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2006.29



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Maison des Sciences Économiques, 106-112 boulevard de L'Hôpital, 75647 Paris Cedex 13
<http://mse.univ-paris1.fr/Publicat.htm>

ISSN : 1624-0340

Persistence of Innovation, Technological Change and Quality-Adjusted Patents in the US Pharmaceutical Industry*

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January 2006

Abstract

This paper analyzes American pharmaceutical firms' persistence in innovating prior to the wave of mergers and acquisitions that accompanied the "Biotech revolution". We evaluate the impact of past innovative activity on firms' innovation propensities using a non-linear GMM estimator for exponential models that allows for predetermined regressors and linear feedback. We find that innovative activity at the firm level depends strongly on the technological importance of past innovations. In particular, breakthroughs depend largely on past innovations' scope, and this effect is likely to deter further pioneering behaviors rather than strengthen incentives to invest on non cumulative R&D. The results also shed light on the importance of small firms for the technological change in pharmaceuticals, and suggest that large firms may persist in using patents strategically to retain sales.

Keywords: Patent Citations, Pharmaceutical Industry, Persistence in Innovation.

Ce papier analyse la persistance à innover des laboratoires pharmaceutiques Américains, antérieurement à la vague de fusions et acquisitions qui accompagna la "révolution des biotechnologies". Nous évaluons l'impact de l'activité passée d'innovation sur la propension courante à innover via des GMM non linéaires appliqués aux modèles de comptage et qui tolèrent des régresseurs prédéterminés avec des rétroactions linéaires. Nous trouvons que l'activité d'innovation au niveau de la firme dépend fortement de la portée de son passé inventif. Plus particulièrement, les découvertes radicales dépendent fortement de la qualité des innovations passées de la firme et cet effet semble la détourner de comportement pionniers plutôt que l'inciter à poursuivre une recherche non cumulative. Les résultats montrent aussi que le niveau de l'activité et le pouvoir de marché des firmes sont négativement corrélés avec l'importance technologique des innovations faites et ne sont positivement corrélés qu'avec les dépôts brevets simples. Les petites firmes apparaissent alors être la principale source du changement technologique tandis que les firmes plus importantes semblent avoir moins d'influence et pourraient donc utiliser le brevet à des fins plus stratégiques.

Mots clés: Citations de Brevets, Industrie Pharmaceutique, Persistance à Innover.

JEL: O31, L12, C23.

*This article benefits from fruitful discussions with MP. Zuniga following our earlier collaboration. I am also grateful to Rodolphe Desbordes, Laura Hering, Etienne Pfister, Faye Steiner, Michelle J. Neuman, Frank Windmeijer and to the various participants of conferences and research seminars where the paper has been presented. The usual disclaimer applies.

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Introduction

Ever since Schumpeter's initial insights (1939), the questions related to firms' efficiency and persistence in innovating have been a recurrent topic of interest.¹ Studies generally shed light on the patterns supporting the technological change by focusing on the forces which determine its innovation dynamics. On the micro-level two fundamental principles rose from this literature and refer either to Schumpeter's "creative destruction" or "creative accumulation".² These two approaches consider differently the link between innovation and market power –which can be either positive or negative– to explain the persistence in innovation activities. It depends on the difference in the fundamental assumption concerning the properties of technology –specific to firms or equally accessible to everybody– and in the nature of innovative process –cumulative or not–³. More generally, innovation may lead to new technologies which undermine old monopolies' position but dominant firms may also benefit from first mover advantage to innovate cumulatively.⁴

Accordingly, size and frequency of innovations made by firms are the fruit of two counteracting forces (see Blundell *et al.* (1999)). On the one hand, the monopolist faces a "displacement effect" which indicates that firms with high market power will have no incentive to win a patent race too quickly as their current revenue streams will be displaced by an entirely new one.⁵ Indeed, entrants may have greater strategic incentives to invest in fundamental research leading to (radical) innovations.⁶ Nelson & Winter (1982) and Kamien & Schwartz (1982) labelled this pattern of innovative activity the "Schumpeter Mark I" in reference to what Schumpeter states in *The Theory of Economic Development* (1934). In this pattern of innovation, research entrants spur the industrial inventiveness, and consequently the technological dynamics, by the competitive pressures they exert on technological incumbent firms. On the other hand, Gilbert & Newbery (1982) and Bud *et al.* (1993) argue that large firms are more likely to innovate persistently mainly because of an "efficiency effect" related to their market dominance. This effect reports the "persistence of monopoly" as being the extent to which leaders will spend more on pursuing innovation in order to maintain their dominant position (e.g. Scherer (1967)). Dominant firms also benefit from barriers to entry and are consequently often recognized as being persistent innovators as it is illustrated in the model of Segestrom & Zolnerek (1999). It follows from this that market leaders should generate a large share of inventions and consequently innovate persistently but cumulatively. This pattern of innovative activity is also known as "Schumpeter Mark II" in reference to *Capitalism, Socialism, and Democracy* (1942).

The persistence in innovation activities is a key feature concerning the patterns of technological change. Fundamental theoretical and political implications follow the comprehension we have to optimize

¹See Scherer (1992), Pavitt (1988), Pavitt & Patel (1994) and Dosi (1988) for detailed discussions on this point.

²For a detailed analysis of these two points see Scherer (1992) and Cefis (2001) among others.

³Cefis (2003)

⁴Segestrom & Zolnerek (1999) explain why industry leaders can often devote substantial resources to R&D by assuming they can improve their own products more easily than can other firms.

⁵Arrow (1962), Reinganum (1982, 1983)

⁶Similar predictions are found in the organizational theory about the failure of incumbent firms to conduct radical innovation because of the diseconomies of R&D, inertia, complacency, etc., which makes harder to achieve returns to radical R&D (see Henderson (1993)).

simultaneously both competition between firms and technological progress. Despite the importance of this concern there is still few empirical evidences on the identification of persistent innovators and their R&D strategies –rather pioneering or cumulative– in a dynamic point of view. This consideration is essential to understanding fully the emergence of new technologies and, conversely, the obsolescence of already existing ones. At the theoretical level, the literature on this area has been far from conclusive, particularly on firms' strategic incentives to engage in pioneering innovation. Mixed results are found and are, in general, extremely sensitive to the core assumptions of the model which are employed.⁷ The goal pursued here is to understand the nature of the relationship between the level of activity (size) and/or market power and innovation activity using the pharmaceutical industry as field of analysis. Several questions arise then:

- i)* Which firms influence the technological change?
- ii)* How persistently do they innovate and with what scope?
- iii)* Which dynamic is at work (persistence) i.e. what role does past innovation activity plays on the firms' current innovative behavior?

Innovations may be distinguished by their nature: "radical" innovations are pioneering discoveries that create new knowledge while "cumulative" innovations describe innovations that improve or upgrade existing knowledge. From the firms' point of view, innovations aim either to create new businesses and new economic perspectives (Schumpeter Mark I) or to maintain already existing businesses by sequential product improvements (Schumpeter Mark II). This is the starting point of the analysis which thus tackles the question on the importance of the quality-differentiating of innovations in the evaluation of the firms' technological efforts and persistence with which they innovate. While in many sectors the patent is seen as a weak instrument of protection,⁸ the focus on the particular case of the pharmaceutical industry is justified by several advantages this sector offers. In fact empirical studies show that the additional profits generated by a patent only have a positive effect on R&D expenditure in pharmaceuticals and biotechnologies.⁹ In addition, given the considerable investments they require, drugs are one category of innovation where the incentive-giving role of patents works best. This sector is therefore particularly pertinent for studies based on patent data to assess innovation activity. Nevertheless, pharmaceutical patenting remains also very heterogeneous and all patents granted are not equal in terms of technological magnitude, newness and industrial use. Besides, it is well known that pharmaceutical firms often rely on patents for anti-competitive practices, notably in order to face competition exerted by generics¹⁰ or by other research intensive firms (i.e. a competition between patents as described in Lichtenberg & Philipson (2002)). This is why in this industry, innovators may well take out hundreds of patents on marginal variations (seen as cumulative innovations) of the same basic invention, to erect a patent "fence" to keep unwanted competitors and imitators out (Davis (2002)). Patenting in the pharmaceutical industry is consequently so essential, that it becomes in some cases an end in itself by protecting business and their associated returns from competition instead of encouraging product innovation.

⁷See Baldwin & Scott (1987), Reinganum (1989), Aghion & Howitt (2000) and Aghion *et al.* (2001) among others.

⁸See Brouwer & Kleinknecht (1999) and Arundel (2001) for detailed discussions on this.

⁹Arora *et al.* (2001).

¹⁰See Langinier (2001, 2004), Arundel & Patel (2003).

In this article we find that innovative activities are persistent and depend strongly on the scope of innovations already made by the firm. The dynamic of innovation is an important feature of innovative activity as a whole, at least in pharmaceuticals. Technological breakthroughs however are likely to deter further pioneering behaviors in the short run rather than strengthen incentives to invest in non cumulative R&D. As firms' level of activity and market power are negatively correlated with the scope of innovations (i.e. their technological influence), this research sheds light on the small firms as being the major sources of the (current) technological change in pharmaceutical. It also suggests that large firms may use patents strategically to retain sales since they mainly grant patents having a low technological values.

Because innovation is often compared with a *black box*, making it difficult to identify innovative behaviors, this study relies on the use of patent citation data as a better measure of firms' innovative activity.¹¹ The information contained in the patent citations makes it indeed possible to take into account the influence, and conversely the dependence, which a given patent exerts on, and undergoes from, technological path.¹² This empirical investigation circumvents the patents' homogeneity hypothesis which is generally used in patent count analysis and preserves the numerous advantages of patent data in studying innovation. This paper's contribution is twofold. By distinguishing "*Leader*" and "*Follower*" patents, understood as pioneering or cumulative discoveries, as well as the innovation's scope according to patent citation criteria (forward and backward citations), the paper evaluates the pharmaceuticals firms' propensities to innovate, that is to say their inventiveness, conditional on past R&D expenditures, internal spillovers, sales and market power in addition to their various patent stocks (i.e. accumulated knowledge). Moreover, the feedback effects of firms' past innovative activity are evaluated on the current propensity to innovate to consider the role that innovation history plays in the firms' technological strategies. By analyzing the dynamics of innovation flows, this investigation therefore assesses the extent to which firms are real sources of knowledge, persistent innovators or rather tend to rely on patents for other purposes like to foreclose competition. Insights are thus given on the way in which "success breeds success" or may lead to some strategic considerations on patent when R&D productivity decreases. Data on patenting and citations, in addition to firms' economic data, has been carefully gathered to obtain a unique unbalanced panel data for 77 traded innovating pharmaceutical firms for the period 1975-95.¹³

The remainder of the paper is organized as follows: *Section 2* surveys the relevant literature and then lays out the basis for the use of patent citations and their advantages for such an analysis. *Section 3* presents the methodology, the variables and the data employed, *Section 4* presents the results and *Section 5* concludes.

¹¹See Trajtenberg (1990), Hall *et al.* (2001) and Lanjouw & Schankerman (2002) for studies using patent citations.

¹²It is important to note that many of the citations are not really issue by the firm, but are added by the inventor's patent attorney or the patent examiner, representing thus inventions that were wholly unknown to the citing inventor. Consequently patent citations are not subjected to any firms' reluctance to cite other patents and are thus almost exhaustively listed in the patent.

¹³However we focus on the period 1975-1991 for two reasons. Firstly to deal with the truncation problem related to forward citation lags (see section "Data and Methodology" and for details Hall *et al.* (2001)). Secondly to avoid bias the wave of mergers and acquisitions in the mid 90's (seen as an external acquisition of knowledge) may induce when analyzing firms' research efforts.

Background

Several reasons motivate this study and justify the choice of the pharmaceutical industry as field of analysis as well as the methodology we employ. First of all, as pointed out by Griliches (1990), to the extent that quality across patents –within a firm’s patent portfolio and across firms– may largely differ it seems important to weigh the patents’ value of a firm relative to other innovations. Indeed, despite its frequent use, counting patents often gives a misleading interpretation of the real productivity of the research sector as shown by Lanjouw & Schankerman (2004). Besides, several papers point out that the lone use of patent count induces a bias in the empirical investigations because patented innovations show only firms that won an innovation race which underestimates innovative behaviors’ assessment.¹⁴ The leadership itself could also be poorly measured by patent data due to the firm’s strategies which may lead them to prefer secrecy to patenting. That explains why some studies are based on innovation surveys –rather than on patent data– to analyze firms’ innovation activity. However, these kind of debates may not be relevant in the specific case of pharmaceutical research insofar as patent race models usually assume that only one competitor can win and be granted a patent. In the specific case of pharmaceuticals, patents rarely narrow the prospects of further patentable inventions as the case of “me too drugs” patents tends to demonstrate. Furthermore, innovation surveys may also present some drawbacks inherent to their qualitative approaches. Notably the definition of innovation, as well as the distinction of its nature (radical or not), remains subjective and presumably heterogeneous. Consequently, to solve these limitations, we apply a methodology which allows us to distinguish more objectively innovations (pioneering discoveries, innovations’ scope) thanks to a quantitative approach independent of the firm’s own admissions and which is specific to patents in a technological sense.

