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Longer Patents for Increased Generic Competition in the US

The Waxman-Hatch Act after One Decade

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Summary

The 1984 Waxman-Hatch Act had two main objectives. Title I was designed to promote price competition by establishing an abbreviated new drug application (ANDA) process for generic market entry. Title II was designed to encourage drug innovation by restoring some of the patent life lost during the lengthy FDA regulatory process. In this paper, we consider whether these twin objectives have been realised during the first decade of the Act's existence.

First, we investigate the pattern of generic and brand name prices and market shares for the major products whose patents expired between 1984 and 1993. A regression model indicates that generic competition has been intensifying significantly in recent periods. Major brand name products now typically lose more than half their market share within the first year after patent expiration. In addition, we examine changes in patent protection for new chemical entities introduced over the period 1984 to 1993. For 1991 to 1993 new drug introductions, the average effective patent life was 11.8 years with 2.3 years resulting from Waxman-Hatch extensions. In the final section of the paper, we consider how the US law compares with that in Europe and discuss possible legislative improvements in the 1984 Act.

The 1984 Drug Price Competition and Patent Term Restoration Act (the Waxman-Hatch Act) is unique in many ways. This law introduced the first change in US drug patent terms since 1861 and represented a delicate political compromise. It simultaneously lowered the barrier to market entry for generic drug firms and increased patent terms for new drugs delayed by FDA regulation. According to Senator Hatch, in his speech introducing the legislation in the Senate, 'the public receives the best of both worlds – cheaper drugs today and better drugs tomorrow'.

The Waxman-Hatch Act became effective on September 24, 1984. Thus, a decade of experience with the legislative scheme has been gained. In this paper, we analyse how the Act has performed in practice, how generic competition has changed under this law, and how it has affected the patent lives of new drugs introduced since 1984. The impact of the Act on consumers and pharmaceutical innovation is also considered. Specifically, we wish to ascertain whether Senator Hatch's forecast that the law would produce both cheaper and better drugs has, in fact, been correct.

1. Generic Entry and Price Competition

Title I of the Waxman-Hatch Act established an Abbreviated New Drug Application (ANDA) procedure for generic drugs. Under this ANDA procedure, to be approved generic drugs need only demonstrate bioequivalence to the pioneer's brand.

Prior to enactment of the Act, generic drugs could not rely on the safety and efficacy data submitted for the branded product and generic drug companies had to duplicate many of the pioneer's tests to gain FDA approval for their drug.[1]

In an earlier article, we examined the effect of generic entry on pricing behaviour and market shares for the period 1984 to 1987.[2] That study included 18 drugs with patents that expired in the period immediately after the passage of the 1984 Drug Price Competition and Patent Term Restoration Act. In this section, we extend our analysis to 22 drugs that encountered generic competition for the first time in the period 1989 to 1993.

As we observed in our earlier study, before the 1984 Act there were a number of factors that led to strong brand loyalty for brand name drugs even after patent expiration. For example, physicians generally gained experience with brand name drugs during the patent exclusivity period, and upon patent expiration they continued to prescribe the brand name drug. Often they had little incentive to prescribe lower cost generic alternatives and many doctors were uninformed about the relative prices of these agents. Furthermore, state anti-substitution laws instituted in the 1950s and 1960s prohibited pharmacists from substituting cheaper generic drugs for equivalent brand name products.

As of the mid-1970s, however, a number of institutional changes affecting pharmaceuticals have resulted in greater price sensitivity. First, state anti-substitution laws have all been repealed. New substitution laws permit, and often require, pharmacists to substitute lower cost generics – unless the physician specifically requires that the brand name product be dispensed (as we will document later, pharmacists generally have a profit incentive to dispense the generic rather than the brand product). In addition, third-party payers, such as Medicaid, instituted requirements limiting reimbursement to generic price levels.

The growth of managed-care programmes, pharmacy benefit managers (PBMs) and health maintenance organisations (HMOs) has significantly increased the incentives for generic utilisation in the last few years. A recent analysis estimated that over 115 million beneficiaries were covered by employer-funded PBM services in 1994, and incentives for generic usage were one of the first steps taken under these plans.[3] These developments make an analysis of recent patent expirations especially interesting at this time.

In this section, after explaining the nature of our data sample for the 1989 to 1993 period, we will compare new findings with our earlier 1984 to 1987 results. The earlier results showed that generic products entered the market at a significant price discount compared with the brand name product and, contrary to the period before the 1984 Act, obtained close to half the market within 2 years.[2] In addition, the brand name product did not compete on a price basis with the generics.

We will also discuss the extent to which price cuts flow through from pharmacies to the final consumer, given that wholesale prices of generic products are less than half those of brand name drugs.

1.1 The 1989 to 1993 Data Sample

We assembled data for a sample of 22 brand name products first exposed to generic competition in the period 1989 to 1993 (table I). Our objective was to include all major products; however, 4 products that just failed to meet the criterion of at least $50 million in sales at the time of patent expiration were also included for some analysis. Thus, the sample comprised 18 major drugs and 4 other drugs.

