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A Computer Simulation Model of Pharmaceutical Innovation

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Introduction

Several of our earlier studies have examined the effects of regulation and other public policies on pharmaceutical innovation and R & D investment levels. Most of these studies have been retrospective in character, involving statistical analyses of firm or industry data. At the current time, however, the drug industry faces a number of developments that are outside the domain of recent historical experience.

One issue, for example, that has generated a great deal of attention has been patent protection for pharmaceuticals. The average effective patent protection period in the U.S. for new drugs has been declining as a result of longer development and approval times. The U.S. Congress is now actively considering a bill that would restore patent time lost during the IND and NDA regulatory periods. The incentive effects of patent restoration on drug innovation will be affected by other government policy programs. These include, for example, proposed regulatory reform measures (which directly influence patent time lost) and government drug reimbursement and substitution policies (which influence the degree of competition from imitative competitors after patents expire).

In a recent set of papers[1], we have attempted to examine this cluster of issues surrounding the patent restoration question. In this regard, we performed a sensitivity analysis of the effect of different patent terms on the expected returns in R & D. This analysis involved, however, a simple partial equilibrium approach which ignored interactions between rival firms or long-run side effects to other variables.

In this paper, we develop a much more elaborate simulation model of the innovative competitive process. Our objectives are to better understand the interdependencies between the key variables driving this process and to analyze the long-run impacts of parameter changes such as patent protection terms.

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Our simulation model involves the analysis of a hypothetical industry situation. It is formulated, however, to incorporate the relevant aspects of new drug competition in pharmaceuticals. Specifically, the firms in our model fund an ongoing portfolio of research projects or investigational new drugs (INDs) of different vintages. Development times are long and probability of success is low. The pay-off distribution for new drug introductions is also highly skewed, in accordance with recent empirical analyses of pharmaceuticals. Successful new drug introductions provide the revenues to firms to engage in new and ongoing R & D projects and simultaneously reduce the available sales revenues to rivals.

This model is run successively over a large number of time periods. As the baseline case for our analysis, the model's parameters are specified with representative values from current drug industry experience (that is, with respect to R & D costs, probability of technical success, the sales revenues distribution of new drug introductions, etc.). We then perform a number of experiments involving deviations from this baseline case. This amounts conceptually to an investigation of different possible future scenarios as determined by several parameters of interest.

The model developed in this paper has many analytical similarities to the evolutionary models studied in several recent papers by Nelson and Winter[2]. As in their work, we focus on how industry structure and innovative performance evolve over time in the presence of different specifications of key determinant factors. However, in contrast to their models, which focus on process oriented technological change and productivity shifts over time, we analyze the case of new product innovation. Competition in pharmaceuticals centers on new product rather than new process innovation and we have formulated our model to reflect this fact.

In order to provide some motivation for working through the mechanics of the model, and also to provide some points of comparison with our past work, we focus on some of the basic policy isssues previously analyzed using other methodological approaches. Specifically, we do several experiments involving alternative specifications about the degree of imitative competition facing innovators (i.e. alternative specification about the length of the patent exclusivity period and the degree of generic competition after patent expiration). Furthermore, we also consider alternative scenarios regarding the richness of "technological opportunities" as reflected in the probability of technical success for research projects. This latter set of experiments is motivated by recent conjectures of a richer technological environment over future periods as a result of several advances in basic biomedical research over the past decade[3]. We also consider the effect of other parameter shifts including changes in the corporate tax rate and regulatory clearance times.

Before turning to a more detailed description of the model and the ex-

periments performed, we present a few qualifications concerning our analysis. We do not view our model, at least at its current stage of development, as a planning or forecasting device regarding future developments in the drug industry. While this is a possible application of our computer simulation model, this requires a much more elaborate specification than is currently the case, especially with respect to complementary activities such as the promotion and marketing of new drugs, firm diversification and investment strategies and international operations. Our analysis is also explicitly concerned only with the research intensive sector of the pharmaceutical industry. Other segments of the industry are reflected in terms of the model's constraints. In addition, we have not tried to duplicate the existing size structure of the drug industry in initializing the model, but rather start out with an arbitrary number of equal-sized, research-intensive firms. Different size structures then evolve over time as a consequence of alternative specifications of the technological, economic, and policy variables present in the model.

