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**Market Structure, R&D and Advertising  
in the Pharmaceutical Industry**

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## ABSTRACT

### **Market Structure, R&D and Advertising in the Pharmaceutical Industry**

by Catherine Mataves<sup>\*</sup>

Recent developments in the literature on market structure have allowed the generation of a few key testable predictions from the theory of strategic behaviour. The seminal model considers one simple but general relationship, that between market structure and market size, focusing on the competitive roles of the endogenous sunk costs of advertising and/or research and development (R&D). Evidence presented in this case study, building on earlier econometric work, shows that such endogenous sunk costs do play a crucial role in the formation of market structure in the global pharmaceutical industry.

## ZUSAMMENFASSUNG

### **Werbung, FuE und Marktstruktur in der pharmazeutischen Industrie**

Jüngere Entwicklungen der Literatur zum Thema „Marktstruktur“ ermöglichen es, robuste testbare Hypothesen aus der Theorie des strategischen Verhaltens abzuleiten. Das grundlegende industrieökonomische Modell geht von einer einfachen, aber allgemein gültigen Beziehung zwischen Konzentration und Marktgröße aus. Dabei wird insbesondere der Einfluß endogener versunkener Kosten für Werbung und/oder Forschung und Entwicklung (FuE) auf den Wettbewerb untersucht. Die empirischen Ergebnisse dieser Fallstudie zeigen, daß endogene versunkene Kosten tatsächlich eine entscheidende Rolle für die Herausbildung der Marktstruktur in der pharmazeutischen Industrie spielen. Die Ergebnisse zeigen jedoch auch, daß unternehmensspezifische Fähigkeiten geeignet sind, die Reaktionsweisen der Unternehmen im Wettbewerb zu erklären.

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## 1 Introduction

The development of game theory has allowed large advances to be made within industrial economics, but it has become clear that game-theoretic models often yield extremely sensitive predictions. Also, unobservables such as the nature of inter-firm competition, information, etc., make the models hard to operationalise as it is very difficult to identify any market characteristic that can act as an adequate proxy. Precisely because there exist many real world strategies, there is no reason to expect a single oligopoly theory that would deliver universal predictions. Yet for the theory to be useful, it must be helpful either in analysing particular industries or in identifying behavioural cross-industry regularities (Shapiro, 1989). Recent empirical work has tended to focus on the former, showing that firm conduct and performance in a particular market can sometimes be explained using some chosen game-theoretic model. Representative examples include Bresnahan (1981), Slade (1987), Hendricks, Porter and Boudreau (1987). However, these ultra-micro studies remain unable to explain widespread empirical regularities.

A seminal contribution that breaks with the 'New Empirical IO' is Sutton (1991). His 'lower bound' approach eschews detailed and sensitive game-theoretic results, but generates a few key robust and testable predictions from the theory of strategic behaviour. Sutton emphasises the strategic choices of sunk costs in a simple and highly general framework, focusing on one simple relationship, the relationship between market structure and market size. He uses cross-section econometric analysis and industry case studies to test his predictions, where the latter provide rather more qualitative evidence on the underlying competitive mechanisms. Homogeneous and advertising intensive (vertically differentiated) industries are analysed. The general empirical results obtained then usefully complement and extend the ultra-micro studies: "the experiences of individual industries can be mapped into special cases of a general theoretical model whose robust results drive the cross-industry regularities" (Sutton, 1991, p. 321).

This paper has two main objectives. First, this industry study complements and reinforces earlier cross-section econometric work (Sutton, 1991; Lyons and Mataves, 1996; Robinson and Chiang, 1996; Lyons, Mataves and Moffatt, 1998). Specifically, by concentrating on the experience of an individual industry, we add to the case evidence accumulated for major national markets in the food and drink industry as detailed in Sutton (1991). An industry study allows a better analysis of the industry dynamics, illustrating how exogenous structural changes feed into the competitive process. Using evidence on observed market share data, we can infer how the underlying competitive mechanisms operate in the pharmaceutical industry. Secondly, in the new theory of industrial structure, the distinction between horizontal and vertical differentiation is crucial. In industries in which vertical differentiation matters, advertising or R&D expenditure is effective in increasing consumers' willingness to pay. Interestingly, the

pharmaceutical industry is both advertising and R&D intensive, allowing the analysis of the relative influences of competition in two types of endogenous sunk costs.

Section two sets out the theoretical framework, based on Sutton (1991, 1996, 1998). Production economies of scale, R&D and advertising each play a central role in the story. We characterise the pharmaceutical industry according to the industry typology developed. In section three, the recent structural changes that have taken place are discussed, and then fed into the theoretical framework in order to derive predictions. In section four, it is demonstrated that the industry level evidence is consistent with the predictions derived, using national concentration data for the period 1987-1993 and global market share data for 1983-1995 (the latest years for which such data could be derived). The final section offers some concluding remarks.

## 2 Theoretical Framework: The Sutton Approach

Following the classification of Sutton (1991), essentially manufacturing industries can be split into two types, which Schmalensee (1992) labelled as Type 1 and Type 2. Type 1 industries are characterised by homogeneous and horizontally differentiated products. Type 2 industries are characterised by vertically differentiated products.

In Type 1 industries, production economies of scale, market size, price competition and entry conditions combine to determine market structure. For a class of two-stage games, it is shown that there is an inverse structure-size relationship.<sup>1</sup> The basic intuition is that as market size increases, profits increase, and given free entry, firms enter until the profits of the last entrant just cover the exogenous overhead costs paid on entry. The more sensitive is price competition to entry, the bigger is the gap between pre-entry and post-entry profits which reduces the extent of entry. Overall, the net effect of an increase in market size must be a rise in firm numbers and reduced concentration. Allowing horizontal differentiation does not substantially alter the argument, except that a range of outcomes becomes possible. Small niche firms may be able to survive as well as multi-product firms who fill many of the gaps and capture a larger market share than in the single product case.

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<sup>1</sup> As a simple example of a Type 1 industry, assume the total value of market demand is fixed at  $S$  (i.e. there is unit elasticity of demand). Straightforward calculations show that if all  $N$  firms in the market have the same constant marginal costs, and competition is Cournot, gross profit will be  $\pi = S/N^2$ . If each firm must incur a fixed cost,  $\sigma$ , upon entry, the free entry zero-profit condition ( $\pi = \sigma$ ) gives the long run equilibrium number of firms:  $N = [S / \sigma]^{1/2}$ .

In Type 2 industries, firms not only compete in price and horizontal product differentiation, but also in their advertising and/or R&D expenditure. In general, such expenditure is a choice variable, and it is this choice of (perceived) quality that highlights the fundamental difference between Type 1 and Type 2 industries.<sup>2</sup> Firms can react to increases in market size by investing in enhancements to (perceived) product quality and so typically increasing consumers' willingness to pay. Intuitively, as market size increases, the incentive to gain market share through the escalation of advertising and/or R&D expenditure also increases, and the consequent rise in overhead costs has a countervailing effect on market structure by increasing the degree of economies of scale. The basic notion therefore is that although there appears to be room for more firms as market size increases, '*the escalation mechanism*' raises fixed costs per firm, possibly even to such an extent that the negative structure-size relation breaks down. Certainly, market structure will be less fragmented than in Type 1 industries.

