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Returns on Research and Development for 1990s New Drug Introductions

Henry Grabowski,[1] *John Vernon*[1] and *Joseph A. DiMasi*[2]

1 Department of Economics, Duke University, Durham, North Carolina, USA
2 Tufts Center for the Study of Drug Development, Tufts University, Boston, USA

Abstract

Background: Previously published research by the authors found that returns on research and development (R&D) for drugs introduced into the US market in the 1970s and 1980s were highly skewed and that the top decile of new drugs accounted for close to half the overall market value. In the 1990s, however, the R&D environment for new medicines underwent a number of changes including the following: the rapid growth of managed-care organisations; indications that R&D costs were rising at a rate faster than that of overall inflation; new market strategies of major firms aimed at simultaneous launches across world markets; and the increased attention focused on the pharmaceutical industry in the political arena.

Objective: The aim of this study was to examine the worldwide returns on R&D for drugs introduced into the US market in the first half of the 1990s, given that there have been significant changes to the R&D environment for new medicines over the past decade or so.

Results: Analysis of new drugs entering the market from 1990 to 1994 resulted in findings similar to those of the earlier research – pharmaceutical R&D is characterised by a highly skewed distribution of returns and a mean industry internal rate of return modestly in excess of the cost of capital.

Conclusions: Although the distribution of returns on R&D for new drugs continues to be highly skewed, the analysis reveals that a number of dynamic forces are currently at work in the industry. In particular, R&D costs as well as new drug introductions, sales and contribution margins increased significantly compared with their 1980s values.

Competition in the research-based pharmaceutical industry centres on the introduction of new drug therapies. In this paper, we examine the returns on research and development (R&D) for new drug entities introduced into the US market in the first half of the 1990s. This research work builds directly on earlier analyses of returns on R&D for the 1970s and 1980s introductions performed by Grabowski and Vernon.[1,2]

Our prior analyses indicate that this industry has exhibited very skewed distributions of returns. In this regard, several significant new classes of drug therapies have been introduced since the late 1970s. Early movers in these classes have obtained the highest returns on R&D. We found that the top decile of new drugs accounted for close to half of the overall market value associated with all the new drug introductions in our 1970s and 1980s' samples.

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latter sub-sample of drugs accounts for a very small share of overall sales for the full sample.

Life-Cycle Sales Profiles

Since data were available for the years 1990 to 2000, 7 to 11 years of worldwide sales values for the NCEs in our sample were provided, depending on their date of introduction into the US market. The next task was to estimate future sales over the complete market life of these products. Twenty years was chosen as the expected market life. This is the same assumption that we utilised for 1980s new drug introductions. We believe this to be a reasonable time horizon for an IRR analysis. Any sales remaining after 20 years of market life are likely to be very small, given the sales erosion experienced by most products from generic competition and product obsolescence. Furthermore, these sales will also be severely discounted by the cost of capital in an IRR analysis.

We utilised a two-step procedure to project future sales values. These steps involve forecasting sales to the point of US patent expiry and then projecting sales in the post-patent period. The two-step approach is illustrated in figure 1 for one of the products in our sample. This product was introduced into the US market in 1992. There are 9 years of sales information and its US patent expires in year 12. By year 9, this product was in the mature portion of its product life cycle. By using a reference life-cycle curve, the product was projected to have relatively stable sales (in constant dollar terms) until year 12. A significant decline is then projected in the period after US patent expiry because of the entry of generic competitors and related economic factors.

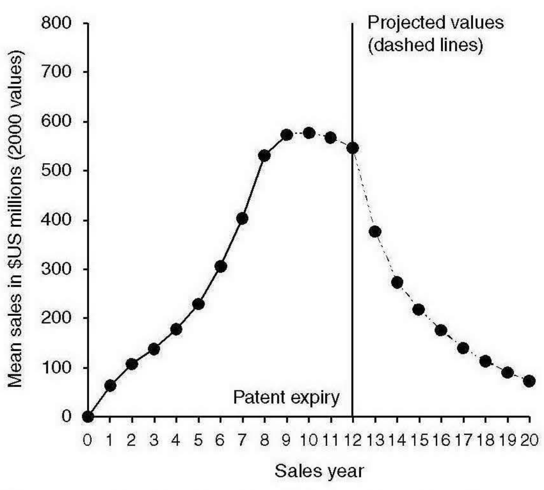

Fig. 1. Actual and projected worldwide sales values for a representative sample product.