For each product, we identified the most popular dosage formulation strength from data audits of IMS America Inc.[4] This data source also provided an estimate of total sales of each dosage formulation strength by manufacturers and wholesalers to

1 Before the 1984 law, generic firms could cite evidence on safety and efficacy published in the scientific literature for post-1962 drugs in lieu of performing these studies. However, since a considerable amount of the evidence needed to obtain FDA approval was not part of any published work, many studies had to be repeated to gain product approval. This was a costly procedure and, consequently, many drugs had little or no generic competition even several years after patent expiration.[1]

Table I. Brand name drugs first exposed to generic substitution during the period 1989 to 1993 included in analysis

Brand name[a]	Generic name	Date of generic entry
Flexeril	Cyclobenzaprine HCl	June 1989
Minipress	Prazosin	June 1989
Asendin	Amoxapine	Sept 1989
Proventil/Ventolin	Albuterol	Jan 1990
Clinoril	Sulindac	May 1990
Minocin	Minocycline	Sept 1990
Procardia/Adalat	Nifedipine	Oct 1990
Tenormin	Atenolol	Aug 1991
Imodium	Loperamide	Oct 1991
Tolectin	Tolmetin	Jan 1992
Aventyl/Pamelor	Nortriptyline	Aug 1992
Feldene	Piroxicam	Aug 1992
Cardizem	Diltiazem HCl	Nov 1992
Dolobid	Diflunisal	Nov 1992
Visken	Pindolol	Nov 1992
Orudis	Ketoprofen	Jan 1993
Lopid	Gemfibrozil	Feb 1993
Sinemet	Caridopa/levodopa	Feb 1993
Corgard	Nadolol	Sept 1993
Naprosyn	Naproxen	Oct 1993
Xanax	Alprazolam	Oct 1993
Lopressor	Metoprolol	Nov 1993

a Some drugs had 2 different brand names (marketed by 2 different companies); both names are included.

drugstore and hospital outlets. Sales values are available in both dollar ($US) and physical units. Using these data, we determined prices at various time intervals after generic market entry for both the brand name products and the generic entrants. Hence, the prices used in this analysis represent the average cost per unit paid by drugstores and hospitals for the most popular dosage formulation strength for each product. Market shares in physical units for brand name drugs and generics were also computed at the same time-points after entry.

1.2 Comparison of the 1984 to 1987 and 1989 to 1993 Periods

Table II provides a summary of findings for the entire period, 1984 to 1993. In particular, it covers 10 drugs that experienced initial generic competition in the 1984 to 1985 period, 8 drugs with initial competition in the 1986 to 1987 period, and 7 drugs with initial competition in the 1989 to 1991 period. As stated earlier, results for the 1984 to 1987 period were reported in our 1992 article,[2] and covered 18 major brand name drugs that first encountered generic competition during those years. We compared those findings with results for a later period. For more meaningful comparison, the earlier study results were divided into 2 periods: 1984 to 1985 and 1986 to 1987.[2] In order to have 2 full years of data after generic entry, only 7 drugs (from the 22 in the 1989 to 1993 analysis) are included in the evaluation for the years 1989 to 1991.

As shown in table II, in the first year after generic entry, the average brand name price index rose by 6% for 1984 to 1985 drugs, 8% for 1986 to 1987 drugs, and 6% for 1989 to 1991 drugs. Hence, the pattern of brand name products not dropping their price to compete with much lower priced generics that was established in 1984 to 1987 continues in the more recent period. Similar small increases in the brand name price index also occurred during the second year after entry.

In contrast to the increases in the brand name price index, substantial decreases in the generic price index took place over the 2-year period (table II). Price decreases of about 35% for generics 2 years after entry occurred in all 3 time periods. Similar patterns were also seen for the ratio of generic to brand name prices, i.e. at entry the generic price was about 60% of the brand name price, and after 2 years it decreased to slightly greater than one-third of the brand name price.

In contrast to the above results, the average generic market share after 2 years did appear to differ between the 3 periods. Indeed, it increased over time. In the first period (1984 to 1985), generics averaged 45% of the market share in physical units. In the second period (1986 to 1987), the generic share increased to 54%, and in the third period (1989 to 1991) it increased even higher to 59% (fig. 1). This finding is consistent with the general

2 One of the 10 drugs in the 1984 to 1985 category actually encountered generic competition in mid-1983.

Table II. Summary of the effects of generic competition on the drug market: 1984 to 1991. Each value is an unweighted average of the values for all drugs in each category

	Drugs[a]		
	1984-1985	1986-1987	1989-1991
Average brand name price index			
At date of entry	1.0	1.0	1.0
1 year after entry	1.06	1.08	1.06
2 years after entry	1.11	1.12	1.10
Average generic price index			
At date of entry	1.0	1.0	1.0
1 year after entry	0.77	0.79	0.86
2 years after entry	0.65	0.67	0.63
Average ratio of generic price to brand name price			
At date of entry	0.63	0.59	0.61
1 year after entry	0.47	0.44	0.49
2 years after entry	0.38	0.36	0.35
Average generic market share in physical units (proportion of total market)			
At date of entry	0.07	0.11	0.13
1 year after entry	0.32	0.38	0.41
2 years after entry	0.45	0.54	0.59

a The drugs include 10 major 1984-1985 drugs and 8 major 1986-1987 drugs, as reported in Grabowski and Vernon[2], and 7 major 1989-1991 drugs.

observation that managed care and other demand side pressures are continuing to increase generic utilisation. Indeed, by disaggregating the recent period and looking at shorter periods after generic entry, we found that the extent of generic utilisation has intensified significantly within the 1989 to 1993 period (section 1.3).

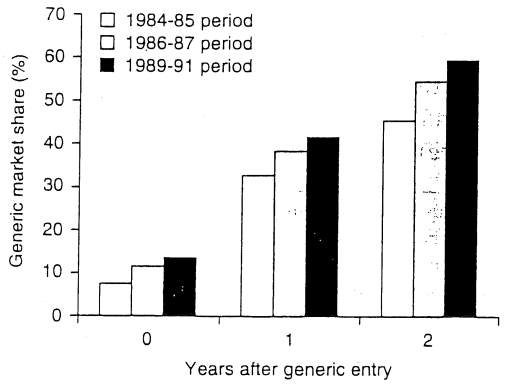

Fig. 1. Growth in unit market shares for generic suppliers during the periods 1984 to 1985, 1986 to 1987 and 1989 to 1991.

