

PIONEERS, IMITATORS, AND GENERICS—A SIMULATION MODEL OF SCHUMPETERIAN COMPETITION*

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A computer simulation model in the tradition of evolutionary models of technical change is developed in this paper. It focuses on R&D competition in new product introductions and is based on data for the U. S. pharmaceutical industry during the 1970s. The sensitivity of innovation levels to the rate of generic competition, regulatory review time, and patent life is examined in the computer simulation experiments. These factors are found to have significant long-run effects on industry structure and innovation levels.

I. INTRODUCTION

In this article we describe a computer simulation model of Schumpeterian competition.¹ Our analysis is put forth in the same spirit and has many analytical similarities to the evolutionary models pioneered by Nelson and Winter.² As in their work, we analyze the relative success over time of firms pursuing different decision strategies, but starting from similar initial positions. However, in contrast to their analyses, our study is directed to the case of new product innovation rather than process-oriented productivity shifts. In addition, to motivate interest in this kind of modeling effort, our analysis draws extensively on detailed micro data and empirical experience from the pharmaceutical industry.³ While we utilize this particular industry to structure much of the analysis, it should be emphasized that we are analyzing a hypothetical industry situation—albeit one that hopefully captures some of the main characteristics of competition in R&D-oriented industries like pharmaceuticals.

There are two qualitatively different types of R&D strategic behavior considered in the model: “pioneering” and “imitative”

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1. This article is a major extension in a number of dimensions of the computer simulation model presented at a conference sponsored by the University of Lund, held at Helsingborg, Sweden, in 1982; the proceedings of this conference are available in Lindgren [1984].

2. See, in particular, Nelson and Winter [1982a,b].

3. For a recent analysis of industry structure and competition in the pharmaceutical industry, see our chapter in Nelson [1982a, pp. 283–360] and the survey article by Comanor [1986].

R&D. Pioneering R&D involves the development of a new family of products with the possibility of very significant therapeutic advances and commercial success to the innovating firm. Pioneering R&D thus offers the firm the opportunity for a "big winner," but the technical probabilities of success for such R&D activities are very low. Imitative R&D, on the other hand, involves the investigation of a known family of products with the hope of developing marginal advances in therapeutic quality. Imitative R&D has more modest commercial success possibilities, but also involves less risk because it has shorter development times and higher probabilities of technical success. Imitators can also key their R&D expenditures to the observed successes of pioneering firms, while pioneering firms are subject to much more fundamental technical uncertainties in their R&D allocations.

A third type of competitive strategy is, of course, generic competition. This involves marketing at a lower price a compound identical to one already on the market. Although we do not explicitly model generic firm behavior in this paper, we do analyze its effect on pioneering and imitative R&D through exogenous shifts in the external environment faced by these firms. The degree of generic competition is a key parameter in our model that influences both pioneer and imitative firm sales in the period after patent expiration.

A major objective of our computer simulation experiments is to consider how innovation and industry structure are influenced by changes in the general environment for technological change. We are particularly interested, for example, in how changes in various government policy measures, such as regulatory and patent policies, influence the rate of innovation and the relative position of the different actors in the Schumpeterian competitive process. Another major issue considered in our computer simulation experiments is how changing opportunities for generic competition affects innovation under different policy regimes. This is, of course, the heart of the classic Schumpeterian issue of static versus dynamic efficiency. It is also an important issue for many R&D-oriented industries such as pharmaceuticals.

The next section of the paper describes the model in much greater detail. Section III discusses the computer simulation experiments, and Section IV presents the results of these experiments. The final section presents some concluding remarks and suggestions for further research.

II. GENERAL DESCRIPTION OF THE MODEL

Competition in our model centers around investments in R&D projects. The firms in our model can be characterized as collections of ongoing projects in various stages of the product lifecycle: discovery, development, market life, or removal from the market. Each year, the firm must make various decisions about its portfolio of R&D projects: i.e., whether to continue funding previously initiated projects; whether to start new projects; whether to exit the industry altogether, etc.

R&D projects that are taken to fruition are eligible for a "draw" from a probability distribution to determine whether the product candidate under development is to be marketed. For those projects with successful marketing draws, there is then another draw to determine "product quality," or commercial potential. After market introduction, a new product starts on a path that follows the typical product lifecycle pattern: sharply rising sales and earnings in early years, stable sales and cash flows in the middle years, and decline in the mature years. This pattern, however, is subject to change as a result of subsequent introductions in its particular market segment or "therapeutic category."⁴

The earnings from successful R&D projects are used to fund future new product candidates. Firms engaged in pioneering R&D, faced with long time horizons and highly uncertain returns, plow back a target percentage of their total earnings into R&D, subject to various constraints. Firms engaged in imitative R&D base their R&D expenditures on both expected and realized earnings from R&D. Our model therefore has a strong recursive character and is very Schumpeterian with respect to these assumptions.

We further assume that pioneering firms pursue only pioneering R&D strategies and imitative firms follow only imitative R&D strategies. While this assumption can be relaxed, analysis of polar decision strategies serves to highlight the long-run viability of these alternative strategies in different market environments.

A. The R&D Investment Process for Pioneers and Imitators

Stylized R&D cash flow patterns on the new product introductions for pioneer and imitator firms are shown in Figure I. Both

4. The idea of distinct market segments based on therapeutic use (e.g., anti-infectives, cardiovasculars, etc.) has been employed extensively in the prior empirical literature. See our survey analysis of the market definition question in the Chien [1979] volume.

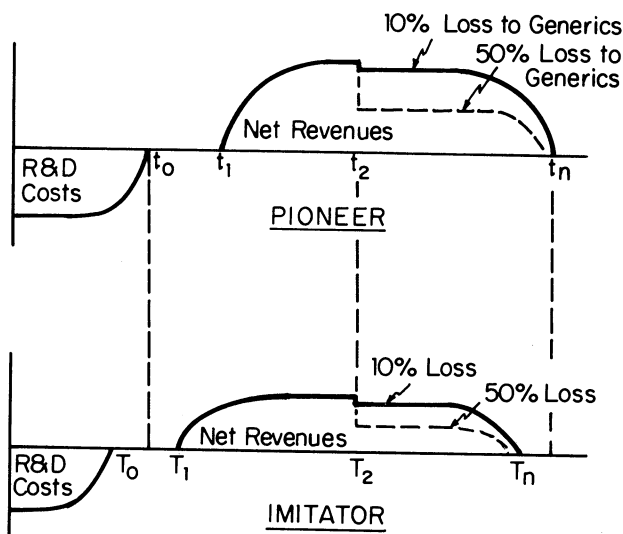


FIGURE I

Comparison of Cash Flows for R&D Investments by Pioneers and Imitators

Notes

a. $t_0 - t_1$ and $T_0 - T_1$ = Regulatory Clearance Times
 t_2 and T_2 = Patent Expiration.

b. The patterns above are *expected* flows at the start of clinical trials. A particular project may be terminated at any stage during R&D. Also for prescription drugs, the net revenues are subject to great uncertainty.

types of firms have qualitatively similar lifecycle patterns: R&D investment, regulatory review, market introduction, commercial sales under patent protection, and patent expiration followed by generic competition. While both kinds of firms go through all of these phases in the same sequence, the expected value of R&D costs and market sales are greater for pioneers than imitators.

Pioneering firms can be viewed as obtaining ideas and leads for new product candidates from scientific research conducted externally to the industry as well as from basic research performed within the firms. A pioneering R&D strategy thus requires a "discovery" phase in the R&D process that imitators do not have to perform. Consequently, the R&D process for pioneers is both longer and costlier. Furthermore, because pioneering R&D is oriented toward the development of compounds with a novel chemical structure, the probability of technical success is lower than that for

imitative R&D. (Specific details on the model's parameters are provided in the Appendix.)

On the output side, pioneering firms face a more highly skewed distribution in terms of market sales potential. In accordance with our empirical work on pharmaceuticals (and more recently, pesticides), most compounds, even those with innovative chemical structures, do not achieve large gains in either clinical efficacy or market sales. At the same time, a small number of compounds can hit the "jackpot" and achieve enormous market success.⁵ The pioneering firm can thus be viewed as a participant in a high stakes game, where the odds of winning on any single project are very small, but the returns to a winner can sometimes be extremely large.

