Effective patent life in pharmaceuticals

Henry G. Grabowski and John M. Vernon

Professors of Economics, Box 90097, Duke University, Durham, NC 27708, USA

Abstract: Effective patent life is lost in pharmaceuticals because of the lengthy time periods required for clinical trials and regulatory approval. A 1984 US law restores some of this lost patent time, while also facilitating generic competition when patents expire. This paper examines this law and the effects of other policy developments on market exclusivity times in pharmaceuticals. It also performs simulation analyses on how proposed legislative reforms would impact on future new drug introductions.

Keywords: Effective patent life; pharmaceuticals; innovation; generic competition.

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Biographical notes: Henry G. Grabowski is Professor of Economics at Duke University and Director of the Program in Pharmaceuticals and Health Economics. John Vernon is Professor of Economics at Duke University and past Chairman of the Economics Department. They have written numerous articles on the effects of regulation on the pharmaceutical industry, as well as other aspects of the economics of pharmaceuticals such as the returns to R&D and economies of scale in R&D.

1 Introduction

Patents play a key role in encouraging the development of new medicines. This follows directly from the economic characteristics of the drug innovation process. In particular, the costs of imitation are extremely low relative to the costs of innovation in pharmaceuticals. It takes several hundred million dollars to discover, develop and gain regulatory approval for a new medicine [1]. However, this is basically an investment in knowledge. Once this information is generated and ascertained by regulatory officials, it is a simple technical matter for an imitator to duplicate the compound for a small fraction of the originator's costs. This is why patents are so essential for investments in drug research and development.

The significant role of patents in pharmaceuticals has emerged in various academic studies. For example, in a study by Levin *et al.* [2] of 130 separate lines of business, pharmaceuticals ranked among the top few in terms of the importance of patents for appropriating R&D returns. In many other research-oriented industries, like computers and semiconductors, factors such as lead time and learning by doing were more important means for obtaining the returns to R&D. In another study examining the role of patents

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for R&D across different industries, Mansfield [3] surveyed the chief research officers of 100 major US corporations. He found that 60% of the innovations commercialized in 1981–1983 by pharmaceutical firms would not have been developed without patent protection. The mean response for all firms surveyed was only 14%.

Patents also play an important role in the emerging biotech industry. The first tier of successful biotech firms (Genentech, Chiron, Amgen) all relied on a strong patent base to develop proprietary technologies. Given the potential agency and information problems associated with the external financing of R&D, patents are considered essential by start-up biotech firms for securing the funding for the expensive and time-consuming clinical testing required to gain FDA approval [4].

An important aspect of patent policy for pharmaceuticals is the length of market exclusivity. In particular, effective patent time is lost by pharmaceutical products because of the long period that a new drug spends in clinical trials and regulatory review. Patents are typically granted years before a product completes its clinical testing and is approved for marketing by the regulatory authorities. In light of this, the USA, Japan and the European Community have all enacted patent term restoration laws. These statutes allow up to five years of patent term restoration to compensate for patent time lost in satisfying regulatory requirements [5].

This paper will focus on effective patent life for new drug introductions in the USA. The US case is interesting on several grounds. First, the USA has the world's leading research-oriented pharmaceutical industry. It also was the first country to enact patent term restoration. The Drug Price Competition and Patent Term Restoration Act also known as the Waxman-Hatch Act, was passed in 1984. The 1984 Act was a compromise that attempted to balance the twin objectives of drug innovation and generic price competition. Generic substitution has become a principal cost-containment strategy used by private and public payers to achieve health care savings. In fact, generic products now account for about 40% of all US prescriptions.

A recent policy development impacting on patent terms in the USA is the General Agreement on Tariffs and Trade (GATT) as implemented by the Uruguay Round Agreement Act [6]. Under GATT, patent terms will equal 20 years from the date of filing as opposed to the prior US system of 17 years from the date of patent grant. There are also transition rules for products with patents in effect or filed before 8 June 1995. An important issue for research is how the patent terms of pharmaceutical products will be affected by the implementation of GATT, both retrospectively and prospectively. This issue is examined for the first time in this paper.

In the next section of the paper, we consider the key economic trade-offs present in determining a public policy toward patent life. We also analyse some of the unique aspects of the pharmaceutical R&D process that bear on this question. We then consider the important historical forces and policy actions determining effective patent life in pharmaceuticals. In the following sections, we examine the effects of the 1984 Act on both generic competition and patent term restoration. We also investigate the impact of GATT on effective patent life in pharmaceuticals. In the last empirical section, we analyse a number of proposed reforms to the Waxman-Hatch Act that were discussed in recent Congressional hearings on the impact of the 1984 Act [7].

2 Some perspectives from economic analysis

Beginning with the pioneering work of William Nordhaus [8], economists have developed various theoretical models seeking to determine the socially optimal patent life. The basic trade-off is between creating incentives for new product development and minimizing the static inefficiency associated with granting market exclusivity for the inventor's product. In a world of perfect information, each product would have its own patent life. This life would equal the number of years that would just induce the developer to bring the product forth. If it were shorter, the product would not be developed at all, and this would result in a social loss. If it were longer, market exclusivity would last longer than necessary, with unnecessary social losses in the form of foregone price competition.

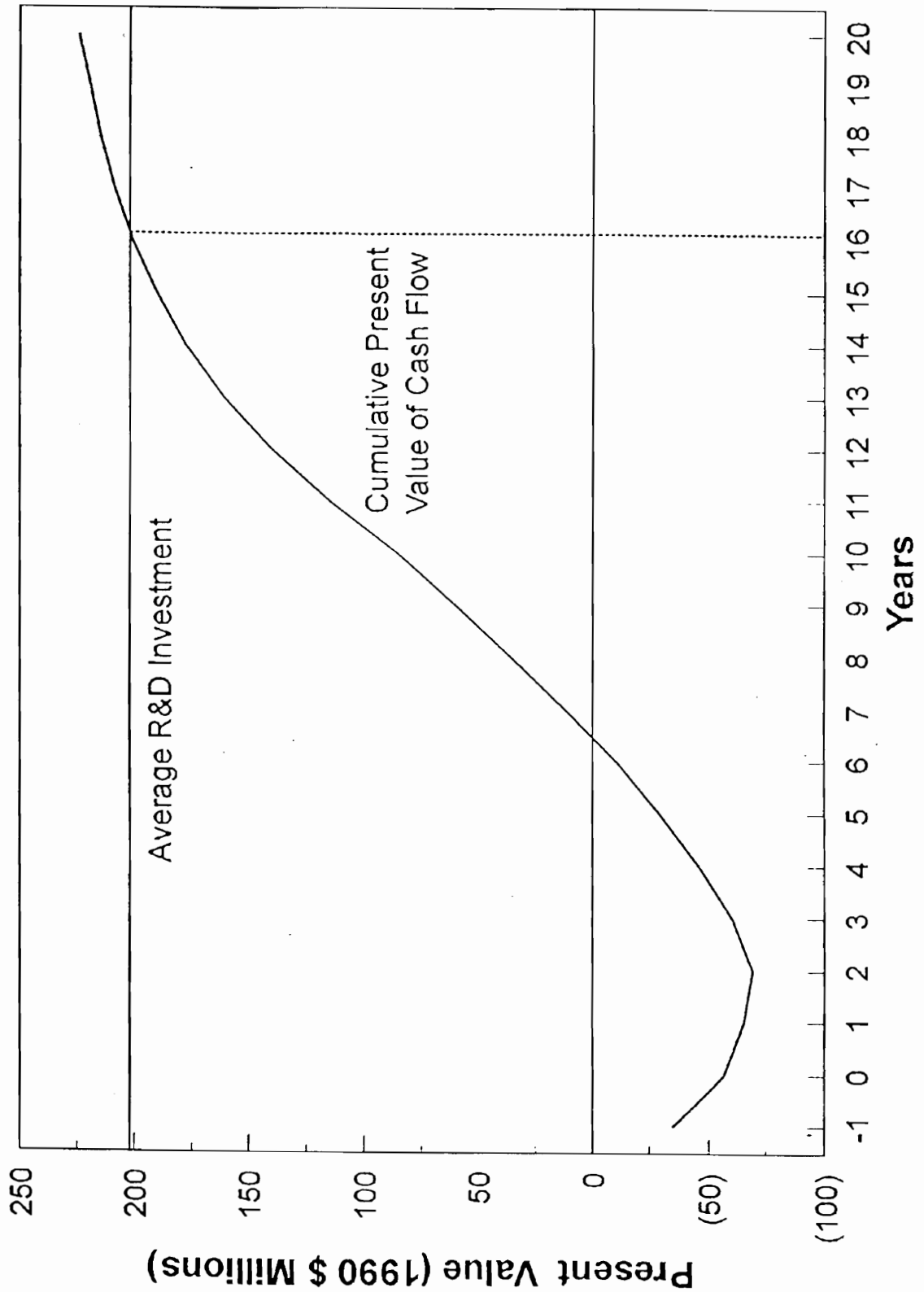
Of course, given a world of imperfect information, the patent life cannot be set individually for each product, or even for each industry. However, theory suggests that changes in patent life should balance social benefits and costs. From a pharmaceutical industry perspective, increasing the patent life will cause some NCEs that would not have been developed to now be introduced – a marginal social gain. On the other hand, for some NCEs the longer patent life will simply postpone the onset of generic price competition – a marginal social cost. When these marginal gains just equal the marginal costs, the patent life is optimal.