1.3 The Recent Period: 1989 to 1993

We focus now on the period, 1989 to 1993, for which we have data on 22 drugs. Table III contains results similar to those in table I, but only the 18 major drugs of the recent period were included. The drugs are divided into 3 categories: 6 drugs that had generic competition initially in 1989 to 1990, 5 drugs that first had generic competition in 1991 to 1992, and 7 drugs that encountered generic entry in 1993.

Results in table III and figure 2 suggest that the trend of increasing generic utilisation is gathering momentum rather dramatically. For example, the average generic market share 18 months after entry increased from 47% for the 1989 to 1990 period to 72% for the 1991 to 1992 period. The average ratio of generic to brand name price fell from 50 to 42% over this same time interval. The last period, the year 1993, is so recent that we can only measure market shares 6 months after entry. During this shorter time interval, generic utilisation increased from 31 to 51% over the 3 periods.

Table III. Summary of the effects of generic competition on the drug market: 1989 to 1993. Each value is an unweighted average of the values for the drugs in each category

	At date of entry	6 months after entry	1 year after entry	18 months after entry
Average ratio of generic to brand name price				
1989-1990[a]	0.59	0.54	0.54	0.50
1991-1992[b]	0.63	0.58	0.47	0.42
1993[c]	0.67	0.46	NA	NA
Average generic market share in physical units (proportion of market)				
1989-1990[a]	0.14	0.31	0.41	0.47
1991-1992[b]	0.20	0.44	0.61	0.72
1993[c]	0.13	0.51	NA	NA

a The average of 6 major drugs first experiencing generic competition in the 1989-1990 period.
b The average of 5 major drugs first experiencing generic competition in the 1991-1992 period.
c The average of 7 major drugs first experiencing generic competition in 1993.
Abbreviation: NA = not available.

The year 1993 may have been unusual in that 2 brand name suppliers initiated new strategies to thwart generic competition. An article in *Business Week*[5] indicates that Upjohn and Syntex, suppliers of the drugs Xanax and Naprosyn, respectively, introduced generic versions of their brand name product in October 1993. By June 1994, according to the article, Upjohn had 90% of the generic market and Syntex had 68%. Our own data, at 6 months postgeneric entry, show total generic shares to be 68% and 77%, respectively. These companies obtained these large market shares by introducing the generic versions before brand patents expired. While this strategy gave them an advantage in being first on the market,[3] it did not slow down generic price cuts. The same article[5] notes that the generic price of naproxen fell to 10% of the price of the brand name product. Whether such aggressive behaviour by brand name firms is profitable and will continue in the future is an open question at this time.

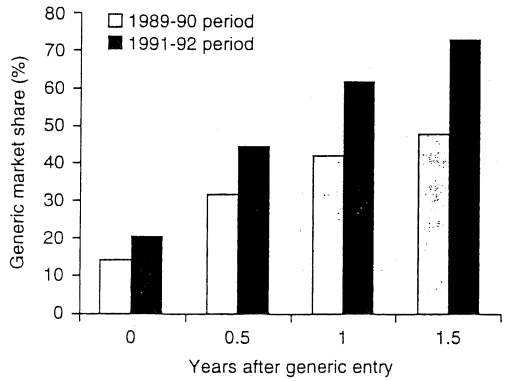

Fig. 2. Growth in unit market shares for generic suppliers during the periods 1989 to 1990 and 1991 to 1992.

We now discuss a regression analysis in which several variables explaining generic market shares 6 months post-entry are considered.[4] The 4 drugs that failed to meet the $50 million sales criterion are included in this sample. In the year before entry, the 4 additional drugs had sales worth between $23 million and $43 million. As indicated earlier, the other 18 drugs had minimum sales of at least $50 million.

The dependent variable in this regression model is taken to be the generic market share 6 months post-entry (GENSH). Explanatory variables are the date of first generic entry (T = 1 is defined as June 1989 and T represents the number of months from that date) and SIZE [total sales of the brand name

3 Being first to the market is an advantage for several reasons. For example, by getting drug chains to stock the first generic version of a drug, pharmacists and customers become acquainted with that particular formulation shape and colour and will not want to change. Also, the initial generic company is usually given the opportunity to simply match a subsequent generic's price and thereby maintain pharmacies' accounts.

4 Regression analysis is explained in depth in several standard econometric texts. See, for example, William H. Greene.[6]

product in the year before generic entry (in billions of dollars)]. The hypothesis is that as SIZE increases so too does the number of generic entrants, because of perceived profitability. The greater the number of generic suppliers the more vigorous price competition is expected to be and, therefore, the larger the generic market share.[5] In this analysis, the variable SIZE ranges from a low of $23 million to a high of $614 million for the 22 drugs. The mean value of SIZE is $208 million.

In addition to the explanatory variables described above, 3 dummy variables were introduced to account for effects of the therapeutic class of the drugs. The dummy variables are ANIF for the anti-inflammatory/muscle relaxant group of drugs, CARD for cardiovascular drugs, and PSYCH for psychotropic drugs. The dummy variables take on the value one if the drug is in the therapeutic class, and zero if otherwise. The sample includes 8 cardiovascular drugs, 7 anti-inflammatory/muscle relaxant drugs and 3 psychotropic drugs, and the remaining 4 drugs are each in a different class (respiratory, anti-infective, antiparkinsonian and antidiarrhoeal).

The estimated equation is:

$$\begin{aligned} GENSH = {} & \underset{(1.83)}{0.09} + \underset{(3.30)}{0.004T} + \underset{(4.64)}{0.58SIZE} + \\ & \underset{(0.56)}{0.04PSYCH} + \underset{(0.04)}{0.002CARD} + \underset{(3.23)}{0.17ANIF} \end{aligned}$$

where the adjusted $R^2 = 0.77$, the total number of drugs (n) = 22, and the t-statistics are in parentheses.