Firms engaging in imitative, or "me too" R&D, have an economic payoff distribution with a smaller expected value and much smaller variance than those doing pioneering R&D. While the imitator definitely faces lower technical risks, it faces the possibility of significant risks as a result of competition from other imitators as well as subsequent new product introductions into its marketing class by pioneering firms. The introduction of a big winner in our model can set in motion a Schumpeterian-like wave of imitation. In other words, there is a possible "crowding out" phenomenon that can occur in the wave of a big winner drug.

B. R&D Competition Across Market Classes

Since we assume that all competition takes place in the context of particular industry submarkets, the allocation of R&D budgets across market categories is a vital micro component of our overall model.

We model this decision by assuming that the ideas of the pioneering firms for new products are primarily generated from the external advance of scientific opportunities and that these are distributed randomly over all product classes. Hence, the odds of a pioneering firm launching a new product in any particular class is assumed to have equal probability across all classes. However, as discussed below, any class that has a major product breakthrough or big winner is assumed to have a temporary "depletion" of the stock

5. See, in this regard, Sections II and III of our NSF Final Report [1983a] and our analysis of pharmaceutical cost and returns in our study published in *Managerial and Decision Economics* [1982]. For a recent analysis of this issue, which also finds skewed returns, see Joglekar and Paterson [1986] and the references cited therein.

of opportunities which prevents that class from having another such winner in the immediately subsequent years.

In contrast to the pioneering firms, imitators target their R&D allocations to therapeutic classes with recent market successes. Hence, their new product launches are a lagged stochastic function of the market introduction pattern of the pioneering firms (with the lags reflecting development and regulatory approval time of imitators). The size of the actual economic payoff for imitative firms is a function of the market sales of the pioneers on which it is targeted as well as the number of competing imitative products coming onto the market in that class over a contemporaneous period.

A key form of interdependence built into the model is that if a pioneering firm is successful in drawing a big winner in a particular therapeutic class, this reduces the probability of another pioneering firm also drawing a second big winner of identical quality in that class in immediately subsequent periods. Specifically, we assume that the stock of technical opportunities is temporarily depleted for that therapeutic category and it takes some time for it to be replenished from R&D conducted by external sources. This is one type of diminishing returns to R&D assumed in the model.

Sales revenues in the model are interdependent in the sense that each firm's new product sales come in part at the expense of established product sales and in part represent an expansion of the total market. In our experiments we assume that the pioneer's new product introductions are more market expanding and less redistributive than the imitator's R&D. Hence, pioneer R&D successes will be a significant determinant of overall industry growth.

C. Total R&D Expenditure Functions

In terms of the total R&D investment budget, pioneering firms plow back a percentage of their net revenues into R&D, subject to constraints on the growth of R&D and the funding of ongoing projects. This assumption reflects the high degree of technical uncertainties surrounding pioneering-type R&D. There is some empirical evidence to support this kind of R&D investment rule.⁶

The pioneers in effect operate with a "target" R&D expenditure to revenue ratio. Firms use the earnings targeted for R&D first to fund ongoing projects and then to initiate new projects. Typically, in periods of rapid earnings growth, a number of new projects

6. See, for example, Caglarcan's doctoral dissertation [1977] and our 1981 paper on the determinants of pharmaceutical R&D and the various references cited therein.

will be initiated. However, a constraint on real R&D expenditure growth is also incorporated to avoid unrealistically sharp increases in R&D from large increases in net revenues.

On the down side, if funds allocated for R&D by pioneers or imitators through the budget 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 retained earnings devoted to R&D in this situation and in effect decrease other outlays (dividends or other expenditures).

The imitator's total R&D investment budget varies over time with the major new product successes of pioneer firms. These successes signal new market opportunities for imitators. When the number of new product introductions with large sales made by pioneers increases, imitators increase their targeted R&D to earnings ratio. Conversely, they decrease it in times of few significant new product introductions. At the same time, adjustments in absolute R&D expenditures are constrained to avoid sharp increases in R&D, as in the case of pioneers.

Our model in effect assumes that major new product launches are influenced to a large degree by external scientific developments, but require significant up-front R&D investment commitments in order for pioneers to recognize and commercially exploit such opportunities. On the other hand, the pace of imitative R&D is largely guided by the observed market successes and more closely resembles traditional economic optimization decisions based on expected returns.

One other decision rule built into the model that deserves comment is the possibility of firm exit. A firm faced with prolonged periods of depressed revenues, because of a lack of new product success, 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 game and terminate its R&D activity. The rule that we employ here is that if the retained earnings initially targeted for R&D drops below 50 percent of what is necessary to fund ongoing projects (in turn requiring a doubling of the R&D to earnings ratio just to fund established projects), the firm stops all R&D activity. 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.

D. Summary of the Model's Key Characteristics

To summarize, the key features and qualifications of the model are listed below.

1. Pioneering firms plow back a fixed percentage of net revenues to finance R&D. Imitators adjust their R&D intensities in proportion to overall profit opportunities, and spend more intensively in more profitable therapeutic categories.

2. Firms "draw" from probability distributions to determine technical success or failure, and then to determine the commercial potential of successes.

3. If firms are unsuccessful in their draws, their net revenues decline. Over some range, R&D to revenues ratios increase to compensate for lower available revenues in funding existing projects. For especially severe cumulative declines, however, the firm will stop R&D and exit the industry.

4. The successful firms find their net revenues and R&D spending rising at an above average rate. Their R&D spending, however, is constrained to annual increases of at most 10 percent.

5. A key factor determining overall industry growth is the rate of new product introductions by the pioneer firms. This is because the new products of pioneering firms are more market expansive and less redistributive than those of imitative firms.

6. There are two kinds of diminishing returns that reduce the returns to R&D as the industry growth rate in new product introduction increases. First, the probability distribution that determines commercial potential is adjusted downward following the introduction of "big winners"—but only temporarily. Second, the degree to which new product sales are redistributive and substitute for existing product sales is subject to change as the industry growth rate in R&D and new product sales exceeds certain threshold levels.⁷

7. Entry by new firms is not allowed. (But "entry" of new products into market segments by existing firms does take place as the profit opportunities in that segment increase. This is the basic competitive mechanism of "imitative" competition discussed above.)

7. Since the firms keep their target R&D to revenue ratio constant for all the experiments discussed in the main part of our analyses, this source of diminishing returns remains a potential rather than operative source of diminishing returns. It would come into play, for example, if firms in the industry decided to increase their R&D to revenue ratios in order to have their revenues grow significantly faster through new products. In order to examine the potential negative effects on growth of an increase in new product cannibalization of existing sales, we examine this issue separately in subsection IV E.

These are the core assumptions of the model. The experiments discussed in the next section consist of changing some policy parameters—for example, patent life—which changes the profitability of R&D and the future growth opportunities for pioneer and imitator firms. We want to observe the consequences in turn for industry innovation and other variables of interest. The model is run over several periods to examine what happens to these variables with the new policy parameters.

One important point to note about the experiments is that the target R&D to revenues ratio for pioneering firms is held constant across the experiments in which different policy parameters are altered. Hence, for example, if patent life increases in a particular experiment, this does not result in an increase in the target R&D to revenues for pioneer firms, even though there may be a plausible rationale *ex ante* for these firms to believe that their returns on R&D have increased. The imitator firms do adjust their R&D to revenues ratio in an adaptive lagged fashion based on the performance of the pioneer firms.

The reason that we have assumed fixed R&D to revenues ratios as opposed to adaptive R&D strategies is basically methodological in nature. In this regard, constant R&D to revenue rules for the pioneering firms mean that changes in the returns to R&D and differential growth rates across these firms induced by the assumed policy changes (rather than adaptive feedback effects on R&D strategy) will be the key driving forces in the model influencing industry innovation and other variables. This is the factor that we wish to direct our attention to in the experiments presented in the next section.