Within the set of Type 2 industries, Sutton (1996, 1998) further analyses the relationship between the nature of technology and market structure to explain why some R&D intensive industries remain unconcentrated. He argues that it is not always the case that in an innovative Type 2 industry, firms move forward along one single technological path making successively better products. Instead, various technologies can be adopted, where a technology is the chosen route for the R&D expenditure. Each technology may lead to several marketable products, where these products may be close or distant substitutes for products associated with another technology. A firm may choose either to: (i) focus on a few technologies, undertaking a lot of R&D per technology; or (ii) spread its R&D expenditure across a wide range of technologies. (i) is associated with the standard '*escalation*' mechanism as previously described. Such industries are termed 'Type 2 high- $\alpha$ '. (ii) is associated with the '*proliferation*' of various distinct technologies, and such industries are termed 'Type 2 low- $\alpha$ '.<sup>3</sup>

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<sup>2</sup> As a simple example of a Type 2 industry, again assume market demand is fixed at  $S$ , and allow consumer utility to depend not just on quantity consumed, but on the product of quantity and  $u$ , where  $u$  is an index of (perceived) product quality. Sutton (1991, Ch. 3) proposes the following relation between endogenous sunk costs,  $E$ , and  $u$ :  $E(u) = [a / \gamma][u^\gamma - 1]$  where  $\gamma > 1$ ; a higher  $\gamma$  corresponds to more rapidly diminishing returns to investment;  $a$  reflects the unit cost of investing. Given strictly positive  $E$ , and noting that in equilibrium firms will invest until  $\frac{d\pi}{du} |_{u=\bar{u}} = \frac{dE}{du} |_{u=\bar{u}}$ , the symmetric subgame perfect Cournot Nash equilibrium with free entry  $(\pi = S/N^2 = E + \sigma)$  generates  $N + N^{-1} - 2 = \frac{\gamma}{2} \left[ 1 - \left( \sigma - \frac{a}{\gamma} \right) \frac{N^2}{S} \right]$ . In the limit, as  $S \rightarrow \infty$ ,  $[N + N^{-1}] \rightarrow [2 + (\gamma / 2)]$  which is a finite constant. Furthermore,  $\text{sgn}\{dN/dS\} = \text{sgn}\{\sigma - (a/\gamma)\}$ , which confirms the possibility that concentration may actually rise with market size.

<sup>3</sup> As a simple example (Sutton, 1996), assume a standard linear demand model, extended to allow

The value of  $\alpha$  will be higher the cheaper it is to improve product performance as this encourages escalation rather than entry. The value of  $\alpha$  will also be higher if there is only one technology, or the closer the substitutability of rival technologies (and associated product groups), as a deviant firm that escalates R&D along its chosen technological path can gain market share from firms that spend less in other technologies.<sup>4</sup>

The crucial theoretical notion therefore is the share of industry sales that can be achieved by a deviant firm that outspends all its rivals along a particular technological path and offers a 'higher-quality' product. In a Type 2 high- $\alpha$  industry, such a firm can capture some given market share, independently of how many other firms are in the market. Thus, Type 2 high- $\alpha$  industries will be associated with high R&D and high concentration. In Type 2 low- $\alpha$  industries, on the other hand, if products are distant substitutes (i.e., a large degree of horizontal differentiation), then a firm that outspends its rivals along a particular technological path can only capture sales for a small product group. Such a firm will not be able to capture market share from rival firms on different paths, and therefore, the incentive to introduce a new variety, i.e., to *proliferate*, is stronger.<sup>5</sup> This implies lower concentration, even if R&D expenditure is high. In Type 2 low- $\alpha$  industries, the escalation of R&D leading to a shakeout of technologies over time will not be observed, but rather a proliferation of technologies, where new ones enter and exist alongside the old.

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goods to differ in quality. Thus,  $U = \sum_k \left[ x_k - \frac{x_k^2}{u_k} \right] - 2\theta \sum_k \sum_{\ell < k} \frac{x_k}{u_k} \cdot \frac{x_\ell}{u_\ell} + M$ , where  $M$ =money spent on outside goods;  $u_k \geq 1$  = the quality of good  $k$ ; and  $\theta$ = the degree of substitution between goods where if  $\theta=1$ , the goods are perfect substitutes. Assume each firm adopts a single technology and is single product. Following Sutton (1991) as in footnote 2, but using a slightly more restrictive functional form for  $E(u)=u^\gamma$  where  $\gamma$  is the cost (or alternatively, the effectiveness) of R&D in raising product quality (performance), the subgame perfect zero profit equilibrium yields  $N=1+\left[\frac{2}{\theta}-1\right]\left[\frac{\gamma}{2}-1\right]$ . For this example, the limiting level of concentration is determined by the values of  $\gamma$  and  $\theta$ . Thus, for a given  $\theta$ , a lower  $\gamma$  implies higher concentration.

<sup>4</sup> The value of  $\alpha$  tells us the extent to which increases in R&D expenditure would increase a deviant firm's market share. For the example in footnote 3,  $\alpha$  is a function of  $\gamma$  and  $\theta$ , neither of which can be directly measured. Empirically, the value of  $\alpha$  can be linked to the R&D to sales ratio and the number of different technologies (which must be proxied).

<sup>5</sup> Inasmuch as there exist any economies of scope in R&D, then for a given market size, this will shift the lower bound to concentration up.



## Characterising the pharmaceutical industry within this framework<sup>6</sup>

Whether concentration is high in an R&D intensive industry such as the pharmaceutical industry essentially depends on how substitutable products associated with different technologies are. If substitutability is low, then in spite of the effectiveness of R&D, concentration may also be low. In the pharmaceutical industry, there exist many therapeutic classes (see Appendix), and a wide range of technologies. Indeed, Temin (1979, p. 444) argues that this industry was transformed after the Second World War by a new research methodology, but there is no one central product: "the revolution in drug research allowed many different drugs to be discovered and promoted." A firm's product range often tends to be horizontally differentiated, making various formulations of the successful drug rather than successive improvements. Each new drug must attain a certain quality standard that is set by the regulatory authority, and differences across firms (see section four) tend to appear more in the number of therapeutic classes covered. Thus, we characterise the pharmaceutical industry as a Type 2 low- $\alpha$  industry. R&D expenditure is among the highest in any manufacturing industry (indicating high R&D effectiveness) and yet concentration is low.<sup>7</sup>

An interesting criticism of the industry characterisation (Type 2 high- $\alpha$  or Type 2 low- $\alpha$ ) is related to the issue of market definition. It can be argued that once the 'right' market has been defined, high R&D and high concentration would be observed. However, in regard to the pharmaceutical industry, this argument is flawed.<sup>8</sup> For example, although manufacturing capacity is easily transferable once the technology is known, the degree of

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<sup>6</sup> Advertising/R&D to sales ratios of 1% provide suitable empirical criteria for industry classification as Type 1 or Type 2. Importantly, these data are used purely to give a 'broad-brush' distinction between those industries identified by the exogenous sunk cost model (e.g. bread, salt) versus the endogenous sunk cost model (e.g., cars, soft drinks).

<sup>7</sup> Mean concentration for industries characterised by both intensive advertising and R&D expenditure was 44% in the US and 40% in the EU market in 1987 (Lyons, Mataves and Moffatt, 1998). Table 6 shows that concentration is much lower in the pharmaceutical industry: 26% for the US, 19% for the EU.

<sup>8</sup> Note average concentration is substantially higher at the therapeutic class level. Cool, Röller and Leleux (1998) estimated mean US concentration to be 46.3% in 1982, and also showed this was relatively stable between 1963-1982. However, this stability may mask significant turbulence (changes in survivor market shares and new drug introductions). Unfortunately, global market size and market share data were unobtainable by therapeutic class. One example of turbulence, however, is in anti stomach ulcer drugs, where the ex-best-seller, Zantac, had a 42% global market share until its patent expired. The pioneer, Tagamet, was introduced in 1977. Zantac was marketed globally in 1983 and became the market leader by 1987; Zantac had fewer side effects than Tagamet, although Tagamet was also considered very safe. Two other H2-blockers were introduced in the late 1980s and did not overtake Zantac. In 1989, a new type of anti-ulcer drug, Losec (a proton pump inhibitor rather than a H2 antagonist) was launched; by 1994, Losec's sales were \$2.2 billion compared to Zantac's \$3.7. It appears the 'exclusivity period' is decreasing (Grabowski and Vernon, 1990; also see PhRMA, 1996, for more examples).

substitution (on the demand side) between and within therapeutic classes is not at all easy to calculate (Caves, Whinston and Hurwitz, 1991). First, one drug might be the typical choice for a particular illness, but not for a certain subset of patients in whom side effects occur. Secondly, there may be several drugs available for a given illness, where the actual choice depends on trial and error to see which one is best for the patient. Thirdly, one drug used for several illnesses may have different substitutes in each use. Finally, drug substitutability does not remain constant over time as new entrants appear, relative prices change, and prescribers' preferences change according to accumulated empirical data on safety and efficacy (Caves, Whinston and Hurwitz, 1991). These difficulties in market definition are due to the splintering of the incentives in R&D (escalation or proliferation), which is in itself endogenous (Sutton, 1996).