While this theoretical modelling approach has not yielded a specific value for the optimal patent life for pharmaceuticals (or any other industry), it does provide a framework for policymakers to keep in mind in considering the relevant trade-off. There are also several empirical characteristics of the innovation process in the pharmaceutical industry which are relevant to the issue of patent life. These relate in particular to the high costs of the R&D process and limited appropriability of drug innovation from other factors.

While drug innovation can have important and unique social benefits, the R&D process is very long, risky and costly compared to most other high-tech industries. Using a representative sample of NCE candidates first entering clinical testing between 1970 and 1982, DiMasi *et al.* [1] found that the average new drug introduction cost 231 million US dollars (1987). This is the capitalized cost at the date of marketing approval using the industry cost of capital to capitalize R&D expenditures. Furthermore, the mean NCE took approximately 12 years from synthesis to market approval, and the average success rate for compounds entering clinical testing was only 22%.

It is instructive for the current analysis to examine the time required by the mean NCE to achieve break even status – that is, cover its R&D costs and earn a risk-adjusted return on its capital. The break-even lifetime is illustrated in Figure 1 for the cohort of 1980 to 1984 industry introductions. The data in this figure combine DiMasi's information on R&D costs and data on cash flows developed in our analysis of R&D returns for 1980–84 NCEs [9]. We find that the breakeven lifetime for the mean NCE introduction in this cohort is a little over 16 years. In particular, this is where the present value of cumulative after-tax cash flows just intersects the present value of the after-tax R&D investment (202 million US dollars in 1990).

Figure 1 Cumulative present value of cash flow versus R&D investment for the mean 1980–84 NCE introduction



Breakeven lifetimes are different of course from patent lifetimes. Most of the products in this cohort have experienced, or will experience, patent expiration before 16 years of marketing life. Several of these NCEs earned significant revenue in the post-patent period due to brand loyalty and the ability of some firms to differentiate their products with new formulations and other changes. However, as discussed below, the erosion of sales for the pioneer product after the onset of generic competition has dramatically accelerated for recent patent expirations. As a consequence, the importance of earning a positive return on investments before patents expire has increased over time, making effective patent life a more important policy parameter in pharmaceuticals.

The significance of Figure 1, taken together with current industry trends on generic competition, is that a long patent life would appear to be a necessary condition on grounds of appropriability to maintain strong incentives for R&D investments in this industry. However, there are several complicating factors. First the distribution of discounted cash flows across NCEs is in fact highly skewed. A few blockbuster NCEs earn several times the average R&D costs. Their breakeven lifetimes are much shorter in value than 16 years. At the same time the majority of products in this cohort have significantly lower discounted cash flows than the mean product, and greater breakeven lifetimes than the 16-year value in Figure 1.

In a world of uncertainty, it is difficult to know *ex ante* exactly which drugs will be the big winners – many NCEs start with this goal but end up as incremental advances or fall by the wayside completely. *Ex post* the top decile NCEs play a disproportionate role in covering the large fixed costs of R&D and enabling the entire portfolio of a firm's R&D projects to earn a positive return. Patent lifetimes in excess of the breakeven lifetimes for the top decile compounds are clearly necessary to sustain the viability of the entire R&D enterprise [10]. But determining the optimal life remains an elusive task.

Another qualification to the analysis presented in Figure 1 is that expected returns on R&D and breakeven lifetimes change over time. They are influenced by trends in R&D costs, product sales life cycles, industry margins, discount rates, competition by close substitutes prior to patent expiration, etc. An important area for further research is to investigate these factors using more recent NCE cohorts[13]. For policy purposes, one ideally would like to have this information on a prospective basis. However, given the long time spans that are involved in R&D and marketing cycles (30 years or more), there will always be considerable uncertainty about prospective returns on R&D, even for the firms participating in the R&D process.

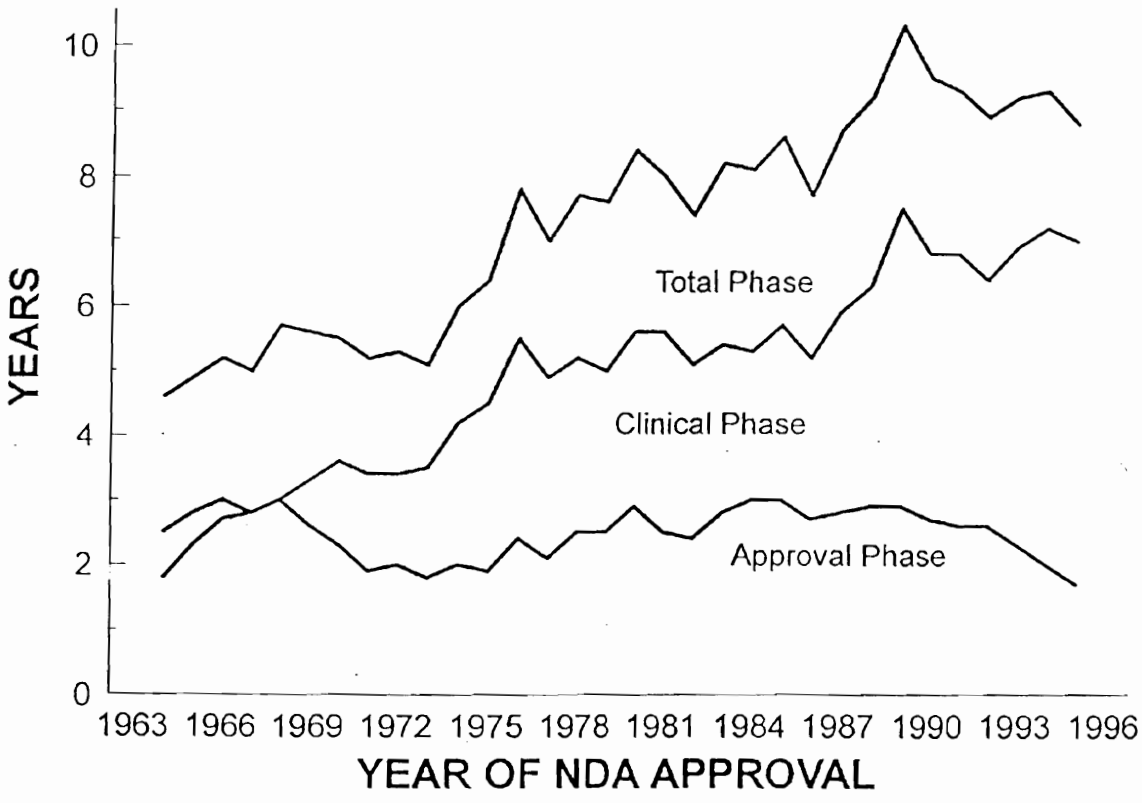
Clearly, the factors affecting optimal patent life are numerous and complex [14]. The best one can say from the perspective of economic analysis is that some of the key characteristics of the pharmaceutical industry suggest a relatively long effective life is socially desirable. By contrast, various industry developments, until recently, have been operating to curtail effective patent terms in pharmaceuticals. As we discuss shortly, the length of patent protection has been a policy instrument that historically has not received much explicit attention by policymakers. Rather, effective patent life in pharmaceuticals has been driven as an unintended consequence of other public policies and broader environmental forces. A looming conflict caused Congress to confront this issue in terms of the 1984 Act. Recent Senate hearings [7] suggest that the patent protection of new drug discoveries is a policy that is likely to receive renewed attention by Congress.

3 Historical policy changes affecting drug patent terms

3.1 Increased drug regulation

An important milestone in the current regulatory regime for pharmaceuticals was the passage by Congress of the 1962 Kefauver-Harris Amendments to the Food, Drug and Cosmetic Act. These amendments required that substantial evidence of efficacy be demonstrated prior to marketing. They also established the investigational new drug (IND) procedures for clinical testing. As these Amendments were codified into FDA regulations, the drug development process became significantly more complex, costlier and lengthier. For example, Figure 2 shows the growth over time in the length of the clinical testing and regulatory review periods between 1963 and 1996. There is a significant upward trend in the average length of time required for clinical testing and regulatory approval.

Figure 2 Mean approval, clinical and total phase times for new chemical entity approvals, 1963–1996



Source: Tufts Center for the Study of Drug Development, 1997

Effective patent life is measured in this study as the time from FDA approval to patent expiration. The growth in drug development times shown in Figure 2 resulted in a corresponding downward trend in effective patent lifetimes. In a previous article, we found that by the early 1980s, the average effective patent life for US new drug introductions was just over eight years [5]. Hence, approximately half of the nominal life of 17 years had been consumed during clinical testing and regulatory review for the representative new drug entity.