The estimated sales decline after patent expiry is based on the experience of major commercial products coming off patent in the 1994 to 1997 period. In particular, we examined worldwide sales losses for a sample of NCEs for a 4-year period following their US patent expiry. The average percentage declines observed were 31, 28, 20 and 20%, respectively. We utilised these percentages to project sales in the first 4 years after patent expiry and, thereafter, a 20% decline until the product's market life is completed in year 20. In our prior work, we found that generic competition is focused on products with significant sales at the time of US patent expiry. Consequently, for the drugs concentrated in the bottom four deciles of our sample (with worldwide sales of less than $US40 million in year 10 of their market life), we assume that the probability of generic competition is very low. For these drugs we assume that sales losses in the mature phase of cycle will proceed at a more moderately declining rate based on the reference curve used for the pre-patent expiry period.

We should note that the percentage declines in sales from generic competition in the US market observed in prior studies are much greater than the worldwide losses in sales for major commercial products observed here.[16] Hence, the decline in worldwide sales in the post-patent period is ameliorated by the lower incidence of generic competition and sales losses outside the US. This may change by the time this cohort actually reaches patent expiry during the current decade, because reference pricing and generic competition are on the rise in many European countries.[17]

Figure 2 provides a plot of the sales life-cycle profile (in $US, 2000 values) for the top two dec-

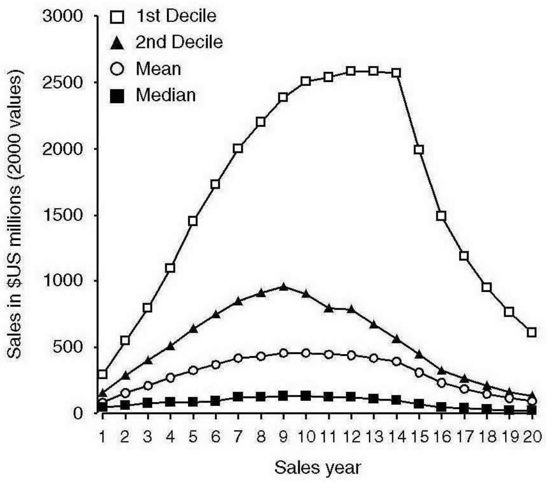

Fig. 2. Worldwide sales profiles of 1990 to 1994 new drug introductions.

iles as well as the mean and median drug compounds in our 1990 to 1994 sample. The sales curves illustrate the highly skewed distribution of sales in pharmaceuticals that was observed for early cohorts. The peak sales of the top decile compounds are several times the peak sales of the second decile compounds. The mean sales curve is also significantly above the median.

Figure 3 provides a plot of mean worldwide sales for the 1990s sample compared with that for the 1980s cohort (in $US, 2000 values). Mean sales have increased significantly in real terms, with peak sales increasing from $US345 million for the 1980s cohort to $US458 million for the 1990s cohort. There is also the suggestion that sales curves have become somewhat steeper in the ascending sales growth stages of the life cycle, with a longer plateau before generic competition and product obsolescence take hold.

Figure 4 shows a corresponding plot of the mean worldwide sales for the top decile compounds in the 1990 to 1994 and 1980 to 1984 periods. This is instructive, given that the prospective returns for top decile compounds are primary drivers of R&D investment activities in pharmaceuticals. For the 1990s cohort, the top decile compounds reached peak sales of more than $US2.5 billion. This may be compared with peak sales of near $US1.8 billion for the 1980s cohort. The peak sales for the 1990s cohort also occur later than for the 1980s cohort.