### **3 Structural Change: Any Predictions?**

This section considers recent structural changes that are important to analyse in some detail in order to derive predictions in the light of the theoretical framework set out in section two. First, the impact of globalisation is analysed, which is defined to include both structural forces and firms' actions. In particular, the Single European Market (SEM) legislation and other regulatory changes are taken into account. The predicted impact on concentration of an increase in global market size, and tougher price competition, are derived. Secondly, the potential effects of the changing discovery process (towards rational drug design) and the cost of innovation on industry concentration are assessed. Finally, the relative importance of the over-the-counter (OTC) sector has been increasing in value terms in recent years. This may make advertising more effective, and consequently, have an impact on inter-firm competition, and hence, concentration.

#### ***Globalisation, Regulation and Price Competition***

Over the past decade, leading firms have been competing more and more at a 'global' level. Moving out of their home markets, particularly European firms entering the US in the 1980s, these firms produce and market their products worldwide, though access to the Japanese market remains relatively more difficult due to extensive non-tariff barriers (Thomas, 1996).<sup>9</sup> Most of the world's Top 20 firms, with approximately 50% of global

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<sup>9</sup> Pharmaceutical exports for all OECD countries increased from 23.5% of total production in 1982 to 28.5% in 1992. Sharp and Patel (1996) indicate the degree of self-sufficiency in the key markets for 1991: Japan was the highest at 82% (German firms took 5%), the US with 70%, Germany with 52%, the UK with 35%. 3 European countries have a significant market share in the US market:

pharmaceutical sales and 85% of R&D expenditure, operate in the key markets of North America, Europe and Japan (Grabowski and Vernon, 1994a). The main driving forces of this globalisation trend are outlined below.

First, competition is tougher due to the emergence of new technologies at the global level, and higher R&D costs. Even if the pricing choice remains region specific, a firm's sunk cost decision may be taken with the global market size in mind, depending on the transferability of the sunk cost across borders (Davies and Rondi, 1996). The results from R&D, unlike advertising expenditure, which is typically dependent on national culture, media and language, are relatively easily transferable across national borders. Once an innovation has been made, it can be exploited anywhere in the world, although some modification or additional testing of the new product may be necessary to conform to local regulations. Additionally, in order to market a product effectively, reinforced by the increase in the demand for OTC products, the leading firms have a presence in all key markets, either through their own marketing and distribution networks, or via a marketing joint venture. Multinationality is thus one indicator, rather than a more conventional trade measure, of the extent of integration.<sup>10</sup>

Secondly, although the pharmaceutical industry remains very highly regulated in the key markets following the thalidomide disaster in the 1960s, there have been important movements towards increased international market harmonisation. In the EU, the SEM legislation removed technical barriers to trade, and allowed firms to more easily access the regional markets. From 1st January 1995, the European Medicines Evaluation Agency (EMA) has recommended drugs for EU-wide circulation, reported any adverse reactions, and coordinated inspections.<sup>11</sup> Firms that supply a local market only negotiate with national agencies. Also, the International Conference on Harmonisation (ICH) was set up in 1990 to bring together regulatory authorities and drug developers from the US, the EU and Japan to internationally harmonise regulatory procedures. In 1996, for

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UK firms with 15%, Swiss firms with 8%, and German firms with 4.6%; US firms had a market share of 19% in Germany, 26% in the UK, and 21% in France.

<sup>10</sup> Indeed, our analysis of leading European pharmaceutical firms in 1993 strongly indicates the importance of foreign markets. One example is Glaxo: sales by origin were 21% in the UK, 21% in the rest of the EU, 44% in the US and 14% in the rest of the world (details of other firms are available on request from the author). Ballance et al. (Ch. 3, 1992) also argue foreign direct investment is more important in this industry than trade.

<sup>11</sup> In the US, the Food and Drug Administration (FDA) approves new drugs, where both safety and efficacy must be shown; in Japan, safety only has to be proven, not efficacy. EU requirements are generally not as tough as in the US (Dranove, 1991), and US approval costs tend to be higher (Senker, Joly and Reinhard, 1996). Of the 154 drugs approved by the FDA between 1990 and 1995, 103 (67%) were first approved outside the US (PhRMA, 1996). In 1992, the Drug User Fee was passed which allowed the FDA to hire more reviewers to speed up the approval process. In 1987, the mean review time was 32.4 months with 21 drugs approved. This had decreased to 17.8 months by 1997 with 53 drugs approved. The statutory standard is six months.

example, an important agreement was reached by the ICH on the appropriate standards for the good conduct of clinical trials. This was implemented in 1997, and means that clinical trials undertaken in the UK, say, will no longer have to be replicated in the US (Internet ICH publication) if the appropriate guidelines are followed. Various other guidelines relating to quality, safety and efficacy such as the number of patients in clinical trials, the length of exposure to the drug, etc., have also been agreed on, and in some cases, implemented.

Thirdly, the common mounting governmental concern over increasing healthcare costs is having a negative impact on pharmaceutical prices, via reducing reimbursement rates and increasing the 'limited lists'. This increases the incentive to market the product globally. In the US, there is very little direct price intervention. However, price competition has recently been influenced by the rapid expansion of health care maintenance organisations (HMOs) which has concentrated drug purchasing, and had the effect of reducing the number of drugs prescribed to only one or two per indication. Virtually all HMOs use limited lists, or so-called formularies, and by 1995, such organisations accounted for 75% of US drug purchases. In the EU and Japan, on the other hand, where the government is the main purchaser, there is substantial price intervention of one form or another.

**Table 1: Market Size at current prices (\$billion)**

<b>Market Size</b>	<b>GER</b>	<b>FR</b>	<b>UK</b>	<b>EU</b>	<b>US</b>	<b>Japan</b>	<b>Global</b>
1987	11.8	10.2	8.2	47.7	39.3	30.2	135.5
1988	12.9	11.6	10.2	55.4	44.0	36.2	156.6
1989	13.3	11.8	10.4	59.4	49.1	36.4	168.0
1990	17.1	14.8	12.1	74.9	53.7	35.7	190.2
1991	17.9	15.0	13.3	80.2	60.8	39.8	208.0
1992	20.3	17.3	15.1	90.2	67.7	43.7	229.9
1993	19.5	17.1	14.9	88.8	70.8	51.1	239.5

*Source:* These 'value of production' data are taken from the OECD 'Industrial Structure Statistics' and account for ethical pharmaceuticals only. The dollar conversion was made using the nominal average exchange rate (OECD Outlook, June 1994).

As the globalisation process continues, this increases effective market size as leading firms have access to new geographical markets. Table 1 shows the increase in actual market size due to factors such as rapidly ageing populations in most advanced industrialised nations, and the substitution of drugs for more expensive forms of healthcare such as hospitalisation/surgery. EU pharmaceutical production, for example, increased at an average annual growth rate of 9.7% (5% in real terms) between 1987 and 1993. Between 1984 and 1993, the increase in the value of production (when measured in constant prices) was 46% for the EU, compared with 30% for the US, and 21% for

Japan (Panorama, 1995). As market size increases, this raises the incentive to escalate advertising and/or R&D expenditure (Sutton, 1991).<sup>12</sup> This yields Prediction 1.