In the early 1980s, declining effective patent lifetimes were more of a potential than actual problem for drug innovators. This was because there were significant barriers to market entry for generic products at that time. Specifically, the FDA determined that generic firms could not rely on the safety and efficacy data submitted by the innovator for post-1962 drug introductions, unless these data were publicly available in scientific literature. In effect the innovator's safety and efficacy data were given 'trade secret' status, and a generic competitor had to duplicate many of the innovator's tests to gain regulatory approval. This was a substantial barrier to entry that significantly inhibited the speed and extent of entry by generics in this period [17].

In this environment, generic firms argued that it was highly inefficient to have to replicate safety and efficacy testing for products that had been utilized for many years by a large number of patients. In addition, they argued that generic products could lead to large savings in pharmaceutical expenditure for both private and public payers. These arguments were positively received in Congress, but there was also concern that the erosion in patent lifetimes could be a significant problem for the future development of new drugs.

3.2 Passage of the 1984 act

The 1984 Waxman-Hatch Act was designed to balance the competing concerns of generic competition and drug innovation. As noted, the official title of this legislation was the Drug Price Competition and Patent Term Restoration Act. This Act lowered the barriers to generic entry while increasing patent terms for new drugs delayed by FDA regulation.

Title I of the Act established an Abbreviated New Drug Application (ANDA) procedure for generic drugs. Under the ANDA process, generic drugs can implicitly rely on the safety and efficacy data of the pioneer product. They have only to demonstrate their bio-equivalence to the brand name product to receive marketing approval. The law also established the rights of generic firms to have the bio-equivalence testing and ANDA review done in the pre-patent expiration period, so that they could enter the market quickly upon patent expiration.

Title II of the Act provided for partial restoration of the patent time lost during the clinical testing and regulatory approval periods. A formula for patent term restoration was embedded in the law. In particular, new drugs were eligible for an extension in patent life equal to the sum of the NDA regulatory review time plus one half of the IND clinical testing time. The law capped extensions at five years and also constrained extensions to a maximum effective patent lifetime of 14 years. In addition, Title I of the law provided for a five-year data exclusivity period in which no ANDAs could be granted for an NCE. Economists and other policy analysts did not have any role in the design of these different provisions on patent term restorations. They emerged after involved negotiations with the different parties.

Title II of the Act also had an important transitional provision. In particular, drugs in clinical testing and already patented at the time of the law's passage (24 September, 1984) were capped at a maximum patent term extension of two years. Because the drug development process spans many years, most new drug introductions made in the 1980s and early 1990s were subject to this cap. It is only relatively recent introductions that have been eligible for the full patent term benefits provided by the law.

3.3 Implementation of GATT

On June 8, 1995, various provisions affecting patents negotiated under the GATT treaty became effective in the USA. Under this law, patent terms are to be 20 years from the date of patent application rather than 17 years from the date of patent grant. In addition, patents in effect or on file before 8 June 1995 are given either a 20-year term from file date or a 17-year term from grant date (i.e., whichever is longer). For drug products in this transition set, a key issue was whether Waxman-Hatch extensions could be added to any GATT-induced increases in patent terms resulting from the switch to a 20-year from file term. Initially, the US Patent Office determined they could not. The courts have recently ruled that firms can add Waxman-Hatch to GATT-induced extensions [19]. However, the constraint of a maximum 14-year effective patent lifetime for Waxman-Hatch extensions is binding under either regime.

One interesting issue considered below is how GATT will affect patent terms in pharmaceuticals in the future. Obviously, for products in the transition set, there will be net benefits to industry patent holders. This is because some products will be eligible for longer lives, while no products will lose patent time. A more interesting issue is what will happen for products filed after June 1995 where patent terms must be based on the new 20-year-from-filing regime. Here there will be both winners and losers. The length of the patent pendency period will be the key determinant in this situation. Products with patent pendency periods of less than three years stand to gain patent time, while those with longer patent pendency periods stand to lose time under the new system. The situation in pharmaceuticals is complicated somewhat by the possibility of Waxman-Hatch extensions which can moderate the expected gains and losses that would otherwise take place. From an overall industry perspective, however, it remains an open question whether pharmaceuticals will experience net benefits or losses for the patents of new product candidates filed after June 1995. We perform some simulation analyses that provide insights on this issue later in the paper.

4 The Waxman-Hatch Act – effects on generic competition

In two earlier papers, we have analysed how generic competition has evolved over the post-1984 period [20,5]. These analyses are briefly summarized here [21]. Our first paper analysed the degree of generic competition for 18 major products first experiencing generic entry in the period 1984–1989. This sample included all the products with initial sales of over 50 million dollars at the time of generic entry. A subsequent paper extended this analysis to 22 major drugs experiencing initial generic entry in the period 1989 to 1993.

A distinctive pattern of competitive behaviour for both generic and brand name firms emerged in the wake of the 1984 Act. First, commercially significant products experienced a large number of generic entrants within a short time after patent expiration. For example, the representative product in our 1984 to 1989 sample had 17 generic competitors by the end of the first year of generic entry and 25 competitors after the second year.

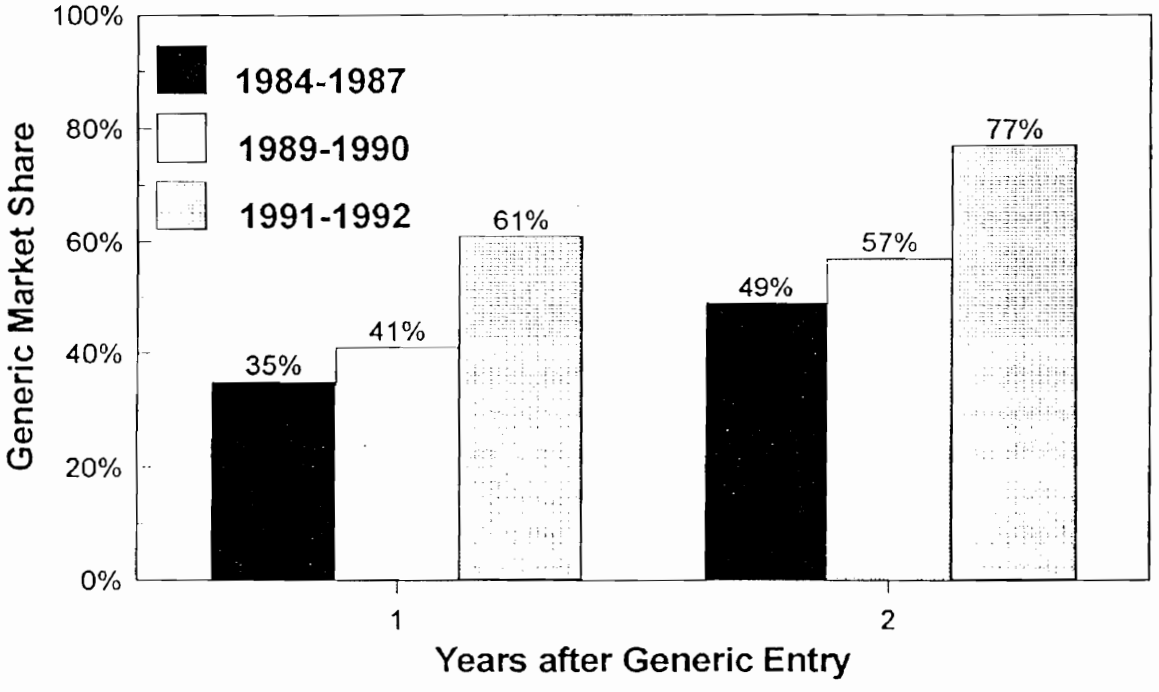
A second important finding was the high degree of price competition exhibited by the generic firms. The initial generic product entered the market at a significant discount to the brand name firm, and this discount grew larger as the number of generic competitors for a particular brand name product expanded over time. For our 1984 to 1989 sample,

generic prices averaged 61% of the brand name product during the first month of generic competition. This declined to 37% by two years after entry. We found that the price of generic products generally converged over time toward product cost, indicating a commodity-type business. However, generic firms could make significant profits as early entrants.

A third important finding was that the pioneering firms did not attempt to deter entry through their pricing strategy. In most cases, the firms continued to increase their prices at the same rate as in the period prior to entry. Hence, the brand name firms pursued what could be characterized as a 'harvesting strategy' – the maintenance of a premium price while market shares erode over time.

This basic pattern of generic competition was observed in both the initial post-84 period and in the more recent 1989-1993 period. The one major change that we observed between the earlier and later periods was a more rapid rate of sales erosion by the brand name products with recent patent expirations. This is illustrated in Figure 3. This figure shows the growth in generic market shares during the first two years on the market for four successive time cohorts. Market share is measured in terms of pills sold of the most popular dosage size. Figure 3 reveals the changing market environment for brand name products experiencing initial generic competition in the 1984–1985, 1986–1987, 1989–1991 and 1992–1993 periods.

Figure 3 Generic market shares for four cohorts



*Measured in terms of pills sold of the most popular dosage size.