Our primary research interest in this paper is to examine how these various factors and constraints interact to determine the innovation performance and structure of this hypothetical industry structure. The multiperiod, multi-firm character of our model allows us to examine the long-run consequences of different research environments or different policy scenarios using the comparative dynamic methodological approach described above. While our results are preliminary in character, they should at the least provide insights into the dynamic workings of new drug introduction processes.

General Description of the Model

As noted in the introduction, pharmaceutical R & D is a very risky enterprise—development times are long and the rewards are uncertain. The R & D intensive firm can be viewed as a participant in a high stakes game, where the odds of winning on any single R & D project are very small, but the returns to a "winner" can be extremely large. In our model, it is useful to consider the firm as a dynamic collection of ongoing projects in various stages of their life—discovery, development R & D, market life or removal from the market.

To obtain representative values of the R & D phase of drug innovation, we rely heavily on the empirical work of Ronald Hansen[4]. Specifically, the R & D process is broken down into discovery, clinical testing and regulatory approval phases. The average duration and expected costs associated with each phase in our model are based on Hansen's estimated values from a study of over 100 new drug candidates spanning the period 1963—1975. Overall, his work indicates a gestation period for a new drug product totaling approximately 11 years in length with expected expenditures of several hundred thousand

dollars for each year of this gestation period. (Details on the specific values used for R & D costs are available in a separate technical appendix that may be obtained from the authors.)

The innovation process then proceeds roughly as follows in our model. Each year, the firm allocates a portion of its available cash flow from past NCEs to existing R & D projects and also initiates new R & D projects if sufficient cash is available. R & D projects that are taken to fruition are eligible for a "draw" to determine if this product candidate is to be marketed. Since only 1 of 10 candidates that begin clinical testing survive to become FDA approved NCEs, we "draw" from a binomial probability distribution reflecting these odds of success. For those projects with successful draws, we then draw from another probability distribution to determine its marketing success. This latter distribution is based on the actual sales distribution of all U.S. NCE introductions for the period 1970 to 1976[5]. It is a highly skewed distribution with a wide variance and most of the density toward the low end. In other words, most introductions have rather modest market potential, but there are a few products that result in very large sales volumes and market shares.

The firm's probability draws to determine the technical and marketing success of its R & D projects that have a major effect on each firm's dynamic path over time. It is possible for a firm to have a run of project successes which correspondingly lead to large cash flows, high R & D, and perhaps future successful NCEs. On the other hand, a run of project failures can lead a firm to cut back on new R & D projects, and even drop out of the business under extreme conditions.

After a new product is introduced, whether it is a major or minor product, sales follow a common life cycle pattern over time. This pattern involves rising sales during its early years, roughly steady sales during its middle periods and declining sales in its final years. A product's net revenues in any period are then obtained by substracting from total sales expenditures for product promotion, manufacturing and administration. These expenditures also follow prescribed dynamic patterns. These were derived from an analysis of the percentage of sales devoted to each of these activities at various points in the life cycle using actual industry data.

Sales revenues realized by the firms in the model are also interdependent in that new product sales come in part at the expense of established product sales and in part represent an expansion of the total market. The relationship specifying what percentage of new product sales are market expanding versus redistributive in nature is one of the parameters that we experiment within our simulation runs. Another form of interdependence built into the model is that if one firm is successful in drawing a "big winner" in a particular therapeutic class, this reduces the probability of any other firm also drawing a big winner in that class in immediately subsequent periods.

A key issue is how to "initialize" the model. In the simulation runs analyzed in this paper, we assume that the industry initially consists of 10 equal sized firms. Furthermore, we assume in year 1 that the firm is already a going concern and owns a portfolio of drugs developed and marketed over the preceding 20 to 30 year period. It is also funding R & D for NCE candidates in various stages of the development process.

To obtain a representative set of values for the initialization of our model, we analyzed the financial data and NCE introductions of 9 large U.S. drug firms. Details on this process are available in the technical appendix. The nine firms were selected because of their high degree of specialization in pharmaceuticals. The initial position of our simulation model is basically the average position of these 9 firms in the year 1970. In point of fact, we assembled sales data on all the NCE introductions for these nine firms since 1946. We then computed average sales revenues for successive vintages of past product introductions (over five year intervals) to obtain a representative portfolio of initial products for the firms in our model.