***Prediction 1:*** *An increase in market size is associated with an increase in the level of advertising and/or R&D expenditure by each surviving firm.*

Consider also the toughness of price competition. Sutton (1991) shows that in Type 1 industries, any exogenous influence that has a negative impact on prices or gross profit margins increases the toughness of price competition. If price competition becomes tougher due to governmental policies or an increase in imports/foreign direct investment, then the result is increased concentration. However, in Type 2 industries, this relationship can be ambiguous. In particular, Symeonidis (1997a, 1997b) shows that the effect of the toughness of price competition on the level of concentration is theoretically indeterminate. Essentially, whether concentration increases or decreases depends on the relationship between endogenous sunk costs and price competition. He shows that as price competition becomes tougher, if advertising/R&D increases or is constant, then concentration must increase. However, a case exists where if advertising/R&D decreases with the intensity of price competition, then this may or may not offset the fall in gross profit caused by lower prices, so concentration may fall or rise. Symeonidis (1997a) looks for empirical regularities, using concentration data at the 4-digit industry classification level post-implementation of the UK Restrictive Trade Practises Act in 1956 (previously allowable restrictive agreements between manufacturing firms were prohibited). He finds that as the toughness of price competition increased, concentration increased irrespective of whether the industry was characterised by exogenous or endogenous sunk costs.<sup>13</sup> This yields Prediction 2.

***Prediction 2:*** *An increase in the toughness of price competition implies an increase in concentration.*

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<sup>12</sup> In Type 2 industries where the escalation mechanism comes into play, this will increase concentration if the direct market size effect is outweighed.

<sup>13</sup> Even if advertising/R&D expenditure decreases, in order for concentration not to rise, it must be a significant decrease to offset the reduction in profits arising from tougher price competition. The most likely outcome is an increase in concentration.

### *The R&D Process and the Cost of Innovation*

There has been a radical shift in the methodology by which new drugs are discovered. The question arises whether this shift has affected the underlying competitive mechanisms in the pharmaceutical industry. Also, the average real cost of introducing a new drug, which we label the 'cost of innovation', has increased. The factors leading to this increase are discussed, and the resulting predicted impact on the level of concentration is derived.

Historically, the technologies by which most drugs were discovered can be traced to random screening of thousands of compounds for efficacy against a given disease, accidental discoveries, or incremental improvements to existing drugs (Schwartzman, 1976). Over the past two decades, 'random drug design' has been replaced by new technologies applying the more focused 'rational drug design'. Due to major advances in basic biomedical knowledge, scientists are now better able to understand biological interactions in the body, and hence design specific drugs to affect these interactions. Since the mid 1980s, drugs have been increasingly manufactured from biotechnological processes rather than chemical. Although the results from biotechnology can be applied within the pharmaceutical industry, the actual scientific advances were achieved outside the pharmaceutical industry and thus exogenous.

As explained in section two, the value of  $\alpha$  depends on the effectiveness of R&D and the substitutability of products associated with different technologies. In a Type 2 high- $\alpha$  industry, if a new technology is introduced which increases consumers' willingness to pay, then the escalation mechanism comes into play. Shakeout occurs as firms race for market share, and the lower bound to concentration will be higher. New technologies displace old.

In a Type 2 low- $\alpha$  industry such as pharmaceuticals, the value of  $\alpha$  may not change because even if biotechnology does become the dominant discovery process, there are many research trajectories (and associated therapeutic classes) over the entirety of the pharmaceutical industry.<sup>14</sup> This implies that the value of  $\alpha$  is not likely to significantly increase, as escalation in one technological trajectory will not cause firms to exit on other trajectories. In other words, the shift from random to rational drug design in the pharmaceutical industry is acting as a natural experiment. In a Type 2 high- $\alpha$  industry,

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<sup>14</sup> For example, Penan (1996) identifies 15 distinct research programs studying Alzheimer's disease alone. These work through two main R&D technologies: neurotransmitter augmentation and cognitive enhancing agents to slow down the neurodegenerative process. Henderson and Cockburn (1996a) assert that leading firms typically invest in 10-15 different research programs, where each program is targeted towards a particular disease area.

we would predict shakeout, and higher concentration in the new equilibrium.<sup>15</sup> In a Type 2 low- $\alpha$  industry, on the other hand, small and mid-sized firms may still be able to survive by becoming more specialised. Suppose leading pharmaceutical firms are active in many therapeutic classes. Not only do these firms incur set up costs to enter each segment (if plant costs are therapeutic class specific) but they also incur the costs necessary to develop a new drug (the cost of innovation). Given the likelihood of capital constraints for mid-sized firms, it may be optimal to devote all R&D efforts to one technology only to capture a large global market share for that particular product line.

Although the new drug discovery process is more efficient, the 'cost of innovation' has increased. The average cost of developing a new drug, or the cost of innovation, was estimated to be \$359 million in 1992 (taking into account compounds that failed),<sup>16</sup> compared with \$231 million in 1987, only five years earlier, and \$54 million in 1976 (Hansen, 1979; Di Masi et al., 1991; Pisano and Wheelwright, 1995). The factors underlying the increase in the cost of innovation are varied. First, if we think of the underlying technological opportunity, then it may be as if the 'easy' drugs have already been developed, i.e., moving away from 'easier' therapeutic areas to areas such as oncology or gerontology (Henderson and Cockburn, 1996b). However, their evidence for 10 leading pharmaceutical firms suggests this is probably not the case. Secondly, even if the discovery process is more efficient, if new drugs are more difficult to find due to the complexity of the compounds, it follows that the costs of doing so are higher. Thirdly, pharmaceutical research is, nowadays, more focused on chronic and degenerative illnesses rather than acute illnesses, mainly due to rapidly ageing populations. Such illnesses tend to require longer and more costly clinical trials (Di Masi et al., 1991). Finally, regulatory requirements are far tougher regarding the safety and efficacy of a new drug.<sup>17</sup> Lengthening development times in clinical trials increase the cost of capital required to undertake R&D. As Table 2 shows, the introduction of new products (NCEs) is slowing. In 1996, only 37 NCEs were launched (Financial Times, 24/4/97), which was the lowest total for several decades.<sup>18</sup>

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<sup>15</sup> Sutton (1996) uses the colour film market as an example of a Type 2 high- $\alpha$  industry where during the shift from black and white to colour film, R&D expenditure escalated, and merger/exit took place. Today, the global market is dominated by just five firms.

<sup>16</sup> There is significant variance in development costs across therapeutic classes (Di Masi et al., 1991; Henderson and Cockburn, 1996b), but there is little evidence of the skewness that is observed on returns to new drugs (Grabowski and Vernon, 1994b).

<sup>17</sup> Average drug development time in the US was 8.1 years in the 1960s, 11.6 in the 1970s, 14.2 in the 1980s, and reaching 14.8 years in the 1990s (PhRMA, 1996). It is estimated that only 1 compound from an initial 5000 will be successfully developed, where clinical trials account for approximately 35% of total R&D costs (PhRMA, 1997) - the average number of trials per new drug application rose from 30 (1977-1980) to 60 (1989-1992).