Furthermore, this investigation concentrates exclusively on the traditional pharmaceutical industry (i.e. drug producers) for different economical and practical reasons. The first one is the fact that many empirical works have shown decreasing R&D productivity in the manufacturing industry which is particularly accentuated in pharmaceuticals.¹⁵ Indeed, such a context gives an interesting point of view with which to evaluate persistency and strategies in innovation activities, especially when distinguishing the technological value of innovations. The pharmaceutical industry is, in addition, one of the most intensive knowledge sectors, devoting more than 20 % of sales to research and development.¹⁶ The average cost to develop New Chemical Entities (NCE) has risen from \$180 million in the eighties up to more than \$800 millions in 2000¹⁷ to reach almost \$1 billion today.

The regulatory framework may have contributed to some extent to rising costs which leads to the decline of R&D productivity and an increasing difficulty for firms to bring innovation onto the market. Because pharmaceutical patents are typically granted at an early stage of the research projects, while clinical tests are still in progress and before being approved, less than 1% of the products examined in the

¹⁴See Kamien & Schwartz (1975).

¹⁵As shown by Dimasi (1991) and Dimasi *et al.* (1999), pharmaceutical innovation costs have dramatically increased since the last decade in part due to the stricter rules on clinical trials, in addition to increasing complexities in technology discovery; see also Henderson & Cockburn (1998).

¹⁶See PhRMA (2000).

¹⁷Source: *Tufts Center for the Study of Drug Development* (2001).

pre-clinical period make it to human testing.¹⁸ Furthermore it takes on average 14 years from laboratory and animal studies to FDA (*Food and Drug Administration*) approval.¹⁹

Technological exhaustion (within a process of so called "creative accumulation") in pharmaceuticals may also explain such a decline. The emergence of biotechnologies and genomics in the eighties, redefined invention methods for drugs from randomly screening of a large number of potentially useful compounds towards a more systematic approach called "rational drug design".²⁰ This revolution of sorts has therefore induced new challenges to the extent that NCE are more and more specific (which can also explain rising costs). Analogously, the role played by competitive entrants compared to dominant firms can shed light on the articulation between "creative destruction" and "creative accumulation" in the discovering of new compounds.

Last, but not least, the pharmaceutical industry is often recognized as the sector where the patent is the more effective and, consequently, the principal industry relying on patents to appropriate returns to R&D and to exclude technological followers. According to the President of the International Intellectual Property Institute "*the pharmaceutical industry is one of three technology-based industries in which the patent virtually equals the product. The others are the chemical industry (including agricultural chemicals) and the biotechnology industry*". More generally, Levin *et al.* (1984) show that a patent is the most effective to appropriate returns in industries with chemical-based technologies, such as pharmaceuticals, which makes it a very convenient field for analyses which proxy innovation activity with patent grants. However firms may also be strategically granted many "poor" patents –as legal right to exclude– to build barriers to entry (foreclosure) or to develop existing inventions in response to increasing difficulties to innovate. To extend market exclusivity on blockbuster drugs (those exceeding US\$ 1 billion of yearly sales) beyond patent expiration, firms use a number of strategies in response to the increasing competition of generics, allowed by policies like the *Hatch-Waxman Act* (1984), and to the threat of technological exhaustion.

Nevertheless, as suggested by Caballero & Jaffe (1993) and Lichtenberg (1998), the pharmaceutical industry remains the sector with the highest rate of creative destruction at the product level despite the fact that less and less pioneering inventions are discovered leading to an erosion of the number of new (technologically) promising compounds invented.

Persistence of Innovation: a State of the Art

A large strand of literature focuses on the persistence with which firms innovate. This literature investigates whether firms innovate persistently or discontinuously over time and attempts to assess the extent to which innovation flows within firms are interdependent over time. Contrasting views are put into light and often underline the role played by financial resources and/or technological leadership resulting from past innovation. These are either seen as an advantage to innovate or as a dead weight which limits future

¹⁸Grabowski (2002).

¹⁹See Viscusi *et al.* (2000).

²⁰This involves exploiting knowledge about the biochemical mechanisms causing a disease to identify or develop chemicals that inhibit such mechanisms, see Pisano (1997).

innovative ambitions. We can summarize that the literature analyzing patterns of innovation agrees on innovative persistence being rather strong among large innovators and that consequently few –persistent– innovators account for the large majority of patenting with quite stable ranking. In other words, these studies confirm the theoretical predictions on persistence only for a restricted group of firms.

In Nelson & Winter (1982) "success breeds success" such that past innovations that meet commercial success are a necessary condition to finance R&D and by consequence to innovate persistently. Analogously, Simons (1995) explains that successful innovations offer technological advantages to innovate thereafter. Thus the cumulative nature of knowledge would induce state dependence in invention flows and consequently persistence in innovation. Considering competition, Arrow (1962) shows that competitive markets generate greater incentives to invest in innovation than concentrated ones.²¹ In the case of free entry, Gilbert & Newberry (1982) show that market dominant firms will preempt potential entrant investment in innovation which leads to persistence in innovation activities. Reinganum (1983) however reinstates Arrow's results by considering the case of uncertain innovations. She shows that a monopolist will seek to avoid overlapping in its product innovation portfolio, and thus will have less incentive to innovate than a competitive entrant. From another point of view, Sutton (1991) considers the sunk costs in R&D investments as an important feature to take into account in studying persistence since they build barriers to entry and create engagements to continue innovation.

At the empirical level, studies focus on the "creative destruction" and "creative accumulation" in the technological dynamics (which of the two effects prevails according to competitive circumstances and firms' characteristics). They point out the differences between dominant firms and competitive entrants in the emergence of new technologies, their improvement and consequently the innovative interactions at work in the technological path design. Schumpeter initiated many debates directing researchers towards the questions dealing with the sources of the technological change but the interaction of market dominance and past innovative activity remains still inconclusive. Several cross-sector studies demonstrate an apparent continuity, or persistence, in the firms' innovative behaviors and, in general, agreed on the fact that only a few innovators account for a large share of innovations and do it continuously (i.e. persistence in innovation is weak as a whole as only a restricted group of firms is concerned). Nevertheless, in almost all cases, the simple patent count, or the R&D activity, is used to proxy the firms' innovative behavior excepting Duguet & Monjon (2004), Peters (2005) and Raymond *et al.* (2005) who use innovation surveys to overcome the limitations of patent data.

Crépon & Duguet (1997) use a panel of R&D performers and patent data to measure innovation in France. They estimate a dynamic count data model that estimates the relationship between the current number of patents to both the previous year number of patent and the amount invested in R&D. They find a rather strong persistence in innovation among formal R&D performers. Marbela & Orsenigo (1999) examine the patterns of innovative entry, exit and survival, using European Patent Office (EPO) data for six European countries through a descriptive analysis. They measure persistence by analyzing the duration of patenting after entry. They found a high degree of turbulence such as the process of entry

²¹See also Aghion *et al.* (2002) who find an inverted U relationship between innovation and competition.

and exit seems to support wide changes over the time in the innovators' population. Hence, a large fraction of new innovators is composed by occasional innovators even if they constitute a significant part of the whole population of innovators, despite a lower share in the total number of patents granted.²² Cefis & Orsenigo (2001) confirm the weakness of persistence in innovation in a comparative analysis of six European countries over the period 1978-93, using a Transition Probability Matrix approach and a Markov chain that distinguishes "great-innovator" and "non-innovators". They assess the probability of remaining in the same stage of patenting and found a strong persistence in the firms' innovative activity. Firms have thus a high probability of staying in their original state, persistent innovators being the principal source of technological change. In addition they find a strong heterogeneity across firms' industry and size. Similar results are found by Cefis (2003) who uses the same methodology for the UK over the period 1978-91 since she finds "*little persistence in general, but strong persistence among 'great' innovators that account for a large proportion of patents requested: innovative activities, at least which are captured by patents, are persistent*".²³ Geroski *et al.* (1997), in a duration analysis (Duration Dependence Weibull Model) that assesses the "*patent spells*"²⁴ in UK over the period 1969-88, find little evidence of persistence at the firm level, even if persistent innovators account, once again, for a large share of the total patenting. They find similar results when considering "major innovations" instead of patent count. Cabagnols (2005) uses the same data to examine the impact of past patenting –the technological accumulation– on the firms ability to be persistent in innovation and finds also a positive and significant relationship.

Concerning the technological specificity of the innovation's patterns, Marbela & Orsenigo (1996) show that the patterns differ systematically across technological classes (referring to Schumpeter Mark I and II), but are remarkably similar across countries for each technological class suggesting there is no country specific effect contrarily to sectors. As a result they found that the process of "creative accumulation" is specific to the electronic and chemical industries whereas the mechanical technologies are closer to a process of "creative destruction". This seems to support the assumption that industries where innovations are primarily based on knowledge (as pharmaceuticals) are more subject to technological accumulation (v.s. pioneering innovation) than others. Thereafter, Marbella *et al.* (1997) wonder if persistence and heterogeneity are associated with a high degree of concentration in the innovative activity and a stability in the ranking of innovators, or whether they are associated to other variables like the firms' size and industrial concentration. As results, contrary to the Schumpeterian hypothesis,²⁵ they found that the market structure doesn't play a clear role in the emergence of innovation while persistence and asymmetry seem to be the fundamental determining causes for it.

²²On this point Duguet & Monjon (2002) explain that in some activities, few innovators patent their inventions (see also Cohen *et al.* (1997), Duguet & Kabla (1998)). Consequently the weak persistence would reflect in fact the weak use of patents in some sectors. In addition patent data would show the persistence of "anteriority" rather than that one of innovation. However in the specific case of the pharmaceutical industry these assumptions do not hold.

²³In an earlier version, Cefis (1996) already found a weak persistence in general but a strong persistence among the greatest and the smallest innovator. By distinguishing firms according to their size and sector, she sheds light on a substantial heterogeneity in the degree of persistence among the firms of the sample.

²⁴i.e. they define the degree of innovation persistence of a firm as the number of consecutive years during which it has a recorded innovative output.

²⁵Nelson & Winter (1982) define the Schumpeterian hypothesis as the fact that "A market structure involving large firms with a considerable degree of market power is the price that society must pay for rapid technological advance".

More recently, Duguet & Monjon (2004) propose to examine if innovation is persistent at the firm level by comparing propensity score and regression methods. They use several innovation surveys on French firms' innovative activity for the period 1986-1996. These data sets give information about the implementation of innovation at the firm level, without any reference to their commercial success or their patenting status. Their results indicate that innovation persistence is strong (a firm that already innovated in the past has a stronger probability to innovate in the future). In addition, the origin of the persistence depends on the size of the firm: the learning-by-doing hypothesis (dynamic increasing returns) seems to play a major role in the small sized firms whereas its weight decreases with the firms' size. Finally the study shows that the importance of dynamic increasing returns should decrease with the formalization of R&D activities. The paper suggests that omitting the dynamic increasing returns leads to underestimating the innovation persistence, especially in small-sized firms. In this vein, Raymond *et al.* (2005) analyze the extent to which the production of innovations is subject to "dynamic economies of scale", or whether "success breeds success". They study the dynamic of innovative achievement and innovation profits in the *Dutch Community Innovation Survey* by estimating a dynamic probit model and find a strong persistence of innovation profits among the multi-period innovators. Recently, Peters (2005) uses data from the *Mannheim Innovation Panel* (manufacturing and service sectors) over the period 1994-2002 through a dynamic random effects discrete choice model. She finds that innovative behaviors are "permanent at the firm-level to a very large extent" and that skilled employees and unobservable individual heterogeneity play an important role in explaining this behavior.