We also used the financial data of these 9 firms for the period 1970—1979 to obtain the fraction of a firm's cash flow to be devoted to R & D. Based on the data from this sample of firms, approximately 28 percent of the available cash flow was allocated to R & D with the remainder divided between dividends, retained earnings and taxes. In the baseline case of our model, we assume firms allocate this particular percentage of their cash flow to R & D. This percentage is then varied in some of the computer simulation experiments.

Hence, for the present, the firm's R & D budget decision rule amounts to allocating a fixed 28 percent of its available cash to R & D. From this amount, ongoing projects are funded first and any remaining funds are then used to initiate work on new NCE candidates. A 10 percent limit on R & D spending increases over previous years is also incorporated into the model to avoid sharp increases in R & D associated with large increases in net revenues. This constraint is in keeping with the fact that the dominant component of R & D outlays is for professional employees and there are limits to how rapidly this activity can be efficiently expanded over time.

On the down side, if funds allocated for R & D through the budget percent decision rule are less than the amount needed for ongoing projects, no new projects are initiated. However, up to a point, existing projects receive continued funding at required levels. This means that firms increase the percentage of cash flow devoted to R & D in this situation and in effect decrease other outlays (dividends or retained earnings). This behavioral assumption is also motivated by the fact that it is not generally efficient for a firm to stop ongoing R & D projects in midstream in downturns because it will essentially have to start over (with new personnel) in upturns.

A firm faced with prolonged periods of depressed revenues because of a lack of new product successes will find funding of R & D increasingly burdensome. The risk of firm bankruptcy increases. This raises the issue of when the firm will withdraw from the market and terminate its R & D activities completely. In this paper we use the following termination rule. If the available cash flow to fund R & D drops below 50 percent of what is necessary to fund ongoing projects (in turn requiring a doubling of the R & D to cash flow ratio from its baseline value of 28 just to fund ongoing projects), the firm exits from the industry. This is, of course, only one of many possible termination rules and in future research we plan to experiment with other alternatives. As we discuss further below, the current rule on termination does not appear to be an excessively restrictive one.

In the aggregate, our model clearly embodies several specific probabilistic, technological, and behaviorial assumptions and rules. We have tried, however, to make the model representative of drug industry conditions and practices in a number of relevant aspects. In this regard, we utilized the results of several empirical analyses of drug innovation and a large array of previously assembled data sets.

As noted above, the initial conditions for our model with respect to each firm's beginning portfolio of R & D projects and existing products are based directly on the composite experience of 9 large research intensive firms in 1970. Given that this is so, one check on the consistency of our model is to run it for a 10 year period and compare the outcomes with those actually observed for these 9 firms over the period 1970 to 1980. We performed this type of consistency check. The model tracked the aggregate experience of these 9 firms reasonably well, at least with respect to the total number of NCEs generated and growth in overall market sales. While this consistency test provides no guarantee as to the reasonableness of the model's results when examining longer time intervals or in considering deviations from this baseline case (as in the experiments analyzed in the next section), it is nevertheless reassuring that it was generally consistent with the experiences of these 9 firms over this interval.

Simulation Experiments and Results

In this section, we begin with a more detailed description of the baseline case of our simulation analysis and then turn to the results of the specific experiments. In our first set of experiments reported in Table 2, we vary our baseline assumption concerning the probability of technical success. In Tables 3 and 4 we examine the effect of changing the effective patent life for different degrees of generic substitution.

Tables 5, 6, and 7 are concerned with the effects of changing alternative parameters of interest. Table 5 shows the effect of reducing FDA regulatory times by one and two years in comparison with the baseline

case. Table 6 considers the impact of alternative income tax rates and Table 7 deals with an assumption concerning-the nature of new product innovation. That is, Table 7 reports the results of several experiments that vary the extent to which new drugs expand the total market as compared with simply substituting for existing drugs.

The "baseline case", mentioned above, refers to the set of parameter values that seems to describe "best" the process of pharmaceutical innovation in the 1970's. Hence, it is used as a benchmark against which we judge the effects of changing parameters. For this reason, it should be useful to provide a more detailed description of this case.

The baseline case

We list below the major assumptions underlying the baseline case that will be changed in the various simulation experiments.