Pre-Tax Contributions and Other Economic Parameters

The next step in the analysis was to obtain revenues net of production and distribution costs (often categorised in the economic literature as 'quasi-rents'). For this purpose, we analysed pre-tax contribution margins in pharmaceuticals during the 1990s. As in prior work, we utilised data derived from the income statements of the pharmaceutical divisions of a number of major multinational drug companies to obtain representative values on contribution margins over time.[1,2]

Our analysis of the data on these firms indicated that average contribution margins gradually increased from 42% in the early part of the 1980s to approximately 45% at the end of the decade. On the basis of these data, we constructed a linear contribution margin schedule over time. In particular, the contribution margin is 42% in the first year of the product life and grows by increments of 0.3%

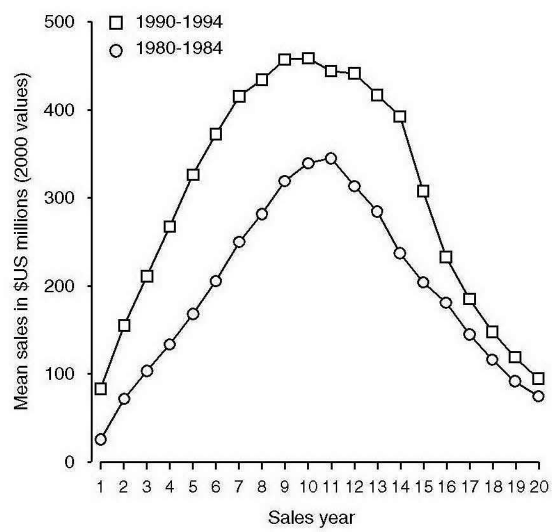

Fig. 3. Comparison of mean worldwide sales curves for new drug introductions in the 1990 to 1994 and 1980 to 1984 samples.

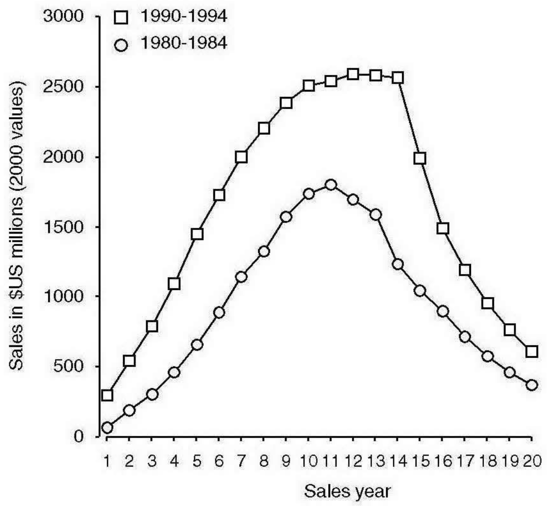

Fig. 4. Comparison of mean worldwide sales curves for top decile drugs in the 1990 to 1994 and 1980 to 1984 samples.

per year. We also assume that contribution margins will continue to rise at this same rate during the current decade. Hence, over the full 20-year life cycle, target contribution margins are expected to rise from 42% in year one, to 48% by year 20, with a mean contribution margin of 45% over the full life cycle.

While we constrained margins to average 45% over the life cycle, we also recognise, as in our earlier analyses, that promotion and marketing expenditures are concentrated in the launch phases of the life cycle. In our prior analysis, we developed the following allocation rule based on a regression analysis of promotional and marketing outlays: promotion and marketing is equal to sales in year 1, declines to 50% in year 2, and falls to 25% in year 3. We retained this assumed pattern on marketing outlays in the present analysis. Interviews with industry participants indicated that the initial post-launch years continue to be the primary focus of marketing and promotion activities.

An analysis performed by Rosenthal et al.[18] indicates that the drug industry's marketing expenses to sales ratios have remained relatively stable around 14% in the 1996 to 2000 period. However, there were some important compositional shifts over this period. The direct-to-consumer advertising to sales ratio increased from 1.2% to 2.2% between 1996 and 2000, at the expense of physician detailing and hospital medical journal advertising.[18]

For the current analysis, we did make one relatively minor change in the allocation and timing of marketing expenditures related to launch. In particular, we estimated pre-marketing launch expenditures in the order of 5 and 10% of first year sales in the 2 years immediately prior to launch. These marketing expenditures are for activities such as pre-launch meetings and symposiums, pricing and focus group studies, and sales force training. Our assumptions concerning the size and timing of these expenditures were guided by a recent survey report on pre-launch marketing expenditures by industry consultants as well as interviews with some of the participating companies.[19]

As indicated above, our model is structured so that margins average 45% over the full product life cycle. Given the assumed pattern of launch expenditures, contribution margins for each product are below representative industry values in the first 3 years of marketing. However, as a product matures, both promotional and administrative costs decline in relative terms, and contribution margins increase over average industry values in the later years of the life cycle.

