

BACKGROUNDER: A Methodology for Counting Costs for Pharmaceutical R&D

November 1, 2001

BOSTON – (November 2001) – Today's announcement by the Tufts Center for the Study of Drug Development — that the average cost to develop a new drug is \$802 million — was based on detailed survey data obtained directly from 10 drug companies. ([See news release.](#)) Here's how the analysis was conducted.

Because drug development is a complex process involving long lead times and substantial technical risks, a reliable estimate of the cost of development accounts for the expense of project failures and the impact that long development times have on investment costs.

Out-of-Pocket Clinical Costs

Data are collected on clinical phase costs for a randomly selected sample of investigational drugs from firms participating in the survey. The sample is taken from a Tufts Center database of investigational compounds. The compounds chosen are all self-originated. That is, their development was conducted entirely under the auspices of the surveyed firm. Licensed-in compounds are excluded because portions of their R&D would have been conducted by non-survey firms. The firms that license-in compounds effectively pay for the licensors' R&D through milestone payments and royalty arrangements. With reasonably efficient markets for licensed compounds, the costs for self-originated compounds can then be generalized.

Average costs for drugs entering a clinical phase (Phase I, II, and III) are computed from the survey data. These phase mean costs cannot be added to obtain either a cost per investigational drug or a cost per approved drug. The reason is that many drugs that enter the clinical testing pipeline will not make it all the way to marketing approval, or even to the late testing phases.

Safety, efficacy, or commercial issues will lead a firm to abandon development of compounds during clinical development. A full cost estimate would also include discovery and preclinical development costs.

Out-of-Pocket Discovery and Preclinical Development Costs

Many costs incurred prior to clinical testing cannot be attributed to specific compounds. Thus, aggregate level data at the firm level are used to impute costs per drug for R&D incurred prior to human testing. Specifically, time series data for each surveyed firm on spending on pre-human R&D and on human testing are obtained, and a ratio of pre-human R&D expenditures to human testing expenditures is determined based on an appropriate lag structure (on average, pre-human R&D expenditures should occur some years prior to the associated human testing costs). This ratio is then applied to an estimate of out-of-pocket clinical cost per drug, which is based on the project-level data, to yield an estimate of the pre-human R&D cost per drug.

Clinical Success and Phase Attrition Rates

To shift from estimates of clinical and preclinical cost per investigational drug to the more relevant cost per approved drug estimates, one needs to estimate and apply attrition rates for clinical phases and an overall clinical success rate. An overall clinical success rate is the probability that a compound that enters the clinical testing pipeline will eventually be approved for marketing. Attrition rates describe the rate at which investigational drugs fall out of testing in the various clinical phases. These probabilities are estimated from data in the Tufts Center database of investigational drugs.

The attrition probabilities are important factors to use in estimating the true average cost per investigational drug. For example, if only one-third of the drugs that enter the clinical testing pipeline ever make it to Phase III testing, then only one-third of the estimated mean cost for drugs that enter Phase III should be used. The overall clinical success rate is used to convert costs per investigational drug to costs per approved drug. For example, suppose that development of investigational drugs costs, on average, \$100. If, however, only one in five investigational drugs will make it to the marketplace, then the cost per approved drug is \$500. Based on this principle, our full cost estimates include the cost of drugs that fail to make it through the development process.

Development Times and the Cost of Capital

Given that drug development is a very lengthy process, the full cost of drug development will depend significantly on the gap between investment and returns. To illustrate, if the out-of-pocket costs for two projects are identical, but one will not yield any income for years, while returns are immediate for the other, then investors and managers will ascribe a higher total cost to the former project. Full cost estimates then require a "capitalization" of the stream of out-of-pocket costs to some point (the date of marketing approval is the standard). To do so, one needs a timeline for a representative drug.

The timeline is constructed from Tufts Center data on average phase lengths and the average gaps and overlaps between successive phases. The periods considered are the time from synthesis to human testing, the three clinical phases (including an animal testing phase concurrent with clinical development), and the length of time from submission of a new drug application (NDA - an application submitted to FDA for marketing approval) to NDA approval.

Finally, once a timeline is established and out-of-pocket costs are allocated over that timeline, the expenditures must be capitalized at an appropriate discount rate. The discount rate should be the expected return that investors forego during development when they invest in pharmaceutical R&D instead of an equally risky portfolio of financial securities.

Empirically, such a discount rate can be determined by examining stock market returns and debt-equity ratios for a representative sample of pharmaceutical firms over a relevant period. The resulting discount rate is an average company cost of capital.

A company's cost of capital is the expected rate of return that the owners of the company require to invest in that company. Capitalizing both the pre-human and clinical testing out-of-pocket cost per approved drug estimates at such a discount rate yields our fully allocated R&D cost estimate. This estimate is a measure of the private sector resource cost needed, on average, to discover and develop a new drug to the point of marketing approval.

About the Study's Author

The Tufts Center study released today was led by Joseph A. DiMasi, Ph.D., director of economic analysis at the Tufts Center for the Study of Drug Development since 1987.

Also participating in the study were Ronald Hansen, Ph.D., associate dean, William E. Simon Graduate School of Business Administration, University of Rochester, and Henry Grabowski, Ph.D., professor of economics, Department of Economics, Duke University.

Prior to joining the Center for the Study of Drug Development, DiMasi was a member of the economics department at the College of the Holy Cross. He received his Ph.D. in economics from Boston College in 1984, and a B.A. in mathematics and economics from the University of Massachusetts at Boston in 1975.

DiMasi has authored numerous articles published in economics and medical research journals. He has served on the editorial board of the Drug Information Journal and currently serves on the editorial board of the Journal of Research in Pharmaceutical Economics. He is the 2001 recipient of the Donald E. Franke Award from the Drug Information Association. In addition to the R&D cost of new drug development, DiMasi also researches success rates in the drug development process, changes in the structure and performance of the pharmaceutical and biotechnology industries, and the role of pharmacoeconomic evaluations in the R&D process.

Earlier Tufts Center Studies on the Cost of Developing New Drugs

Today's announcement that the average cost to develop a new drug exceeds \$800 million is the third comprehensive study in a Tufts Center series that originated more than two decades ago.

The first study, in 1979, applying a similar comprehensive methodology used in the current study, established for the first time the true cost to develop a new drug. At that time, the number was \$54 million, in 1976 dollars.

Then, in 1991, the Tufts Center updated the study and pegged the cost at \$231 million, in 1987 dollars.

About the Tufts Center for the Study of Drug Development

Based in Boston, Mass. and affiliated with Tufts University, the Tufts Center for the Study of Drug Development, (<http://csdd.tufts.edu>) provides strategic information to help drug developers, regulators, and policy makers improve the quality and efficiency of pharmaceutical development, review, and utilization. The Tufts Center conducts a wide range of in-depth analyses on pharmaceutical issues and hosts symposia, workshops, and public forums on related topics throughout the year.

For more information, call the Tufts Center at 617-636-2170.

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