As shown in Figure 3, more recent time cohorts are characterized by much more intensive generic competition. The values are particularly striking for the 1992–1993 cohort of brand name products. In particular, generic drugs captured a 64% share of total units sold after one full year on the market. This increased to 73% after the second year. This may be compared to the 1984–1985 cohort. For that cohort of brand name products,

generics achieved shares of 32% and 45% after one and two years, respectively [24].

In sum the Waxman-Hatch Act was a major catalyst for the extensive price competition and generic utilization now occurring in the US market. The growth of managed care and other related demand-side changes have also been important factors underlying the rapid increase in generic usage that has taken place during the past decade [25]. However, without the steep reduction in the cost of generic entry made possible by the Waxman-Hatch Act, it is clear that the generic market would have evolved in a much different manner.

5 Effective patent life for 1984 to 1995 NCEs

If Congress had only created the ANDA process with the 1984 Act, it would have resulted in significant disincentives for pharmaceutical R&D and innovation. As noted in the last section, average effective patent life in the early 1980s had decreased to less than nine years or approximately half the nominal life of 17 years. Title II of the Act was designed to promote drug innovation by providing patent restoration for future NCE introductions.

We now have over a decade of experience with this aspect of the 1984 Act. In this section, we consider the effective patent life (EPL) and the contribution of Waxman-Hatch extensions for the new drugs introduced between 1984 and 1995. Furthermore, given that the USA Court of Appeals for the Federal Circuit has ruled that Waxman-Hatch extensions can be added to GATT-induced increases in EPL (under the transitional rules for drugs with patents still in effect on 8 June 1995), we have incorporated this ruling into the present analysis. Information on patent expiration dates and extensions was obtained from the US Patent and Trademark Office and the FDA's 'Orange Book.'

When analysing the effective patent life for a specific NCE, we follow the approach employed in our prior work. In particular, if multiple patents exist for a particular NCE, we focus on the patent chosen for patent restoration (only one patent per NCE is eligible for extension under the 1984 Act). The strongest form of patent protection in pharmaceuticals is a patent on the molecule itself (i.e., a compound patent). This is also the patent typically chosen for Waxman-Hatch extensions. A firm can also obtain a patent on the product's composition, use, and the process utilized to make it [27].

In this paper, we include the effects of GATT on effective patent life for the first time. For patents that were still in force on 8 June 1995, the expiration date is determined by whatever yields the longer patent life: either the 17-year term from the patent grant date or the 20-year term from the patent filing date. After determining effective patent life on this basis, the Waxman-Hatch restorations were added in accordance with the provisions of the 1984 Act [28]. As before, patents that expired prior to 8 June 1995 have their Waxman-Hatch extensions based on a term of 17 years from the grant date. Our approach is consistent with the procedures and outputs of the US Patent Office. They provided a list to us of patent expiration dates and Waxman-Hatch term restorations that included most of the NCEs in our sample [29].

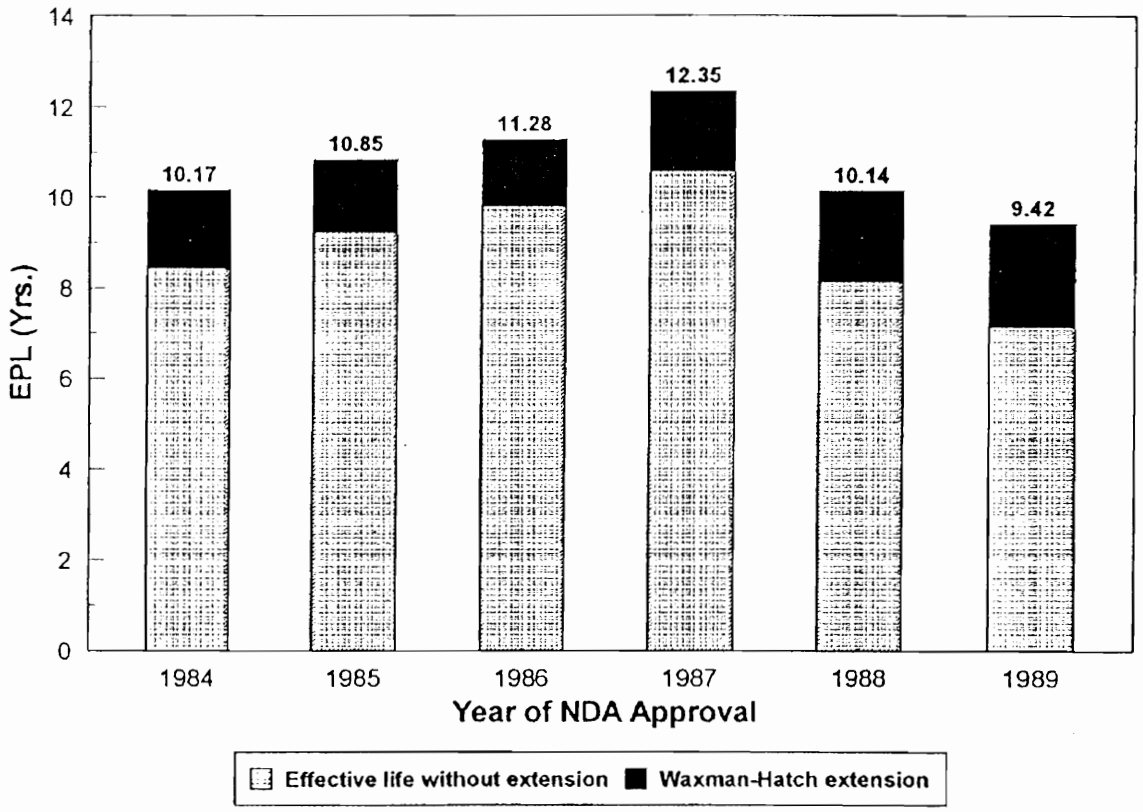
As in our earlier research, if the effective patent life for an NCE is less than five years after considering all its compound, composition and use patents, the five-year FDA regulatory exclusivity term provided under Title I of the Act is substituted for that NCE's EPL. A seven-year exclusivity term is also possible for 'orphan drugs' under the 1983 Orphan Drug Act. In this and prior work, we include orphan drugs only if they have a

patent that provides longer intellectual property protection than the seven-year orphan drug exclusivity period. We adopted this approach because our primary interest here is with patent protection and extensions associated with the Waxman-Hatch Act. The Orphan Drug Act has been analysed extensively elsewhere [31].

5.1 The 1980s cohort

We consider first the effective patent life of the 102 NCEs approvals over the period 1984 to 1989 [32]. Figure 4 shows the average effective life (post-GATT) and the Waxman-Hatch extensions by the year of NDA approval. The average EPL for all 102 NCEs in this cohort is 10.8 years with a mean Waxman-Hatch extension of 1.8 years. Figure 4 indicates that there is considerable variability in EPL from year to year, but there is no particular trend evident in this series. Among other factors, the EPL in a given year will be significantly affected by the composition of NCEs by therapeutic class. Specifically, certain types of drug therapies have significantly shorter expected development times than others (e.g., anti-infectives *versus* psychotherapeutics).

Figure 4 Effective patent life for 1984–1989 NCEs



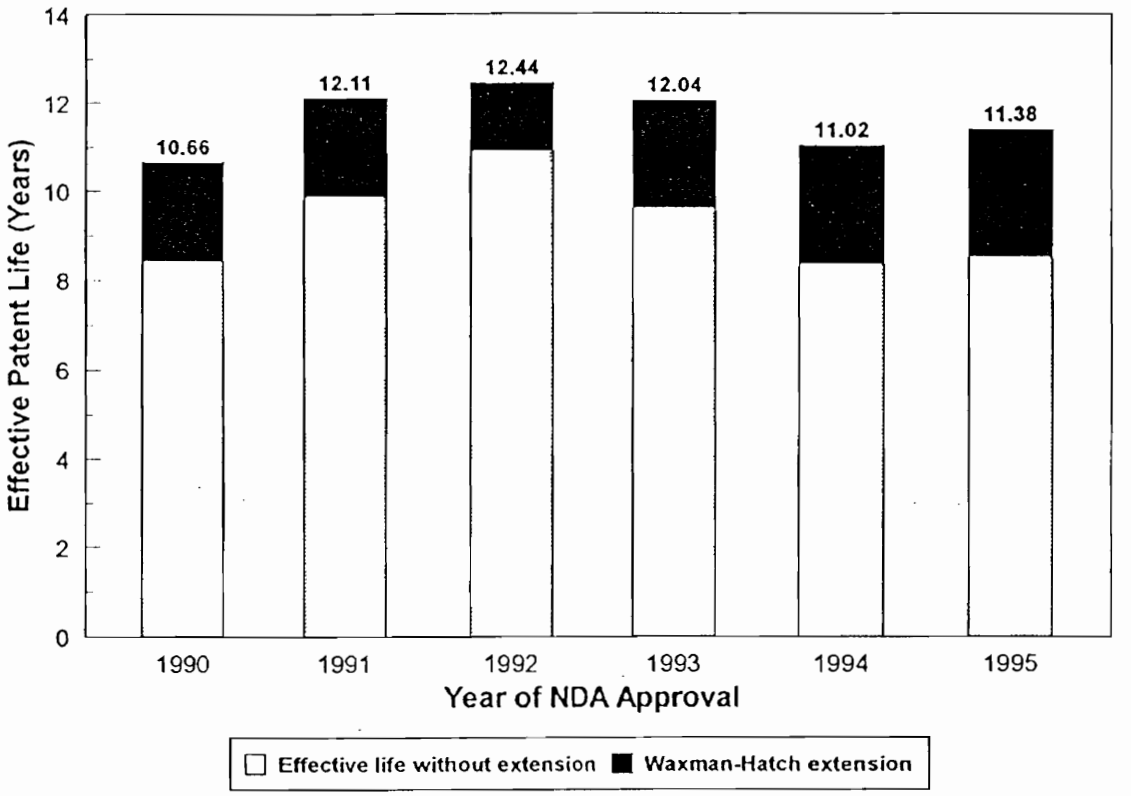
The vast majority of 1980 NCEs were already patented and in clinical testing on the date that the 1984 Act was passed. Hence, these NCEs are eligible for a maximum two-year extension. In fact, 60 of the 74 NCEs that obtained positive patent term extensions in this cohort received exactly two years as a result of their pre-1984 testing status. Only three NCEs received patent term extensions in excess of two years because they were 'post-84' INDs. Eleven NCEs in this cohort had positive patent term extensions that were less than

