

**Inertia in the Assessment of Technological Innovations:
An Examination of the FDA Approval of New Drugs**

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Prior studies examined firms' inertia favoring the exploitation of existing knowledge and hindering the exploration of novel knowledge. However, the effects of externally-driven inertia in the assessment of innovations by outside parties remain understudied. Even when a firm overcomes its own inertia and introduces an innovation based on novel knowledge, it still faces hurdles to demonstrate the merits of that innovation to relevant outside parties. I focus on endorsements of innovations by the scientific community as an important mechanism engendering inertia in the assessment of subsequent innovations. I show that, although scientific endorsements facilitate the assessment of a technological innovation, they hinder the assessment of a subsequent innovation that builds on a different type of knowledge, especially when the subsequent innovation pioneers novel knowledge. To examine inertia in the assessment of innovations I focus empirically on the FDA approval of new drugs. I constructed a unique dataset that identifies the mechanisms of action underlying new drugs. Because pharmacological mechanisms of action capture the key knowledge on which drugs build, this empirical context enables the investigation of how innovations building on some knowledge paradigms influence the assessment of a subsequent innovation based on different knowledge.

Prior research showed that firms' inertia towards the exploitation of existing knowledge helps explain why most innovations refine or recombine existing knowledge whereas innovations based on novel knowledge emerge only occasionally (Nelson and Winter, 1982; Van den Belt and Rip, 1987; Dosi, 1988; Anderson and Tushman, 1990). Firms create and revise routines to better exploit existing knowledge (Levitt and March, 1988; Cohen and Levinthal, 1990; March, 1991) and, as a result, experience inertia that inhibits the generation of innovations based on novel knowledge (Tushman and Anderson, 1986; Mitchell, 1989; Henderson and Clark, 1990). However, we know substantively less about externally-driven inertia in the assessment of technological innovations, which affects the success of innovations even when firms overcome internal inertial pressures. In this paper I examine the existence of inertia in the assessment of innovations by outside parties.

Technological innovations are an important source of competitive advantage (Rumelt, 1984; Barney, 1991; Nelson, 1991). Yet, in the process of creating innovations firms cannot ignore the constraints imposed by outside parties such as governmental agencies, regulatory structures or professional communities that play a key role in assessing innovations (e.g. Nelson and Winter, 1982; Van de Ven and Garud, 1989; Tushman and Rosenkopf, 1992). Technological innovations can result from the refinement or recombination of existing knowledge, or from the application of novel knowledge (Henderson and Clark, 1990; Fleming and Sorenson, 2001). Even when a firm overcomes its own inertia towards the exploitation of existing knowledge and introduces an innovation based on novel knowledge, it still needs to demonstrate the merits of that innovation to relevant outside parties (Anderson and Tushman, 1990; Garud and Rappa, 1994; Wade, 1995; Hargadon and Douglas, 2001).

The assessment of technological innovations is uncertain. Regulatory structures are established by legal mandate to mitigate the uncertainty inherent in the assessment of particularly complex innovations, thus preventing market failure due to quality uncertainty (Akerlof, 1970; Bodewitz, Buurma and De Vries, 1987; Noll, 1989). However, regulators face uncertainty in regard to how innovations fare along different performance dimensions and which performance dimensions are relevant to the assessment of innovations (Nelson and Winter, 1982; Anderson and Tushman, 1990; Wade, 1995; Martin and Mitchell, 1998). Prior research showed that third-party endorsements help outside parties mitigate the uncertainty they face when assessing the prospects of a new organization (Rao, 1994; Stuart, Hoang and Hybels, 1999; Higgins and Gulati, 2003). Based on the arguments that this literature developed I expect that endorsements of an innovation by the scientific community mitigate the uncertainty that regulators face when assessing that innovation. This study focuses on the influence of endorsements of innovations introduced previously on the assessment of a subsequent innovation based on different knowledge.