The statistical results of this analysis are interesting. As expected, the coefficients of the 2 explanatory variables, T and SIZE, are both positive and both are statistically significant. Of the 3 therapeutic class variables, ANIF is the only statistically significant variable. Hence, results indicate that anti-inflammatory/muscle relaxant drugs lose some 17 percentage points of the market share more to generics than do other types of drugs when measured 6 months after initial generic entry.

The regression explains more than three-quarters of the variation in generic market shares across the 22 products. Consistent with the results in table III, the coefficient of T indicates that drugs first exposed to generic competition in more recent years experience greater market losses to generic competitors. This 'vintage' effect has a value of approximately 5 percentage points per year. Thus, a drug first encountering generic competition in June 1993 lost 20 percentage points more of its unit market share after 6 months than one first encountering generic competition in June 1989, all other things being equal. In addition, the coefficient of SIZE indicates that increasing the revenue of a drug by $100 million will lead to a greater generic market share of about 6 percentage points.

The pricing pattern and market shares for the longest period permitted by our data (3.5 years) were also assessed. Results for the average relative price and generic share for the 7 major drugs that encountered generic entry for the first time in 1989 to 1990 are shown in figure 3. 14 quarters after entry, the average generic market share was 71% and the ratio of generic to brand name price was 34%. As can be seen, the price ratio declined very slowly after about quarter 8, when it reached 41%. In contrast, the generic market share continued to increase throughout the period. Generic market share in quarter 8 was 53%, and it increased to 71% in quarter 14.

1.4 Price Reduction Benefits to Consumers

As discussed earlier, the 1984 Act was designed to benefit consumers by encouraging generic competition upon patent expiration. Clearly, as tables II and III indicate, generic prices are generally much lower than brand name drug prices. For example, table III shows that for drugs encountering generic entry in 1993, the generic drug price 6 months after entry was 46% of the brand name price, representing a 'price cut' of 54%. In a competitive retail distribution sector, one would expect

5 A recent report of an econometric study of generic competition includes a table in which price reductions are shown to increase with the number of generic suppliers.[7]

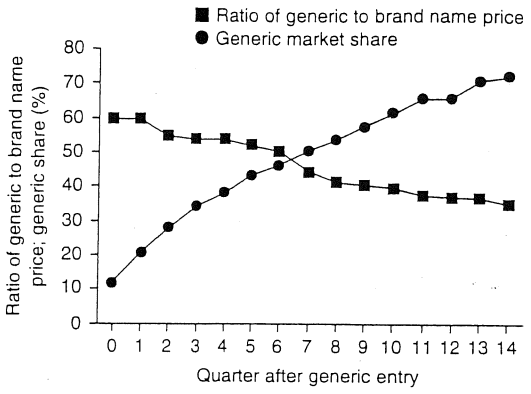

Fig. 3. Trend in relative prices and unit shares for generic suppliers for 7 drugs experiencing initial generic entry in the 1989 to 1990 period.

price cuts at the wholesale level to flow through to consumers.

However, the extent of competition in the retail market for prescription drugs is open to question. Among other factors, the price and quality information that is available to consumers can be relatively costly to obtain. This suggests that drug stores possess some market power in their pricing of prescription drugs.

It is possible that pharmacists earn a higher profit per unit on the lower price generic drugs, thereby appropriating some of the potential gains to consumers from lower manufacturers' prices. This possibility has been investigated by Masson and Steiner[8] and Bloom et al.[9] for time periods predating the 1984 Act. Both studies found that drug store margins on generic products are higher on both a percentage and absolute basis. However, since these analyses were undertaken there has been a dramatic increase in the growth of generic drugs as a result of the 1984 Act and other factors. It is therefore useful to examine this issue for the post-1984 Act period.

To examine prices at the retail level, we assembled data on the total number of prescriptions, average prescription size and total amount spent by consumers for the drugs in our sample (1984 to 1987). These data were collected in the IMS National Prescription Audit. Using the most popular dosage formulation strengths prescribed, we computed prices of the brand and generic drug on a per pill basis. Because of data availability problems, we were able to obtain complete data on only 15 of the 18 drugs in our 1984 to 1987 sample. Using the IMS Drug Stores Audit, we also obtained matching data for the wholesale prices paid by pharmacists for these drugs on a per pill basis.

Table IV provides a summary of this analysis (detailed data on each drug are given in table V). As indicated, all prices are measured 1 year after generic entry. Table IV shows that the average margin on generic products of 13.24 cents exceeds that of brand name drugs (9.86 cents). This occurs despite the fact that the average wholesale price for brand name drugs is 33.38 cents compared with only 14.85 cents for generic competitors. Hence, the average percentage markup for generics is 89% compared with 30% for brand name drugs. These results are consistent with those of Masson and Steiner,[8] who found that the dollar margin on generics was higher than that on brand name drugs for 23 of the 37 drug entities that they assessed. We found that for 13 of the 15 drugs, the absolute generic margin exceeded that of the absolute margin for the brand name drug. Masson and Steiner also argued that there tends to be a greater overestima-

Table IV. Average drug store prices[a] and margins for brand name and generic products: 1984 to 1987 sample[b]

	Brand name price	Generic price	Generic to brand name price ratio
Wholesale	33.38	14.85	0.44
Retail	43.24	28.09	0.65
Absolute markup	9.86	13.24	
Percentage markup	30%	89%	

a All prices are measured in US cents per pill 1 year after generic market entry took place.

b See table V for data on the individual drugs included in this sample.