two years because they bumped up against the 14-year maximum EPL constraint for Waxman-Hatch extensions [33].

5.2 The 1990s cohort

Figure 5 shows the EPLs by approval year for the new drugs introduced between 1990 and 1995. This figure indicates that the average EPLs in the 1990s centre around an 11- to 12-year range. The mean for all 126 NCE introductions in the 1990–1995 period is 11.7 years with an average Waxman-Hatch extension of 2.33 years. In the last two years of this period, when virtually all of the drugs involve post-84 INDS, the average extension is close to three years in length.

Figure 5 Effective patent life for 1990-1995 NCEs

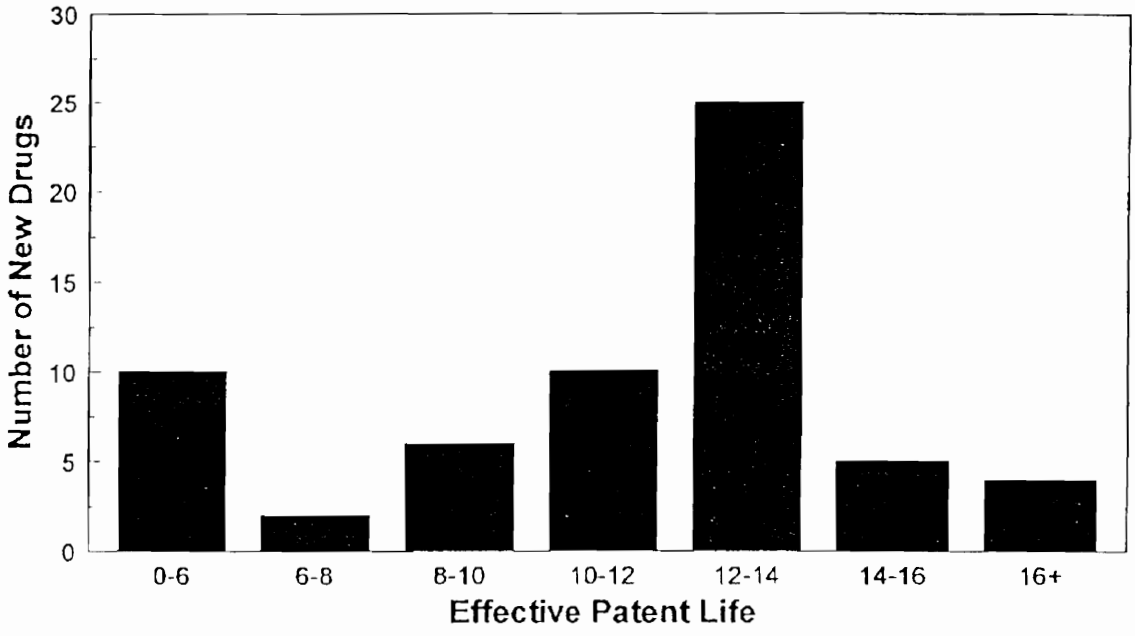


In contrast to the 1980s cohort, 85% of 1990 NCEs were not in clinical testing in 1984 and hence are not subject to the two-year cap on extensions [34]. However, patent term extensions for this cohort are significantly affected by the other caps and rules embodied in the law. For example, 38 NCEs have their restoration times shortened by the 14-year constraint on EPL. In addition, 32 NCEs have patent term extensions that cluster between 2.5 and 5.0 years in length. This relatively tight clustering reflects both the five-year cap on extensions, and the rule that time lost in the IND process is subject to only 1/2 credit toward restoration. The effect of relaxing these different constraints and rule on long-run EPL in pharmaceuticals is considered later in the paper.

Figure 6 shows the frequency distribution of EPLs for the 62 NCEs approved over the last three years of this sample (1993-1995). The mode of this distribution is the 12- to 14-year EPL interval. This finding reflects the fact that a large number of NCEs are

effectively constrained to a 14-year EPL under the 1984 Act. At the same time, there are a significant percentage of NCEs with EPLs below ten years (18 NCEs or 29% of the total sample). This latter group includes nine NCEs that had to rely on the five-year FDA regulatory exclusivity period to obtain their maximum protection.

Figure 6 Frequency distribution of EPLs – 1993–1995 NCEs



5.3 The effect of GATT

A final issue worth considering in this section is the patent term benefits resulting from GATT. Table 1 shows the net effect of GATT on EPLs for 1980s and 1990s NCEs. This analysis incorporates the relevant Waxman-Hatch extensions in both the pre- and post-GATT situation. Overall, the net effects of GATT are relatively modest. For 1984-89 introductions, there was an increase in EPL of only 0.21 years. For the 1990-95 cohort, the increase is 0.40 years.

Table 1 Net benefits of GATT for 1984-1995 NCEs

	Time Cohorts	
Average EPL	*1984-89 NCEs*	*1990-95 NCEs*
(a) Under GATT	10.79 yrs	11.70 yrs
(b) Without GATT	10.58 yrs	11.30 yrs
Difference	0.21 yrs	0.40 yrs

Notes

1 Total sample for 1984–89 cohort is 102 NCEs, 20 of these NCEs have increased EPLs from GATT and the other 82 NCEs have no change in EPLs.

2 Total sample for 1990–95 cohort is 127 NCEs, 49 of these have increased EPLs as a result of GATT and the other 78 NCEs have no change in their EPLs.

The main reason for this modest impact was the small proportion of NCEs that realized positive benefits from GATT [35]. In the case of the 1980's cohort, only 22 of the 102 NCEs had an increased EPL from switching to the 20-year term. The expiration of patent protection prior to 8 June 1995 was the primary factor making NCEs ineligible for any GATT benefits in this cohort.

For 1990s NCEs, this was not the case since all but three had patents still in effect on 8 June 1995. However, only 49 of the 127 NCEs had gains under the 20-year term. The factors keeping more NCEs in the latter sample from realizing any gains from a 20-year term were:

1 the NCE's patent pendency period was greater than three years;

2 the addition of the Waxman-Hatch extensions resulted in an effective cap on EPL of 14 years under both regimes;

3 an NCE obtained its maximum term protection from the five-year ANDA exclusivity provision of the Law in both regimes [36].

In sum, under the transition rules, the net gains in EPL for pharmaceutical products are relatively modest. They average approximately five months for recent NCE introductions. For future NCEs with patents filed after 8 June 1995, firms will have to utilize the 20-year from filing date patent term and figure all Waxman-Hatch extensions based on this expiration date. As discussed, over the long run this switch to a 20-year term can result in positive or negative net benefits to the industry. This issue is considered in the next section where data on the distribution of patent pendency periods for 1990s NCEs are considered to analyse this issue.

6 Hypothetical effect of GATT in the long run

In this section, and the following, we will present some results that we have obtained in analysing a database of 105 NCEs introduced in the US in the period 1990–1995. The main issue here is to measure the effect of GATT in terms of patent extension.

We focus on what we term the long run. The long run refers to a comparison between two hypothetical worlds: one in which Waxman-Hatch is fully phased in and the patent life is the grant date plus 17 years, and the other in which Waxman-Hatch is fully phased in and the patent life is determined by the GATT rule of the filing date plus 20 years. As we have noted previously, all drugs with patent filing dates after 8 June 1995 must use the GATT rule of the filing date plus 20 years. Hence, we use 1990s NCEs to perform a hypothetical experiment in order to estimate what the future effect of GATT might be.