Given this state of the art on persistence in innovation, an interesting addition to the literature would be to look at the nature of these inventions (technological scope, newness...) from a quantitative point of view and the different behaviors that might emerge following the firms' characteristics. In this vein, Lerner (1997) examined whether strategic behavior can be identified in the decision to introduce new products in a high technology industry: the disk drive sector. Consistently with models rising doubts about the persistence of monopoly, he found that greater innovative activity is shown by the firms which follow the leader. This result supports the idea that a second mover advantage exists in technological races. Such an assumption may be tested in a dynamic approach of innovative activity. Empirical works which study persistence by distinguishing innovation "qualities" or "scope" are very scarce. Such a dimension seems however fundamental to take into account, especially in the pharmaceutical industry where the "quality" –i.e. the technological magnitude– of new product is often seen as weak. In Geroski *et al.* (1997), an effort was made in this sense by taking into account the simple counting of patents and the number "major innovations" made at the firm level, i.e. those being technically innovative and commercially successful. However, this criteria may be questionable to the extent that the commercial success should be carefully interpreted and thus may be related to the brand-name or even the firm's advertising among other (unobservable) parameters. Since this definition involves a commercial success, the firms considered as innovative are likely to be innovation leaders or commercial leaders. Our study suggests several patent quality measures, exclusively based on forward and backward patents' citations. These quality measures only refer to the innovations' importance in a technological sense and thus allow to proxy for firms' innovation activity in a sharper way than the simple patent count.

Distinguishing Innovations Quality

Patent count, as a proxy for the firms' innovative activity, generally leads observers to assume a perfect homogeneity of quality between and within patent portfolios. Distinguishing the importance of inventions would however permit to identify the *real* sources of technological change in the industry. Taking into account the dynamic effects in such a question could offer valuable insights on the relationships existing among the persistence in innovating, the nature of the firm's R&D output and the inventors' characteristics (size, market dominance, R&D intensity, etc).

To describe how cumulative innovations are made, and consequently to understand the innovations' technological magnitude, we suggest several patent citations-based measures. The main idea supporting this methodology (widely recognized in the literature)²⁶ is that the simple observation of firms' patenting activity is an unsatisfactory measure of the real innovative effort. This is in particular the case when firms patent intensively, regardless of the innovations' quality, following a defence and/or blocking-entry strategy as shown in Lanjouw (1998) and Lanjouw *et al.* (1998).²⁷ More generally, firms may also differ in terms of competence in innovating (depending on history and on other factors like the position on the supply chain), some of them being more specialized in fundamental research than others and consequently generate more technological spillovers. In the next section we also present some of the strategic use of patents that may explain differences in quality patenting. Overall, the simple patent count should therefore be interpreted carefully. Whereas technological breakthroughs are able to impel the technological change, others just deepen into an already existing knowledge. Thus some innovations may have a greater impact on technological change than others because they may provoke new technological perspectives. According to this, the main findings of the literature dealing with the firms' innovative behaviors may be contrasted, particularly concerning the persistence in innovating over the time. Hence, by distinguishing the nature of innovations, this paper shows that persistence differs widely according to innovation quality, pioneering discoveries following a "one shot" process in the short run (even if they are presumably generated by the same firms) whereas other innovations are more persistent from one year to the next.

Up to now, some authors have attempted to estimate the private value of patents through their renewal patterns or by evaluating the stock-market value generated by patents announcements, among other techniques. Pakes & Schankerman (1984) and Schankerman & Pakes (1986) have proposed to proxy quality of patents by building the value of patent rights and their distribution value for the UK, France and Germany during the post-1950 period using renewal patent data²⁸. Guellec & Pottelsbergue (2000) study patents' values by evaluating the probability of obtaining a patent grant at the European Patent Office in function of the technological value of innovation, patenting and innovation strategies (collaboration etc.) followed by applicants at the international scale.

²⁶See Scherer, 1967, Pakes & Griliches, 1980 and Griliches, 1990 among others on this point.

²⁷As shown by previous studies, there are important differences in R&D performance across industries and firms, and the way firms rely on patents to appropriate sales; see Scherer (1967), Griliches (1990), Levin *et al.* (1987), Cohen & Levin (1989), Arundel & Kabla (1998).

²⁸They show that the variation in the quantity of patents in different cohorts tended to be negatively related to the variation in their mean values. As the authors pointed out, this finding implies that exclusive reliance on patent counts for measuring secular trends in the value of patented output could be quite misleading.

Trajtenberg (1990) is the first to construct an indicator of the value of innovation by weighting patent grants with the citations they received. He finds a close association between citation-based patent indices and independent measures of the social value of innovation in the field of a particular innovation. An interesting methodology to build a quality-innovation index has been proposed by Lanjouw & Schankerman (1999). Using information on individual patents (the number of claims, the forward and backward citations and the family size) to build composite index of quality, they find in particular, that the patent quality index shows significant power in predicting which patents will be renewed and which will be litigated. Further, Lanjouw & Schankerman (2004) show that research productivity is negatively correlated with the patent quality index whereas it is positively correlated with the stock market valuation of patented innovations. Through an empirical investigation concerning 100 US manufacturing firms, the authors show that the use of this quality adjusted measure of innovation could explain the so-called *R&D paradox*: the apparent decline in research productivity in the decade 1980-89.²⁹ As they argue, it is likely that firms face a trade off between "quality" (i.e. importance or scope) and "quantity" of innovation such as one should expected a negative relationship between patent counts and the average patents' quality at the firm level, conditional on R&D. Such a result, as the authors indicate, would generate a different relationship between R&D and simple patent counts as compared to R&D and quality-adjusted patents.

The Strategic Dimension of Patents

An important aspect of patents may be their potential strategic dimension as surveyed in Encaoua *et al.* (2000) and more specifically in Crampes *et al.* (2005). Hence, Hall & Ziedonis (2001) examine the "patent paradox" i.e. the fact that firms do not rely to patents to appropriate return of R&D more in the 1980s than before despite an unprecedented surge in patenting, they show that the "1980s strengthening of U.S. patent rights spawned a 'patent portfolio race' among capital-intensive firms". They consequently underlined the use of patents as a strategic variable to build legal rights to exclude competition in the semiconductor industry. In the study based on a survey questionnaire by Cohen *et al.* (2000), firms seem to rely on a large range of mechanisms to protect the profit due to innovation. They found patents tend to be the least emphasized whereas secrecy and lead time seems to be the most used strategies in the majority of the manufacturing industries. In the specific case of the pharmaceutical industry however, firms may more rely on patents as strategic variable to preserve their business from competition than in other sectors.³⁰ The main reasons supporting this opinion stand on the fact that secrecy is an extremely weak instrument of protection because of the (publicly available) clinical trials required in the development of each drugs and also because the pharmaceutical firms' outcomes are closely linked with the life of princeps' patents. As a consequence, to extend market exclusivity on drugs beyond patent expiration, a number of strategies are implemented to deter entry in order to preserve monopoly power. Among them, Carlton & Gertner (2002) show that "the combination of dynamics, uncertainty, and market power leads to one of the most important features of many R&D-intensive industries .an important form of competition is

²⁹Hence Lanjouw & Schankerman (1999, 2004) consider that if innovation varies widely in value, a part of heterogeneity is due to innovation at birth. As a result they show how it is possible to foresee the "value" of an innovation via the four indicators mentioned above. The composite indicator contains the number of forward and backward citations, the claims and the family size of each patent and is estimated as one-factor latent variable model where the conditional mean is a linear combination of the indicators.

³⁰See Scherer *et al.* (1959), Mansfield *et al.* (1981), Mansfield (1986) and Levin *et al.* (1987).

in R&D to replace the existing technology winner that has static market power with another based on improved technology". Hence, patenting around existing chemical entities ("me too drugs", ever-green patenting, etc.) have indeed become an important strategy followed by pharmaceutical firms.³¹ The increasing threat of generics, allowed by policies like the *Hatch-Waxman Act* (1984), may consequently motive research intensive firms to use patents as a strategic variable to maintain their revenue. Such strategy imply *evergreening* that occurs when a brand-name manufacturer "stockpiles" patent protection by obtaining separate patents on multiple attributes of a single product.³² To evergreen their products, Carlton & Gertner (2002) explain that the originator company will develop a "life-cycle management plan" composed not only of patent strategies, but an entire range of practices aimed at limiting or delaying the entry of a generic product into the market. Some of the evergreening strategies are line extensions and so-called next-generation drugs.³³ Patenting around existing chemical entities seems however to be more and more sought by pharmaceutical firms as shown by Lichtenberg (1996). Much of sequential innovation thus results from internally generated research and sequential product innovation which constitute an important feature of the pharmaceutical industry. Hence 60% of the new drugs approved in the 1990s were for "new formulations" or "new combinations" of already approved compounds. According to the Pharmaceutical Research and Manufacturers of America (*PhRMA*) "industry data indicate that of the \$26 billion spent by U.S. firms on pharmaceutical research in 2000, \$5 billion (19 %) was spent on post-launch R&D for new indications, new formulations, and other improvements to existing products. Sequential product innovation is spurred by and fosters competitive pressures." These market developments, carefully balanced with protections for seminal intellectual property, have spurred additional innovation and competition. Hence, brand-name manufacturers introduce new dosage formulations that provide, *a priori*, superior therapeutic properties than the original formulation, and introduce over-the-counter versions of products. In parallel, breakthrough drugs may also face competition within their initial patent life from other branded drugs of the same therapeutic class.³⁴ Consequently, the research intensive firms tend to rely heavily on product differentiation to achieve competitive advantage over other branded rivals what, to a certain extent, can be considered as one strategic use of patent. Further, with the increasing generic competition allowed by the Hatch-Waxman Act, branded manufacturers tend to develop improved products to retain sales which can be another strategic use of patent.³⁵

Strategic patenting to enclose sub-markets in order to face competition from other research intensive firms (i.e. brand name manufacturers) or production intensive firms (i.e. generics producers), may influence the technological change by extending, to some firms, the legal right to exclude imitators up to a foreclosure possibility on a whole technology. Statistically, the strategic dimension of patents may

³¹See Lichtenberg (2000, 2001).

³²These patents can cover everything from aspects of the manufacturing process to tablet color, or even a chemical produced by the body when the drug is ingested and metabolized by the patient (see European Generic Medicines Association: www.egagenerics.com).

³³Some of the evergreening strategies are also switching from prescription-only to over-the-counter status, exclusive partnerships with chosen generics manufacturers, direct-to-consumer advertising, defensive pricing strategies or even more to establish a subsidiary generics unit to compete in the generics market before independent generics companies are allowed to do so.

³⁴See the "between patent competition" in Lichtenberg & Philipson (2002).

³⁵A recent example is that one of *Mopral*, which has recently lost its patent protection, which carried out AstraZeneca to launch *Inexium*, an improved version, simultaneously with the entry of its generics.

bias the observation of firms' innovative efforts based on patents data. Indeed, it remains difficult to distinguish strategic patenting from creative accumulation since in both cases patents are granted.

Data and Methodology

This study pursues several research goals. *First*, an analysis at the patent level is conducted in order to make a distinction of *Leader* and *Follower* (or pioneer and incremental) patents, on one hand, and to distinguish patents in term of technological value on the other hand. These distinctions are made thanks to the number of citations made and/or received per patent. *Second*, an exploration of the pharmaceutical firms' persistence to innovate, conditional on the different kind of innovations' stocks, is presented. *Third*, the feedback effect –the dynamics showing the persistence of innovation over the time– of the different patent grants is explored through an innovation function equation.

We use two data sources. Firstly, we extracted patent data from the NBER patent data file, by Hall *et al.* (2001) concerning USPTO (*United States Patent and Trademark Office*) utility patents granted in the classes 424 and 514 (*Drug, Bio-Affecting and Body Treating Compositions*) over the period 1973-1999. Secondly, we gathered firms' patent data and match it by using the firms' CUSIP (*Committee on Uniform Security Identification Procedure*) identifier code with individual economic data from Standard & Poor's COMPUSTAT annual industrial files database that covers the period 1975-1995.³⁶ Data are thus reduced to a sample of 77 pharmaceutical firms patenting at the USPTO between January 1975 and December 1994. We build firms' quality-adjusted portfolio of patents as the sum of total patents weighted by their citation index which is also provided by the NBER.

Micro-Level Data from COMPUSTAT concerns R&D spending, capital stock, number of employees, net sales, capital expenditures, cash flow, and operating income (constant thousand US\$ 94). After merging the two data sources and keeping only firms having been granted patents at least three times consecutively at USPTO, we end up with a rather small sample of 77 pharmaceutical firms in a unbalanced panel data covering the period 1975-95. Contrary to other studies, we consider only firms who patent regularly. By this focus we want to consider innovative behaviors among real inventors: in the pharmaceutical industry only few patents become drugs³⁷ and laboratories must test hundreds of patented molecules before obtaining a result which will has a chance to be claimed an authorized drug. This relatively reduced sample eliminates the bias that may exist when considering also firms that rarely patent. True drugs inventors have to test many new chemical entities (NCE) and consequently have to be granted many patents before obtaining a new promising compound to commercialize.