The model is also structured to provide for capital expenditures on plant and equipment (P&E). As in our model for the 1980s cohort, we assumed overall capital expenditures for P&E to be equal to 40% of tenth year sales. Half of these outlays are assumed to occur in the first 2 years before marketing and the other half during the initial 10 years of the product's market life. These assumptions imply an average capital investment to sales ratio of 3.3% over the full product life cycle. This is generally consistent with data from pharmaceutical industry income statements.

In particular, we checked the reasonableness of our assumptions by comparing this implied 3.3% capital investment to sales ratio with the corresponding ratios observed on industry income state-

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ments during the 1990s. We found that the drug industry capital investment to sales ratio averaged about 7.0% during the 1990s. However, the latter value includes investment for R&D as well as production, marketing and administrative facilities. In our model, provisions for capital investment in R&D facilities are included in the cost estimates provided by DiMasi et al.[5] Accordingly, we asked some industry members involved with strategic planning for information on what percentage of their P&E expenditures was devoted to R&D, versus other firm activities. We obtained a range of 40 to 50% of total capital expenditures devoted to R&D. Given this range, the capital investments to sales ratio for non-R&D activities implied by our model is consistent with the observed data from company income statements.

For working capital, it was assumed that accounts receivables are equal to 2 months of annual sales and inventories are 5 months of sales (valued at manufacturing cost). These are also based on the analysis of balance sheet data of major pharmaceutical firms. Working capital is recovered at the end of the final year of product life.

Effective Tax Rates

Our analysis of returns is conducted on an after-tax basis. In our prior studies of returns, we computed average effective tax rates based on analysis of income statement data from eight major pharmaceutical firms. The average effective rate was 35% for the 1970s cohort and 33% for the 1980s cohort. A comparable analysis for the 1990s cohort yielded an effective tax rate of 30%. This is the rate used in our baseline case. The difference between the nominal corporate tax rate (34%) and the average effective tax rate of 30% reflects various credits and deferrals such as the R&D tax credit and manufacturing tax credits for plants in Puerto Rico.[2]

After-tax cash flows are also influenced by the tax treatment of depreciation. In our analysis, cash flow in each year is equal to after-tax profits, plus depreciation charges. Accelerated depreciation, as specified in the US tax code, results in tax deferrals and positive cash flow in the early years of a product's market life. This reverses in the latter years of a product's life.

Summary of Economic Values

Table II provides a summary of the key economic inputs to IRR and NPV analysis for the 1990 to 1994 NCEs cohort compared with the corresponding values for the 1980 to 1984 cohort. R&D investment levels have roughly doubled in real terms, in both uncapitalised as well as capitalised dollar terms. On the revenue side of the equation, sales-life curves have shifted upward significantly. This is reflected in higher peak sales for the 1990 to 1994 cohorts ($US458 million compared with $US345 million for 1980 to 1984 NCEs). While sales have not grown at the same rate as R&D costs, contribution margins have increased in the 1990s, implying higher operational profits from a given level of sales. How all these factors balance out from a returns-on-investment standpoint is a major issue addressed in the analysis that follows. The industry's cost of capital, effective tax rate, and capital investment-to-sales ratio have changed only marginally for the current cohort compared with the 1980s sample.

Table II suggests that R&D investment expenditures are growing over time relative to sales revenues and the other activities of pharmaceutical

Table II. Key economic values for internal rate of return analysis for the 1990 to 1994 versus 1980 to 1984 new chemical entities (NCEs)

Economic parameter	1990 to 1994	1980 to 1984
Average R&D costs[a]		
pre-tax uncapitalised	$US416 mil	$US196 mil
after tax capitalised	$US480 mil	$US251 mil
Peak sales for mean NCE[a]	$US458 mil	$US345 mil
Contribution margin[b]	45%	40%
Cost of capital	11%	10.5%
Effective tax rate	30%	33%
Capital-to-investment sales ratio	3.3%	3.4%

a R&D costs and sales are all expressed in 2000 values.
b Average contribution margins over the full product life cycle; launch costs are concentrated in early phases of life cycle, so margins are lower in initial years and higher in later years.
mil = millions; **R&D** = research and development.

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