- The probability that a chemical entity which begins clinical trials will be approved for marketing is 1 out of 10. Varying this parameter can be viewed as a way of altering "technological opportunity".
- The total time from discovery through FDA approval of the New Drug Application (NDA) is 11 years. Discovery takes 3 years, followed by clinical testing, and then 28 months for NDA approval. By shortening this time period, we can take into account efficiency gains in FDA regulatory procedures.
- The time pattern of marketing is that sales increase steadily from year 1 to year 10, remain constant (in real terms) from year 10 until year 20, and then decline to a relatively low level for the last 5 years of commercial life. This time pattern can be modified to represent varying length patent periods and varying degrees of generic competiton upon patent expiration.
- An effective income tax rate of 37.5 percent is assumed for the baseline case. As discussed above, this was the average rate paid by our 9 firms sample in the early 1970's. We will consider the consequences of both higher and lower tax rates in our analysis.
- New drugs introduced reduce old drug sales in the relevant therapeutic category. Letting α = fraction of new drug sales removed from old drugs sales and β = fraction of old drug sales below which further reductions are not permitted, we assume α = .25 and β = .50. Varying α and β can be viewed as changing the character of new drug innovation—from pure substitution at one extreme to market expansion at the other.

Of course, there are numerous other important assumptions that underlie the model. However, they are common to all of the simulations and are therefore relegated to the technical appendix.

As discussed earlier, we begin the simulations with ten firms all of identical size. Each firm has $57.1 million (1967 dollars) in net revenues

in year 1. Our "industry" therefore has total net revenues of $571 million in the initial year. Other variables that we shall be interested in are the market share of net revenues accounted for by the largest four firms and the flow of new chemical entities (NCEs) generated by the industry. The initial market share of the top four firms is, of course, 40 percent since each firm has a 10 percent share.

Because of the probabilistic character of our simulation model, a single simulation of the model over 50 years is not very meaningful. Hence, we have replicated each simulation ten times and computed the mean values of the variables of interest. For example, for the baseline case, the observations for industry net revenues, NCEs and, in year 50, market share of the top 4 are shown in Table 1.

Table 1. Illustration of method: each simulation was replicated ten times and mean values computed

	Net Revenues	Market Share 4 Firms	NCEs
Run 1	963	70.3	11.8
Run 2	815	58.7	8.6
Run 3	698	75.9	5.6
Run 4	459	65.4	6.4
Run 5	671	85.9	4.8
Run 6	549	74.2	4.2
Run 7	861	87.4	9.6
Run 8	696	87.1	10.0
Run 9	750	69.4	9.4
Run 10	829	83.7	9.4
Mean	729	75.8	8.0
Standard Error	(47)	(3.1)	(.8)

Of course, the standard errors shown in parentheses under the means could be reduced by increasing the number of runs. For example, we tried one experimental set of 50 runs and obtained an estimate of $717 million in net revenues with a standard error of $29 million. Balancing computer costs against the number of experiments, however, led us to choose ten runs as reasonable.

Several important characteristics of the baseline case should be noted. First, industry net revenues increased in real terms over the 50 year period from $571 million to $729 million. This is an implicit annual growth rate of about .5 percent from the introduction of new products. (The model abstracts from other sources of market growth such as population increases, demographic change, etc.) This growth rate rises to 1.5 percent for the higher probability of technical success used as the datum in several model runs.

A second characteristic of the baseline case is that the market share of the top four firms rises from 40 percent to 75.8 percent[6]. This tendency

toward concentration is typical of other simulation studies of this sort[7]. Although all firms begin of equal size, some firms will inevitably "draw" the more profitable NCEs and this in turn provides them with larger R & D budgets to finance more draws in the future. There is, however, considerable dynamic instability in individual firm market shares and in the identity of the market leaders. This, in accordance with empirical findings on market share, changes over time in progressive industries like pharmaceuticals[8].

A final observation about the baseline case is that the average number of NCEs annually rises from about 6.2 NCEs for years 1 through 5 to 8 NCEs for years 46 through 50. This is, of course, consistent with the assumed real growth built into the model.

Our baseline case was constructed from drug industry performance data centered around the early Seventies. This was not a period of particularly rapid technological growth for the industry and this helps to explain the relatively low annual growth rate in sales revenues generated by the baseline assumptions. Nevertheless, this set of values provide a convenient reference point from which to gauge various parameter shifts in the model. As discussed above, we also analyze alternative regimes concerning technological opportunity that yield much greater real growth rates.