The database contains approximately 10,000 patents referred at USPTO. In this study, we focus on the innovations that concern exclusively NCE and we do not take into account other products. This

³⁶Matching between two sources has been made through an intermediary file the containing CUSIP code (Hall *et al.* (2001)) and the corresponding corporate company name and USPTO's assignee code. Since Compustat includes firms that are traded in the US stock market (manufacturing firms) our final database concerns mainly American Pharmaceutical Firms.

³⁷It is well known that in the pharmaceutical industry very few of patents granted will become commercialized drugs and the failures during the clinical trials are enormous (see works of Grabowski).

choice is motivated by the fact that the NCE represent the most important share of the R&D effort made by firms and because strategic behaviors are expected on this market segment. The remaining patenting (excluding drugs) is assumed to represent a noisy measure of the real innovative effort made by firms and a weak share of their revenue. This paper deals therefore exclusively with pharmaceutical firms who extract their revenues from the commercialization of drugs because it is assumed to be the core of innovative activity in pharmaceuticals. We build firms' total patents portfolio weighted by their citation intensities, in addition to the explaining variable of total patents counts. Stocks of R&D, non-weighted and weighted patents are built following the perpetual inventory method using a 15% depreciation/obsolescence rate as traditionally used in the literature.³⁸

We address the problem of truncation related to patents and citations by implementing the methodology proposed by Hall *et al.* (2001). There is an important lag between patent applications and patent grants (in average about two years) so we observe only a small fraction of the patents applied which eventually will be granted as we approach the last year of patent data. Patent counts should then be corrected using weighting factors according to the estimated application-grant empirical distribution (*ibid.*)³⁹. Similarly, to deal with the problem of truncated citations, Hall *et al.* (2001) propose to estimate the shape of the citation-lag distribution, i.e. the fraction of lifetime citations (defined as the 30 years after the grant date) that are received in each year after the patent grant. Accordingly, the total citations for any patent (for which we observe a portion of its citation life) is estimated by dividing the observed citations by the fraction of the population distribution that lies in the time interval for which citations are observed. It is assumed that this distribution is stationary and independent of overall citation intensity. Although the normalization of citations reduces the striking contracting tendency at the end of the period, it does not eliminate the problem completely. Because our empirical study focuses on the period 1975-1991, it minimizes such a bias. The main reason of the shortening of our panel to 1975-1991 is however that it limits the problems inherent to the wave of mergers and acquisition (M&A) that characterized the pharmaceutical industry in the mid-nineties. This restructuration of the sector is indeed assumed to introduce a bias in the observation of innovative activities –at the firm level– since the acquisition of knowledge cannot be taken into account.

Distinguishing Innovations from Patents and Citations

Originality Index

In order to distinguish patents in terms of "*Originality*" or technological specificity, we use a citation-based measure suggested in Henderson, Jaffe and Trajtenberg (1998). Innovation *Originality* constitutes a measure of the firms' innovation technological specificity since it captures the extent to which a patent cites a wide range of technological classes or is rather concentrated on few technological areas. As shown by Cockburn & Henderson (1998) and Henderson & Cockburn (1996), pharmaceutical firms which are

³⁸See Griliches (1989), Hall & Mairesse (1995).

³⁹We use patent data from 1975, patent stocks are built for those firms patenting before this year. Therefore we do not need to adjust the patent counts for application lags but we will have to adjust the patent counts for the last periods. Patent counts beyond 1993 (since only about half the patents applied for in 1994 are observed due to grand lags).

more technologically diversified have been found to enjoy a stronger R&D productivity (R&D economies of scope). The measure of *Originality* is a Herfindahl concentration index such as:

$$Originality = 1 - \sum_{k=1}^{N_i} \left(\frac{N_{cited_{i,k}}}{N_{cited_i}} \right)^2 \quad (1)$$

where k is the index of patent classes and N_i is the number of different classes to which the cited patents belong.

Thus, if a new patent cites patents that belong to a narrow set of technologies, the originality score will be low, whereas if it cites patents in a wide range of fields would render a high score (notice that $0 \leq Originality \leq 1$ and that higher values represent less concentration and hence more originality). Consequently *Originality* measures the technological diversification of the innovator's R&D. A high score implies that the firm was held on a broad range of fields to innovate whereas a lower score implies that the innovator's R&D has been concentrated on a small set of fields (patent classes).

Citations-Adjusted Patents

As a measure of innovation technological "quality" or "scope", we weight the patent count by the number of citations each patent received (the number of forward citations). It captures the technological impact of an invention as reflected by the number of patents which cite it. It is important to note that the listing of patent citations is made by the patent examiners and not by the patentor itself: there is consequently no potential bias due to the firms' claims. Hence our variable *Citation Adjusted Patent* (CA) measures the (yearly average)⁴⁰ number of citations received per patent and represents one of our proxy for the firms' innovative activity. Such a variable increases with the number of forward citations and decrease with the number of patents granted by the firms. So the larger the number of citations a patent has received, the greater its "quality" or "scope". However, to track the pioneering behavior this measure is not completely satisfactory insofar as it does not refer to the citations made (which can proxy for the degree of novelty) but only on the citations received (which proxy for the technological importance).

Leader and Follower Patents

We separate patents in two categories which denote both their technological novelty and their importance. Compared with the simple patent weighting by citations received, this patent distinction considers both citations received and made (respectively forward and backward citations). Consequently we characterize, at the same time, the novelty of each innovation and its influence on the technological path (i.e. its technological value or influence). Such a distinction reports to a certain extent the pioneer and incremental inventions provided by our firms.

The measure of the leading or pioneering aspect of an invention considers a patent as *Leader* if its forward citations exceeds the yearly industry mean⁴¹ whereas its backward citations remains inferior to

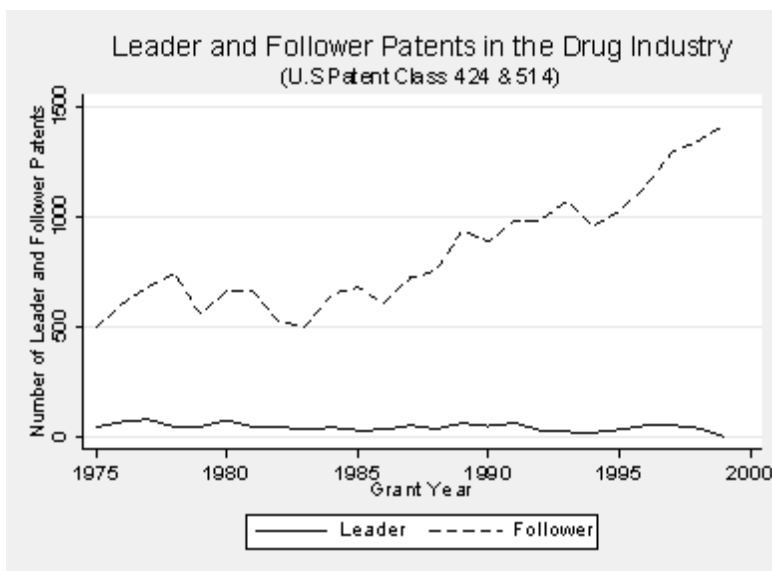
⁴⁰Because our data are yearly aggregated at the firms level, the weighted patent count is represented by the ratio of yearly citations received by the number of patents granted.

⁴¹It would be possible to use the median instead of the mean but there is no notable differences between the two calculation.

the yearly industry mean (considering the citations in the patent classes 424 and 514).⁴² As a consequence a *Leader* patent is defined relatively to the other patents granted the same year. Such patents exhibit, in comparison to the mean, of a greater influence on the technological path design **and** of a lower dependence on existing technologies. As a consequence, *Leader* patents are those which, apparently, lead the technological change, thanks to a relatively strong creativity which is widely diffused in the industry. We define *Follower* patents as the remaining patents of the sample so that they represent all patents which are not considered as pioneers ($Leader + Follower = Total\ of\ patents$). *Follower* patents are those which have received at most as many citations as the yearly industry mean and which have made at least as many citations as the yearly industry mean. *Leader* and *Follower* patents are defined relative to the yearly industry means so that there is no bias due to forward citations lags in addition to the precautions mentioned earlier. To our knowledge, few empirical works have differentiated the inventions in such a way. Duguet (2002), for example, distinguishes incremental and radical innovations on the basis of the firms' claims in a innovation survey which may be subjected to the drawbacks mentioned earlier.

For the full period (before having shortened the panel to 1975-91) we have the following trends in the granting of *Leader* and *Follower* patents:

Figure 1



Source: own calculations from NBER Patent Data File

The number of *Follower* patents apparently increases over the time whereas the number of *Leader* patents granted shows a slower and contracting movement along the period. The propensity to grant pioneering discoveries decreases over the time, especially since the mid eighties (the Hatch Waxman Act

⁴²Forward and backward citations included in this mark cover the period 1963-2000; as a consequence we consider all citations received up to 2000 whatever the granting date. As our study only cover the period 1975-91, patents granted in 1991 can receive citation up to year 2000. In addition, as mentioned previously, recall patent citations used in all the study have been normalized following the methodology proposed by Hall *et al.* (2001).

was enacted in 1984). The ratio of these two indicators (see appendix) confirms a relative decline in the *Leader* patenting compared to the *Follower* patenting. In fact, fewer and fewer patents propose radical technological change which assumes improvement strategies characterize the period considered probably as a response to the new competition impulsed by biotech firms. It could imply a greater use of internal knowledge if firms seek to stand on their previous inventions to introduce new products. Yet firms can also improve technologies that are not their own discoveries.

Internalized Spillovers

When a patent stands on the patented firm's previous innovations, it indicates a process of internalized spillover that can be evaluated through the number of self-citations that are made (the extent to which a patent cites the previous patents granted by the firm).⁴³ According to Hall & *al.* (2001) an interesting issue is that "presumably citations to patents that belong to the same assignee represent transfers of knowledge that are mostly internalized, whereas citations to patents of 'others' are closer to the pure notion of (diffused) spillovers." In other words, few citations to rival firms, or others entities, would mean that the firm does not rely on external spillovers as much as it relies on internal knowledge. The figure in the appendix shows that the use of self citations increases dramatically over the period. Hence the firms of our sample apparently rely more and more on their previous inventions to innovate. Such a trend highlights the increasing difficulties to innovate radically over the time i.e. to create new knowledge. Empirically these observations coincide with the introduction of the *Hatch-Waxman Act* (enacted in 1984)⁴⁴ which provides incentives to support the development of generic versions of off-patent drugs and permit patent owners to recover time lost during FDA approval. As shown by the figures 1 and 2, it is possible to hypothesize that the pharmaceutical firms seek to retain their sales through product development strategies in order to face the pressure exerted by generics. More generally our data confirm previous empirical findings relating a decrease of inventiveness in pharmaceuticals: fewer and fewer pioneering inventions are discovered leading to an erosion of the number of new (technological) promising compounds invented.

In the pharmaceutical industry our proxies of innovation based on citations criteria (*Leader*, *Follower*, *Citation-Adjusted* patenting) allow us to measure the propensity to improve already existing solution rather than to create technological breakthroughs. They are thus means to put into evidence the kind of strategy of research led by the current pharmaceutical firms and how the past innovative activity of these firms may influence their present innovative behaviors. Several patent stocks are therefore built for further employment in the knowledge production functions for each firm.

⁴³The percentage of self-citations is computed as in Hall *et al.* (2001): for each patent that has an assignee code we count the number of citations that it made to (previous) patents that have the same assignee code, and we divide the count by the total number of citations that it made.

⁴⁴Since the law's passage, the generic industry's share of the prescription drug market has jumped from less than 20 % to almost 50 % today. The economic realities of non-innovator commodity production allow generics to enter the market at a significant discount, and for prices to decrease with increased generic entry. Before the 1984 law, it took 3-5 years for a generic copy to enter the market after the expiration of an innovator's patent. Today, generic copies often come to market as soon as the patent on an innovator product expires. Prior to the *Hatch-Waxman Act*, only 35 percent of top-selling innovator medicines had generic competition after their patents expired. Today, almost all innovator medicines face such competition (see *PhrMA* (2002)).