Table V. Drug store margins for brand name and generic products measured 1 year after market entry of the generic version of the drug. Prices and margins are measured in US cents per pill

	Wholesale prices		Retail prices		Margin	
	brand name	generic	brand name	generic	brand name[a]	generic[b]
Indomethacin	23.29	13.35	33.13	24.91	9.84	11.56
Tolazamide	30.7	18.29	38.48	27.58	7.78	9.29
Methyldopa	15.47	9.81	19.92	16.24	4.45	6.43
Chlorpropamide	28.12	5.02	36.01	14.23	7.89	9.21
Ibuprofen	15.51	7.81	26.74	17.67	11.23	9.86
Lorazepam	27.81	13.91	40.51	24.49	12.70	10.58
Diazepam	24.37	5.64	31.18	16.88	6.81	11.24
Propranolol	18.78	7.56	22.94	14.89	4.16	7.33
Metoclopramide	21.65	10.91	30.14	20.65	8.49	9.74
Flurazepam	25.94	14.97	38.46	28.45	12.52	13.48
Doxepin	25.66	9.90	34.21	22.49	8.55	12.59
Haloperidol	59.66	36.05	73.51	55.74	13.85	19.69
Clonidine	22.19	6.34	27.65	13.68	5.46	7.34
Verapamil	23.67	12.86	31.05	22.13	7.38	9.27
Cefalexin	137.82	50.39	164.67	101.33	26.85	50.94
Average	33.38	**14.85**	**43.24**	**28.09**	**9.86**	**13.24**

a The absolute margin for each drug. This is calculated as the difference between the retail and wholesale price of the brand name product.

b The absolute margin for each drug. This is calculated as the difference between the retail and wholesale price of the generic product.

tion of generic wholesale prices than of brand drug prices in the IMS data. If true, this implies that generic drugs are even more profitable relative to brand name products.

However, these much lower generic prices do not give the expected benefit to consumers. For example, using data from table IV, the ratio of the average generic price to the average brand name price at wholesale is 0.44. One might incorrectly conclude that the 1984 Act has given consumers generic prices that are 56% lower than brand name drug prices. However, the ratio of the average generic price to brand name price at the retail level is 0.65. The true price reduction to consumers resulting from generic substitution of brand name products is therefore only 35%.

This smaller price reduction results because the retail markup of wholesale prices is not a proportional one (see above). While we do not argue that the same percentage markup should apply, a conservative approach would be to assume that in a competitive retail sector the absolute margin of the brand name product could be viewed as a minimum absolute margin of the generic. That is, if there are pharmacy costs that are independent of the cost of drug acquisition – as there obviously are – then it would seem reasonable to take the absolute brand name margin (9.86 cents) as a reasonable floor for the generic margin (rather than the actual margin of 13.24 cents).[6] If this is done, then the generic retail price would be 24.71 (14.85 + 9.86) cents. The ratio of generic price to brand name price at the retail level would then be 0.57. The true price reduction associated with generic substitution in this hypothetical situation would then be 43%. Therefore, manufacturers' relative prices cannot be used to measure benefits to consumers.

The analysis presented here must be qualified by the fact that the IMS data source does not include all of the discounts that wholesalers offer to pharmacy retailers and also excludes rebates that

6 We term this 'conservative' because it seems reasonable to assume that there must be at least some pharmacy costs that are positively related to the wholesale price, e.g. inventory costs. If so, then the generic absolute margin in a competitive retail sector would be less than the brand absolute margin.

manufacturers give to managed-care institutions. Indeed, results in this section are relevant primarily to the cash out-of-pocket consumer market. The managed-care market needs to be studied separately using alternative data sources.

As noted earlier, a problem from a public policy perspective is the cost of information on the quality and price of drugs to consumers. It is not clear what policy measures could be taken to improve this situation (substitution laws in some states initially required 100% pass through of savings to consumers, but this did not lead to increases in generic dispensing[8]). It is worth noting, however, that all potential savings created by vigorous generic competition at the manufacturer level do not seem to be passed through to consumers.

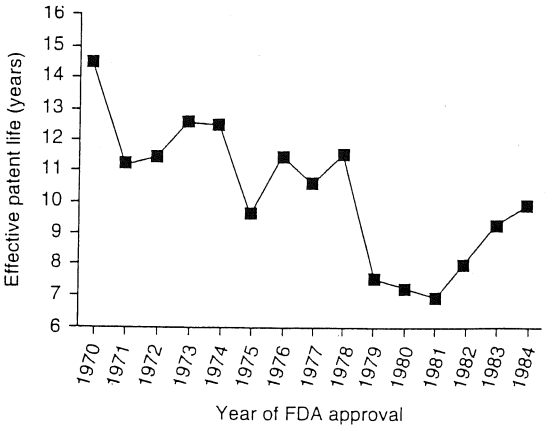

Fig. 4. Average effective patent life by year of FDA approval for the period 1970 to 1984.

2. Patent Restoration

In Title II of the Waxman-Hatch Act, Congress sought to reverse the decline in effective patent life that had been occurring over the prior 2 decades. Both clinical testing and FDA regulatory approval times steadily lengthened after 1962, when the Kefauver-Harris Amendments were enacted (for a survey of the literature see Grabowski and Vernon,[10] chapters 2 and 3). Because drug firms must apply for patents early in the development period, effective patent life by the early 1980s was significantly less than the nominal patent life of 17 years.[7]

Figure 4 shows the average effective patent life for US new chemical entities (NCEs) during the period 1970 to September 24, 1984 (for an analysis of effective patent life in the pre-1984 period, see Eisman & Wardell[11] and Kaitin & Trimble[12]). While there are clearly annual fluctuations in this series, there is also a strong downward trend in patent life over time, which is reflected by average effective lives for the 3 successive periods 1970 to 1974, 1975 to 1979, and 1980 to 1984 of 12.4 years, 10.0 years and 8.1 years, respectively. Thus, the average effective patent life in the period just before the enactment of the 1984 law was approximately half the nominal life of 17 years.