Results of experiments

Our first experiment, reported in Table 2, was designed to examine the effects of a shift in technological opportunity. As discussed, the baseline case utilizes representative parameter values characteristic of the Seventies. This results in a relatively low growth rate in industry net revenues and perhaps embodies excessively pessimistic assumptions concerning future introductions, given the advances that have occurred in basic biomedical research in recent periods.

Accordingly, for our first experiment we examine the following kind of shift in technological opportunity. Assume that the chances of technical success for any R & D project increase to 1 in 8 from 1 in 10 odds assumed for the baseline case. In effect, this assumes a 25 percent increase in the odds of technical success (from .10 to .125), or a 25 percent increase in the chance of any research project resulting in a new product introduction.

The results in Table 2 indicate a strong response in both revenue growth and the level of NCE introductions to this shift in technical opportunity. In particular, a 25 percent increase in the technical success parameter results in an approximate doubling of NCE introductions (from 8 to 15.5 per year) and a tripling of the annual growth rate in industry net revenues from new product introductions (from .5 to 1.5 percent per year). This multiplier effect of technological success parameter reflects both an "R & D productivity" effect (more NCEs from a given

Table 2. Simulation of 10 Firms over 50 Years Assuming Alternative Probabilities of Technical Success as Indices of Technological Opportunity

	.10 Probability of Technical Success (Baseline Case)	.125 Probability of Technical Success
Avg. Annual NCEs of Industry	8.0 (.8)	15.5 (1.3)
Net Revenues of Industry	729 (47)	1276 (117)
Market Share of Top 4 Firms	75.8 (3.1)	74.0 (1.9)
Avg. No. Firms Dropping Out	.5	.2

Notes:

a. Each experiment was repeated 10 times; hence, values above are averages of the 10 replications and numbers in parentheses are standard deviations.
b. Values generally refer to year 50 with the exception of "Avg. Annual NCEs" which averages years 46—50. Of course, "Number of Firms Dropping Out" refers to the complete 50 year period.
c. Net Revenues equal sales less production and promotion costs and are in millions of 1967 dollars. Market share refers to net revenue share. Industry net revenues in year 1 equal 571.

level of R & D investments) as well as a "cash flow availability" effect (higher level of internal funds available for R & D investment throughout the 50-year period). These two effects working together produce a compound interactive impact on NCE introductions and industry revenue growth.

The market share of the top four firms shows no significant change over the baseline case. As we shall see in later tables, this variable appears to be relatively insensitive to our various experiments, with one exception. The exception is that a rise in market share occurs when the number of firms dropping out of the R & D rivalry averages over one firm per run. In the first five tables the average number of firms dropping out is always less than one. In Table 7, the assumptions become sufficiently harsh to produce higher numbers of drop-outs, and consequently, higher market shares.

Because of the importance of technological opportunity to the observed long-run growth in new product introductions and net revenues, most of the experiments considered below were performed using the alternative assumptions of "high" and "low" technological opportunity as reflected in these two different assumptions on the technical success parameter.

The experiments presented in Table 3 and 4 are designed to examine the effect of alternative patent lifetimes and generic substitution rates on industry performance. The two cases analyzed in Table 2 assumed a product life of 25 years. In this set of experiments we assume effective

patent lives of 17, 12, and 8 years[9]. By an effective patent life of 8 years, we mean that the firm's patent expires 8 years after market introduction and the product becomes vulnerable to a loss in revenues from generic competition. The amount of the reduction in net revenues is, of course, an important assumption itself. Hence, two different assumptions on substitution rates are employed: a mild reduction of 10 percent and a much larger reduction of 50 percent.

The results presented in Table 3 are computed under the assumed regime of low technological opportunity (i.e. a technical probability of success equal to .10). Hence, they are appropriately compared to the baseline case presented in Column 1 of Table 2. The results of these experiments are not especially surprising. The mild substitution of rival products upon patent life expiration causes the effect of shortened patent life to be mild itself. The industry net revenues and NCEs are virtually unchanged from the baseline case with the 10 percent substitution rate assumption. However, the 50 percent substitution rate results in a much greater impact. The 8-year patent life 50 percent substitution case, in particular, results in a reduction in NCEs to 5.6, from the baseline level of 8.0, and to decline in net revenues to $524 million from $729 million.