Sample construction for the hypothetical calculations reported here began with the 127 1990–1995 NCE introductions in our prior analysis. We then eliminated 14 drugs with no patents or ones that, because of short patents, obtain their longest protection from the five-year exclusivity period. The reason for this was to focus on extensions and effective patent terms that can be impacted by the different rules of the new and prior US patent systems. In addition, we omitted eight other drugs that have not received Waxman-Hatch extensions. These were drugs that either did not apply for an extension, were late in applying and thereby were barred from getting an extension, have their case under appeal at the PTO, or for some other reason had extensions of zero even though they could have received positive extensions [37].

The patent pendency period is, of course, the time from the filing date to the patent grant date. For our sample, the average time was 3.8 years, with a rather skewed distribution. Table 2 shows this skew – the top 20% in terms of the length of pendency averaged 8.49 years. Since GATT increases patent life by three years (but measured from filing rather than grant), and the date from filing to grant averages 3.8 years, one would expect GATT to have a slightly negative effect on the average EPL. (The positive actual effect for GATT found in the previous section was, of course, due to the fact that in the transition period firms only use the filing plus 20-year rule if it is more beneficial than the grant plus 17-rule; this option is unavailable in the Long Run studied here.)

Table 2 Patent pendency

	Years
Quintile 1	8.49
Quintile 2	4.43
Quintile 3	2.90
Quintile 4	1.93
Quintile 5	1.24
Average for 105 NCEs	3.80

In our analysis of the long run case, a major issue is whether firms will continue to behave in the same way as they have in the past with regard to the filing of patent applications. That is, in the past the patent life was determined by grant date plus 17 years, and long patent pendency periods did not matter. Of course, in the future, it will matter greatly since the life will be determined by the earliest date of filing referenced in the patent. It is not uncommon for new filings to be continuations of earlier filings that were abandoned. For example, the firm and patent examiner may not agree on the scope of the claim being sought, causing the firm to abandon the original filing, but also to continue the process while new data are being obtained to buttress the claim. In addition, new research may lead to changes in the scope of claims made in the original application.

In our work reported here it is assumed implicitly that the filing behaviour will not change with respect to the earliest filing date. Discussions with patent attorneys seem to support this view, although there is some uncertainty on this issue. The argument is that firms may not reference all prior filings in the patent as in the past and this would lead to longer lives; however, this is also a risky strategy and could lead to the patent not being obtained at all. Few pharmaceutical firms would appear to be willing to engage in such risky behaviour.

Another possible qualification is that a new 'provisional' application is now available in the USA. A provisional application can be in effect for up to a year, and its filing date does not start the 20-year clock running. This provisional application has been available in Europe for some time and patents filed in Europe typically take advantage of it. It is also worth noting that Europe operates on a 'first to file' rule while the US uses a 'first to invent' rule when deciding which of competing inventors receives the patent. Hence, there is an incentive to file more quickly in Europe than in the USA. It is difficult to estimate at this time what the overall effect on filing behaviour will be of the new provisional patent option now available in the USA.

Table 3 presents the summary results for our long run comparison of two hypothetical worlds – one in which only the file date plus 20 years is in effect and the other in which

only grant date plus 17 years is available. The main finding is that the average EPL for all 105 NCEs in the new GATT world of 20-year terms is 12.46 years, and this is less than the life of 12.80 years under the traditional 17-year term that it replaces. The benefit of GATT is therefore negative, and equals –0.34 years. The table also shows the distribution by quintiles for the two cases. It is interesting to note that the average patent life for the fifth quintile (the average for the 21 NCEs with the shortest lives) declines by almost a full year under GATT – from 9.25 to 8.39.

Table 3 Estimated future benefits of GATT ('Long Run' Case)

Quintiles	*Effective Patent Life under File + 20 yrs. (a)*	*Effective Patent Life under Grant + 17 yrs. (b)*	*Benefit of GATT (a) – (b)*
1	14.31	14.88	–0.57
2	14.00	14.00	0
3	13.61	13.72	–0.11
4	11.97	12.15	–0.18
5	8.39	9.25	–0.86
Avg 90-95	12.46	12.80	–0.34

In examining the benefits of GATT on a drug by drug basis, there are some interesting findings. First, of the 105 drugs, 23 came up against the 14 year cap in both worlds, so the benefit of GATT was zero for these drugs. Second, more drugs had positive benefits (43) than had negative benefits (39). However, because the average negative benefit was larger in absolute value than the average positive benefit, the overall average was a negative 0.34 years.

7 Effect of Waxman-Hatch modifications

In 1996, the Senate Judiciary Committee, chaired by Senator Orrin Hatch, held a hearing to re-examine the Waxman-Hatch Act. As Senator Hatch explained, the Act in 1984 was carefully balanced. However, he observed that "the cost of research has risen dramatically since 1984, as has the time needed to bring a pharmaceutical product from discovery to pharmacy". Hence, the hearing was intended to answer the question as to whether modifications to the Act were needed.

Another issue considered at these Hearings was the fact that the European Community has recently adopted a patent restoration law with more favourable incentives for drug innovation in several respects. For example, the EC law embodies a five-year cap on extensions but has set 15 years as the maximum EPL for patent term extensions. It also allows full credit for patent time lost in the clinical testing period. Japan also has a patent restoration act with far fewer restrictions than the Waxman-Hatch Act, including full credit on time lost in clinical testing and no maximum EPL for extensions [38]. Furthermore, both the EC and Japan also have longer exclusivity periods in which generics cannot enter the market relying on the pioneer's data [39]. These international differences provide another perspective for possible reforms in the Waxman-Hatch Act.

A variety of changes in the rules for computing patent restoration, therefore, have been proposed recently to Congress (i.e., repeal of the 14-year cap on EPL, the five-year cap on extensions, full credit for clinical and testing time, etc.) However, the empirical effects of these changes on patent life have not been analysed. Hence, given the result reported in the previous section, that GATT may shorten effective patent lives, and the interest in modifying Waxman-Hatch for other reasons, we use our sample of 105 NCEs to analyse the effect of modifications in the Act. We now turn to some simulation results of relaxing certain Waxman-Hatch rules.

For this simulation analysis, we chose as our baseline case, the long-run world in which only the GATT rule of file date plus 20 years is available. This is the most relevant assumption in a prospective analysis of future new drug candidates. In particular, we are focusing here on NCEs currently in the initial part of the R&D process or not yet in the R&D pipeline (i.e., NCEs patented after June 8, 1995).

Table 4 shows how the effective patent life changes for various modifications in the Waxman-Hatch rules. For example, in row (1) we change only one rule – the overall 14-year cap on EPL that can be achieved under Waxman-Hatch is raised from 14 years to 15 years. This single change leads to an increase of 0.32 years. As shown in the last column, 40 of the 105 NCEs had positive gains from raising the cap by one year. Similarly, row (2) shows that if the 14-year cap were raised to 16 years, the increase in average patent life would be 0.48 years. However, only 25 NCEs benefit from this extra year (i.e., the change from 15 years to 16 years). Similarly, raising the cap to 17 years is subject to further diminishing returns in terms of the incremental gain and the number of NCEs benefiting from the change [41].

Table 4 Sensitivity analysis of Waxman-Hatch constraints

	Patent Life (a)	*Baseline Life (b)*	*Gain (a)–(b)*	*No. NCEs with Gain**
(1) Raise 14 cap to 15	12.78	12.46	0.32	40
(2) Raise 14 cap to 16	12.94	12.46	0.48	25
(3) Raise 14 cap to 17	13.02	12.46	0.56	11
(4) Eliminate 5-year cap	12.87	12.46	0.41	31
(5) Count testing time fully	12.67	12.46	0.22	27
(6) Do (1) & (5) together 'The EC Case'	13.10	12.46	0.64	67
(7) Do (1), (4), (5) simultaneously	14.36	12.46	1.90	90

* In the cases of (2) and (3), this column gives the number of NCEs with additional gain over the previous case. E.g., 25 is the number of NCEs that gain by increasing the 15-year cap to 16 years.

Independently eliminating the five-year cap (row 4) and providing full credit for patent time lost in the IND phase (row 5) results in comparable impacts on mean patent life as raising the cap on 14-year effective life to 15 years. However, fewer NCEs benefit and the distribution of NCEs which do benefit is very different. In row (6), we consider the case involving the simultaneous provision of full credit for patent time lost during clinical testing and a 15-year EPL cap while retaining the five-year cap on extensions. This case in fact embodies the main features of the European Community law governing patent term restoration. The results for row (6) indicate a synergistic effect from relaxing these two restrictions simultaneously. The gain is 0.64 year and 67 NCEs benefit.