Building on Kuhn's (1996 [1962]) work on scientific paradigms and the related notion of technological paradigms (Nelson and Winter, 1982; Van den Belt and Rip, 1987; Dosi, 1988; Anderson and Tushman, 1990), I argue that endorsements by the scientific community of innovations building on certain types of knowledge hinder the assessment of a subsequent innovation based on different knowledge. Further, I argue that these inertial effects of prior endorsements pose a greater challenge to the assessment of a subsequent innovation that deviates from existing technological paradigms by pioneering novel knowledge than to the assessment of a subsequent innovation that builds on existing knowledge. Finally, I argue that scientific endorsements of an innovation constitute an important mechanism that the firm sponsoring that

innovation can use to partly overcome this externally-driven inertia, especially when the innovation pioneers novel knowledge.

By examining the influence of scientific endorsements on the regulatory assessment of innovations, this paper expands our knowledge of the inertial forces that help shape the ordered pattern observed in technological evolution (Nelson and Winter, 1982; Van den Belt and Rip, 1987; Dosi, 1988; Anderson and Tushman, 1990). Prior research emphasized the role of firm-level inertia: the procedures and routines that a firm establishes to better exploit existing knowledge hinder its ability to generate innovations based on novel knowledge (Tushman and Anderson, 1986; Mitchell, 1989; Cohen and Levinthal, 1990; Henderson and Clark, 1990). However, inertia also exists outside the confines of the firm and affects outside parties involved in the assessment of innovations. Hence, besides firm-level inertia relating to the types of innovations that firms generate, externally-driven inertia in the assessment of innovations by outside parties also affects technological evolution.

This paper also adds to our understanding of sociology of technology (Tushman and Nelson, 1990). Prior literature showed that firms establish linkages with the scientific community in order to access external knowledge that is relevant to technological innovations (e.g. Arora and Gambardella, 1990; Rosenberg, 1990; Powell, Koput and Smith-Doerr, 1996; Zucker, Darby and Armstrong, 2002). This paper draws attention to the fact that the influence of the scientific community on technological innovations is not only cognitive but also normative: the scientific community, besides being an important source of inputs to firms' research, is also an important referee in the assessment of the outputs of firms' innovative activities.

To examine the assessment of innovations by outside parties I focus empirically on the FDA approval of new drugs. I constructed a unique dataset that identifies the mechanisms of

action underlying pharmaceutical drugs to capture the knowledge on which they build. The generation of new drugs involves both the finding of new drugs based on existing mechanisms of action and the application of a new mechanism. Even when a pharmaceutical firm succeeds in finding a new drug to treat a medical condition, it still needs to obtain FDA (U.S. Food and Drug Administration) approval before commercializing the innovation. The approval of a new drug by the FDA is characterized by uncertainty about the drug's efficacy and safety. I examine the influence of scientific endorsements of drugs introduced previously on the FDA assessment of subsequent new drugs.

THE REGULATORY ASSESSMENT OF NEW DRUGS

Pharmaceutical firms invest on average more than 800 million dollars in the discovery and development of a new drug (DiMasi, Hansen and Grabowski, 2003), and experience high uncertainty when searching for a new drug that will achieve the desired therapeutic effect. The search for a new drug to treat a medical condition involves understanding the causes of the disease and synthesizing molecular entities that will act on mechanisms associated with these causes. Drug discovery in a therapeutic class is guided by mechanisms of action, which refer to the knowledge about pharmacology and human physiology that establishes the pathways through which drugs achieve the desired therapeutic effect (Reuben and Wittcoff, 1989). Pharmaceutical firms' effort to find a new drug can either target a new molecular entity that builds on an existing mechanism of action or aim at the application of a new mechanism. The use of a new mechanism potentially results in significant improvements in terms of safety or efficacy, the two key parameters that guide the assessment of new drugs. However, the validation of a new mechanism is characterized by high uncertainty and often takes a long time.