<sup>18</sup> Since 1960, the majority of NCEs have been discovered in the EU. Japan has the lowest percentage

**Table 2: Number of NCEs introduced by country of origin**

<b>Country</b>	<b>1961-70</b>	<b>1971-80</b>	<b>1981-90</b>
W. Europe	509	375	243
US	201	152	117
Japan	80	75	126
<b>TOTAL</b>	<b>790</b>	<b>602</b>	<b>486</b>
<b>World Total</b>	<b>844</b>	<b>665</b>	<b>506</b>

*Source: Ballance et al (1992, p. 86)*

*Notes: 1961-1980: Italy=112; Fr=272; Ger=191; UK=73. 1981-1990: Italy=42; Ger=37; Fr=31; UK=21 (Earl-Slater, 1993, p. 91). Note that i) some NCEs introduced are genuinely original, others may be marginal improvements; ii) these data are by country of origin, not firm of origin.*

The increase in the cost of innovation sets a lower limit on the size of a firm, and this size effect is further reinforced by the following two stylised facts (Grabowski and Vernon; 1990, 1994b): (i) the return to new drugs is highly skewed, a few 'blockbusters' dominate the product ranges of the major firms;<sup>19</sup> and (ii) only the top 30 drugs worldwide cover average R&D costs. Interestingly, smaller firms are disproportionately affected by both of these factors. In the long run, firms must cover total fixed costs or exit/merge. Therefore, even if there is variance in the cost of innovation across therapeutic classes, smaller firms will be at a disadvantage compared with larger firms who may better diversify their portfolio and absorb the risk of failure. Additionally, in order to recoup R&D costs, extensive marketing is essential to launch the new drug effectively, which works against small and mid-sized firms.

Let the fixed and sunk outlay required to achieve quality level,  $u$ , be written as  $F(u)=\phi +E(u)$  where  $\phi$  = cost of innovation;  $E(u)=u\gamma$ , as in our earlier example (footnote 3). Then, an increase in the cost of innovation,  $\phi$ , is analogous to an increase in the exogenous overhead costs a firm would pay upon entry into the market. However, it has no effect on  $\gamma$  (the effectiveness of R&D). It follows that it has no effect on the asymptotic level of concentration as market size becomes very large. For any given market size, however, concentration will increase (Sutton, 1991, p. 79-81). This yields Prediction 3.

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of NCEs, which may reflect the extremely protected domestic market, although Japan has overtaken the US in the last decade. However, if the number of breakthrough NCEs is considered, then between 1970-1983, US firms developed 42%, whereas Japanese firms only developed 4% (Ballance et al, 1992; Thomas, 1996).

<sup>19</sup> In 1993, Zantac accounted for 44% of Glaxo's sales, Tenormin accounted for 47% of Zeneca's, Augmentin (22%) and Tagamet (19%) accounted for 41% of SKB's, and Cipro (23%) and Adalat (20%) accounted for 43% of Bayer's (derived from company accounts).



**Prediction 3:** *As the cost of innovation increases, the minimal level of concentration for any given market size will increase.*

### ***Prescription Drugs versus OTC Products***

Prescription drugs which offer a therapeutic advance have a first mover advantage that tends to be overcome only if later entrants offer a distinct therapeutic benefit, and not just a lower price (Bond and Lean, 1977). Even once the patent has expired, pioneer products tend to keep a large market share due mainly to prescribers' existing familiarity with the product, and successful marketing (Caves, Whinston and Hurwitz, 1991). Thus, entry is made difficult on the demand rather than the supply side, through the stock of goodwill and prescribers' concerns over quality differences. These effects are now somewhat weaker due to governmental concern over rising costs forcing doctors to prescribe more cost-effectively via generic substitution, the increasing importance of HMOs (in the US), and better information (Grabowski and Vernon, 1992).

New products (and processes) are protected by a patent whose typical life is twenty years. A patent's approximate effective length was, until recently, ten years only, primarily due to the length of development time in clinical trials. There have since been changes made to patent law in all the key markets. In the US, the 1984 Waxman-Hatch Act extended the patent life for 5 years. Similar patent extension was legislated in Japan in 1986. Within the EU, the 1993 Supplementary Protection Certificate also extended the patent for up to 5 years. Additionally, in the US, the 1984 Act stipulated that the innovator must provide data to firms who wish to market the drug as a generic post-patent.<sup>20</sup> Thus, although the monopoly period was increased, the effective time between patent expiration and generic entry was reduced to zero. Consequently, the generics' share of the US prescription drug market by volume rose from 18.6% in 1984 to 40.4% in 1993. In 1993, generics accounted for approximately 15% of the EU market, although this varies across member states, and 7% of the Japanese market (Scrip Yearbook, 1995).

Product life cycles are becoming shorter due to the reduction in the effective patent life, the increased ability by rival firms to use rational drug design to produce close substitutes ('me-too' drugs), and generic competition. In response, leading firms have both offered a wider range of formulations of their best-selling drugs, and attempted to switch a formulation of the product to the OTC sector.

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<sup>20</sup> It used to be the case that for a generic introduction, many of the same trials had to be replicated to prove safety and efficacy. This slowed down entry. Since this act was passed, a firm need only show bioequivalence.

If leading firms switch a post-patent modified version to the OTC market, then the market will gain in importance (in value terms) relative to prescribed pharmaceuticals. For prescription only drugs, marketing is carried out through two channels: (i) by sales representatives (commonly known as 'detailers'); and (ii) in medical magazines. In the OTC market, on the other hand, advertising takes place as in a typical advertising intensive industry, via the mass media, because the products are sold directly to the final consumer. As market size increases, this would be associated with escalating advertising outlays (see Prediction 1), which work in the same direction as an increase in the cost of innovation,  $\phi$ , i.e., increasing concentration.

Perhaps more interestingly, as the OTC market expands, this implies an increase in the effectiveness of advertising that, in turn, implies an increase in the value of  $\alpha$  (Sutton, 1996).<sup>21</sup> This can be understood as follows. In the prescribed pharmaceuticals sector, leading firms maintain large sales networks. Once a new drug is developed, substantial detailing occurs. When prescribing doctors have been informed once or even a few times about the drug's therapeutic effectiveness, any further promotion may be quite redundant. If a saturation level is reached, then in terms of the theoretical framework, maintaining a large sales network is analogous to adding to the exogenous overhead costs paid upon entry (see Sutton, 1991; also Prediction 3). Thus, there will be no effect on the limiting level of concentration. However, this is not the case within the OTC market. As long as one deviant firm can convince some proportion of consumers to buy its product, through escalating its advertising expenditure as compared to its rivals, then the lower bound to concentration is bounded away from zero, no matter how large the market becomes (Sutton, 1991). Finally, inasmuch as both advertising and R&D are used as competitive weapons (assuming they are imperfect substitutes), this will increase the aggregate overhead costs incurred and so raise equilibrium concentration (Lyons and Matraives, 1996, H3, p. 99).<sup>22</sup> This yields Prediction 4.

**Prediction 4:** *Given the level of effectiveness of R&D, a rise in the effectiveness of advertising implies a rise in  $\alpha$ , and hence in the minimal level of concentration for any given market size.*

<sup>21</sup> In an advertising intensive industry, if the market is defined such that advertising covers all a firm's products in that market, then this is equivalent to assuming that the number of technologies is one (a Type 2 high- $\alpha$  industry).

<sup>22</sup> The example in footnote 2 can be easily generalised to two perceived quality enhancing expenditures,  $E_1$  and  $E_2$ , where  $E(u) = \left[1 + \frac{\gamma E_1}{a}\right]^{\frac{1}{\gamma}} \left[1 + \frac{\beta E_2}{b}\right]^{\frac{1}{\beta}}$ . In the limit, as  $S \rightarrow \infty$ ,  $\left[N + N^{-1}\right] \rightarrow \left[2 + \left(\gamma\beta / 2(\gamma + \beta)\right)\right] < \left[2 + (\gamma / 2)\right]$  so the limiting level of concentration is higher with two types of endogenous sunk costs

#### 4. Evidence

In this section, evidence is presented in support of Predictions 1-4. Prediction 1 states that an increase in market size is associated with escalating advertising and/or R&D expenditure. Prediction 2 states that concentration must rise if price competition becomes tougher (as long as advertising/R&D expenditure is constant or increases). Prediction 3 states that an increase in the cost of innovation,  $\phi$ , implies an increase in concentration for any given market size. Prediction 4 states that given the level of effectiveness of R&D, an increase in the effectiveness of advertising will increase the value of  $\alpha$ , and so the minimal level of concentration.