In addition, it should also be noted that the changes in policy parameters being considered generally have a marginal effect on the expected returns to R&D for pioneer firms. While some of the changes in policy variables considered below do involve a significant departure from historical experience, their expected effects on rates of return on R&D generally are in the range of only a few percentage points.⁸ Since the inherent uncertainty arising from externally

8. Internal rates of return were computed for a sample of the data generated, and indicated that the variation across experiments was relatively small. For example, the rate of return for pioneers for the baseline case in Table III was 9.8 percent. A one-year reduction in FDA time, an experiment in Table III, produced an 11.0 rate of return. However, because of the length of the product lifecycle, the number of years of data that could be used was severely restricted. For example, most of the calculations involved projects beginning in years 11–14 and ending, respectively, in years 47–50. This led us to view the observed values on the rates of return somewhat skeptically. However, the analysis was sufficient to give us a general feel for the sensitivity of returns to the experimental shifts in the policy variables.

determined technological opportunities is likely to dominate these changes for pioneering firms, large shifts in their R&D to revenues plowback rule would not be expected from the experimental changes in the policy variables analyzed here. However, the reader should keep the constant R&D to revenue assumption in mind when interpreting the results presented below. For very large changes in several policy parameters, adaptive changes in R&D decision rules might be logically expected. This could be incorporated into the model in future work.

A more detailed description of the model is presented in the Appendix. At this point the reader should have a basic appreciation of the main components of our dynamic computer simulation model of R&D competition in pharmaceuticals. Further understanding of the simulation experiments should become apparent from our discussion below.

III. THE NATURE OF COMPUTER SIMULATION EXPERIMENTS

Our experimental runs incorporate parameter estimates for R&D costs, technical and commercial success probabilities, sales revenue distributions, and other parameters that are representative of the pharmaceutical industry during the decade of the 1970s. Furthermore, the baseline case of our model includes values on the environmental and policy-determined variables that are also representative of the 1970s. The Appendix provides a discussion of parameter estimation.

The main policy variables that are analyzed in the simulation experiments are regulatory review times, patent life, and the degree of sales loss to generics after patent expiration. These variables are depicted in the stylized R&D cash flow patterns for pioneers and imitators previously shown in Figure I. In particular, regulatory review time for pioneers is given by $t_0 - t_1$, patent life by $t_1 - t_2$, and the degree of generic competition by the percentage loss in sales after patent expiration.

Based on our previous empirical analysis of R&D investment patterns in pharmaceuticals, we assume that the average discovery phase for pioneers is three years in length, followed by a development period of eight-plus years (which includes a regulatory review period of 28 months). Since only pioneers have to perform discovery research, this implies an effective patent life, on average three years shorter for pioneers than for imitators. Consistent with this fact, we

assume in the baseline case that patent life for pioneers is equal to eight years and for imitators it is equal to eleven years.⁹

After patent expiration, we further assume for the baseline case a loss of sales to generic competitors of 5 percent (in dollar terms) in the first year and 10 percent in all subsequent years of market life. This is roughly consistent with the findings of a study done by Statman [1981] of patent expirations in drugs over the period 1970 to 1978.

Our first set of computer simulation experiments compares the baseline case, based on data representative of the 1970s, with a world of much greater expected generic competition (reflective of the way the pharmaceutical industry is currently developing in the 1980s).¹⁰ In particular, our first deviation from the baseline case assumes that the average expected loss to generics will be 50 percent (25 percent in the first year) after patent expiration.¹¹ The effects of this change on cash flows of pioneers and imitators are shown by the dashed lines in Figure I. In short, we are interested in how the rate of innovation will change in a world of increased generic competition and how other aspects of industry performance evolve over time.

As one can see from the lifecycle pattern illustrated in Figure I, increased generic competition reduces the returns to R&D and the cash flow available for new R&D investment projects. The size of the resulting impact on industry innovation levels will depend importantly on how the returns to R&D of the pioneer firms are affected. This in turn will be sensitive to the patent lifetimes. With very short patent exclusivity periods (e.g., less than five years), sharp increases in generic shares can be expected to produce large negative impacts on the R&D returns of imitators. As patent life

9. Average effective patent times for pharmaceuticals during the 1970s are examined in Eisman and Wardell [1981]. They found the average effective patent life on all new introductions in 1979 was 9.5 years (midway between our estimates for pioneers and imitators). In addition, there was a strong downward trend evident over time.

10. The factors encouraging generic usage in drugs include the repeal of state anti-substitution laws, the spread of reimbursement programs for limiting payments to the lower priced drug alternatives, the growth of health maintenance organizations, and the increased promotion of generics by discount pharmacies. In addition, a recent law restoring some of the lost patent life for innovations on future new product introductions also has a provision that makes it easier for generic competitors to obtain regulatory approval without additional safety or efficacy testing. This is a change from past practices. See Grabowski and Vernon [1986].

11. In our 1986 paper we found that the rate of sales loss to generics by major brand products coming off patents in recent years has increased significantly. For example, Indocin, a leading anti-inflammatory drug lost 50 percent of its market by the second year of generic availability while Valium and Inderal lost 25 percent of their sales within the first quarter of generic availability.

increases, however, the negative effect of increasing generic competition on R&D returns can be expected to moderate and become relatively insignificant for patent lifetimes that approach the nominal life of seventeen years. The patent life assumed in our baseline case—eight years—would appear to be in the midrange in this regard. It is short enough so that significant impacts on industry innovation levels might be expected to be observed from increased sales gains by generics, but not so short that R&D returns for the pioneering firms are likely to be drastically reduced or pushed into the negative range.

Another point to note from Figure I is that increased generic competition reduces the cash flow of pioneering drugs more than imitators, given the former's longer R&D investment periods and shorter effective patent lives. This will be true even if sales losses to generics are comparable in percentage terms for pioneers and imitators. However, it may be more realistic to assume that sales losses of pioneers will be greater in percentage terms given their larger market shares and higher implicit profit margins compared with imitative products. Some different scenarios in this regard will be considered in our computer simulations.

One of the policy measures recently instituted by Congress to provide innovation incentives for pharmaceuticals, food additives, and medical devices is a restoration of some patent time lost during the pre-market regulatory period.¹² Hence, this is also an interesting issue to analyze in our simulation experiments. The effect of increased patent protection on the cash flow of pioneer firms is illustrated in the upper panel of Figure II. The gain in cash flow from patent restoration is shown by the hatched area. It is a roughly rectangular area equal to net revenue loss to generics times the length of patent restoration. As discussed above, increased patent life can be expected to moderate the effects of generic competition on the returns to R&D of innovators. At the same time, one would also expect that patent restoration effects on industry innovation levels to be subject to diminishing returns as one increases the length of life significantly beyond baseline values. In order to gain

12. The Drug Price Competition and Patent Restoration Act was passed in September 1984. Its provisions are published in the Congressional Record S10981-S10990 (Sept. 12, 1984). This Act restores for future new drug introductions some of the patent time lost during the clinical testing and regulatory review period. At the same time, it facilitates generic competition after patents expire by making entry relatively easy for generic products. For an initial analysis of the laws of economic effects, see Grabowski and Vernon [1986].