If Congress had only instituted ANDAs under the 1984 Act, without also addressing the reductions that had occurred in effective patent life because of increased regulation and other factors, there would have been significant adverse consequences for drug innovation incentives.[8] Title II of the Act was designed to restore a portion of the patent life lost during the clinical testing and regulatory approval periods. In particular, the Act provides new drugs with an extension in effective patent life equal to the sum of the New Drug Application (NDA) review time plus one-half the Investigational New Drug (IND) clinical testing time. It allows a maximum extension of 5 years, and extensions are capped at 14 years of total effective patent life.

The law also provides for a 5-year data exclusivity period in which no ANDAs can be granted for an NCE. This is designed to provide a basic 5-year protection period for NCEs with patents that have already expired, and for those with very short

7 Effective patent life in this analysis is measured from the date of FDA marketing approval to the date of patent expiration.

8 The 1984 Act not only established the ANDA procedure for post-1962 drug introductions, but also gave generic producers the right to perform their bioequivalence testing and FDA applications in the pre-patent expiration period.

terms after patent restoration. This data exclusivity does not absolutely prevent a generic competitor from entering the market. However, during this 5-year period, generic drug applications cannot rely on data from the brand name drug, but require their own safety and efficacy data in order to receive FDA approval. This is a very high cost barrier that would usually preclude generic entry during the first 5 years of market life.

The law also had some transitional features. In particular, INDs in clinical testing on September 24, 1984, were eligible for a maximum patent term extension of 2 years. Hence, the full benefits of the Act were confined to drugs in the discovery or preclinical testing phases at the time of the law's passage. The Act also retrospectively granted an ANDA exclusivity period of 10 years to drugs approved for marketing in the period January 1, 1982, through September 23, 1984.

Another statute passed in the same period as the Waxman-Hatch Act was the 1983 Orphan Drug Act. This Act provided a variety of incentives for drugs indicated for treatment of 'orphan' indications or rare diseases, subsequently defined in the law as disease indications affecting less than 200 000 US patients. These incentives included a 7-year exclusivity period for orphan drugs. In the following analysis we exclude orphan drugs, for which no other patent protection exists other than this 7-year exclusivity. We do so because our primary interest in this paper is patent term extensions associated with the Waxman-Hatch Act.[9]

2.1 Waxman-Hatch Patent Extensions

When computing effective patent life for a specific NCE, we look first to see if a compound patent exists. This is the strongest form of patent protection available for pharmaceuticals. Compound patents are also typically the patents chosen for extension by drug firms (only one patent per NCE is eligible for extension under the 1984 Act). If no compound patent exists, an NCE's composition or use patent is used to compute effective patent life. If the effective life is less than 5 years after considering all available compound, composition or use patents, the 5-year data exclusivity term provided under the Act for all post-1984 NCEs is used to compute effective life.

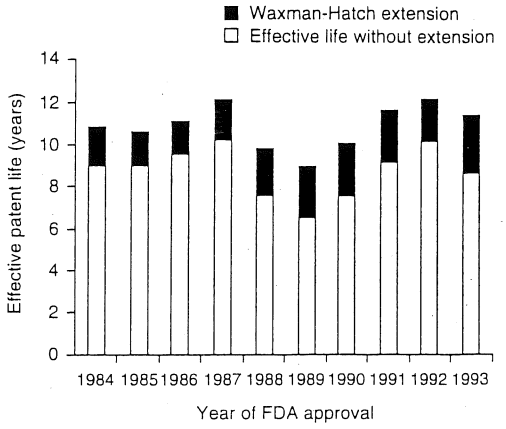

Fig. 5. Average effective patent life and Waxman-Hatch extensions by year of FDA approval, 1984 to 1993.

Figure 5 shows the average annual effective patent life for NCEs approved for marketing between September 24, 1984, and December 31, 1993 (i.e. the post-Waxman-Hatch period). The average effective patent life of these NCEs, including the extension, varied from 9.0 years in 1989 to over 12 years in 1992. The average extension allowed by the Waxman-Hatch Act, also shown in figure 5, has grown over time.

The period since 1991 is the most relevant for the purpose of judging the benefits of the 1984 Act. Prior to 1990, only a handful of NCEs were eligible to receive patent extensions in excess of 2 years (i.e. the transition cap). There were, however, some NCEs with little or no effective patent life that received the ANDA exclusivity protection of 5 years. Starting in 1991, however, an increasing number of new drug introductions in each year were eligible for the full benefits of the Act because they

9 Inclusion of this set of orphan drugs in our analysis would yield a downward bias over time to our effective patent life series. This is because the number of orphan drugs has increased over time, and the 7-year exclusivity term is shorter than the average effective patent life for other NCEs. For an analysis of the Orphan Drug Act see Shulman et al.[13]

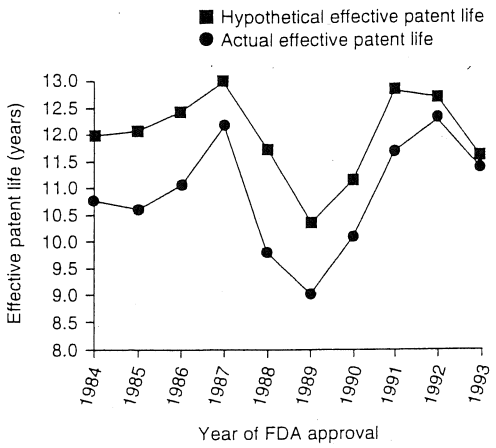

Fig. 6. Actual effective patent life versus hypothetical effective patent life, assuming no transitional caps on patent term extensions.

entered clinical trials after the 1984 Act was passed. This point is illustrated in figure 6, which shows convergence over time between the actual effective patent life and a hypothetical effective patent life curve. This hypothetical curve is computed under the assumption that all NCEs in each year receive the full benefits of the Act. By 1993, all but 2 drugs in that year's cohort received the full patent restoration benefits.