Consider Prediction 1. Table 3 shows how expenditure on R&D and advertising has varied in the UK (and also the US when looking at R&D) over the past decade. Looking at the evidence on advertising expenditure,<sup>23</sup> observe that the UK advertising to sales ratio has remained more or less constant, at an average of 1.4%. This implies that as UK market size has been increasing, advertising expenditure has also been increasing, which is consistent with Prediction 1. Additionally, substantial increases in advertising expenditure have been within direct-to-consumer advertising (Pharmaceutical Online), implying that the effectiveness of advertising has indeed increased. This supports Prediction 4.<sup>24</sup> It is when considering firm R&D expenditure that the results are most striking. The R&D to sales ratio has been increasing over time, implying that R&D expenditure is increasing faster than market size. The direct market size effect is then outweighed and we would predict merger and/or exit, as the least efficient firms would not be able to cover their total costs in the long run (see Table 7).

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<sup>23</sup> Only UK advertising data are available. However, advertising is typically dependent on local media, culture and language, and if the theory is correct, the underlying competitive mechanisms would be broadly similar across countries. Thus, if UK advertising expenditure is increasing over time, we would expect to observe similar trends in other countries; i.e., the UK is acting as the representative market. Access to both UK and US R&D to sales ratios allows these to proxy trends in the global market.

<sup>24</sup> OTC products account for approximately 20% of the overall market by value, increasing their market share via the promotion of self-medication for common illnesses such as headaches, colds and hayfever, and the development of new sectors such as nicotine patches. 1993 global market size was \$38.9 billion (US=\$11.3; Europe=\$9.2; Japan=\$8.8). The 1993 advertising to sales ratios were 9.7% for France, 16.3% for Germany, 17.2% for Italy and 13.4% for the UK (Scrip Yearbook, 1995). In the US, direct advertising to consumers is now higher than promotion to medical journals. The 1995 figures were \$356m and \$346m respectively (FT, 24/4/97). By 1996, approximately \$600 million was spent, with only 10 firms accounting for more than 90% of the total (Scott-Levin Inc, 10/10/97).

**Table 3: UK and US Firm Expenditure on Advertising and R&D Industry (\$million)**

	1981	1983	1985	1987	1989	1991	1993
UK R&D	594.4	572.7	602.1	1089.9	1513.9	2077.6	2476.0
UK R&D/S	11.3	11.7	11.8	13.5	14.7	15.6	17.4
US R&D	1866.2	2663.1	3370.7	4503.2	6019.3	7923.6	10473.0
US R&D/S	8.3	9.7	10.7	11.5	12.3	13.0	14.8
UK Ads	66.2	65.2	65.5	111.1	130.9	155.2	166.7
UK Ads/S	1.3	1.3	1.3	1.7	1.5	1.4	1.4

*Source:* R&D/S = R&D to sales ratio; Ads/S = advertising to sales ratio; UK: Central Statistical Office (CSO production data); Register-MEAL (Ads data); CSO Business Monitor MO14 (R&D data); US: OECD (production data); PhRMA (R&D data).

Table 4 shows the variation in R&D expenditure since 1983 as a proportion of gross output in the 'Big 4' EU member states, the US and Japan. In 1983, the lowest R&D to sales ratio was in Japan which was a protected domestic industry. This can be explained as follows. Given the smaller protected market initially, Japanese firms had less incentive to invest heavily in R&D (assuming high R&D is strongly correlated with drug discovery), as the market over which such fixed costs could be spread was relatively small (Sutton, 1991). As globalisation has opened up new geographical markets to Japanese firms, and also led to more competition in the Japanese market, this has raised the incentive to escalate R&D in order to capture a larger global market share.<sup>25</sup> Between 1983 and 1992, R&D expenditure increased in Japan. Table 4 also shows that the R&D to sales ratio was initially higher where there was more deregulation and/or the market size was larger, so that expenditure could be spread over a wider area. The US is both the most deregulated and largest domestic market, and in absolute terms, R&D expenditure is the highest there. Overall, the evidence on the increase in both advertising and R&D expenditure is consistent with Prediction 1.

<sup>25</sup> Ballance et al. (Ch. 7, 1992) state that the Ministry of Health and Welfare began to remove entry restrictions in the 1980s. By 1990, foreign multinationals had a 15% share of the domestic market. Japanese firms had relied on licensing agreements to sell their products abroad, but are now beginning to invest abroad. FDI has been growing at 10% annually since 1989 (Scrip Yearbook, 1995). In 1992, Takeda's export sales were 10%, and Sankyo's were 8% of their total sales.

**Table 4: International Comparison of Firm Expenditure on R&D (%)**

	<b>1983</b>	<b>1987</b>	<b>1992</b>
<b>USA</b>	10.6	10.6	14.3
<b>Japan</b>	6.7	7.5	9.8
<b>Germany</b>	8.4	9.6	9.2
<b>France</b>	7.1	8.4	8.7
<b>Italy</b>	7.6	6.3	8.1
<b>UK</b>	11.7	13.5	16.3

*Source: Sharp and Patel (1996). Total R&D measured as a percentage of gross output.*

Now consider Prediction 2 relating to increases in the toughness of price competition. Table 5 shows the 1991 price levels in the major EU member states. Observe first that drugs were relatively cheaper in France and Spain, and relatively more expensive in the Netherlands and Denmark. Table 5 also shows the continuing divergence in pharmaceutical prices across the EU, due mainly to the varying institutional social security systems (Panorama, 1995).<sup>26</sup> However, the variance has decreased over time (see also European Economy, 1996, p. 135).<sup>27</sup>

In the majority of the key markets, there have been attempts to reduce healthcare costs. For example, prices were cut by 2.5% on reimbursable drugs in 1993 in the UK, and the increase in fundholding doctors who control their own budgets put extra pressure on prices. In Germany, post-unification, the government introduced a reference pricing system (where drugs are grouped by therapeutic class) for the first time, and at the beginning of 1993, there was a 5% cut on all prices not already controlled. In Japan, at the beginning of 1993, there was an 8% price cut on reimbursed drugs. In the US, the rapid growth of HMOs and the increase in generic substitution has intensified price competition. Although there continues to be substantial variation in the pricing systems for reimbursed medicines across the industrialised nations, the evidence suggests that

<sup>26</sup> There are various market distortions: for example, France and Italy offer higher prices if firms locate production in the country; even though Spain and the UK do not intervene in price setting, a maximum level is set on the rate of return. In 1989, the Transparency Directive was adopted; national authorities must clearly set out their pharmaceutical pricing procedures (Klepper, 1992).

<sup>27</sup> Danzon (1996) provides a cross-country comparison for 1992 weighted average prices (at the manufacturers' price level); the drugs included are matched on the basis of molecular content and therapeutic category. Constructing a Laspeyres index based on the price per kilogram of the active ingredient (weighting by US quantity volumes) shows that prices are higher in Japan and Switzerland than in the US (28% and 5% resp.), but are considerably lower in France (43%), Italy (26%) and the UK (32%). Note these types of price comparisons depend on the sample of drugs selected, the inclusion of generics, and the weighting scheme, and moreover, are sensitive to the index used.

prescribing doctors must be more accountable, and prescribed drugs more cost-effective. This supports Prediction 2 where if advertising/R&D expenditure increases, combined with tougher price competition, then concentration must increase.