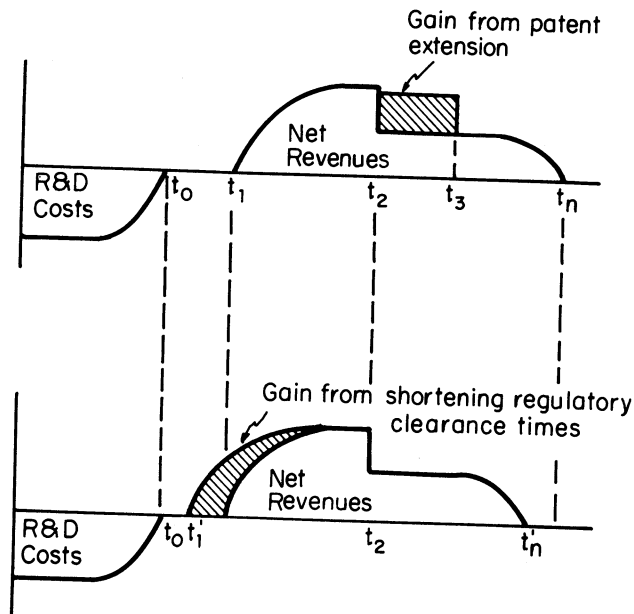


FIGURE II
Effects of Alternative Policies on Cash Flows of Pioneers

Notes

$t_2 - t_3$ = Patent Life Extension

$t_0 - t'_1$ = Reduced Regulatory Clearance Time.

insights into this issue, we focus on patent life increases of three and six years in our experiments.¹³

Another policy action that can significantly affect innovation incentives in industries subject to pre-market regulatory approval is reduced regulatory clearance times. In the lower half of Figure II the effect of reduced regulatory clearance times on the sales revenues from R&D is illustrated. Reductions in regulatory clearance times largely increase the effective patent life. However, in contrast to patent restoration, they also increase cash flow up front in the product life cycle. As a result, returns on R&D are signifi-

13. The Bill passed by Congress would increase the patent life for future new drugs up to five years using a formula based on the length of the regulatory testing and review periods. There are also other constraints on the length of patent restoration permitted. See our 1986 paper on this issue.

cantly enhanced, and firms will also have opportunities to fund new R&D projects sooner and to experience greater growth over time compared with equivalent gains in net revenues from patent restoration. As a consequence, one might expect a year of total reduced regulatory review time to have a much more significant effect on innovation levels compared with a year of increased patent life. In the experiments we consider regulatory lag reductions of one and two years in value.¹⁴

One might also expect reductions in regulatory lags to have a proportionately greater effect on the cash flows of pioneering products compared with imitative ones. This follows from the fact that the cash flows of pioneering firms are more concentrated in the first half of the lifecycle than for imitative products. Hence, it is reasonable to postulate that reduced regulatory lag would tend to benefit the relative position of firms pursuing pioneering R&D strategies versus imitative ones. This hypothesis will be considered in the experiments.

In sum, regulatory review time, patent life, and the extent of generic competition are factors that are currently undergoing change for the pharmaceutical industry (and other R&D-oriented industries subject to pre-market regulatory approval). Hence we think our experiments should offer insights into the sensitivity of R&D and innovation levels to prospective changes in these factors. It should be kept in mind, however, that our model is basically of a hypothetical industry, with some of the parameters based on empirically observed values of pharmaceuticals, rather than a literal model of the U. S. pharmaceutical industry. Hence, we are primarily interested in seeing whether the experimental outcomes exhibit the general properties outlined above and are not overly concerned with the exact values that emerge from the experiments.

IV. COMPUTER SIMULATION EXPERIMENTS

A. *The Baseline Case*

A key issue is how to "initialize" the model. In the simulation runs analyzed in this paper, we assume that the industry initially

14. As discussed above, the average new drug in the United States took over two years to gain approval during the 1970s. The FDA has recently begun to implement a number of procedures to try to streamline the regulatory review process. This includes parallel review of new drug applications by several divisions, time deadlines for such reviews, etc. The FDA is also looking into various changes in its regulatory procedures at the clinical testing stage with an eye toward speeding up this part of the process. Their goal is to reduce regulatory review times by at least six months and to shorten regulatory-induced delays in the clinical period by comparable amounts. For a discussion of these procedural changes, see Grabowski and Vernon [1983b].

TABLE I
 BASELINE CASE—TEN PIONEER AND TEN IMITATOR FIRMS

	Year 1	Year 50 ^a
1. Net sales revenues—industry (mil. \$) ^b	1,144	2,320
2. Leading 4-firm market share (%)	20	42
3. Market share—pioneers (%)	50	56
4. Market share—imitators (%)	50	44
5. Total R&D outlays—industry (mil. \$)	320	609.6
6. Average R&D outlays—pioneers (mil. \$)	16	32.5
7. Average R&D outlays—imitators (mil. \$)	16	28.5
8. Annual introductions—industry	21.0	33.9
9. Annual introductions—pioneers	6.0	10.9
10. Annual introductions—imitators	15.0	22.9

a. Each experiment was repeated 10 times; hence, values are averages of the 10 replications. Values in column 2 are for year 50 with the exception of "Introductions," which averages years 41–50.

b. Net Revenues equal sales less production and promotion costs and are in millions of 1967 dollars. Market shares refers to net revenue share.

consists of twenty equal sized firms—ten firms doing only imitative R&D and ten firms doing pioneering R&D. 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 performing R&D for projects in various stages of the development process.¹⁵

The first row of Table I summarizes the initial conditions in year 1 for each computer simulation run. There are 20 equal sized firms with net revenues of 57 million dollars each in the first period. Hence, our 20-firm industry has total net revenue of just over 1 billion dollars in year 1. Total R&D expenditures for pioneer and imitative firms are initially equal to 16 million dollars (28 percent of net revenues). There is also an expected value of twenty-one new introductions annually based on the number of projects in progress—six new products from pioneering firms and fifteen from imitators.

The second column of Table I shows the outcomes of our simulation model for the baseline case after 50 years have elapsed. Given the fact that product lifecycles span several decades in industries like pharmaceuticals, we choose a period this long in

15. To obtain a representative set of values for the initialization of our model, we analyzed the financial data and new drug introductions of nine large U. S. drug firms. 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 firms (in terms of net sales revenues and R&D expenditures) in the year 1970.

order to be able to observe potentially significant shifts across each market class. Each experiment was also replicated ten times, and the values in Table I are the means of ten replications.¹⁶ Several interesting characteristics are worth noting. First, industry net revenue increased in real terms over the 50-year period from 1.14 billion to 2.32 billion dollars. This implies a real annual growth of 1.4 percent from the introduction of new products. (The model abstracts from other sources of market growth such as population increases, demographic changes, etc.)

With respect to the distribution of market shares, the average market share of the pioneers is significantly larger than that of the imitators in year 50 (56 to 44 percent). This reflects the higher rates of return on R&D for pioneers compared with imitators under the baseline set of assumptions.¹⁷ At the same time, imitators have a greater number of annual NCE introductions, but these have a much smaller average sales than those of the pioneering firms. The pioneering firms also perform higher aggregate R&D expenditures in year 50, consistent with their larger market shares and revenues.

A second characteristic of the baseline case is that the market share of the top four firms rises from 20 percent to 42 percent. Some tendency toward increased concentration is typical of other simulation studies involving investments in projects with variable outcomes. In particular, some firms can be expected to "draw" the more profitable introductions 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 throughout the 50-year period.

In order to convey some insight into the behavior of individual firm performance, we have selected randomly four pioneers from one computer run. The four firms were those that ranked first, fourth, sixth, and tenth in net revenues in year 50. Figure III plots the net revenues of the four firms over the 50-year period. While industry net revenues aggregated over all firms and over all runs are generally stable, it is clear from the figure that the performance of individual firms are subject to considerable variability. This reflects the skewed nature of R&D outcomes assumed in this model.

16. The choice of ten replications reflected a tradeoff between further reduction in the standard error of the mean estimates and higher computer costs. This issue is discussed in our earlier paper presented at the Helsingborg Conference (see footnote 1).

17. For one subset of years sampled the rate of return for pioneers was 10.5 percent and for imitators was 10.1 percent. See footnote 8 for a discussion of how these rates of return were calculated, and various qualifications.

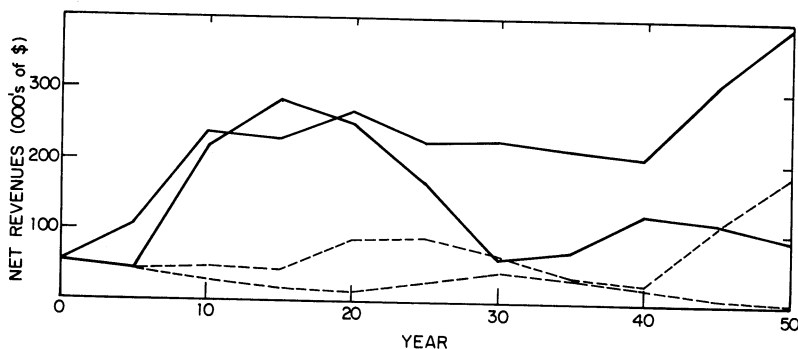


FIGURE III
Net Revenues for Four Pioneers

B. Changes in Generic Competition after Patent Expiration

Our next set of experiments analyzes alternative scenarios regarding the degree of generic competition an innovator confronts after patent expiration. As discussed above, our baseline assumptions on generic competition more or less reflect recent experience in pharmaceuticals—a moderate loss of sales after patent expiration, in the range of 10 percent. Assuming that the future environment will witness much more competition from generics, we now analyze some scenarios that reflect this possibility.

