprojects is supplemented with data from the *Orange Book.*

5. R.M. Abrantes-Metz, C.P. Adams, and A.D. Metz, "Pharmaceutical Development Phases: A Duration Analysis," *Journal of Pharmaceutical Finance, Economics, and Policy* (forthcoming).

6. See DiMasi et al., "The Price of Innovation."

7. See Abrantes-Metz et al., "Pharmaceutical Development Phases."

8. There is evidence that time in regulatory review has fallen in recent years, particularly after 1995. Ibid. E.R. Berndt et al., "Industry Funding of the FDA: Effects of PDUFA on Approval Times and Withdrawal Rates," *Nature Reviews: Drug Discovery* 4, no. 7 (2004): 545–554, estimates this duration as having fallen from 24.2 months to 14.2 months between 1992 and 2002. However, our shorter estimates may be attributable to censoring bias toward observing completed durations for quicker drugs.

9. J.A. DiMasi and H.G. Grabowski, "R&D Costs, Innovative Output, and Firm Size in the Pharmaceutical Industry," *International Journal of the Economics of Business* 2, no. 2 (1995): 201–221, presents variation in costs of development by groups of firms where the authors also measure variation in actual expenditure by firm.

10. The date used is the first date we have for the drug's human clinical trials and could be from any phase.

11. R. Henderson and I.M. Cockburn, "Scale, Scope, and Spillovers: The Determinants of Research Productivity in the Pharmaceutical Industry," *RAND Journal of Economics* 27, no. 1 (1996): 32–59.

12. P.M. Danzon, A.J. Epstein, and S. Nicholson, "Mergers and Acquisitions in the Pharmaceutical and Biotech Industries," NBER Working Paper no. 10536 (Cambridge, Mass.: National Bureau of Economic Research, 2004).

13. DiMasi and Grabowski, "R&D Costs."

14. Thanks to an anonymous reviewer for pointing this out.

15. See DiMasi and Grabowski, "R&D Costs."

16. The categorizations are done by Pharmaprojects and come with the data. The therapeutic categorization is the most inclusive and the most aggregate. The categorization is based upon a European marketing system.

17. See C. Adams and V.V. Brantner, "Spending on New Drug Development," December 2005, http://papers.ssrn.com/sol3/papers.cfm?abstract_id=869765 (accessed 18 January 2006).

18. See DiMasi et al., "Research and Development Costs"; and DiMasi et al., "R&D Costs and Returns."

19. The previous section explains how the success rates were calculated.

20. See Navigant Consulting, "Navigant Consulting Estimates the Worldwide Market for Rheumatoid Arthritis Will Increase to Nearly $15 billion by 2009," 30 March 2004, http://www.corporate-ir.net/ireye/ir_site.zhtml?ticker=nci&script=410&layout=0&item_id=509944 (accessed 20 December 2005). DiMasi et al., "R&D Costs and Returns," presents a more detailed discussion of the relationship between development costs and returns.

21. Abrantes-Metz et al., "Pharmaceutical Development Phases," uses similar data and a full duration model and also finds that AIDS/HIV drugs move through the development process fairly quickly.

22. DiMasi et al., "R&D Costs and Returns."

23. Thanks to an anonymous reviewer for pointing out this possibility.

24. DiMasi et al., "Research and Development Costs."

25. The authors present clinical costs because of a lack of cost data on preclinical costs by therapy.

26. According to M. Meadows, "The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective," *FDA Consumer,* FDA Pub. no. 02-3242 (Washington: Food and Drug Administration, 2002), most HIV drugs have been approved under accelerated approval provisions.