**Table 5: EU pharmaceutical prices 1981-1991** (Unweighted EU mean = 100)

	<b>1981</b>	<b>1986</b>	<b>1988</b>	<b>1991</b>
Belgium	89	80	87	96
Denmark	*	*	126	135
France	84	69	74	63
Germany	128	152	118	97
Italy	78	72	87	102
NL	*	140	136	132
Spain	*	61	72	81
UK	121	123	110	114

**Source:** Burstall and Senior (1992)

Predictions 2-4 imply an increase in concentration. Importantly, the 'correct' geographic market must be considered: if competition is indeed taking place at the global level, then there should not exist any systematic pattern at the national level. In other words, concentration may increase or decrease at the national level, as firms locate wherever is efficient. However, if higher global concentration is not observed in our data, then given the increase in advertising and R&D expenditure already shown, combined with tougher price competition, the evidence would not support Predictions 2-4. Table 6 shows any changes in national (including the EU) concentration since 1987. Observe that concentration is, for the most part, fairly stable over this time period. At the EU level, concentration has decreased by 3 percentage points over this seven year period, which is a relatively large change for a fairly short time period. Interestingly, it appears that there is no systematic pattern in the movement in national and EU concentration at the 3-digit level.

**Table 6: The 4-firm concentration ratio by the value of production**

<b>Germany</b>	<b>CR4</b>	<b>UK</b>	<b>CR4</b>	<b>France</b>	<b>CR4</b>
1987	26	1986	34	1985	11
1991	28	1993	35	1992	11
<b>Italy</b>	<b>CR4</b>	<b>EU</b>	<b>CR4</b>	<b>USA</b>	<b>CR4</b>
1987	17	1987	19	1979	26
1991	15	1993	16	1986	26

*Note:* The Japanese 1990 5-firm CR is 21.4% (Sharp and Patel, 1996).

*Source:* German and Italian data are derived from the firm size distributions (resp. by sales and employment). UK and US (1986) data are derived from their Censuses of Production; French data were provided by INSEE. Finally, the source for the 1979 US CR4 is IMS America, as reported in Cool, Röller and Leleux (1998).

Now consider changes in global concentration. Table 7 details the extent of the recent merger activity in the pharmaceutical industry. Table 8 shows the changes in global market shares between 1983 and 1995. Since the 1989 merger of SmithKline with Beecham to the Ciba Geigy-Sandoz merger forming Novartis in 1996, the industry has been rapidly restructuring itself leading to a consolidation of firms at the top. Table 7 shows that this restructuring has been dominated by global (inter-regional) activity. There has also been a substantial increase in the creation of joint ventures: both RJVs, particularly between large multinational firms and biotech start-ups (Casper and Mataves, 1997), and marketing joint ventures.

**Table 7: Mergers and Acquisitions** (all values in billion)

<b>1985</b>	Monsanto (US) and Searle (US).
<b>1988</b>	Eastman Kodak (US) acquired Sterling (US) for \$5.1.
<b>1989</b>	SmithKline Beckman (US) and Beecham (UK) merged. Bristol-Myers (US) and Squibb (US) merged. Dow (Merrell) (US) and Marion (US) merged. American Home Products (AHP) (US) acquired AH Robins (US) for \$3.2.
<b>1990</b>	Rhone-Poulenc (Fra) acquired Rorer (US) for \$3.5. Roche (US) bought 60% of Genentech (US) (biotech firm) for \$2.1.
<b>1993</b>	Merck (US) paid \$5.9 for Medco (US distributor). Synergen (US) and Amgen (US) merged (\$2.6 billion).
<b>1994</b>	Ciba Geigy (Ch) paid \$2.1 for 50% of Chiron (US biotech firm). AHP (US) acquired American Cyanamid (US) for \$9.8. Roche (Ch) acquired Syntex (US) for \$5.1. SmithKline Beecham (UK) paid \$2.9 for Sterling Health (US) and resold part of it to Bayer (Ger) for \$1. Eli Lilly (US) paid \$9 for PCS (US distributor).
<b>1995</b>	Glaxo (UK) acquired Wellcome (UK) for \$14. Hoechst (Ger) acquired Marion Merrell Dow (US) for \$7.1. Pharmacia (Swed) and Upjohn (US) merged. Rhone-Poulenc Rorer (Fr) acquired Fisons (UK) for \$1.7 and BASF (Ger) acquired Boots (UK) for \$1.3.
<b>1996</b>	Ciba-Geigy (Ch) and Sandoz (Ch) merged forming Novartis.
<b>1997</b>	Roche (Ch) acquired Boehringer Mannheim (Ger) for \$11 billion.

Observe the huge amount of merger activity in 1995. This may be explained by the fact that R&D works with a lag which has also been lengthening over time. Given that the average NCE takes between 12 and 15 years to bring to the market, no immediate impact from changes in R&D expenditure on the level of concentration would be expected. Table 4 clearly shows that R&D expenditure escalated from 1987, but only recently has merger activity been substantial. In the UK, for example, the number of world-class pharmaceutical firms was reduced from six to three in 1995. Boots Pharmaceuticals was acquired by BASF, Fisons was acquired by Rhone-Poulenc Rorer (RPR), and most importantly, Glaxo and Wellcome merged (forming the world's largest pharmaceutical firm). Although the firm-level company account evidence shows that it is currently true that mid-sized firms can compete with the industry's leaders in a limited line (e.g., Zeneca, UK), some of the recent merger activity, as shown in Table 7, indicates that a mid-sized firm may be less able to survive if it wants to be an innovator. (e.g., Fisons/RPR or Upjohn/Pharmacia).<sup>28</sup> This is the impact of the cost of innovation

<sup>28</sup> Alternatively, it may be that due to the wide range of available technologies, the data mask changes in therapeutic class concentration. In other words, concentration could be increasing at the therapeutic class level but could still be decreasing overall if indeed firms are specialising more.



effect as stated in Prediction 3.

**Table 8: Top 20 Market Shares (%) Worldwide: 1983- 1995**

Company	1995 Share	Rank	1992 Share	Rank	1988 Share	Rank	1983 Share	Rank
Glaxo Wellcome (UK) <sup>a</sup>	4.5	1	3.8	1	2.7	2	1.2	17=
Merck (US)	3.5	2=	3.6	2	3.2	1	3.1	1
Hoechst Marion Roussel <sup>b</sup> (Ger)	3.5	2=	2.6	4	2.5	3	2.5	4
Bristol-Myers Squibb <sup>c</sup> (US)	3.1	4	2.8	3	1.6	12=	1.7	10=
American Home Products (US)	3.0	5	2.0	9=	2.1	6	2.6	2=
Pfizer (US)	2.9	6=	2.0	9=	1.6	12=	2.4	5
Johnson & Johnson (US)	2.9	6=	1.9	13	1.5	16=	1.9	8
Roche (Ch)	2.6	8	2.1	7=	1.5	16=	1.8	9
SmithKline Beecham <sup>d</sup> (UK)	2.5	9=	2.2	5=	1.3	21=	2.3	6
Ciba-Geigy (Ch)	2.5	9=	2.2	5=	2.2	5	2.6	2=
Rhone-Poulenc Rorer (Fr)	2.2	11	1.8	14=	1.3	21=	1.1	19=
Bayer (Ger)	2.1	12	2.0	9=	2.3	4	1.7	10=
Eli Lilly (US)	2.0	13	2.0	9=	1.7	9=	2.1	7
Sandoz (Ch)	1.9	14=	2.1	7=	2.0	7=	1.7	10=
Schering-Plough (US)	1.9	14=	1.5	16=	1.4	18=	1.4	14
Astra (Sweden)	1.8	16=	1.1	22=	Not Top 25		Not Top 25	
Abbott (US)	1.8	16=	1.8	14=	1.7	9=	1.0	21=
Upjohn Pharmacia <sup>e</sup> (US/Sw)	1.7	18	1.3	18	1.4	18=	1.3	15=
Sankyo (Jap)	1.6	19=	1.0	24	Not Top 25		0.8	24
Takeda (Jap)	1.6	19=	1.5	16=	2.0	7=	1.0	21=
<b>TOTAL SALES (\$billion):</b>	<b>250.0</b>		<b>229.9</b>		<b>156.6</b>		<b>86.7</b>	
<b>TOP 10 SHARE (%)</b>	<b>31.0</b>		<b>25.4</b>		<b>22.4</b>		<b>23.0</b>	
<b>TOP 20 SHARE (%)</b>	<b>49.6</b>		<b>41.6</b>		<b>37.7</b>		<b>36.6</b>	

**Source:** Adapted from *Financial Times*, 25/3/96; Sharp and Patel, 1996; Ballance et al 1992; Bogner, Thomas and McGee, 1996. Total sales are derived from the OECD 'Industrial Structure Statistics'.