In Table II, we report the results of a simulation experiment that assumes a 50 percent loss in sales to generics in the post-patent period. This compares with the only moderate sales loss to generics made in the baseline case. The assumption on effective patent life for pioneer and imitator firms (eight and eleven years, respectively) is maintained in this new simulation run.

As one can see immediately from this table, the rate of innovation and other performance variables in our model are highly sensitive to this assumed increase in the degree of generic competition. Industry revenues and R&D expenditures are reduced by approximately 30 percent and new product introductions by 20 percent compared with the baseline case. (The latter is reproduced in column 1 of Table II for purposes of comparison.) All of these variable changes are statistically significantly at normal confidence intervals.¹⁸

While the experiment analyzed in Table II assumes comparable sales losses (in percentage terms) by both pioneer and imitative

18. The statistical test used was the standard test for the difference of two sample means, where each sample was of size ten.

TABLE II
THE EFFECTS OF INCREASED GENERIC COMPETITION IN THE POST-PATENT PERIODS

	Alternative assumptions ^a		
	10% sales loss to generics after pat. exp. (baseline case)	50% sales loss to generics after pat. exp.	60% for pioneers 40% for imitators after pat. exp.
1. Net sales rev.—industry (mil. \$)	2,320.	1,647.* (-29.0)	1,519.* (-34.5)
2. Leading 4-firm market share (%)	42.	41.	41.
3. Market share—pioneers (%)	56.	54.	51.
4. Market share—imitators (%)	44.	46.	49.
5. Total R&D outlays—industry (mil.\$)	609.6	431.3* (-29.2)	388.5* (-36.2)
6. Average R&D outlays—pioneers (mil.\$)	32.5	22.6	18.9
7. Average R&D outlays—imitators (mil.\$)	28.5	20.6	19.9
8. Annual introductions—industry	33.9	26.9** (-20.6)	25.6* (-24.5)
9. Annual introductions—pioneers	10.9	9.0	7.0
10. Annual introductions—imitators	22.9	17.9	18.5

a. Numbers in parentheses for variables in rows 1, 5, and 8 are percentage changes from the baseline case in column 1. Tests of statistically significant differences from the baseline case were also calculated for these variables. A single asterisk indicates significance at the 1 percent level, a double asterisk indicates the 5 percent level, and a triple asterisk the 10 percent level.

In the first year after patent expiration, the loss to generics is assumed to be one half that for the remaining periods (which is shown in the column headings).

(Also see notes to Table I.)

firms after patent expiration, it is probably more realistic to expect that the sales losses of pioneer products to generic competition will be greater. This is because these products command larger market shares and implicitly enjoy higher profit margins. As a consequence, they are a more attractive target to generic firms.

In column 3 of Table II we assume that the sales loss two years after patent expiration will be 60 percent for pioneer firms and 40 percent for imitative firms. This assumed difference, of 20 percent, which actually may be quite conservative, leads to greater observed relative declines in the R&D expenditures and net revenues of the pioneering firms. These values can be expected to diverge further as the assumed impact of generic firms is concentrated more heavily on the pioneer firms because their returns to R&D are disproportionately affected.

The observed negative impact of generic competition on innovation levels is consistent with the characteristics of the R&D process shown in Figure I. In particular, one has long gestation periods and high up front R&D costs coupled with moderately short patent lives. As a consequence, increased generic competition sets in relatively early in the product lifecycle and results in lower cash flows and rates of returns on new product introductions. This, in turn, also means that fewer R&D projects are initiated by pioneers and imitators and the compound rate of growth is correspondingly reduced over the 50-year period.

In interpreting these results, two qualifications of our model that work in opposite directions should be borne in mind. First, the pioneers' target R&D to revenue ratios are held constant over the different experimental scenarios. An adaptive R&D to revenue assumption (with target ratios adjusting to expected returns) would necessarily result in larger declines in innovation than those observed in Table II. At the same time, we assume that the character of R&D projects undertaken by pioneer firms are unaltered at reduced plowback levels. In other words, pioneer firms in our model are assumed to be unable to forecast *ex ante* the returns from particular R&D projects; hence, they are unable to screen out the marginal projects when reducing R&D outlays. Relaxing this assumption and allowing them to do so would reduce the negative impact on innovation associated with increased generic competition observed in Table II.

Keeping these qualifications in mind, the results in Table II are still suggestive of significant long-run tradeoffs between dynamic and static measures of industry performance. Compared with the

baseline case, the implicit generic "fringe" of the industry has expanded severalfold by year 50 under the assumptions in columns 2 and 3 of Table II. Increased generic competition clearly brings significant benefits to consumers in the form of lower prices for established products as well as lower effective industry concentration levels. At the same time, the rate of innovation by pioneering firms is reduced, and we have lower rates of new product introductions and growth for the industry as a whole. While we are not in a position to evaluate this classic Schumpeterian tradeoff from a welfare perspective, the results in Table II suggest that the tradeoff will be quantitatively significant for the representative parameter values utilized in this analysis.

As discussed above, two policy measures that will affect the tradeoff between generic competition and innovation are changes in effective patent life and regulatory review time (as shown in Figure II). We now turn to an analysis of these policies.

C. Changes in Effective Patent Life

As noted above, Congress has recently passed legislation that restores some of the patent time lost because of regulatory-induced delay in marketing for industries like pharmaceuticals that are subject to pre-market approval. Our objective here is to see how sensitive innovation rates are to patent term restorations of the magnitude allowed by the new legislation.

Accordingly, in Table III we treat the case of a 50 percent sales loss to generics as a new baseline case. We then assume that patent life has increased by three years for both pioneer and imitative firms (i.e., to eleven years for pioneers and fourteen years for generics).¹⁹ (Column 1 of Table III displays for purposes of comparison the new baseline case, which is identical to column 2 in Table II.)

The outcomes in Table III indicate that a three-year extension in effective patent life restores much of the reduction in innovation and revenues previously observed as resulting from increased generic competition. In particular, industry R&D and net revenues increase by over 20 percent relative to the baseline case shown in column 1. Approximately three-fourths of the losses observed in

19. The three-year extension assumed here is consistent with a retrospective analysis of actual new product introductions for the pharmaceutical industry over the period 1976 to 1981. If this new legislation had been in effect at the time that these new introductions had entered clinical trials, we found their effective patent life would have been extended an average of 2.9 years under the new legislation. See Grabowski and Vernon [1986].

TABLE III
THE EFFECTS OF PATENT EXTENSION AND SHORTENING REGULATORY CLEARANCE TIMES IN A REGIME OF INCREASED GENERIC COMPETITION

	50% Sales loss to generics after patent exp. (baseline case)	Three-year extension in patent life ^a	Six-year extension in patent life ^a	One-year reduction in FDA times ^b	Two-year reduction in FDA times ^b
1. Net sales revenues—industry (mil.\$)	1,647.	2,031.*** (23.3)	2,158.* (31.0)	2,133.** (29.5)	2,341.* (42.1)
2. Leading 4-firm market share (%)	41.	46.	44.	42.	46.
3. Market share—pioneers (%)	54.	55.	55.	57.	58.
4. Market share—imitators (%)	46.	45.	45.	43.	42.
5. Total R&D outlays—industry (mil.\$)	431.3	527.5*** (22.3)	572.8** (32.8)	568.9** (31.8)	649.6* (50.6)
6. Average R&D outlays—pioneers (mil.\$)	22.6	28.6	31.4	30.9	37.7
7. Average R&D outlays—imitators (mil.\$)	20.6	24.1	25.9	25.9	27.3
8. Annual introductions—industry	26.9	31.2*** (16.0)	32.8** (21.9)	32.6** (21.1)	35.0** (30.1)
9. Annual introductions—pioneers	9.0	10.0	11.2	11.3	12.1
10. Annual introductions—imitators	17.9	21.2	21.7	21.3	22.9

a. The three-year extension in patent life is from the baseline value of 8 years for pioneers and 11 years for imitators. A similar argument applies to the six-year extension.
b. The one-year reduction in regulatory time results in products being introduced into the market one year sooner and, hence, also implies a one-year increase in effective patent time. A similar argument applies to the two-year reduction.
(Also see notes to Tables I and II.)