An Innovation Equation

Propensity to Innovate: Distinguishing the Nature of Innovations

A key focus of interest in this paper is the estimation of an innovation equation I_{it} where I denotes either the *Non-Adjusted* patent count, the *Citation-Adjusted* patent count or the *Leader* patent count which are described above. Following Hausman *et al.* (1984) and Blundell *et al.* (1999), for a latent variable of innovation I_{it} , we consider the knowledge production function:⁴⁵

$$I_{it} = f(x_{it}, \eta_i) \quad (2)$$

where x_{it} is a vector of firm i characteristics (e.g. past R&D investments) and unobservable invariant firm-specific factors are represented by the term η_i . It represents permanent unobservable differences across firms affecting the production of innovation firms (appropriability conditions, marketing strategy or financial characteristics). This relationship is derived as the outcome of a firm's optimal search rule for innovation (Blundell *et al.* (1995), Reinganum (1989)) where the search process is assumed to generate innovations in future periods. I_{it} represents the several patent-based proxies for innovations made by the firm i at time t described previously. Because the number of patents is a non-negative integer, we adopt count data regressions as described by Hausman *et al.* (1984) and Blundell *et al.* (1999). We model the conditional mean as a multiplicative or log link function of explanatory factors as:

$$\begin{aligned} I_{it} &= \exp(x'_{it}\beta + \eta_i) + \varepsilon_{it} \\ &= \mu_{it}v_i + \varepsilon_{it}, \quad \text{for } i = 1, \dots, N \text{ and } t = 1, \dots, T \end{aligned} \quad (3)$$

where $\mu_{it} = \exp(x_{it}\beta)$, $v_i = \exp(\eta_i)$ and ε is a disturbance term with expected value 0. x_{it} is a vector of observed explanatory variables, and β is the corresponding vector of parameters to be estimated including lagged values of firms' market share, R&D expenditures and stock of knowledge, etc. The full empirical model is defined as:

$$\begin{aligned} I_{it} &= \exp(\beta_1 \log(\text{Sales})_{it-1} + \beta_2 \log(\text{R\&D})_{it-1} + \beta_3 \text{MS}_{it-1} + \beta_4 \text{G}_{it-1} + \beta_5 \text{Self} + \eta_i) + \varepsilon_{it} \\ \text{for } i &= 1, \dots, N \text{ and } t = 1, \dots, T; \text{ where } I_{it} = \{NA_{it}, CA_{it}, L_{it}\} \end{aligned} \quad (4)$$

In this specification, firms' innovation propensity is conditional on previous market power, measured by the lagged value of total sales $\log(\text{Sales})_{it-1}$, R&D effort $\log(\text{R\&D})_{it-1}$, market-share MS_{it-1} , and internal spillover (*Self-Citation* propensity) Self_{it-1} . Considering the dynamics of innovation, we first introduce the lagged knowledge stock variables $G_{NA, CA, L; t-1}$ (where subscripts NA refer to *Non-Adjusted* patent stock $G_{NA, t-1}$; CA to *Citation-Adjusted* patent stock $G_{CA, t-1}$; and L to *Leader* patents stock $G_{L, t-1}$) into the knowledge production function (see Blundell *et al.* (1999) for a comparable specification). Secondly, we introduce the lagged flows of the firm's innovations. A patent is considered as a *Leader* if it has made fewer citations than the mean value for patents of the same application year while

⁴⁵See also Hausman *et al.* (1984); Winkelmann & Wimmermann (1992); Crepon & Duguet, (1997); Blundell *et al.* (2000), among others.

receiving more citations (normalized) than the average of these same patents. Thus, in a (yearly) cross-sectional basis, we identify the *Leader* patents (i.e. the pioneering discoveries having had a large impact on the technological path), as those that determine the technological dynamic of the pharmaceutical industry. These *Leader* patents are assumed to generate the process of creative destruction in a technological sense, since they open a new technological path, replacing existing knowledge (i.e. innovations).⁴⁶

The expected effects of market share and total sales on innovation propensity are ambiguous. Strategic considerations imply that the marginal benefit of an innovation (an additional increment to the firm's innovation stock, $G_{i,t}$) may be more valuable to a market leader than to a follower as shown through the "*efficiency effect*" described in Gilbert & Newbery (1982). In contrast, dominant firms may be more reluctant to innovate as they find it more profitable to exploit existing innovations.⁴⁷ This case thus illustrates the Reinganum's "*cannibalization*" model (1989) or "*displacement effect*". The self citations show how the firm relies on the previous inventions it made to generate NCE. On the one hand, it is expected that it influences positively on the *Non-Adjusted* patenting because of the product development strategies described previously, and negatively for the *Leader* patenting if we hypothesis that self citations exhibit the cumulative nature of innovation within firms. On the other hand, the internal spillover effects may also help to generate high quality innovations because they represent a technological advantage as the firm exploits its knowledge to invent. If we hypothesis that pioneering discoveries follow a multi stage process of invention requiring several knowledge, self citations may have a positive influence. As a result of these two possible impacts, the potential effect of internalized spillover (i.e. self citations) on the firms' innovation propensity and persistence in innovating is undetermined.

Individual knowledge stock variables are obtained by accumulating past patents granted: $G_{i,t} = I_{i,t} + (1 + \delta)G_{i,t-1}$. The stock of knowledge increases continuously by the addition of new patents, but it also continuously decreases at the constant depreciation/obsolescence, rate δ (15%).⁴⁸ Knowledge-stocks should exert a positive effect on the propensity of the firm to innovate as there are dynamic returns in the production of innovation. Cumulated technological experience facilitates in some way current R&D productivity: R&D economies of scale (see Teece (1980), Cohen & Levin (1989), Chandler (1990)), learning-by-doing, and learning-by-learning effects (see Rosenberg (1987) and Cohen & Klepper (1996)). Concerning dynamics of innovation it is expected to find higher persistence in low quality patenting for firms that use patent as a strategic variable to preserve market power, whereas highest quality (i.e. *Leader*) patenting should be less persistent over the time since it requires –presumably– large R&D spending and may need developments to be commercialized. Concerning the *Citation-Adjusted* patenting the expected effect of lagged patenting is more ambiguous because it capture two dimensions: that one of the number of patent granted (–) and that one of the number of citations received (+). We also

⁴⁶The process of creative destruction in drugs is to some extent limited, both economically and technologically. First, as we mentioned previously (Henderson & Cockburn (1993, 1994)), pharmaceutical firms may enjoy each different "patent" prize as patents may cover similar technological innovations (e.g. patenting around, evergreening patenting etc.). Second, economically, firms may keep their market power in specific therapeutic domains through lead time, brand reputation strategies, and other first-mover advantages.

⁴⁷They may also rely on alternative strategies to keep market power as presented earlier (technological foreclosure...).

⁴⁸Initial values of $G_{i,t}$ correspond to the pre-sample stock of patents for firms patenting before 1975, otherwise patent' stocks for firms appearing after 1975 are calculated according to the perpetual inventory method following Griliches (1989) or Hall & Mairesse (1995).

include two additional lagged terms referring to the firms' innovation degree of *Originality* and the firms' citations (received) share. They constitute the yearly mean value of firms' patent portfolio. The firms' citation share represents the share the firm own in the industry total forward citations (i.e. the sum of citations received) by patents granted in classes 424 and 514. It thus measures the degree of technological leadership. If technology-leaders have stronger incentives to remain in the innovation race, it should enter positively for the firms' innovation propensity as mentioned in Segestrom & Woniereck (1999) then Hörner (2001). Nonetheless, its impact must differ *a priori* according to the quality level of patenting (see Henderson (1993)).⁴⁹

Estimation Method for a Linear Feedback Model (LFM)

An important feature of our study is the estimation of a dynamic model (i.e. including linear feedback) to assess the persistence with which firms innovate. Given the panel dynamic specification of the model, several practical problems have to be handled: first, the autocorrelation problems imposed by the lagged variables. These lagged variables are by nature dependent on past disturbances, which makes it a pre-determined variable in the equation. Second, we have to deal with the time series cross-section nature of data and account for the presence and features of the unobserved components of residuals (i.e. non-observed heterogeneity). Third, the appropriate lag length of the auto regressive-distributed lag model have to be determined.

A series of strong assumptions must be respected in order to apply traditional OLS or panel data estimators. Including the lagged dependent variable as one of the regressors makes pooled OLS as well as classic error component estimators obsolete. Poisson or Negative Binomial models, because they assume that the regressors are strictly exogenous, cannot be used as mentioned by Montalvo (1997) and Blundell *et al.* (2000). The count panel data literature has largely focused on estimating models for patenting and the returns to R&D investments. A seminal paper of Hausman *et al.* (1984) initiated a growing literature estimating patent and innovation production functions using the Generalized Method of Moments (GMM) estimator allowing for correlated firm specific effects and weakly exogenous inputs.⁵⁰ It involves estimation of a dependent variable as a function of its lagged value and other endogenous, pre-determined and exogenous variables in the presence of unobserved heterogeneity. The model is estimated in two stages using the residual of the first stage to compute an optimal weighting matrix, which is subsequently used in the second stage. As we analyze the effects of lagged innovation flows on the current propensity to innovate, we employ the nonlinear GMM method discussed and implemented by Windmeijer (2002) –*ExpEnd*– and used in similar conditions by Kim & Marschke (2005) then Salomon & Shaver (2005).⁵¹

⁴⁹Likewise, a weak citation-share indicates that other firms or competitors own a larger part of the new technology. Hence competitive spillovers may have a negative rivalry effect on a firms' likelihood to apply for a patent : the more competitors invest in R&D, the less a firm is likely to invent a new technology (see Loury (1979), Lee and Wilde (1982)).

⁵⁰See the development of the quasi-differencing approach of Chamberlain (1992) and Wooldridge (1991, 1997) by Montalvo (1997), Cincera (1997), Crépon and Duguet (1997), Blundell *et al.* (1999) and Blundell *et al.* (2002).

⁵¹The different parameterization between the multiplicative feedback model (MFM) and the liner feedback model (LFM) (Blundell *et al.* (1999), Cincera (1998)) implies that, in comparison to the LFM, the coefficients $\beta E(I_{it})$ in the MFM measures the short run impact of a change in X_{it} . As explained by Blundell *et al* (1999), in the MFM the nonlinear dynamic makes it difficult to judge the stability properties of the model and the potentially important feedback parameter

The conditional mean in the LFM is defined as:

$$\begin{aligned} E(I_{it} | I_{it-1}, x_{it}, v_i) &= \gamma I_{it-1} + \exp(x'_{it}\beta)v_i \\ &\equiv \gamma I_{it-1} + \mu_{it}v_i \end{aligned} \tag{5}$$

We implement the Arellano and Bond test for first and second order serial autocorrelation of residuals ($AR(1)$, $AR(2)$) in the differenced error terms to test the validity of the set of instruments (reported at the bottom of each table). If it is not serially correlated, the difference residuals should be characterized by negative first-order serial correlation and the absence of second-order serial correlation (which is the case for all our equations). Then, the Hansen test (–two steps– SYS-GMM) of over-identifying restrictions is applied: it tests for correlation between the instruments that are excluded from the second stage model and the residuals. It conducts a test for the null hypothesis that the remaining theoretical orthogonality restrictions are equal to zero (see Hansen (1982) and Sargan (1985)). Failure to reject the null hypothesis indicates that the instruments are valid, and then supports the validity of the model specification (which is the case for all our equations).

Empirical Results

Table 1 presents summary statistics describing the data. Averaging across all firms and years, our sample spent on average \$283 in R&D and has average sales of \$2,786 (thousand US\$ 1994) whereas the average market share is 0.5% with a rather large standard error (0.9). When looking at the innovations made by firms, expected values are found since the yearly *Non-Adjusted* patenting is widely stronger than the *Leader* patenting (on average for 10 patents applied only one is a *Leader*). Our firms grant in average 25 patents over the period with (approximately) 3 *Leader* and 22 *Follower* patents (recall we keep only patents granted in classes 424 & 514). On average our firms receive 6 citations per patent and the ratio of total citations received by each patent stock is almost 23 (versus a maximum of 135). Patent stocks appear very heterogeneous: 25.4 in average but 536.5 in max (recall patent stocks are continuously depreciated over the time and consequently values are not integer). This first exploration of the data thus first indicates that they are relatively few innovations made in volume compared with *Non-Adjusted* patenting. In addition, important differences appear across firms when looking at the standard errors for the whole of the variables, which suggests a large dispersion of the values and consequently a strong heterogeneity among the firms and/or the periods considered.