The search for a therapy to treat the Alzheimer's disease illustrates the importance of mechanisms of action in drug discovery. Dementia was primarily considered an amorphous mental disorder until the emergence of the cholinergic hypothesis proposing that the mental disorder was associated with decreased levels of the enzyme cholinesterase. The cholinergic hypothesis offered a road map for the development of drugs to treat the Alzheimer's disease: to find molecular entities that inhibit the destruction of cholinesterase. The first cholinesterase inhibitor, the drug named tacrine, was discovered in 1987. The approval of this pioneering drug by the FDA six years later "validated the cognitive tests that had recently been developed to gauge drug efficacy for the disease and provided clear guidelines on how to conduct clinical trials for AD" [Alzheimer's disease] (Travis, 2005: 732).

Following the discovery of a promising new drug, the sponsoring firm must conduct extensive clinical trials to detect any possible harmful effects, determine how the drug is metabolized, discover side effects, show interactions with other drugs, and define the appropriate dosage. Upon completion of clinical trials, the firm compiles all data and submits a New Drug Application (NDA) to the FDA. An NDA usually contains more than 100,000 pages (Macher and Boerner, 2006). Despite the voluminous documentation that the sponsoring firm submits to regulators, pre-approval clinical trials are insufficient to determine the full spectrum of the drug's effects. As a result, FDA officers face uncertainty when assessing a new drug and, instead of resolving that uncertainty, evaluate whether the expected benefits outweigh potential risks (CDER, 2005). Since the FDA makes decisions about new drugs under uncertainty, FDA officers need to take into account the reputational damage following the approval of unsafe drugs, which can result in greater political scrutiny and loss of the agency's autonomy (GAO, 1990, 2000; Carpenter, 2004a; Olson, 2004).

All new drugs need to receive FDA approval before introduction in the US market. However, there is considerable variation in FDA approval times across drugs (Carpenter and Fendrick, 2004). The time that regulators spend in the assessment of a new drug has a direct impact on the time elapsed before a novel therapy is available in the market and on the ability of the sponsoring firm to appropriate value from that innovation. The longer the time that the FDA spends to assess a new drug, the lower the profitability achieved by the sponsoring firm (DiMasi, 2002) and the shorter the period of effective patent protection (Grabowsky and Vernon, 1982). In the next section I discuss the influence of endorsements on the assessment of innovations and relate my arguments to the FDA assessment of new drugs.

THEORY DEVELOPMENT

The creation of regulatory agencies is an attempt to reduce the complexity involved in the evaluation of innovations: lacking the means to assess a complex innovation, customers can rely on the seal of approval conferred by regulatory agencies (Akerlof, 1970; Bodewitz, Buurma, DeVries, 1987; Noll, 1989). However, regulators also face uncertainty when assessing technological innovations. Different technological paradigms, each building on a different type of knowledge, usually coexist in a product category (Nelson and Winter, 1982; Dosi, 1988). Because one technology rarely dominates other technologies across all dimensions of merit, the assessment of technological innovations entails a tradeoff between different performance dimensions. As a result, the assessment of innovations involves uncertainty not only about how innovations fare along different performance dimensions but also about the very criteria that are relevant to the task (Anderson and Tushman, 1990; Wade, 1995; Martin and Mitchell, 1998).

Prior research showed that social references assuage the uncertainty inherent in the assessment of organizations and innovations. Even if an organization is convinced about its

prospects, it must lead relevant outside parties to the same conclusion (Thompson, 1967: 88). Outside parties resort to social references to mitigate the uncertainty involved in the assessment of an organization (Thompson, 1967; Meyer and Rowan, 1977; DiMaggio and Powell, 1983). Social references are also relevant to the assessment of innovations. People manage the uncertainty involved in the assessment of an innovation by drawing on a socially acceptable frame of reference (Burt, 1987).

Third-party endorsements by relevant institutional constituents represent an important social reference that mitigates the uncertainty inherent in the assessment of organizations. Endorsements of a service organization by licensing agencies increase the confidence of resource providers in the prospects of that organization (Baum and Oliver, 1991). Endorsements of a start-up company by prominent exchange partners mitigate the uncertainty faced by potential investors when assessing the value of that company (Stuart, Hoang and Hybels, 1999). Endorsements of a young firm by the scientific community help that firm establish its legitimacy (Zucker and Darby, 1997; Higgins and Gulati, 2003). These arguments suggest that endorsements of an innovation by the scientific community assuage the uncertainty that regulators face when assessing that innovation.