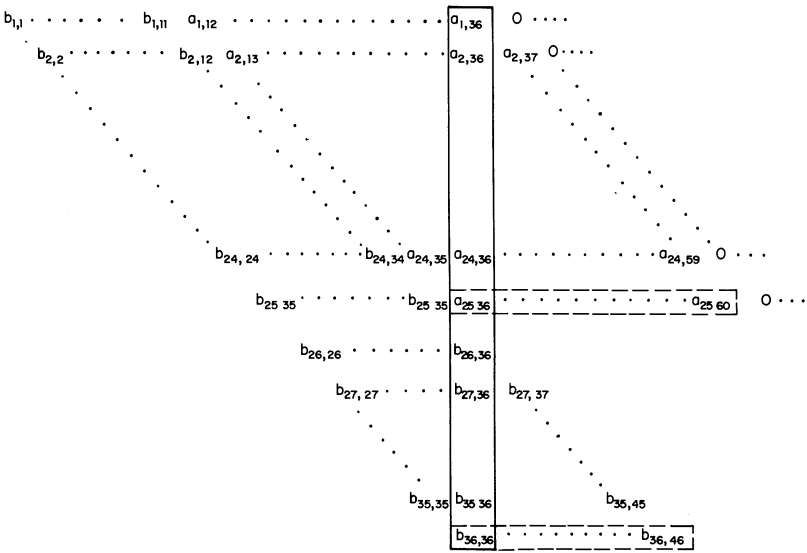


FIGURE IV
Matrix of Net Revenues and R&D Expenditures for a Pioneer Firm

Notes

- a. a_{ij} = net revenues of firm from NCE's of vintage i in year j
- b. b_{ij} = R&D expenditures of firm on NCE's of vintage i in year j .

these variables are thus restored by a three-year increase in patent life. Furthermore, the relative position of pioneers and imitators is left virtually unchanged.

Overall, these results suggest that patent life extension can significantly influence the rate of innovation. Our results also suggest, however, that the positive effects on innovation of increasing patent life are subject to sharply diminishing returns. In column 3 of Table III we consider the case of a six-year increase in patent life for pioneer and imitative firms. There is a positive increase in both industry revenues and R&D expenditures compared with the three-year patent extension case in column 2, but it is very small. This indicates that the positive stimulus of increased patent life is disproportionately concentrated in the early years of the product life and relatively little is gained in terms of the stimulus for innovation by extending effective patent life to approach the full nominal value of seventeen years (given the other parameter values assumed in our simulation).

This diminishing returns phenomenon observed here reflects two interrelated factors: first, the reduced effect on the returns to R&D of adding fixed revenue dollars at later intervals in the product cycle; and second, the gradual fall off in the level of revenues that occurs over the product cycle as a product matures due to new product entry. Hence restoring patent life well into the product life results in both smaller cash flows and reduced growth potential for research-intensive firms.

D. Changes in Regulatory Clearance Times

Another potential way of reducing the tradeoffs between static and dynamic performance would be greater "efficiency" in the regulatory review process.

Our next set of experiments examine the effect of reduced regulatory clearance times on industry revenues and innovation levels. In particular, columns 4 and 5 of Table III report the outcomes for experiments in which regulatory clearance times are shortened by one and two years, respectively. We assume in this analysis that the costs of discovery and development are unchanged and that the review process at the end is shortened by one or two years. This is an oversimplification but is a generally conservative way of modeling the effects of regulatory changes discussed above.²⁰ As in the analysis of changes in patent life, we consider this change in a regime of rapid generic competition (i.e., 50 percent substitution rates after patent expiration).

The results in Table III indicate a strong sensitivity of innovation levels to changes in regulatory clearance times. Indeed the one-year reduction in regulatory review-time causes an approximately 30 percent increase in industry revenues and R&D outlays. There is also some tendency for reduced regulatory times to disproportionately benefit pioneer firms as reflected in the market share figures in Table III. The results in Table III also indicate diminishing returns in moving from one to two years reduction in review times, but much less severe than observed in the case of patent life extension. The differences in values observed for revenues, R&D expenditures, and introductions are all statistically significant in moving from one- to two-year reductions in review times. This is not true, however, when moving from three- to six-year increases in effective patent life.

20. In particular, we assume that all reductions in regulatory delays, whether they occur during the clinical testing period or the review period, are realized during the end of the development period when regulatory review takes place.

In sum, reductions in regulatory approval times, because they increase effective patent life as well as the cumulative sales realized throughout all the earlier years of the product lifecycle, have powerful economic effects on the rate of innovation and the position of innovators in our model. Moreover, our experiments indicate that the stimulative effects on innovation of a year reduction in regulatory approval times is approximately equivalent to five to six years of increased patent life. This latter finding is perhaps surprising in view of the plowback character of R&D investment inherent in the present model. However, if a firm is able to increase its cash flow at the beginning, rather than the middle, or end, of its lifecycle, it is able to initiate new projects sooner and also realize returns on them sooner. Over time, this leads to a compounding effect on industry revenues similar to other economic models of growth.

One final point is that increased patent life and reduced regulatory times are not mutually exclusive. We have analyzed them independently here in order to gain insights into their relative effects on innovation levels. In particular, patent restoration by design is supposed to compensate for time spent in regulatory review. Hence, any reductions in review time achieved through more efficient regulatory procedures will operate to reduce the amount of patent time extension (and vice-versa). Our results suggest, however, that the effects of reduced regulatory review times will significantly outweigh equal time changes in effective patent life operating in an offsetting direction. Hence, the potential "drag" on the stimulus to innovation from regulatory reform due to offsetting change in patent life should be minimal in nature. This was confirmed by examining some cases experimentally in which this interactive nature between these policy variables was specifically considered.²¹

E. Additional Experiments

While the main focus of our simulation experiments has involved an analysis of the factors enumerated above —i.e., generic competition, patent life, and regulatory review times—we also performed some additional experiments to test the robustness of our findings to the initial conditions and parameter specifications. In this section we consider the sensitivity of our findings to the number of firms participating in the industry, to the extent to

21. In this regard, we found that a two-year reduction in regulatory review time coupled with a two-year loss in patent life still resulted in significant gains in industry revenues and R&D levels. These were in excess of 30 percent or approximately three-fourths of that observed from regulatory reduction alone.

which new product sales are market expanding versus redistributive in nature, and to the "richness" of technological opportunities. These additional simulations also suggest some interesting directions for future research.

In terms of the number of firms, we examined the alternative of an industry starting with ten firms rather than the twenty assumed above. These were evenly divided between pioneers and imitators as before. The model was stable to this change of specification, and the results were similar to those in Tables I through III.

Our next sensitivity test relates to the extent to which new products are market expanding or redistributive. This is governed by a parameter α that equals the fraction of new drug revenues that "cannibalize" existing drugs in a therapeutic category. For example, $\alpha = 0.25$ means that a new drug introduced with revenues of \$100,000 would cause \$25,000 of revenues of competitive drugs to be lost.²²

This parameter plays an important role as a potential source of diminishing returns in our model. In particular, consider the case where the firms in an industry decide to increase their R&D outlays relative to their revenues in order to grow faster through new product innovation. One would expect α to increase in these circumstances. The idea, of course, is that a significant increase in new product introductions in any given time span is likely to result in increased duplication of therapeutic properties and therefore increased cannibalization of the products marketed.