- *Table 1 about here* -

Propensity in Innovating

Table 2 displays the estimations on the innovation equation using GMM-Wooldridge Estimation on our different proxies for the firms' innovation. Columns 1-3 display results of *Non-Adjusted* patents, whereas *Leader* patents are sensitive to large innovation counts. In a similar study, Blundell *et al.* (1999) implement both specifications and both models are found to yield similar estimates for the main parameters of interest. Although a non-nested comparison has suggested a preference for the LFM specification.

columns 4-7 concern estimations of *Citations-Adjusted* patents and columns 7-9 concern estimations of *Leader* patents. The sets of instruments used are reported at the bottom of the table. For each equation we consider either the firms' different patent stocks effect on the current propensity to invent (column 3, 6 and 9) or the feedback exerted by innovations made in the previous period (column 2, 5 and 8).

- *Table 2 about here* -

Results indicate that the role played by internal spillover, the Self-Citations variable, is significant to explain the *Citation-Adjusted* and especially the *Non-Adjusted* patenting (column 1 & 4) which suggests firms rely on their previous inventions to "patent around". The effect is the largest for the simple patent count and is not significant for the *Leader* patenting (column 7). Product developments indeed lead to low quality innovations (in a technological sense) and consequently improved technologies tend to be less cited than others. Considering the specifications 1-3, the weak stability of this variable shows that it captures the dynamic process of innovation: the coefficient, even if positive, strongly decreases when introducing the patent stock (column 3) and the sign becomes negative (column 2) when a lagged dependant variable is introduced.

Concerning the role played by market power, interesting results are found: the firms' market share is negatively correlated with the *Citation-Adjusted* patenting and positively with the *Non-Adjusted* patenting while it is not significant to explain the *Leader* patenting. The amount of sales of the previous period confirms that the firms' level of activity (or size) is negatively correlated with the quality of inventions: the smallest firms seem therefore to be the most cited and thus have the largest technological influence. In addition the coefficient of the amount of sales is significant and negative to explain the *Leader* patenting confirming that quality comes essentially from firms with a low commercial activity (presumably a low financial leadership). Consequently, if the firms' market power is not significant to explain the pioneering behavior, the amount of sales, as proxying for the firms size and/or level of activity, seems to matter. These results then confirm the Reiganum's cannibalization model finding: dominant firms have few incentive to provoke the technological change by fear of conflicts in their product portfolio and overlaps in their source of revenue it may cause.

About dynamic effects there is, at first sight, a certain persistence, from one year to another, in patenting and especially in *Citation-Adjusted* patenting. However, concerning the pioneering behaviors (*Leader* patenting) a deterring effect is found since the feedback's coefficient is negative.⁵² Hence, on the one hand the previous period *Leader* patents applied is likely to deter the innovator to provide further *Leader* innovations even if, on the other hand, quality patenting seems to have a persistent trend at the firm level. Consequently, providing quality (i.e. widely cited patents) seems to be a continuous behavior

⁵²Because of the nonlinear functional form, negative coefficients on the lagged dependent variable in the LFM cannot be interpreted straightforwardly as the integer-valued autoregressive (INAR) model does not really allows for that. However, in reference to Salomon & Shaver (2005) who also found negative coefficients with a comparable specification, our interpretation of a negative lagged dependant variable is that firms with positive innovation counts in $t - 1$ often realize zero counts in t , once controlling for firms specific effects.

whereas the radical change, through the creation of technological breakthroughs (i.e. *Leader* patents), appears to be less persistent from one year to another and consequently more sequential. The *Leader* patenting appears therefore to be a "one shot" process for the innovators in the very short run. However more lags are needed in our equation to generalize this process (see *Table 3, 4 and 5*).

Another interesting finding is the role played by the various patent stocks in the propensities to innovate.⁵³ Stocks are always positive and significant which suggests, as expected, that the firms' knowledge base plays positively in the propensity to innovate. Nevertheless, the patent stocks' coefficients are rather small but increase with the technological importance of the patenting considered and thus is relatively strong for the *Leader* patent stock. Hence it appears that the *Leader* patent stocks are strongly correlated with the current *Leader* patenting suggesting only some firms are responsible for a large share of the technological breakthroughs even if, in addition, such patenting is not persistent in the short run. The comparison between column 8 & 9 thus shows that the pioneering discoveries follow a non continuous dynamics. The radical technological change seems emerge from non persistent innovators (but which are *a priori* the same) whereas the quality innovations seems to be the fruit of small sized persistent innovators.

The R&D expenses are always significant and positive even if substantial differences across coefficients suggest a greater importance for the *Leader* patenting, then for the *Citation-Adjusted* ones and least for the *Non-Adjusted* patenting. Consequently, as expected, the level of R&D expenses is correlated to the importance of inventions: the higher the R&D expenses the larger the probability to grant *Leader* patents. It is interesting to note that the simple patent count is slightly connected with the past R&D expenses, compared to the other patenting. It thus reinforces the hypothesis of the (large) firms' strategic use of their patenting without (or with a weak) real innovative motivations. Considering the diversification of the R&D, the *Originality* score is always positive and a particularly large effect is found for the *Leader* patenting. Recall that innovations' *Originality* constitutes our measure of firms' R&D diversification.⁵⁴ Hence, confirming previous studies, pharmaceutical firms which are more diversified in their knowledge base (larger scope of R&D) are found to enjoy a stronger R&D productivity (due to R&D economies of scope). Surprisingly this R&D diversification is found to have the largest impact on *Leader* patents and the lowest on *Citation-Adjusted* patents. The scope of R&D therefore stimulates the newness and importance of research output even if the effect is relatively low when considering only the importance of innovations disregarding newness (*Citation-Adjusted* patents). The diversification of R&D therefore appears to be an important factor contributing to pioneering discoveries. It suggests that spillover occurring between technological classes support the firms' inventiveness. To a certain extent, such an importance of *Generality* for *Leader* patenting highlights the potential importance of the links (i.e. strategic interactions) between the different sectors for the pharmaceutical research (presumably biotechnologies/pharmaceutical and chemical/pharmaceutical).

⁵³According to the perpetual inventory method used, a 15% depreciation rate means a patent value is close to zero after 20 years.

⁵⁴See Cockburn & Henderson (1998), Henderson *et al.* (1998) and Henderson & Cockburn (1996).

Finally these estimations suggest at first sight that small firms are more cited whereas large firms appear to be mainly technological developers through a strong (*Non-Adjusted* and possibly strategic) patenting activity. In addition it appears that patent stocks play differently than the feedbacks of previous period patenting. Indeed, while the *Non-Adjusted* and *Citation-Adjusted* patent stocks have a significant but rather small impact on the current propensity to innovate, the *Leader* patent stock is relatively important. Given the importance of feedback effects of lagged *Leader* patenting, such results may appear contradictory at first sight. However, if we consider pioneering behaviors are not persistent from one year to another but persistent on the long run (presumably between 5 and 20 years considering the depreciation rate used in the stock calculation) it suggests that some (relatively) occasional inventors have the greatest technological impact by innovating. This highlights the role played by the competitive (entrants) research intensive firms for the technological path design in pharmaceuticals. We bring more precision thereafter by widening the window of feedbacks.

Dynamic of Innovation

Tables 3, 4 and 5 display the estimations of the firms' persistence in innovating over the time (the dynamic model). Table 3 displays results of *Non-Adjusted*, whereas Table 4 concerns estimations of *Citations-Adjusted* and Table 5 shows estimations of *Leader* patenting. The sets of instruments used are reported at the bottom of each table. We analyze the feedback of past innovations up to four years before the current propensity to innovate as a means to characterize the firms' persistence in innovation. For each equation we assess the feedback's effect of firms' innovating activity in $t-1$, $t-2$, $t-3$ and $t-4$ on their current innovation flows. We firstly present results on *Non-Adjusted* then on *Citation-Adjusted* and *Leader* patenting. The equations assessing the persistence with which firms innovate confirm previous findings: innovation quality is negatively correlated with the level of activity (firms size) and the strongest persistence concerns the *Citation-Adjusted* patenting whereas the *Leader* patenting exerts a deterring effect on future pioneering behaviors up to three years after.

The role of R&D expenditures is always significant and positive regarding the different patenting propensities but its score is increasingly large according to the technological importance of innovations. Hence, as expected, the technological influence (the propensity to be cited) and the innovation novelty are linked with the firms' effort in R&D. Cohen & Kleppers (1996) suggest that innovations are not directly linked between them and only the continuity in the R&D expenses ensures the persistence in innovating. The simultaneous inclusion of both the R&D expenses and past innovations variables in our equations thus allows us to test this assumption. Our results finally reject the Cohen & Kleppers' prediction since the R&D score is always significative as well as the past innovative activity. Consequently the persistence in innovating does not reflect only a continuous flow of R&D expenses insofar as the past innovating activities remain significative despite the significance of the R&D expenses. At the firm level, innovations are consequently related between them confirming Duguet & Monjon (2002)'s findings. We now detail the different dynamics of innovation according to our three dependant variables proxying for firms' innovation activity: *Non-Adjusted*, *Citations-Adjusted* and *Leader* patent counts.

Persistence of Patenting (*Non-Adjusted* patents)

At the simple patent count level, the feedbacks are almost always significant at the 1% level. There is however no evidence of a decrease following the importance of lags introduced in the equation and, when comparing columns 1 and 4, it even seems that the coefficients tend to increase. That means the *Non-Adjusted* patenting does not erode itself over the time and consequently that firms are strongly persistent in using patents.

Considering the research efforts, the coefficient of R&D expenditures is always positive and decreases a little when the importance of feedbacks increases. It suggests that the more persistent patenting over the time do not need the largest expenses in R&D. If we hypothesize that some strategic use of patents are at work, the interpretation of the R&D's decreasing coefficient is straightforward: the building of barriers to entry, product development and other foreclosing strategies represent a weak innovative behavior which need few expenditures in R&D, once controlling for firms effects. Such a result suggests the *Non-Adjusted* patenting as a whole capture some behaviors that are not related to innovation as the strategic patenting.

Considering the firms' market shares, the coefficient tends to increase with the importance of feedback. It means the more persistent firms in granting patents are also those who benefit from the largest market power. Because the amount of sales' coefficient follows the same trend one may therefore deduct this effect is proper to the firms' size: largest firms are the most persistent in granting patents.

- Table 3 about here -

The dynamic analysis at the level of the *Non-Adjusted* patenting seems to support the assumption according to which largest firms (those having the largest level of activity and market share) are those who have the greatest use of patents without having the research effort that would however be necessary to innovate in the same proportion. *Table 3* thus justifies our methodology –the use of different proxies for firms innovations– by showing that continuous patent flows do not reflect necessarily persistence in innovation but persistence in patenting and possibly a strategic use of it.

Persistence of Innovating (*Citations-Adjusted* patents)

Similarly with Duguet & Monjon (2004), in our the *Citation-Adjusted* equations, the coefficient of lagged innovations decreases with the importance of the lag, which suggests that some kind of knowledge depreciation takes place and consequently a strong entry barrier to innovation seems to exist. In contrast to their findings, our coefficient remains almost always significant at the 1% level, regardless of the number of lags (up to four years). Hence the pharmaceutical industry seems to be characterized by a *learning-by-doing* which is depreciating as time goes on.

Compared with *table 3*, the coefficient of R&D is stronger and increases significantly with the importance of lags. In addition to the rejection of the Cohen and Kepler's hypothesis, we deduct that persistence in *Citation-Adjusted* patenting reflects indeed a true innovative behavior since firms tend to

increase their R&D expenses when the *Citation-Adjusted* patenting goes on. This confirms previous findings in the literature (presented earlier): the *Citation-Adjusted* patenting is a better proxy for innovation than the *Non-Adjusted* one since it results from larger R&D efforts.

Considering sales and market shares, coefficients are always negative what confirm that largest firms have a lower technological impact in innovating than others. As the importance of the coefficient of market share increases with the importance of lags, *table 4* suggests the more persistent firms in *Citation-Adjusted* patenting are also the smallest: market domination is inversely proportional with the technological influence.

- **Table 4 about here** -

Results which are presented in *table 4* confirm the importance of smallest firms in the pharmaceuticals' technological dynamics. They seem to be a major source of technological change to the extent that pharmaceutical patents widely cite their inventions which therefore have a large impact at the industrial level. To a certain extent one may assume that small firms are competitive entrants who threat market dominants of technological exhaustion.

Persistence of Pioneering Behaviors (*Leader* patents)

About the *Leader* patenting, the feedbacks impact always negatively but with increasingly small coefficients according to the importance of lags. The firms' pioneering behavior thus tends to reduce further innovative ambitions even if this effect decreases with time. This is straightforward to interpret: some firms canalize their innovative effort (R&D expenditures for instance) leading to some occasional technological breakthroughs which then limit their future inventive capacities in the short run. Consequently the pioneering behaviors seem to be not bearable by the firms for each period and there is no possibility of persistence with such innovations. It is possible that the time needed to create a technological breakthrough does not allow persistence from one year to another. Another explanation is supported by the coefficients of the R&D expenditures that show the *Leader* patenting needs exceptional expenses in research that are probably not bearable continuously.