Table 3. Simulation of 10 Firms over 50 Years for Alternative Patent Lifetimes and Substitution Rates, Assuming a .10 Probability of Technical Success

		Substitution Rate After Patent Expiration	
		10 Percent	50 Percent
Effective Patent Life of 17 Years	Avg. NCEs	7.0	7.0
	Net Revenues	695	734
	Top 4 Firms' Share	77.0	73.4
	Avg. No. Drops	.3	0
Effective Patent Life of 12 Years	Avg. NCEs	8.4	7.2
	Net Revenues	804	664
	Top 4 Firms' Share	74.9	82.0
	Avg. No. Drops	.3	.3
Effective Patent Life of 8 Years	Avg. NCEs	7.7	5.6
	Net Revenues	713	524
	Top 4 Firms' Share	77.8	77.4
	Avg. No. Drops	.1	.5

Notes:

a. Each experiment was repeated 10 times; hence, values above are averages of the 10 replications.

b. Values generally refer to year 50 with the exception of "Avg. Annual NCEs" which averages years 46—50. Of course, "Number of Firms Dropping Out" refers to the complete 50-year period.

c. Net Revenues equal sales less production and promotion costs and are in millions of 1967 dollars. Market share refers to net revenue share. Industry net revenues in year 1 equal 571.

Table 4. Simulation of 10 Firms over 50 Years for Alternative Patent Lifetimes and Substitution Rates, Assuming a .125 Probability of Technical Success

		Substitution Rate After Patent Expiration	
		10 Percent	50 Percent
Effective	Avg. NCEs	14.7	14.8
Patent	Net Revenues	1281	1222
Life of	Top 4 Firms' Share	70.4	70.9
17 Years	Avg. No. Drops	0	1
Effective	Avg. NCEs	14.0	12.2
Patent	Net Revenues	1179	927
Life of	Top 4 Firms' Share	73.3	74.6
12 Years	Avg. No. Drops	.1	.1
Effective	Avg. NCEs	15.2	9.0
Patent	Net Revenues	1206	668
Life of	Top 4 Firms' Share	71.1	74.3
8 Years	Avg. No. Drops	.1	.5

Notes: See Notes a, b, c of Table 3.

The experiments reported in Table 4 concerning alternative patent terms and substitution rates, under this assumed regime of greater technological opportunity, are qualitatively similar to those reported in Table 3. The appropriate comparisons are now with Column 2 of Table 2. The mild substitution effect, in Table 4, again gives rise to only minor effects of shorter patent lives. However, the 8-year patent life 50 percent substitution assumption of Table 4 shows large reductions in NCEs and net revenues. NCEs fall from 15.5 to 9 and net revenues fall from $1276 million to $668 million. In percentage terms these reductions are larger than those of Table 3, where the probability of technical success was lower.

The results of the simulation experiments in Tables 3 and 4 are consistent with our earlier partial equilibrium analyses of the impacts of the patent and substitution rate variables. In particular, we found a firm's expected returns on R & D were affected in an interactive manner by these variables[10]. Significant impacts on expected returns were observed only when patent terms dropped below 10 to 12 years in value combined with substitution rates of appreciable size. Our analyses here, which involves a more general equilibrium analysis of this same question, indicates that the long run time paths of industry NCE introductions and net revenues are similarly influenced by changes in the degree of imitative competition faced by innovating firms.

In Table 5 we turn to a different experiment. The key parameter here is the efficiency of the FDA regulatory process. The total drug development and regulatory approval period is shortened from 11 years (the baseline case) to 10 and 9 years to examine the impact of FDA efficiency. The results are in accord with expectations. For the baseline case in

Table 5. Simulation of 10 Firms over 50 Years Assuming a .10 Probability of Technical Success and Alternative Reduction in FDA Regulatory Period

		Baseline Case	8 Year Patent, 50 % Substitution Case
Initial Regulatory Period	Avg. NCEs	8.0	5.6
	Net Revenues	729	524
	Top 4 Firms' Share	75.8	77.4
	Avg. No. Drops	.5	.5
1-Year Reduction	Avg. NCEs	9.4	6.8
	Net Revenues	801	548
	Top 4 Firms' Share	76.9	79.9
	Avg. No. Drops	.5	.3
2-Year Reduction	Avg. NCEs	9.8	7.4
	Net Revenues	982	627
	Top 4 Firms' Share	74.7	79.9
	Avg. No. Drops	.1	.3

Notes: See Notes a, b, c of Table 3.

d. The 8-year effective patent life refers only to baseline case. The effective patent life increases to 9 years for a 1-year reduction in approval time, and to 10 years for a 2-year reduction.

the first column of Table 5, NCEs increase from 8 to 9.4 for a one-year reduction, and from 8 to 9.8 for a two-year reduction.