The 1991 to 1993 cohort had an average effective patent life of 11.8 years. This is probably representative of the average patent lives of NCEs currently coming on to the market. If Congress had not included the patent restoration section of the 1984 Act, the representative NCE in this cohort would have had an average effective patent life of 9.5 years. Hence, the Act has produced a significant increase in patent protection periods for new drug introductions. However, it should be emphasised that there is also considerable variability in this average effective life. For example, in the 1991 to 1993 cohort there were 31 NCEs (44%) that had an average effective patent life equal to or greater than the 14-year upper limit on Waxman-Hatch extensions and, conversely, there were 19 drugs (27%) with patent lives shorter than 10 years (excluding those with only orphan drug protection). There were also 11 orphan drugs with 7-year exclusivity as their main property rights protection.

2.2 GATT Extensions

One interesting recent development for pharmaceutical patents was the passage by Congress of Public Law 103-465, which implements the General Agreement on Tariffs and Trade (GATT) in the United States. Under GATT patent exclusivity, terms are 20 years from the date of patent application, rather than 17 years from the date of the patent grant. Patents filed on or after June 8, 1995, are, and will be, governed by this new rule, which brings the United States in accord with the rest of the world.

GATT also has a discretionary transitional feature for patents in effect on June 8, 1995. This permits firms to elect either the 20-year term from patent application or the 17-year term from patent award. An unresolved issue is whether patent term restorations previously granted under the Waxman-Hatch Act can be added to the 20 years from filing term under the GATT transitional law. The Patent and Trademark Office determined that they could not be,[14] but this ruling was overturned by the Federal District Court in October 1995.[15] This court decision is currently under appeal.

NCEs patented after June 8, 1995, are covered by a 20-year term from the date of application, as instituted by the GATT Agreements. Waxman-Hatch extensions will then be added to this expiration date.[15] Overall, the GATT law could add another year or so of effective patent life to some as yet unpatented NCEs compared with the duration of patent they would generally have received under the old patent law regime. For example, if the US Patents Office took 2 years to grant a patent to a representative NCE under the prior 17-year regime, then the shift to the new regime of a 20-year patent from the date of filing means the patent for this NCE would expire 1 year later. The Waxman-Hatch time extension would be added to this later expiration date. This would mean a later patent expiration unless this is counteracted by the 14-year constraint. Indeed, a growing number of

NCEs are now being extended to the maximum 14-year effective life by Waxman-Hatch extensions, and this will counteract the GATT-induced increases in patent life for these drugs.

3. Summary and Conclusions

As we discussed at the beginning of the paper, the objectives of the Waxman-Hatch Act were to facilitate generic entry into the pharmaceutical market in order to spur drug price competition, and also to provide a positive stimulus for drug innovation.

In terms of the first objective, the Act has clearly been a tremendous success. The level of generic competition is very different one decade after, compared with before, the Act. In the early 1980s, the level of generic dispensing in the US was around 10%. By contrast, in the mid-1990s, the level of generic prescribing approached 40%.[16] Furthermore, there are more than 100 drugs coming off patent between 1992 and the year 2000, with current market sales of more than $25 billion. As a consequence, one analyst projects that generic drugs will account for more than 65% of all new prescriptions by the turn of the century.[17] The Waxman-Hatch Act is not the only explanation for this new world of extensive generic usage. The growth of managed care and other related demand-side factors have also played a major role. But the 1984 Act, by making entry into the market relatively easy for generic products, was a prerequisite for the dramatic changes that have occurred in this past decade.

Our analysis of major new drugs coming off patent indicates that the extent of generic competition has continued to accelerate in recent years. In particular, drugs that have come off patent since 1991 experienced unit sales losses to generics of over 50% during the first several months of generic competition. This is a much more rapid rate of loss to generics than was observed for similar drugs coming off patent between 1984 and 1989.[10]

Consumers and purchasers of pharmaceuticals have clearly been major beneficiaries of the increased generic competition since 1984. While we have not performed precise accounting, the cumulative savings to consumers and payers would be in the billions of dollars. Pharmacists also appear to be significant beneficiaries of the Act, given the larger absolute price markups on generic drugs compared with their brand name counterparts.

The effects of the 1984 Act on the incentives for drug innovation are more complex to evaluate. The Act has clearly led to significant patent extensions on recent new drug introductions. For example, the average effective patent life for new drugs coming to the market in the 1991 to 1993 period was 11.8 years, with an average extension of 2.3 years. Moreover, 43% of these NCEs had effective patent lives of 14 years or more (14 years is the upper limit for extensions under the Act).

While patent periods have increased, there is also a much more rapid rate of sales decline after patents expire. One must balance these two effects when assessing the impact of the law on new drug returns. Given the many other changes that have also taken place in the market-place for new drugs over the past decade, it is not clear what the relevant baseline for undertaking this type of analysis should be.

One major finding that has emerged from our ongoing studies of the returns from research and development for new drug introductions in the 1970s and 1980s is that product lifetimes are shortening over time. In other words, despite the movement towards longer effective patent lives, product life cycles are plateauing earlier in the pre-patent period and they are also subject to much more rapid rates of sales decay when patents do expire (for a summary of our work on the 1980 to 1984 cohort of new drug introductions and a discussion of preliminary findings for the 1980 to 1989 cohort, see Grabowski and Vernon.[18] This reflects increased price sensitivity in the pharmaceutical market because of managed care, as well as the increased

10 The 18 drugs from the 1984 to 1989 period experienced a 54% loss after 2 years of generic competition, while drugs from the 1991 to 1993 period experienced this rate in less than a year.

availability of substitute therapies and generic competitors for major brand name products.