**Notes:** This Table shows the Top 20 for 1995 and how they ranked in 1992, 1988 and 1983.

*a* Wellcome: 1992=1.2; 1988=0.9; 1983=1; *b* Marion Merrell Dow: 1992=1.2; *c* Squibb: 1988=1.4; 1983=1.1; *d* Beecham: 1988=1.2; 1983=1.2; *e* Pharmacia: 1992=1.2

Firm level evidence (derived from company accounts) shows that of the leading UK firms in 1993, for example, only Glaxo and SKB operated in several therapeutic classes; Glaxo has a leading position in internal medicine and respiratory; SKB in anti-infectives and internal medicine. Smaller firms such as Zeneca and Wellcome are far more specialised; world-wide, Zeneca leads in one technology only, oncology; and Wellcome (acquired by Glaxo in 1995) in anti-virals.

Table 8 shows the changes in the global market shares of the leading twenty pharmaceutical firms between 1983 and 1995. Up until 1988, although firms were changing rank, market shares remained pretty stable. Between 1988 and 1995, the global market shares of the Top 10 firms increased from 25.4% to 31%, an increase of 5.6 percentage points in concentration. This is a significant ( $z=3.56$ ) increase and also indicates that given that market size increased over this time period, the largest firms are growing more quickly than market size. Also, the second rank of firms (11th to 20th) gained market share, rising from 16.8% in 1992 to 18.6% in 1995.<sup>29</sup> Overall, this significant increase in global concentration is consistent with Predictions 2-4.

This section has shown that the data support expectations. It is interesting to ask, however, what the alternative hypothesis would be. It is clear that the alternative is not that the pharmaceutical industry is a Type 1 industry, as in such industries, firms compete in price only. Only within the generic pharmaceutical sector where firms are commodity producers, do firms compete in price. As market size increases, we would expect prices to tend to marginal cost as the number of firms become very large in this segment of the market.<sup>30</sup>

The alternative hypothesis, in the context of this case, is that the pharmaceutical industry is a Type 2 high- $\alpha$  industry. The arguments put forward in section two concerning the nature of the technology indicate this is unlikely. If this industry were a Type 2 high- $\alpha$  industry, the expectation would be that given the observed increase in advertising and R&D expenditure, combined with tougher price competition, the pharmaceutical industry would become extremely concentrated, with the new technology of rational drug design displacing the old. This is not what is being observed. The evidence on concentration indicates that although the industry is becoming more consolidated, the two leading firms still only have a global market share of around 4.5%. This is a high level of fragmentation in an industry characterised by two types of endogenous sunk costs, and is due to the proliferation mechanism at work, rather than the escalation mechanism. Only in the OTC market would we expect the escalation mechanism to dominate, and concentration to be correspondingly higher.

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<sup>29</sup> Using a standard t-test, it was found that within the top 10, the difference in mean market share between 1983 and 1988 or 1992 was insignificant. However, the difference was significant at the 1% level when comparing 1983 (or 1988) and 1995, and this was also true at the 10% level when comparing 1992 and 1995. The same significance pattern is observed within the Top 20.

<sup>30</sup> Sutton (1991) provides a nice example of the frozen food market, in which a dual market structure emerged. In the retail sector, firms escalated advertising expenditure as market size increased, and concentration is high. In the non-retail sector, firms competed on price, and there are a large number of smaller firms.

## 5 Discussion and Concluding Remarks

Various structural changes have occurred in the pharmaceutical industry in recent years. These include increased international regulatory harmonisation, governmental attempts to control rising healthcare costs combined with rapidly ageing populations, and a substantial increase in the cost of innovation,  $\phi$  (mainly through the lengthening development time). These structural changes have had an important impact on the competitive process, and given the observed increase in advertising and R&D expenditure and the toughness of price competition, we predicted that concentration would increase. This increase would take place not at the national level, but at the global level. The evidence indeed showed no systematic pattern in changing market shares at the national and EU level, but concentration has significantly increased at the global level. Overall, the basic competitive mechanisms in the pharmaceutical industry are consistent with the Sutton approach to market structure. The recent increases in global concentration can be traced primarily to a rise in  $\phi$ , but there is an important secondary influence that has worked in the same direction which is the increasing effectiveness of advertising as the OTC market expands.

The fascinating aspect of the competitive process in pharmaceuticals is why this industry continues to remain relatively fragmented, given that it is both advertising and R&D intensive. We argued this is due to the nature of the technology such that the incentive to proliferate dominates the escalation mechanism. The pharmaceutical industry is a Type 2 low- $\alpha$  industry. Although the mode of discovery is changing, through the introduction of biotechnology into the competitive arena, we argued that the value of  $\alpha$  is likely to remain constant over time. This implies that the pharmaceutical industry is unlikely to become extremely concentrated. In other words, even if biotechnological processes do win out, due to the existence of many research trajectories (and associated therapeutic classes), escalation along one technological trajectory is unlikely to cause firms on other trajectories to exit. Interestingly, any changes in the value of  $\alpha$  will be observed through an increase in the effectiveness of advertising. It is predicted that the escalation mechanism will come into play in the OTC market, i.e., firms will compete as in a typical Type 2 high- $\alpha$  market, with an escalation of direct-to-consumer advertising in response to any increases in market size. This may have a substantial concentrating effect in this sector of the industry.

However, although the pharmaceutical industry is a Type 2 low- $\alpha$  industry, there are, nevertheless, limits to how unconcentrated it can be. This is due to the existence of a firm size threshold, which has increased because of the following two factors. First is the increase in the cost of innovation linked with the skewness of the rate of return on a new drug. Secondly, a global marketing/distribution network is necessary in order to exploit a new drug effectively. Both of these factors work against small firms. Also, these factors

are independent of the nature of technology in the pharmaceutical industry.

Finally, an interesting avenue for future research is to analyse the role of firm-specific competencies. These may determine how the different leading firms react to the underlying Type 2 mechanisms, where the external dynamics of the market and the internal resources of the firm may combine to determine the R&D expenditure, advertising expenditure and product line.

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## **Appendix: Therapeutic Classes in the Pharmaceutical Industry**

Cardiovascular:	anti-coagulants, haemophilia, beta-blockers, diuretics, hypertension, cholesterol reducers
Respiratory system:	anti-histamines, asthma, cough medicines, bronchitis, cystic fibrosis
Anti-infectives:	antibiotics, antimalarial, anti-virals, vaccines, AIDS
Pain Control:	analgesics, anaesthetics, anti-arthritis, anti-gout, migraine, bone products (for rheumatism, etc.)
Internal medicine:	antacids, anti-nauseants, contraceptives, enzymes, hormones, laxatives, digestants, anti-ulcerants, immuno-suppressants, anti-obesity
Mental Health/CNS:	anti-convulsants, sedatives, Parkinson's disease, Alzheimer's, anti-depressants, multiple sclerosis
Topical:	dermatologicals, haemorrhoids, feminine hygiene preparations, ophthalmic
Cancer Therapy:	cancer therapy (oncology), anti-emesis in cancer treatment
Miscellaneous:	nutrients, vitamins, diabetes, diagnostics