An interesting comparison of the magnitudes involved is provided by the second column of Table 5. That is, the second column refers to the 8-year effective patent, 50 percent substitution case. Given the initial assumption about drug development and approval period length, the 8-year patent cuts NCEs from 8 to 5.6 per year. Now if we also assume a two-year reduction in the FDA regulatory process, we note that this reduction can be largely, though not completely, offset. That is, the last row and column of Table 6 shows NCEs annually of 7.4. Furthermore, this latter value is larger than the 7.0 NCEs observed for the 17-year 50 percent substitution case reported in Table 3. Hence, a two-year "up-front" gain in regulatory approval time is equivalent to several years tacked on to the end of a product's lifetime with respect to the realized innovation levels observed in our model.

Table 6 provides a comparison of the effects of various income tax rates. The baseline case, which was based on actual tax rates of nine firms, translates into a nominal rate of 37.5 percent. For comparison, we used a nominal rate of 46 percent (the legal rate assuming no exclusions, special credits, etc.) and a low rate of 25 percent. The results are as expected, given our assumption about how firms decide on their R & D budgets. That is, with higher cash flows resulting from lower taxes, higher R & D budgets lead to higher net revenues and NCEs. The quantitative effect of the tax rate parameter is in fact quite strong. An increase of the tax rate to 46 percent causes the annual flow of NCEs to

drop by over 20 percent while a decrease in the tax rate to 25 percent causes the flow of NCEs to increase to over 30 percent of the appropriate baseline value. The latter finding, of course, is conditional on the maintenance of a non-diminishing stream of technological opportunity (i.e. a constant probability of technical success and distribution of product sales) despite increasing resources devoted to R & D investment over time.

Table 6. Simulation of 10 Firms over 50 Years Assuming Alternative Nominal Income Tax Rates

		.10 Probability of Technical Success	.125 Probability of Technical Success
Tax Rate of 46 %	Avg. NCEs	5.8	12.1
	Net Revenues	624	1025
	Top 4 Firms' Share	78.0	70.8
	Avg. No. Drops	.4	.1
Tax Rate of 37.5 % (Baseline Case)	Avg. NCEs	8.0	15.5
	Net Revenues	729	1276
	Top 4 Firms' Share	75.8	74.0
	Avg. No. Drops	.5	.2
Tax Rate of 25 %	Avg. NCEs	11.5	20.0
	Net Revenues	932	1655
	Top 4 Firms' Share	67.2	70.1
	Avg. No. Drops	.1	.1

Notes: See Notes a, b, c of Table 3.

Table 7. Simulation of 10 Firms over 50 Years Assuming Alternative Assumptions about the Competitive Effect of New Drugs on Old Drug Revenues

		.10 Probability of Technical Success	.125 Probability of Technical Success
$\alpha = .25$, $\beta = .50$ (Baseline Case)	Avg. NCEs	8.0	15.5
	Net Revenues	729	1276
	Top 4 Firms' Share	75.8	74.0
	Avg. No. Drops	.5	.2
$\alpha = .50$, $\beta = 1.0$	Avg. NCEs	6.3	13.0
	Net Revenues	519	927
	Top 4 Firms' Share	83.5	74.8
	Avg. No. Drops	1.6	.4
$\alpha = 1.0$, $\beta = 1.0$	Avg. NCEs	3.6	5.6
	Net Revenues	281	364
	Top 4 Firms' Share	87.7	83.5
	Avg. No. Drops	2.8	2.7

Notes: See Notes a, b, c of Table 3.

d. α = fraction of new drug revenues removed from old drug revenues.
e. β = fraction of old drug revenues below which no further cuts allowed.