Finally, in the last row of the table we consider the effects of making three changes simultaneously

1 an increase in the cap on effective patent life to 15 years,

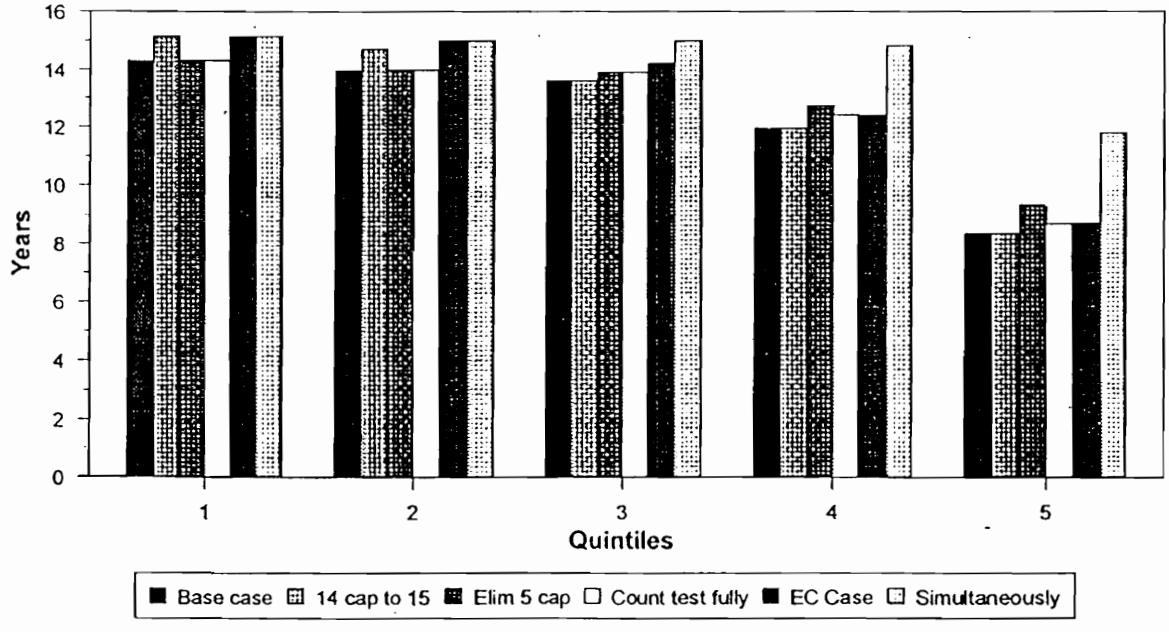
2 elimination of the five year cap on extensions and

3 provision of full credit for patent time lost in the IND phase.

This leads to an increase of 1.9 years. Some 90 NCEs would benefit from this change. Hence, the synergistic effect is quite strong when one relaxes all three restrictions simultaneously. It amounts to roughly an extra year in EPL over what one obtains by adding the effects from separately relaxing each restriction.

Figure 7 shows the effect of the changes on the patent life distribution. We show the average of the 21 NCEs with the longest patent lives as quintile 1, the average of the 21 with the next longest as quintile 2, etc. Hence, in addition to the average change for all 105 NCEs reported in Table 3, the figure shows some further interesting effects. For example, raising the 14-year cap to 15 years benefits only the top two quintiles. Eliminating the five -ear cap, on the other hand, benefits only the drugs with shorter patent lives. Similarly, the provision of full credit for time lost in the IND phase benefits the NCEs with shorter patent lives. The 'EC case' benefits all groups but tends to have its most synergistic impact on the middle quintile. Finally, the simultaneous changing of three constraints, row 6 in Table 3, also benefits all groups but tends to benefit the NCEs with shorter lives the most.

Figure 7 Effect of modifying Waxman-Hatch rules on patent life distribution



8 Concluding remarks

This paper has examined the impact of two major public acts on effective patent life in pharmaceuticals. The 1984 Waxman-Hatch Act provided a basis for pharmaceuticals to recover some of the patent time lost in the lengthy clinical testing and FDA review process. The Act also facilitated generic drug competition by lowering the regulatory barriers on generic entrants. A second law impacting drug patents was the Uruguay Round Agreements Act of 1994, implementing the GATT provision that US patent terms are to be 20 years from the date of filing rather than 17 years from the date of patent grant.

An important result reported in Table 1 is that the actual EPL after Waxman-Hatch and GATT extensions averaged 10.79 years in the 1984–89 period and almost a year longer in the 1990-95 period, or 11.7 years. The average annual contribution in EPL from Waxman-Hatch extensions during the 1990 to 1995 period is 2.33 years. There is an upward trend in the size of Waxman-Hatch extensions as fewer NCEs are constrained over time to the transitional cap of two years. With respect to GATT transition rules, we found the effect on EPLs was small in both the 1980–84 and 1990–95 periods. In particular, GATT contributed 0.21 years and 0.40 years of extra patent life respectively. A major difference in the two cohorts is that the majority of the 1980s NCEs were not eligible for GATT, while all but three 1990s NCEs were.

We also performed a long-run simulation experiment on the future effect of GATT utilizing a comprehensive sample of 105 NCEs from the 1990 to 1995 period. A principal result that is somewhat surprising is that the change from a patent term based on 17 years from the grant date to the GATT rule of 20 years from the filing date may well result in shortening EPLs. Based on this experiment, the average effective patent life would decline by 0.34 years in the future when GATT is fully in place. The reason is the long patent pendency period that had characterized some NCEs. Of course, this result must be qualified by our assumption that the first filing of the patent application by firms will exhibit the same general pattern in the future as it has in the 1990–1995 period.

In sum, our retrospective and prospective analyses indicate the effects of Waxman-Hatch and GATT on EPL have been modest to date. This is especially true when one contrasts these impacts to the changes in generic competition facilitated by the 1984 Act. In two earlier papers, we found that the degree of generic competition has grown dramatically in the post-84 period. By the mid-1990s, major drug products confronting patent expiration typically lost more than half their sales within the first several months to generics entering the markets. This is a major difference from the pre-84 period. This experience, along with other developments, has prompted some in Congress to consider whether the rules on patent term restoration should be changed.

The last section reported a sensitivity analysis of various modifications in the Waxman-Hatch Act on patent lives. For example, we examined the effects of eliminating the five-year cap on patent extensions, providing full credit for patent time lost in the IND phase, and raising the 14-year cap on EPL life to 15 years. These changes, performed independently, produced increases in the average EPL in the range of 0.2 and 0.4 years. Only when we relaxed some or all of these provisions simultaneously did we obtain significantly larger 'synergistic' increases in EPL. In addition, the distribution of effects from these changes is quite different. Relaxing the five-year constraint on extensions and permitting full credit for IND testing tends to benefit NCEs with shorter patent lives. Increasing the 14-year cap on EPLs benefits NCEs with longer lives.

These findings should be a useful input to the emerging policy debate on possible reforms in the 1984 Act. Further analysis along these lines is also a desirable direction for future research. Although selecting a given set of rules for patent restoration will always give rise to vexing trade-offs, policymakers should be well informed about the consequences of different interventions.

References and Notes

1 DiMasi, J.A., Hansen, R., Grabowski, H. and Lasagna, L. (July 1991) 'Cost of innovation in the pharmaceutical industry', *J. Health Econ.*, Vol. 10, pp.107–142.

2 Levin, R.D., *et al.* (1987) 'Appropriating the returns from industrial research and development', *Brookings Papers on Economic Activity*, No. 3, pp.783–820.

3 Mansfield, E. (1986) 'Patents and innovation: an empirical study', *Management Science,* Vol. 32, No. 2, pp.173–181.

4 Grabowski, H.G. and Vernon, J.M. (1997) *The Search for New Vaccines: The Effects of the* ***Vaccines for Children*** *Program*, Washington, D.C., American Enterprise Institute.

5 Grabowski, H.G. and Vernon, J.M. (1996) 'Longer patents for increased generic competition: The Waxman–Hatch Act after one decade', *PharmacoEconomics*, Vol. 10, Suppl. 2, pp.110–123.

6 Public Law No. 103-465, 108 Stat. 4809 (1994).

7 US Senate, Judiciary Committee (1996) Hearing on the Drug Price Competition and Patent Term Restoration Act.

8 Nordhaus, W.D. (1969) *Invention, Growth, and Welfare: A Theoretical Treatment of Technological Change*, Cambridge, MIT Press.

9 Grabowski, H.G. and Vernon, J.M. (1994) 'Returns to R&D on new drug introductions in the 1980s', *J. Health Econ.*, Vol. 13, pp.383–406.

10 In a prior study, we performed some simulation analyses relevant to this issue. This was done in the context of examining the effects of price controls directed to breakthrough products (one of the possible outcomes of Clinton's Health Security Act). In particular, we curtailed the returns on the top decile NCEs to a breakeven rate of return, while leaving the expected returns on all other NCEs unchanged. The effects on R&D returns were striking. This change caused the representative NCE to go from a moderate positive net present value to a highly negative one. See the summary of these results in Grabowski [11] and also the discussion in Scherer [12].

11 Grabowski, H.G. (1994) *Health Reform and Pharmaceutical Innovation*, Washington, D.C., American Enterprise Institute.

12 Scherer, F.M. (1995) 'US industrial policy and the pharmaceutical industry', in Adrian Towse, (Ed.) *Industrial Policy and the Pharmaceutical Industry*, London, Office of Health Economics, pp.26–39.

13 Joe DiMasi and colleagues at Tufts University Center for the Study of Drug Development are undertaking an updated study of R&D costs. Aggregate industry data suggest that real R&D costs have grown significantly over the past decade [11]. At the same time, there is evidence that pharmaceutical firms are making strong efforts to reduce development times and launching new drugs on a global basis in order to achieve more rapid market diffusion, given the dramatic decline in sales revenue that now typically occur when patents expire.