The coefficients of R&D are indeed the strongest compared with other proxies for innovation: the quality ranking of innovation thus follow that one of the R&D expenses.

- **Table 5 about here** -

Table 5 exhibits the large needs of R&D expenditures to grant a *Leader* patent compared to other innovations. The main finding concerns the deterring effect of past pioneering behaviors on the current *Leader* patenting: firms who have granted *Leader* patents in the past three years have a strong probability to obtain a zero count in the following year. When comparing this result with column 9 of *table 2* we can deduce that firms are the same since the *Leader* patent stock is significantly positive to explain the *Leader* patenting.

Overall Results on Firms' Persistence in Innovating

The effects of size and market power found in table 3 are confirmed. Whereas the amount of sales (the firm's size) increases the probability to grant patents, with increasingly important coefficients according to the number of lags, it reduces the probability to provoke the technological change: the coefficients are always negative concerning the Quality-Adjusted (*Citation-Adjusted* and *Leader*) patenting. The role played by the market dominance (market share) is the same, even if in both cases the coefficients are stronger.

As a result, whereas the market power increases the probability to be a persistent patentor, it decreases the propensity to provide highly cited patents and this effect increases with the importance of feedbacks. Concerning the *Leader* patenting these coefficients are not significant. This is a key result of the paper insofar as it sheds light on the effect of market dominance, or size, on innovation in the pharmaceutical industry. Dominant firms are indeed persistent "innovators" without regard to the quality of inventions (thus they patent continuously), suggesting a strategic use of patents to block entry and maintain revenues. Nevertheless, dominant firms do not have a strong technological influence which must result of the smaller firms' innovative activity, being apparently the real sources of technological change.⁵⁵

Considering the effects of internalized spillovers (as measured by the number of Self-Citations made by the firms) the effect appears to be the strongest for the *Leader* patenting. Surprisingly this result suggests that pioneering discoveries emerge from a pattern where the internal knowledge of the firm plays a strong role. It supports the idea of an innovative process standing on some internal competencies and knowledge which are needed to fully develop a real technological breakthrough. To a certain extent this result highlights a process where innovations result from an accumulation of competencies, as in Rosenberg (1976). However, according to our results the impact of internal knowledge decreases over the time. This mitigates the Scotchmer (1999)'s results about cumulative innovation: internal knowledge benefits more to the pioneering discoveries than to other innovations.

An interpretation of these results indicates larger pharmaceutical firms innovate in a *closed loop* (see Fudenberg & Tirole (1984)) that leads them to have a strategic management of their innovative capacity, conditioned by their past innovations. Innovations are thus indeed linked between them at the level of the firm but differently according to the patenting characteristics. Whereas innovative (patenting) persistence is found to be strong, especially for the quality patenting, the pioneering patenting deters further *Leader* inventions even if, considering stocks, breakthroughs seem to be the fruit of the same firms. In addition, the strategic use of patent and other foreclosing strategies (product developments, evergreening) seems to play a significant role in pharmaceutical.

⁵⁵Similar conclusion where found with linear IV-GMM in an earlier version of this paper. It implies that our results are robust to alternative specifications.

Concluding Remarks

This paper analyzes the American pharmaceutical firms' persistence in innovating just before the wave of mergers and acquisitions that followed the "Biotech revolution". We evaluate the impact of past innovative activity on firms' innovation propensities using a non-linear GMM estimator for exponential models that allows for predetermined regressors and linear feedback. Hence, an empirical investigation on *Non-Adjusted*, *Citation-Adjusted* and *"Leader"* patents has been presented both on innovation propensities and persistence in innovation. We find that innovative activity at the firm level depends strongly on the scope of past innovations. The results also shed light on the importance of small firms in the dynamics of innovation in pharmaceutical industry, and suggest that large firms persist in using patents strategically in order to preserve their revenues by setting up barriers to entry with blocking patents or even more by evergreen their products. Pharmaceutical innovation in general, and pioneer innovation in particular, depends largely on past quality innovation made by firms, and this effect may likely deter further *Leader* innovations rather than strengthen incentives to invest on pioneering invention. In addition, the strategic use of patents seems to be an important feature of the pharmaceutical industry and well announce the wave of concentration that follows our period of analysis which will be explored in further analyses.

The estimates suggest that in the pharmaceutical industry the *"displacement effect"* is likely to dominate the potential *"efficiency effect"* attributed to market dominant firms when we relax the patent homogeneity assumption. Further, (large) pharmaceutical firms may find it more profitable over time to make incremental innovation –product developments and strategic patenting– rather than high quality innovations. When considering how persistently pharmaceutical firms innovate, the functioning of innovation seems to support the hypothesis that the pioneering behavior, at the firm level, is not persistent whereas the *Citation-Adjusted* patenting is eroding on the short run and the simple patent count appears to be more stable over the time. A key result of the paper is thus that technological breakthroughs need large investments in R&D that limit the ability of firms to be persistent sources of radical technological change (from one year to another). However, the *Leader* patenting seems to come often from the same firms as evidenced by the positive impact of *Leader* patent stocks. The *Citation-Adjusted* patenting is strongly persistent over time and essentially comes from the small firms' inventive efforts.

Consistent with research by Lanjouw & Schankerman (2004) there is an apparent decline of research productivity in the American manufacturing industry during the period considered. In the pharmaceutical industry in particular, quality R&D productivity seems to have decreased in the last decade. Our results suggest that the smaller firms are responsible of the major technological changes occurring in the pharmaceutical industry whereas the large pharmaceutical firms tend to be, on average, technological followers (i.e. developers of existing technologies). This result extent to the pharmaceutical industry the findings of Lerner (1997) who finds that in the disk drive industry the firms who follow the (technological) leader display the greatest propensity to innovate. Consequently technological followers appear to be those which grant the most patents whereas the real technological change (the *Leader* patenting) seems to result of a one shot process or come from the smallest firms when considering the *Citation-Adjusted* patenting. Our results thus confirm the advanced hypothesis of increasing difficulties to innovation in

the pharmaceuticals: dominant firms are not the sources of the technological change but bring onto the market many low quality innovations. Such a finding could be related to diseconomies of R&D and organizational inertia related to big laboratories. Like Marbela & Orsenigo (1996), which found that a process of "*creative accumulation*" characterizes the knowledge based industries, our results show that in the pharmaceutical industry there is no persistence at the pioneering patenting level and a rather strong product development strategy. However innovators seem to be more persistent regarding to the *Citation-Adjusted* patents what exhibits a persistent quality patenting (especially from small firms), punctuated by occasional technological breakthroughs. On this study, the pattern of innovation in the pharmaceutical industry identifies the small firms as the source of the technological change.

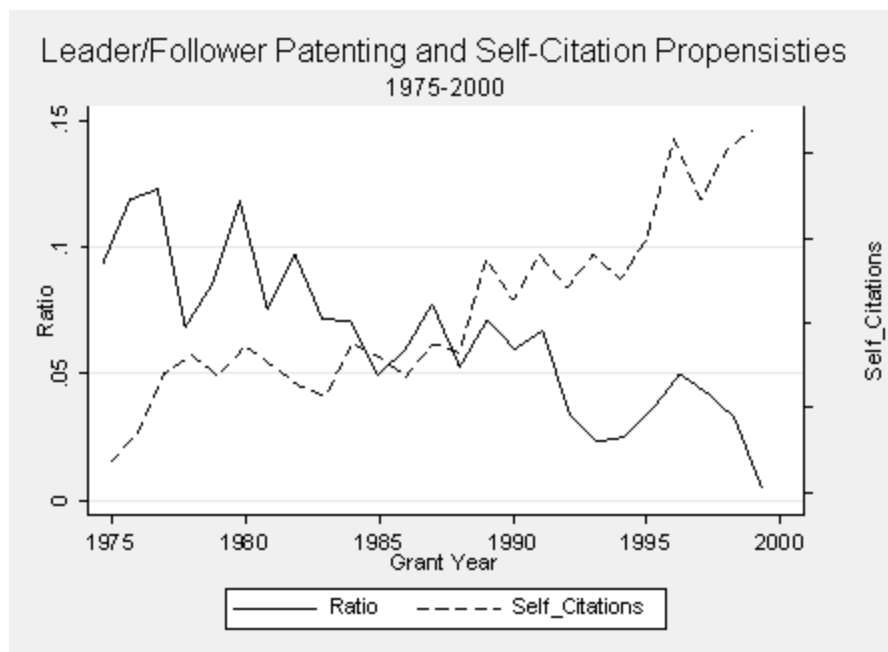
Finally, there are implications for patent policy, particularly the questioning of the optimal patent length as well as the optimal scope of protection offered by patents. Additional follow up research may also be considered. A first step will be to assess the impact of our proxies of innovation on the firms' financial performance. Secondly, an analysis of the relationship existing between entrant and incumbent firms is needed to fully understand the strategies that are currently emerging in the drug industry. To this end, mergers and acquisitions and other technological interactions between firms should also be analyzed.

Appendix

Table 1. SUMMARY STATISTICS

| Patenting Firms T3 (77 firms) | Obs. | Mean | Standard Dev. | Min. | Max. |
|-------------------------------|------|----------|---------------|------|----------|
| Sales | 1085 | 2786.416 | 5362.877 | 0 | 43992.59 |
| Market Share | 1085 | .5094704 | .9133403 | 0 | 4.717773 |
| R&D Expenditures | 1085 | 283.2219 | 546.97 | 0 | 4833.788 |
| Generality (mean) | 1085 | .1130722 | .1966503 | 0 | .9024943 |
| Originality (mean) | 1085 | .0950629 | .17544 | 0 | .8175583 |
| Citations received (nor.) | 1085 | 78.10945 | 216.2227 | 0 | 2098.684 |
| Patents | 1085 | 5.621198 | 14.67009 | 0 | 115 |
| Leader patents | 1085 | .4562212 | 1.493272 | 0 | 21 |
| Follower patents | 1085 | 5.164977 | 13.57932 | 0 | 108 |
| Citations Share | 1085 | .0069771 | .0186747 | 0 | .1871287 |
| Patent Stock | 1085 | 25.35753 | 68.66387 | 0 | 536.527 |
| Citations per Patent | 1085 | 6.116834 | 13.78752 | 0 | 135 |
| Citations stock/Patent | 1085 | 22.92756 | 52.56765 | 0 | 352.5332 |
| R&D Stock | 1085 | 1084.876 | 2269.905 | 0 | 15166.15 |
| Leader Patents Stock | 1085 | 2.623058 | 7.080935 | 0 | 56.64452 |
| Follower Patents Stock | 1085 | 22.73448 | 62.20354 | 0 | 485.4362 |