Our final table, Table 7, concerns the assumption about the nature of new product innovation. Our baseline assumption is that for every dollar of new drug sales in a therapeutic category, $.25 of existing drugs' sales in that category are removed. We also assume that once 50 percent of the existing drugs' sales are removed, no further reductions are allowed. This set of assumptions is varied in Table 7. For example, the last row shows the case in which new drugs are viewed as primarily substitutes for existing drugs rather than as net additions to the market. The results are striking. For this latter case, NCEs fall from 8 to 3.6 and net revenues fall from $729 million to only $281 million.

As mentioned earlier, these latter rather strong assumptions—making new drugs complete substitutes for established drugs—have significant negative effects on profitability and lead to a relatively large number of firms dropping out. This, in turn, gives rise to a substantial rise in the top four firms' market share. In effect, the expected lifetime for any new drug introduction is severely curtailed by the sales of future new drug introductions in its therapeutic class, so that R & D investments must be recaptured in a very short time frame. This further increases the risk of bankruptcy (or withdrawal from the R & D game) and leads to increased market concentration over time.

The extent to which new products displace established entities is of course an empirical question. This will vary from product to product and over different time periods. In point of fact, average new product lifetimes have been lengthening over time in pharmaceuticals. The simulation results in Table 7 emphasize, however, the importance of this parameter to firm survival probabilities and market concentration levels.

Concluding Remarks

In this paper we have described a simulation model of a hypothetical pharmaceutical industry that competes through new product innovation. The model is designed to capture many of the characteristics of new product rivalry in the U. S. industry, although we do not claim it to be a forecasting model. The objective of the model is to examine how various policy constraints and technological factors interact to determine the long-run structure and performance of the industry.

It is useful to summarize briefly some of the broad findings of the simulation experiments. First, our results underscore the importance of "technological opportunity" factors in determining the level of new product introductions and net revenue growth over time. In terms of our analysis, we varied the probability of technical success as one key index of technological opportunity. This parameter had a very large multiplier effect on the annual level of new product introductions. Another technological factor with large quantitative implications was the extent to which introductions were market expanding versus redistributive in nature.

While technological opportunity factors have a strong determinative effect on an industry's potential for innovation, economic factors also have an important influence on whether this potential is realized or not. In particular, we examined a number of policy factors which jointly affect the cost and returns to industry R & D and the availability of internal funds for R & D investment. We found that new product introductions were especially sensitive to regulatory and tax policy impacts. Patent terms and substitution rates had a lesser effect on innovation levels, but one that was strongly interactive in nature. These findings therefore suggest the important role that public policy can have in terms of providing a stimulative or repressive environment with respect to the realization of technological opportunities.

There are also clearly a number of interesting directions for further research suggested by this modeling effort. Our analysis here abstracts from several possible strategic interactions that might be fruitfully analyzed in future work. For example, firms might be assumed to pursue an adaptive strategy over time in their R & D budget decision rather than investing a constant fraction of available resources. There are a number of other such refinements of this kind that might be incorporated into future modeling efforts. Nevertheless, the results observed here for the variables investigated (annual flow of NCEs, industry net revenues and market share of the largest four firms) are interesting and generally in accord with intuition. These findings, although preliminary in nature, appear to provide a promising basis for further research.

Notes

1 See, for example, Grabowski and Vernon (1982 a, b)
2 See Nelson and Winter (1982 a, b).
3 See, for example Magnet (1981); Bylinsky (1976).
4 Hansen (1978); also in *Issues in Pharmaceutical Economics,* edited by R. I. Chien, Cambridge, Mass.: Lexington Books, 1979.
5 Details concerning this distribution can be found in Grabowski and Vernon (1982 a).
6 Overall 4 firm concentration ratios for the pharmaceutical industry are in the range of 25 percent. However, we are examining a much more selective industry grouping in our simulation experiments—the new product segment of the research intensive sector. The four largest firms in our research intensive sample of 9 firms accounted for over 60 percent of that group's sales. Also concentration levels within particular therapeutic classes are generally quite high. See Grabowski and Vernon (1982 b).
7 See the discussion of this phenomenon in Scherer (1980); also in Nelson and Winter (1982 a).
8 See D. L. Cocks (1975).
9 Because of the long development and regulatory approval time, the average effective patent time in pharmaceuticals now averages less than 10 years. See in this regard, Eisman and Wardell (1978).
10 See our table on this question in Grabowski and Vernon (1982 b).