14 In this regard, the original Nordhaus model has been generalized to take account of various factors including the presence of rivalry, patent races, spillovers, patent scope and other factors. For a further discussion, see Chapter 17 of Scherer and Ross [15] and Gilbert and Shapiro [16].

15 Scherer, F.M. and Ross, D. (1990) *Industrial Market Structure and Economic Performance*, third edition, Boston, Mass, Houghton Mifflin Co.

16 Gilbert, R. and Shapiro, C. (1990) 'Optimal patent length and breadth', *RAND J. Econ.*, Vol. 21, pp.106–112.

17 There were also demand-side barriers to generic prescribing and substitution. The state anti-substitution laws had only recently been repealed in many states. Furthermore, the health care system in the USA was dominated by fee-for-service reimbursement. In that system, physicians were the key decision-makers, and they often exhibited strong brand loyalty to the brand name products. Hence, many physicians in that era prescribed the brand name product and prohibited generic substitution on their prescriptions by checking 'do not substitute' and taking other such actions as required by state law [18]. Managed care was in its infancy, and only a small segment of the market was very price sensitive, e.g., state Medicaid programs. The market's receptivity to generic usage has changed dramatically with the growth of managed care penetration over the past decade and other related demand-side changes. This is discussed further in Section 4.

18 Masson, A. and Steiner, R.L. (1985) *Generic Substitution and Prescription Drug Prices: Economic Effects of State Drug Product Selection Laws*, Federal Trade Commission.

19 Merck & Co., Inc. versus Kessler, 1996 US App. LEXIS 6296 (Fed. Cir., April 4, 1996). The USA Court of Appeals for the Federal Circuit affirmed a lower court ruling that the Waxman-Hatch extension could be added to either the traditional 17-year term or the new 20-year term. The only exception is with respect to patents still in force on June 8, 1995 only by virtue of their Waxman-Hatch extension. In this latter case, the firm is entitled to the longer of the 20-year term without an extension or the 17-year term with an extension.

20 Grabowski, H.G. and Vernon, J.M. (1992) 'Brand loyalty, entry, and price competition in pharmaceuticals after the 1984 drug act', *J. Law and Econ.*, Vol. 35, No. 2, pp.331–350.

21 Studies of generic competition in the pre-1984 period by Statman [22] Caves *et al.* [23], and other researchers had revealed little generic entry or competition for a period spanning several years after patent expiration. The main exception was antibiotic drugs. This therapeutic category, in fact, was governed by a separate monograph system in the pre-1984 period in which generic firms could enter the market by demonstrating that their compound met the standards for the product set forth in the monograph. As discussed above, other types of drug products had to repeat safety and efficacy testing (if this information was not publicly available in the scientific literature). This constituted a very significant entry barrier, and little generic competition occurred in these classes.

22 Statman, M. (1981) 'The effect of patent expiration on the market position of drugs', in Robert B. Helms (ed.), *Drugs and Health*, Washington, D.C., American Enterprise Institute, pp.140–166.

23 Caves, R.E., Whinston, M.D. and Hurwitz, M.A. (1991) 'Patent expiration, entry and competition in the US pharmaceutical industry', *Brookings Papers on Economic Activity; Microeconomics*, pp.1–66.

24 The rate of generic sales erosion has become so rapid for major products in recent periods that many brand name firms have begun using a 'two tier' pricing approach to patent expiration. Under this strategy, the brand name firm either licenses rights for a generic product to another firm or produces and markets it through a separate subsidiary while maintaining the market presence of the original product at a premium price. Furthermore, the brand name firm will typically launch the generic version in advance of the patent expiration date in order to take advantage of possible first-mover advantages. These two-tier pricing strategies have achieved mixed commercial success to date. They are also under the continued scrutiny of the FTC for possible anti-trust violations.

25 Over this period, an increasing share of pharmaceutical prescriptions have been turned over to pharmacy benefit management firms (or PBMs). They employ a variety of strategies to achieve cost savings in pharmacy expenditures. Generic substitution is one of the core strategies employed by PBMs [26]. Strong financial incentives are typically incorporated into the benefit plan design to insure high rates of generic substitution once a product becomes multi-source (e.g., lower co-payments on generic products, caps set equal to the generic price reimbursement, mandatory generic utilization, etc.). Our work also indicates higher absolute margins are earned by pharmacists on generic products which give them a strong incentive to dispense these products whenever possible [5].

26 Grabowski, H.G. and Mullins, C.D. (1997) 'Pharmacy benefit management, cost–effectiveness analysis and drug formulary decisions', *Soc. Sci. Med.*, Vol. 45, No. 4, pp.535–544.

27 Process patents are considered the weakest form of protection in pharmaceuticals because more than one process can usually be employed to produce a particular compound.

28 As noted in [19], patents still in force on 8 June 1995 only by virtue of the Waxman-Hatch Act cannot add the Waxman-Hatch extensions to the 20-year term from filing date. It also should be noted that for some NCEs, the increased life from a later expiration date due to GATT is exactly offset by a shorter Waxman-Hatch extension. This will be the case when the 14-year constraint on Waxman-Hatch extensions is binding under both determinations of patent life. In these circumstances, firms do not receive any net benefits in terms of increased effective patent life. However, in principle, they receive some possible benefits in terms of patent scope. This is because at the point in time when the Waxman-Hatch extension goes into effect, the scope of patent protection narrows to cover only approved FDA extensions. However, a generic firm that wants to come on the market with a new indication during the Waxman-Hatch restoration period would have to do a regular NDA, not an ANDA, on the new indication.

29 Karin Tyson of the US Patent Office provided a list of patent expiration dates and extensions that were compiled by the Special Program Law Office as of May 1997. This list has now been put on their internet site and is regularly updated under the title, Patent Terms Extended Under 35 USC – 156. For those NCEs in our sample whose extensions were not yet approved by the US PTO, we used the Federal Register notices of the FDA to obtain the relevant IND and NDA periods. These data were then coupled with information on patent filing and grant dates (which is available on the US Patent Office web site) to compute effective patent life and Waxman-Hatch extensions. Another source of information on patent expiration dates is provided by the FDA's web site listing and publication on approved drug products (often denoted as 'The Orange Book'). These data are also available through FOI Services [30].

30 FOI Services, Inc. (1997) *Drugs under Patent, 1997*, Gaithersburg, Maryland, FOI.

31 Shulman, S. *et al.* (1992) 'Implementation of the Orphan Act: 1983–1991', *Food and Drug Law J.*, Vol. 47, No. 4, pp.363–404.

32 We separated our analysis of the 1980s period from that of 1990s introductions because the transition features of the 1984 law are much more important for 1980s NCEs. In addition, the ability of NCEs to benefit from the GATT transition rules differs significantly across the two periods.

33 Fourteen NCEs had potential extensions constrained to zero because they had EPLs in excess of 14 years. Furthermore, three NCEs had zero extensions because they failed to apply to the PTO for an extension (this must be done within 60 days from NDA approval). Finally, 11 NCEs obtained their primary protection from the five-year exclusivity period.

34 In this cohort, 20 of the 127 NCEs had their extension capped at two years because they were in clinical testing and already patented on September 24, 1984.

35 The NCEs that actually switched to the 20-year term received an average increase in EPL of just over one year (reflecting an average patent pendency period for these NCEs of approximately two years).

36 Of the 127 NCEs in the 1990s sample, 3 NCEs had patents which expired prior to June 8, 1995, and 15 NCEs had their maximum protection under the five-year exclusivity provision in either case. Of the remaining 109 NCEs, 57 had patent pendency periods of less than three years, leaving them with longer EPLs before the application of the Waxman-Hatch extensions. However, eight of these NCEs were constrained to a 14-year EPL (i.e., after applying the Waxman-Hatch extensions in both the pre- and post-GATT worlds). This leaves 49 of the 127 NCEs with positive net benefits from GATT in the 1990s cohort.

37 The drugs are Ornidyl, Aredia, Vantin, Cognex, Flumadine, Univasc, Azelex, and Sular. Removing these drugs from the sample changes only slightly the results in Table 1. That is, the benefit of GATT for the full sample for 1990s NCEs was 0.40 years; the benefit for the sample used here is 0.42 years.

38 Redwood, H. (1990) *Pharmaceutical Patent Term Restorations for the 1990s*, Oldvicks Press.

39 For further discussion of the EC law, see Hansen and Hill [40]. As noted, both the EC and Japanese laws have a five-year cap on product extensions as in the USA, but are less restrictive in other dimensions. In this regard, individual EC countries have enacted data exclusivity periods of six to ten years compared to the five-year period in the USA. The European Commission is currently considering harmonizing the data exclusivity period to ten years for all EU countries.

40 Hansen, B. and Hill, C. (June 1994) 'Obtaining an SPC in Europe', *Patents and Licensing*, pp.27–30.

41 Eliminating the 14-year cap completely is almost the same as changing it to 17 years. The EPL increases by only 0.06 years over the 17-year cap, and only six NCEs benefited.