When making a final analysis, policy makers must consider whether current rules on property rights for pharmaceuticals, devised in a very different market environment, provide the optimal amount of stimulus for the drug innovations of tomorrow. In a computer simulation model of the effects of different public policies on innovation,[19] we found that the length of patent protection was a very important policy instrument for the pharmaceutical market, albeit one that was subject to diminishing returns. In particular, we found that the positive stimulus to innovation was disproportionately concentrated in the first decade of market life, with significant diminishing returns as one extended patents to the full nominal life of 17 years.

If policy makers are to consider changes in the 1984 Act, we think the first priority should be for products that have little or no effective patent life. In particular, attention should be focused on new drug candidates that must rely on the 5-year data exclusivity for their basic protection. We do not know how many potentially useful compounds have not reached the market because of too little patent protection. However, we do know that 5 years is a very short term in which to recover the hundreds of millions of dollars of research and development investment required for a typical new drug introduction.[20]

The European Community recently enacted patent restoration and data exclusivity policies for pharmaceuticals. The new European Community law resembles the US law in many respects. As in the US, patent term restoration in the European Community is subject to a cap of 5 years. In addition, patents cannot be extended beyond an effective life of 15 years (compared with 14 years in the US).[11] However, in one very important respect the European Community law has a more favourable incentive for drug innovation. Patent time lost during the clinical development period in the European Community is eligible for 100% restoration versus 50% in the US. The differential treatment of patent time lost during clinical testing produces unintended distortions in patent term extensions. This is currently a particularly relevant policy issue because clinical development periods have been increasing for recent US drug introductions, while NDA approval times have been declining.[22] Another major difference between the US and the European Community is that the latter has a data exclusivity period of 6 to 10 years.

From the standpoint of societal welfare, it is also especially important that research and development projects capable of producing medical breakthroughs be encouraged. An undesirable feature of the current US rules on patent term restoration is that breakthrough products subject to very high risks and above-average expected development periods will end up with below-average effective patent lives (other factors being equal). This is another undesirable consequence of the fact that patent time lost in the development period is eligible for only 50% credit in the US. Hence, this provision of the 1984 Act warrants particular attention by Congress when it considers revisions in the patent restoration law. We believe that US legislators should also consider an increase in the minimum period of protection that new drugs enjoy against generic competition. This should be done in light of the changing economics of the drug innovation process over the past decade, including those emanating from the generic competition section of the 1984 Waxman-Hatch Act.

11 In contrast with the US, generic products in the European Community cannot undergo bioequivalence testing or apply for marketing approval until after the patent expires. For further discussion of the European Community law see Hansen and Hill.[21]

References

1. Grabowski H, Vernon J. Longer patents for lower imitation barriers: the 1984 Drug Act. Am Economic Rev 1986; 76 (2): 195-8
2. Grabowski H, Vernon JM. Brand loyalty, entry, and price competition in pharmaceuticals after the 1984 Drug Act. J Law Econ 1992; 35: 331-50
3. Mandelker J. Get the most out of your PBM. Business and Health 1994; November: 37-41
4. IMS America Inc. US drug store and hospital sales (1989 to 1993). Plymouth Meeting (PA), IMS America

5. The drugmakers vs. the trustbusters. Business Week 1994; September 5: 67
6. Greene WH. Econometric analysis. New York: McMillan, 1990
7. Caves RE, Whinston MD, Hurwitz MA. Patent expiration, entry, and competition in the US pharmaceutical industry: an exploratory analysis. Brookings Papers on Economic Activity: Microeconomics 1991. Washington DC: Brookings Institute: 1-48
8. Masson A, Steiner R. Generic substitution and prescription drug prices: economic effects of state drug product selection laws. Staff Report of the Bureau of Economics, Federal Trade Commission, Washington DC: October 1985
9. Bloom B, Wierz DJ, Pauly M. Cost and price of comparable branded and generic pharmaceuticals. JAMA 1986; 256 (18): 2523-30
10. Grabowski H, Vernon J. The regulation of pharmaceuticals: balancing the benefits and risks. Washington: American Enterprise Institute for Public Policy Research, 1983: 14-48
11. Eisman M, Wardell W. The decline in effective patent life of new drugs. Res Management 1981; 21: 18-21
12. Kaitin KI, Trimble AG. Implementation of the drug price competition and patent term restoration of 1984: a progress report. J Clin Res Drug Devel 1987; 1: 263-75
13. Shulman S, Bienz-Tadmor B, Seo PS, et al. Implementation of the Orphan Act: 1983-1991. Food and Law J 1992; 47 (4): 363-404
14. Patent and Trademark Office. Determination of new expiration dates of certain patents. Federal Register, Vol. 60, no. 109, June 7, 1995
15. Hoffmann La Roche Inc., et al. *vs* Bruce Lehman, *vs* District Court for the Eastern District of Virginia, Civil action no. 95-1236A, Alexandria, Virginia, Oct 16, 1995
16. Morrison S. Prescription drug prices: the effects of generics, formularies and other market changes. Congressional Research Service Report for Congress, August 17, 1983
17. Shaw HK. Catalysts for change: the impact of generic drugs on the pharmaceutical industry. Spectrum, Report 38, Decision Resources, Burlington, Mass: December 28, 1992
18. Grabowski H, Vernon J. Prospects for returns to pharmaceutical R&D under health care reform forthcoming. In: Helms RB, editor. Competitive strategies in the pharmaceutical industry. Washington DC: AEI Press, 1996
19. Grabowski H, Vernon J. Pioneers, imitators and generics – a simulation model of Schumpeterian competition. Q J Econom 1987; 101: 491-525
20. DiMasi J, Hansen R, Grabowski H, et al. The cost of innovation in the pharmaceutical industry. J Health Econ 1991; 10: 107-42
21. Hansen B, Hill C. Obtaining an SPC in Europe. Patents and Licensing 1994; Jun: 27-30
22. DiMasi J. A new look at US drug development and approval times. Tufts Center for the Study of Drug Development, Tufts University, Boston, Mass., 1996

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