To illustrate the quantitative impact of this parameter, α was increased from its value in the baseline case of Table I by 20 percentage points. The result was a 28 percent decline in net revenues and a 23 percent decline in annual introductions. The negative effects of an increase of α on the returns to R&D are therefore quite large.

For our next sensitivity test, we modeled increased technological opportunities by assuming a greater likelihood of major therapeutic advances compared with the distribution based on the 1970s. This scenario produced results qualitatively similar to the findings obtained in Tables II and III, but with much higher rates of growth in R&D, new product introductions, and revenues. With the research-oriented firms on higher growth paths, the negative effect on innovation of increased generic competition is also greater (in

22. This description oversimplifies the exact mechanism employed in the computer programs. Also, separate values of α for pioneers and imitators are used. A more detailed exposition is contained in our paper in Lindgren [1984].

absolute terms). The implicit tradeoff between dynamic and static competition is thus accentuated by an increase in technological opportunities.

There are some additional considerations, however, relative to this scenario. If an industry were to experience a significant positive structural shift in technological opportunities, one might also expect new entry into the industry. This possibility of entry, particularly into specific segments of the industry experiencing rapid technological advance, is an interesting institutional phenomenon that might be fruitfully studied in future research.²³

An alternative scenario that we also investigated was the possibility of a declining industry situation based on reduced technological opportunities. The previously reported findings hold qualitatively for the reduced technological opportunities case as long as the industry returns from R&D are positive. If industry returns becomes negative, however, the industry enters a declining growth phase. In this situation there is an increased probability of firm exits, and the industry evolves over time to a smaller size with fewer R&D projects and new product introductions.²⁴

In addition to these experiments, we also examined the stability of our findings to other changes in initial conditions. In general, the results were stable so long as the parameters do not depart radically from historical values.²⁵

V. CONCLUSIONS

In this paper we have performed various experiments using a computer simulation model of Schumpeterian competition. While the model is intended to be exploratory in nature, we have utilized data from the pharmaceutical industry extensively in specifying the

23. One segment of the pharmaceutical industry that has experienced entry in recent years in response to new technological developments is the biotechnology area. So far entry has been mainly in the form of small venture capital firms into the discovery and research phases of the R&D process. See Chapter 4 of the OTA study [1984] on commercial biotechnology for a discussion of biotechnology firms active in the drug area.

24. One interesting finding observed for the declining industry case concerned the relative behavior of pioneer and imitator firms. Because the latter are more responsive to market returns, they begin cutting back R&D projects well in advance of pioneers. On the other hand, pioneers are engaged in long-term R&D and do not respond to low observed returns until the threat of bankruptcy becomes large. Hence, our declining industry model is also characterized by a relative decline in the R&D efforts and market position of imitators versus pioneers. This, of course, is only one possible dynamic path in a contracting industry situation, but one that highlights the different decision horizons between pioneers and imitators.

25. We examined the sensitivity of our findings to the R&D revenue targets for pioneer and imitators and the constraints on R&D growth over time.

model's relationships and parameters. We have also focused on a set of conceptual and policy issues that are relevant currently to the pharmaceutical industry as well as several related R&D-oriented industries.

In common with many other studies of Schumpeterian competition, our study suggests that a significant long-run tradeoff exists between dynamic and static competition. Our computer simulation experiments further indicate that this tradeoff is quite sensitive to policy-determined variables such as the length of patent exclusivity periods and pre-market regulatory review times. Hence, there appears to be considerable scope for policymakers to influence the terms of the classic Schumpeterian tradeoff when making decisions that are ostensibly directed to other concerns (such as regulatory review procedures).

The results of this computer simulation approach are preliminary in nature and caution should be exercised in applying them to particular current policy issues. The model is based on a number of strong assumptions. These include the fact that (1) the initial number and size distribution of pioneer and imitator firms is selected arbitrarily; (2) the duration of the R&D process is fixed; (3) the R&D expenditures of pioneer firms are based on a simple plowback decision rule; (4) no entry occurs from outside the industry; and (5) activities and practices in other countries are not considered.

There are a number of potentially interesting directions for further research. One such direction might involve the intensive modeling of a single firm or small group of firms from the perspective of an evolutionary model. We are currently investigating this possibility.

APPENDIX

In this appendix we turn to a more specific description of the simulation model. Since the computer program consists of some 1,800 statements, we can describe only the key features of the model here. Our description is mainly concerned with a pioneer firm, but we shall indicate how an imitator firm differs, as appropriate.

The Discovery and Development of New Products

First, we have what could be termed an "R&D production function." This relates the innovative outputs of pioneers stochastically to their R&D inputs. In symbolic terms, one has the following

kind of relationship for the pioneer firms:

$$(1) \quad N_{ijt} = f(R_{ijt}^m, \dots, R_{ij,t-m}^m, u_p),$$

where

N_{ijt} = number of new product introductions of i th firm in therapeutic class j for period t ;

R_{ijt}^m = R&D expenditures by i th firm on projects of vintage m for therapeutic class j in period t ;

u_p = a binomial random variable defining the odds of technical success for a pioneering firm.

A basic question is how the R&D expenditures in equation (1) are determined for each vintage of new product candidates. To obtain representative values for these R&D expenditures, we relied heavily on the empirical work of Hansen [1979]. Hansen obtained data on over 100 pharmaceutical industry R&D projects for the period 1963–1975. In his analysis the R&D process is broken down into discovery, clinical testing, and regulatory approval phases. Hansen found a total gestation period for a new drug product of approximately eleven years. Table IV presents his R&D cost estimates for the eleven years. We should note that these are *expected* costs per New Chemical Entity (NCE) entering clinical trials. Hence, we abstract from the fact that some drop out early and do not complete the full eleven years. The expected costs average in all

TABLE IV
EXPECTED COST PER NCE ENTERING CLINICAL
TRIALS FOR EACH YEAR OF DEVELOPMENT AND
REGULATORY REVIEW PERIOD

Year	Cost (thousands of 1967 dollars)
1	275
2	275
3	322
4	322
5	219
6	252
7	222
8	144
9	118
10	66
11	1

Source. Hansen [1979].

NCEs that enter clinical trials regardless of what point in time they might be terminated.

Equation (1) indicates that for each project that the pioneering firm funds according to the schedule given in Table IV, it will be eligible for a draw at the end of the eleventh year of its R&D expenditures. The probability of technical success for the pioneering firm (the u_p variable) is set equal to 0.10. This is based on data collected by the Center for the Study of Drug Development (see Wardell et al. [1978]). Their study utilizes the full population of all U. S. new drug entities undergoing clinical testing to arrive at this estimate of one in ten odds for a new product success.

Determination of Sales Revenues

For each successful draw for a new product introduction, a second draw is taken to determine the product's projected commercial success. This gives rise to a second relationship for the pioneer firm:

$$(2) \quad S_{ijt} = g(N_{ijt}, v_p),$$

where

S_{ijt} = projected sales in the tenth year of marketing life for products introduced by the i th firm in therapeutic class j in year t ;

v_p = a random variable.

This second draw to determine commercial success is from a distribution of 50 equally likely outcomes. The sales distribution referred to is presented in Table V and is based on the sales distribution of U. S. NCEs introduced over the period 1970 to 1979. If the category has experienced a "big winner" in the last five years, the sales distribution available to the NCE is adjusted to exclude that outcome. (The big winners are those with sales of 11,000 and over.)

Since the sales values in Table V refer to tenth year sales only, we must now describe how these tenth year sales are transformed into a stream of net revenues over a 25-year life. A set of " F " multipliers, given in Table VI transforms the tenth year sales value into the stream of projected net revenues over time. The F factors incorporate a number of assumptions concerning production costs, promotion costs, and the time pattern of sales revenues. A discussion of the data sources used is provided in Grabowski and Vernon [1982].