Figure 2



Source: Author's calculations from *NBER Patent Data File*

Table 2 : GMM-Wooldridge Estimation
 Patenting and Quality-Adjusted Patenting: Pharmaceutical Firms (1975-1991)

| | Non-Adjusted Patents | | | Citations-Adjusted Patents | | | Leaders Patents | | |
|-----------------------------------|-----------------------|-----------------------|-----------------------|----------------------------|------------------------|------------------------|-----------------------|-----------------------|------------------------|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| Lt-1 | | | | | | | | | |
| CAt-1 | | | | | 0.7710 (0.0039)*** | | | | -0.2396 (0.0566)*** |
| NAt-1 | | 0.3020 (0.0166)*** | | | | | | | |
| Log (SALES)t-1 | 0.2758 (0.0638)*** | 0.2885 (0.0670)*** | 0.2507 (0.0623)*** | -0.2335 (0.0164)*** | -0.2704 (0.0367)*** | -0.2192 (0.0215)*** | -0.3081 (0.1584)* | -0.1547 (0.1778) | -0.3456 (0.1549)** |
| Log (R&D)t-1 | 0.1846 (0.0550)*** | 0.2436 (0.0737)*** | 0.2146 (0.0405)*** | 0.3058 (0.0142)*** | 0.4814 (0.0386)*** | 0.3629 (0.0238)*** | 0.9776 (0.1477)*** | 0.7591 (0.1869)*** | 1.0400 (0.1814)*** |
| Market Share t-1 | 0.5459 (0.0298)*** | 0.5868 (0.1060)*** | 0.3713 (0.0522)*** | -0.2075 (0.0135)*** | -0.5262 (0.0333)*** | -0.2879 (0.0213)*** | -0.2428 (0.3115) | 0.1018 (0.3385) | -0.4529 (0.4604) |
| Citations Share t-1 | 9.2923 (0.6046)*** | -0.6743 (0.7069) | 6.8644 (0.6976)*** | 0.6351 (0.0626)*** | -2.5381 (0.5067)*** | -2.4173 (0.1667)*** | 47.0613 (27.5860) | 5.8227 (2.5178)** | 6.1456 (19.2542) |
| Innovation Originality t-1 | 1.6099 (0.0985)*** | 2.3675 (0.2047)*** | 1.5240 (0.0729)*** | 0.3372 (0.0106)*** | 0.1157 (0.0363)*** | 0.1583 (0.0278)*** | 3.5190 (1.3130)** | 3.3820 (0.7747)*** | 4.0000 (0.9435)*** |
| Self Citations t-1 | 0.4379 (0.0601)*** | -0.1387 (0.0715)** | 0.2014 (0.0636)*** | 0.1502 (0.0067)*** | 0.2594 (0.0509)*** | -0.4582 (0.0645)*** | 1.5176 (1.4166) | 0.7524 (0.4489)* | 1.1011 (1.1022) |
| GNA t-1 | | | 0.0053 (0.0005)*** | | | | | | |
| GCA t-1 | | | | | | 0.0067 (0.0001)*** | | | |
| GL t-1 | | | | | | | | | 0.1327 (0.0547)** |
| AR(1) | -2.2778** | -2.1355** | -2.3046** | -2.0369** | -2.7030** | -2.1770** | -1.2404 | -1.1770 | -1.2474 |
| AR(2) | 1.4769 | 1.3041 | 1.4097 | -1.0756 | -0.7864 | -1.6421 | 0.6215 | 0.2667 | 0.5661 |
| Sargan Overident. Test | 39.9866 | 35.1394 | 41.4776 | 44.6007 | 42.5118 | 43.0607 | 14.6936 | 12.1246 | 14.7414 |
| DOF | 41 | 38 | 41 | 41 | 38 | 41 | 14 | 13 | 14 |
| Instrumental Variables | 6 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 7 |
| Number of Observations | 854 | 854 | 854 | 854 | 854 | 854 | 854 | 854 | 854 |
| Number of Firms | 77 | 77 | 77 | 77 | 77 | 77 | 77 | 77 | 77 |

Robust Standard Errors in parentheses. GNA, GCA, GL are (patents) knowledge stocks.
 * significant at 10%; ** significant at 5%; *** significant at 1%

| IV (all) = | Log (SALES) t-2 ; Log (R&D) t-2 ; Citations Share t-2 ; Innovation Originality t-2 ; Self Citations t-2 and Time Dummies | | |
|------------------------|--|-------------------|--|
| | Capital Stock t-2 | Capital Stock t-1 | Capital Stock t-1 (No Sequential) |
| Sequential IV = | Log (SALES) t-2 | Log (R&D) t-2 | Log (SALES) t-2 ; Log (R&D) t-2 ; Citations Share t-2 ; Innovation Originality t-2 ; Self Citations t-2 and Time Dummies |
| IV = | NA t-3 | GNA t-2 | CA t-3 GCA t-2 L t-3 GL t-2 |

Estimation has been implemented using *ExpEnd* Gauss Code (Windmeijer, 2002).

Table 3 : GMM-Wooldridge Estimation
 Non adjusted Patenting (Persistence to Patent): Pharmaceutical Firms (1975-1991)

| | Non-Adjusted Patents (NA) | | | |
|----------------------------|---------------------------|------------------------|------------------------|-----------------------|
| | 1 | 2 | 3 | 4 |
| NA t-1 | 0.2194 (0.0073)*** | 0.2212 (0.0323)*** | 0.1580 (0.0234)*** | 0.2594 (0.0306)*** |
| NA t-2 | | 0.4256 (0.0391)*** | 0.0575 (0.0139)*** | 0.3308 (0.0417)*** |
| NA t-3 | | | 0.0381 (0.0162)** | 0.0027 (0.0211) |
| NA t-4 | | | | 0.2836 (0.0185)*** |
| Log (SALES) t-1 | 0.2019 (0.0647)** | 0.3135 (0.0641)*** | 0.2280 (0.0658)*** | 0.2746 (0.0951)** |
| Log (R&D) t-1 | 0.2628 (0.0574)*** | 0.2893 (0.0675)*** | 0.3419 (0.0675)*** | 0.2916 (0.1035)** |
| Market Share t-1 | 0.5930 (0.0557)*** | 0.3881 (0.1234)** | 0.5195 (0.0611)*** | 0.6838 (0.2022)*** |
| Citations Share t-1 | 3.0054 (0.2219)*** | 40.4953 (3.2367)*** | -1.3427 (0.7817)* | 8.0792 (3.2081)** |
| Innovation Originality t-1 | 2.0976 (0.0962)*** | 2.5207 (0.4321)*** | 2.8708 (0.2813)*** | 3.3847 (0.6392)*** |
| Self Citations t-1 | -0.0624 (0.0519) | 0.2202 (0.2202)*** | -0.3366 (0.0930)*** | -0.6691 (0.2783)** |
| AR(1) | -2.7849** | -2.2537** | -2.2924** | -1.8295* |
| AR(2) | 1.2923 | 0.2497 | 1.2109 | 0.9240 |
| Sargan Overident. Test | 43.6485 | 38.9202 | 31.5590 | 35.7278 |
| DOF | 42 | 39 | 36 | 33 |
| Instrumental Variables | 8 | 9 | 10 | 11 |
| Number of Observations | 854 | 777 | 700 | 627 |
| Number of Firms | 77 | 77 | 73 | 68 |

Robust Standard Errors in parentheses.

* significant at 10%; ** significant at 5%; *** significant at 1%

| | | | | |
|-----------------|---|--------------|------------------------|-------------------------------|
| IV (all) = | Log (SALES)t-2; Log (R&D)t-2 ; Citations Share t-2 ; Innovation Originality t-2 ; Self Citations t-2 ; Stock (Dep.Var.)t-1 and Time Dummies | | | |
| Sequential IV = | Capital Stock 1-2 | | | |
| IV = | NAt-2 | NAt-2; NAt-3 | NAt-2; NAt-3; NAt-4 | NAt-2; NAt-3; NAt-4; NAt-5 |

Estimation has been implemented using *ExpEnd* Gauss Code (Windmeijer, 2002).

Table 4 : GMM-Wooldridge Estimation
 Citations-Adjusted Patenting (Persistence to Innovate): Pharmaceutical Firms (1975-1991)

| | Citations-Adjusted Patents (CA) | | | |
|-----------------------------------|---------------------------------|------------------------|------------------------|------------------------|
| | 1 | 2 | 3 | 4 |
| CA t-1 | 0.8019 (0.0037)*** | 0.7674 (0.0035)*** | 0.8411 (0.0032)*** | 0.7867 (0.0039)*** |
| CA t-2 | | 0.0340 (0.0039)*** | 0.0551 (0.0069)*** | 0.0559 (0.0085)*** |
| CA t-3 | | | -0.0010 (0.0076) | -0.0018 (0.0075) |
| CA t-4 | | | | 0.0062 (0.0033)* |
| Log (SALES) t-1 | -0.2765 (0.0164)*** | -0.2470 (0.0346)*** | -0.2841 (0.0759)*** | -0.2431 (0.0833)** |
| Log (R&D) t-1 | 0.4746 (0.0232)*** | 0.4644 (0.0291)*** | 0.5565 (0.0690)*** | 0.5854 (0.0841)*** |
| Market Share t-1 | -0.4258 (0.0175)*** | -0.5545 (0.0327)*** | -0.6290 (0.0552)*** | -0.6595 (0.0615)*** |
| Citations Share t-1 | -6.3376 (0.2208)*** | -2.6953 (0.4687)*** | -6.0990 (0.4690)*** | -3.0237 (0.7494)*** |
| Innovation Originality t-1 | 0.0269 (0.0384) | 0.2239 (0.0468)*** | 0.1575 (0.1123) | 0.3415 (0.1056)** |
| Self Citations t-1 | 0.0815 (0.0583) | 0.2318 (0.0565)*** | 0.1957 (0.2039) | 0.4766 (0.2403)* |
| AR(1) | -2.8642** | -2.6623** | -2.6830** | -2.5109** |
| AR(2) | -0.7149 | -1.0598 | -1.2019 | -1.2582 |
| Sargan Overident. Test | 46.3420 | 42.3981 | 39.8911 | 34.0426 |
| DOF | 42 | 39 | 36 | 33 |
| Instrumental Variables | 8 | 9 | 10 | 11 |
| <i>Number of Observations</i> | 854 | 777 | 700 | 627 |
| <i>Number of Firms</i> | 77 | 77 | 73 | 68 |

Robust Standard Errors in parentheses.

* significant at 10%; ** significant at 5%; *** significant at 1%

| | | | | |
|------------------------|---|---------------------------------------|--|--|
| IV (all) = | Log (SALES)t-2; Log (R&D)t-2 ; Citations Share t-2 ; Innovation Originality t-2 ; Self Citations t-2 ; Stock (Dep.Var.)t-1 and Time Dummies | | | |
| Sequential IV = | Capital Stock 1-2 | | | |
| IV = | CA _{t-2} | CA _{t-2} ; CA _{t-3} | CA _{t-2} ; CA _{t-3} ; CA _{t-4} | CA _{t-2} ; CA _{t-3} ; CA _{t-4} ; CA _{t-5} |

Estimation has been implemented using *ExpEnd* Gauss Code (Windmeijer, 2002).

Table 5 : GMM-Wooldridge Estimation
Pioneer Patenting (Persistence to Open Tech.Path): Pharmaceutical Firms (1975-1991)

| | Leaders Patents (L) | | | |
|-----------------------------------|------------------------|------------------------|------------------------|------------------------|
| | 1 | 2 | 3 | 4 |
| Lt-1 | -0.3369 (0.0602)*** | -0.2749 (0.0533)*** | -0.4830 (0.0668)*** | -0.5379 (0.0692)*** |
| Lt-2 | | -0.1150 (0.0359)*** | -0.4145 (0.0215)*** | -0.3880 (0.0346)*** |
| Lt-3 | | | -0.3304 (0.0274)*** | -0.3476 (0.0272)*** |
| Lt-4 | | | | -0.0090 (0.0446) |
| Log (SALES)t-1 | -0.1311 (0.1174) | -0.2205 (0.1665) | -0.0252 (0.1246) | -0.1372 (0.1217) |
| Log (R&D)t-1 | 0.7589 (0.1108)*** | 1.0422 (0.1606)*** | 0.6110 (0.1141)*** | 0.8674 (0.1463)*** |
| Market Share t-1 | 0.7317 (0.4767) | -0.1040 (0.3140) | 0.5331 (0.3789) | 0.3549 (0.3198) |
| Citations Share t-1 | 1.5049 (1.6224) | -0.6474 (1.5049) | 1.8712 (2.0462) | 1.9788 (2.2969) |
| Innovation Originality t-1 | 2.9983 (0.6544)*** | 3.9153 (0.9106)*** | 1.3071 (0.2068)*** | 1.6606 (0.3225)*** |
| Self Citations t-1 | 2.2774 (0.0533)*** | 0.6719 (0.2354)** | 0.5079 (0.2496)** | 0.1711 (0.2396) |
| AR(1) | -0.9598 | -0.9847 | -1.3617 | -1.1248 |
| AR(2) | 0.3017 | 0.9289 | 1.1675 | 0.6704 |
| Sargan Overident. Test | 16.0015 | 16.8592 | 19.3368 | 17.4663 |
| DOF | 15 | 14 | 13 | 12 |
| Instrumental Variables | 8 | 9 | 10 | 11 |
| <i>Number of Observations</i> | 854 | 777 | 700 | 627 |
| <i>Number of Firms</i> | 77 | 77 | 73 | 68 |

Robust Standard Errors in parentheses.

* significant at 10%; ** significant at 5%; *** significant at 1%

| | | | | |
|-------------------|---|------------|---------------------|---------------------------|
| IV (all) = | Log (SALES)t-2; Log (R&D)t-2 ; Citations Share t-2 ; Innovation Originality t-2 ; Self Citations t-2 ; Stock (Dep.Var.)t-1 and Time Dummies | | | |
| IV = | Capital Stock t-1 | | | |
| IV = | Lt-2 | Lt-2; Lt-3 | Lt-2; Lt-3; Lt-4 | Lt-2; Lt-3; Lt-4; Lt-5 |

Estimation has been implemented using *ExpEnd* Gauss Code (Windmeijer, 2002).

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