TABLE V
 FIFTY EQUALLY LIKELY OUTCOMES FOR TENTH
 YEAR U. S. SALES REVENUES OF NCEs
 (thousands of 1967 dollars)

0	500	6,500
0	800	8,400
0	900	11,000
0	950	15,000
0	950	16,000
5	1,800	19,400
10	2,000	23,000
15	2,000	25,000
50	2,800	25,200
50	2,900	33,200
50	3,000	34,100
100	3,300	52,100
120	3,700	52,200
150	4,400	56,700
250	4,900	104,000
300	5,000	165,000
400	6,000	

Source. International Medical Statistics, Inc. and forecasts by the authors. See Grabowski and Vernon [1982] for details.

These U. S. net revenues are then converted into projected worldwide net revenues by applying a multiplier. Our baseline assumption is that the multiplier is 1.65. (This assumes that foreign sales are 65 percent of U. S. sales for the typical new product introduction.) This value was based on an analysis of several representative products for the drug industry [Grabowski and Vernon, 1982].

The projected net revenues that are determined by this process are upper bound estimates on a new product's sales and are subject to erosion over time. The reason for this is that the projected revenues do not take account of substitution from future new product introductions which are endogenously determined in each computer simulation experiment. The amount of sales erosion from future substitutes will depend upon the parameter "alpha" that measures the extent to which new drugs cannibalize older drugs. The alpha values for the baseline case are 0.20 for pioneers and 0.40 for imitators. See our paper in Lindgren [1984] for a more detailed explanation of this mechanism.

Up to this point we have been discussing the situation of the firm pursuing pioneering R&D activity. For the case of firms

TABLE VI
F FACTORS FOR CONVERTING TENTH YEAR U. S. SALES REVENUES TO U. S. NET
REVENUES

Year	F	Year	F
1	0	14	0.54
2	0	15	0.54
3	0	16	0.50
4	0.2343	17	0.45
5	0.3354	18	0.40
6	0.3995	19	0.35
7	0.4230	20	0.30
8	0.4557	21	0.25
9	0.4940	22	0.20
10	0.54	23	0.15
11	0.54	24	0.10
12	0.54	25	0.05
13	0.54		

undertaking imitative R&D, the number of new drug introductions in any therapeutic class is also based on a R&D production function relationship like that given by equation (1). However, there are a number of differences in the specification of this relationship. First, it is assumed that the imitator firms do not have to undertake any discovery activity. Hence the required R&D expenditures for an imitator firm to undertake a draw are essentially the expenditures shown in Table IV for the pioneer firms, but only for years 4 through 11 (the development stage). The gestation period for imitators is correspondingly reduced to eight years. Second, the probability of success for imitative R&D is taken to be one in eight rather than the one in ten assumed for pioneering firms. Third, the distribution of tenth year sales from which the imitator firm draws also differs from that given in Table V. In particular, the distribution excludes the extreme tail completely, i.e., the big winners, and has a much lower mean and variance than that for the pioneer firms.

This combination of assumptions on R&D inputs and outputs for the imitative firms results in a projected rate of return that is smaller in value than that for pioneer firms. This is appropriate given the lower risks entailed in imitative R&D activity.

Total R&D Expenditures Functions

A third basic relation in the model is the determination of the pioneering firm's total R&D expenditures in a particular time

period. The firm's target R&D expenditures is determined as a percentage of its net revenues subject to various constraints. Symbolically, one has the equation,

$$(3) \quad R_{it} = h(\Pi_{it}, X_{it}),$$

where

- R_{it} = total R&D investment expenditures for the i th firm in period t ;
- Π_{it} = net revenues for the i th firm in period t generated from all its product's sales;
- X_{it} = a vector of variable constraints on the relationship between R&D and net revenues for the i th firm in period t .

The target R&D decision for the pioneering firm in our model is to allocate 28 percent of its net revenues to R&D. This figure was derived as an average for nine representative pharmaceutical firms over the 1970-to-1979 period. However, in any given period the R&D to revenue ratio in our simulation model can rise above or fall below this 0.28 value. In particular, to avoid sharp increases in R&D because of sharp increases in net revenues, a 10 percent limit on R&D spending increases over the previous year is incorporated into the model. On the downside, if funds available for R&D are less than the amount needed for ongoing projects, it is assumed that the funds are diverted from elsewhere so that existing projects need not be terminated. However, no new projects are undertaken in periods of revenue decline.

The model also has a termination rule for firms experiencing revenue declines of a persistent and significant character. In particular, if available funds targeted for R&D are less than half those necessary to support ongoing projects (thereby requiring an R&D to revenue ratio more than double the target ratio to support prospects in the pipeline) the firm exits from R&D competition. Its existing product portfolio is then allowed to mature and decline over time.

The R&D investment equation for imitator firms is given by the relation,

$$(3') \quad R_{it} = h(\Pi_{it}, NPS_t, X_{it}),$$

where

- NPS_t = an index of pioneering new product introductions across all classes in recent periods.

The imitator's R&D investment function is also related to its available earnings. However, the target ratio of R&D to revenues for imitator firms also varies over time with the observed new product successes of pioneering firms (this is captured by the NPS_t variable in equation (3')). This variable is in effect a signal of market opportunities for imitator firms. When a number of significant new product introductions have been made recently by pioneers, imitators increase their targeted R&D to revenues ratio. Conversely, they decrease it in times of few significant new product introductions. This assumption, together with the targeting of imitator's R&D expenditures to therapeutic categories that have experienced significant new product introductions makes the imitator's R&D sensitive to future earnings potential as well as current earnings availability.

Mechanics of the Computer Model and Simulation Experiments

We present in Figure III a representation of how the computer program keeps track of a firm over time. The matrix shows net revenues and R&D expenditures by vintage and by year for a representative pioneer firm. In particular, a_{ij} equals net revenues of the firm from NCEs of vintage i in year j . Similarly, b_{ij} equals R&D expenditures of the firm on NCEs of vintage i in year j . Thus, the first row of the matrix shows a stream of 11 years of R&D expenditures on the first vintage of NCEs, followed by a stream of 25 years of net revenues received from this first vintage. (Imitators require only eight years of R&D expenditures since they do not perform discovery research.)

The column of elements contained in the rectangular box can be viewed as a snapshot of the firm's financial position in year 36. The firm receives revenues from 25 vintages of NCEs, including revenues from the last year of the commercial life of vintage 1, the next to the last year of the life of vintage 2 drugs, etc. The dashed box that includes the element $a_{25,36}$ contains net revenues for all drugs of vintage 25. These net revenues are determined in year 36 by draws from probability distributions as discussed above (equation (2)). The b elements in the column for year 36 are the R&D expenditures that must be made in year 36 to support ongoing projects of vintages 26 through 35. The lower dashed box that includes the element $b_{36,36}$ shows R&D expenditures for NCE candidates of vintage 36. These values are determined in year 36 by the target R&D revenue decision rule discussed above (equation (3)).

After the elements in the two dashed boxes are filled in, the program simply indexes to year 37. In year 37 the program fills in the net revenues for vintage 26 and R&D expenditures for NCE candidates of vintage 37. This is the essence of how the firm is tracked over the 50-year period of the simulation experiments.

We next explain how we initialize the model, i.e., how we obtained the column of a 's for year 1. The a 's were based on data for all NCEs marketed by a sample of nine pharmaceutical firms for the period 1946 to 1970. The years were divided into five groups of five years each. We then computed the tenth year U. S. sales figure for each group and then divided this amount by five years and nine firms to get the mean. These means were 1946–1950: 1,625; 1951–1955: 1,991; 1956–1960: 6,637; 1961–1965: 3,640; and 1966–1970: 3,040. These tenth year sales values (in 1967 dollars) were converted into U. S. net revenues by the appropriate F multipliers in Table VI.

The computer simulation experiments involve changes in the assumed values on patent life, percentage of sales lost to generic competitors, and regulatory review time. These can all be conveniently handled by changing the F values for the baseline case presented in Table VI. For example, the F values can be directly adjusted to reflect a 50 percent reduction in U. S. net revenues in, say, years 9 through 25 (which corresponds to the eight-year patent life–50 percent loss to generic competitors case). Similarly, a change in regulatory review time can be accomplished by a shift in the schedule of F values forward or backward and a corresponding adjustment in the F values where appropriate (as illustrated in Figure II).

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