One of the distinctive features of the scientific community is the disclosure of discoveries in scientific journals (Zuckerman and Merton, 1971; Dasgupta and David, 1987). Firms publish in scientific journals to receive the “ticket of admission” to the scientific community, which enables them to access external scientific knowledge (Rosenberg, 1990; Henderson and Cockburn, 1994; Gittelman and Kogut, 2003). Publications in top scientific journals, besides ensuring the status of firms as members of the scientific community, constitute a form of endorsement. Top scientific journals maintain rigid criteria for publication and their

reputation is directly tied to the academic standard they maintain (Zuckerman and Merton, 1971; Merton, 1973). An article in a premier scientific journal “bears the imprimatur of scientific authenticity, as given to it by the editor and the referees whom he may have consulted” (Ziman, 1968: 111). Hence, top scientific journals function as a form of expert intermediaries that endorse the research portrayed in those publications (Zuckerman, 1999; Rindova et al., 2005).

The arguments above suggest that endorsements of an innovation by the scientific community increase regulators’ confidence in the quality of that drug. As a result, publications in top scientific journals about a new drug facilitate the regulatory assessment of that innovation, thus reducing the time that FDA officers require to review that drug before granting regulatory approval. However, although scientific endorsements of a drug facilitate the assessment of that drug by the FDA, they might also engender inertial forces that affect the assessment of a subsequent new drug.

Inertia Stemming from Prior Endorsements

Kuhn’s (1996 [1962]) work on philosophy of science highlighted the importance of scientific paradigms in the accumulation of scientific knowledge. In broad analogy with the Kuhnian perspective on scientific progress, the literature on technological innovations emphasized the role of technological paradigms in technical advance (Dosi, 1982; Nelson and Winter, 1982). A key defining element of a technological paradigm is the knowledge used to address the technical problems of the respective product category. Scientific paradigms guide scientists’ research in a given field and, likewise, technological paradigms guide innovators’ efforts to find new products. Technological evolution in a product category occurs through the accumulation of innovations building on the knowledge underlying existing paradigms and the occasional emergence of a new paradigm based on novel knowledge.

The consolidation of a technological paradigm in a product category shapes innovators' "beliefs about what is feasible or at least worth attempting" (Nelson and Winter, 1982: 258-59). Besides, a technological paradigm has an important exclusion effect in that it constrains "the technological imagination of engineers and of the organizations they are in", making them "blind" with respect to possibilities that lie outside that paradigm (Dosi, 1982: 153). At the same time that a technological paradigm enables firms to design routines and decision-making processes in order to better exploit the underlying knowledge, it also hinders firms' ability to generate innovations based on a different type of knowledge (Tushman and Anderson, 1986; Mitchell, 1989; Henderson and Clark, 1990). By favoring the exploitation of the underlying knowledge, a technological paradigm plays an important cognitive function that underlies the ordered pattern observed in technological evolution.

In addition to the cognitive function, a paradigm also has an important normative function. A scientific paradigm determines not only the direction in which scientists conduct research but also the assessment of scholarly contributions. When a new scientific paradigm emerges, "there are usually significant shifts in the criteria determining the legitimacy both of problems and of proposed solutions" (Kuhn, 1996 [1962]: 109). A new scientific paradigm, although it may lend itself to the prediction of some phenomena unexplained by the prevailing paradigm, usually fails to predict all the range of phenomena that the prevailing paradigm explains. The fact that different scientific paradigms usually explain different problems makes a direct comparison between them difficult, which hinders the assessment of a new paradigm. Whereas the cognitive function of a scientific paradigm ensures that research effort is focused on that paradigm, its normative function increases the hurdles for its replacement by a new paradigm.

Likewise, technological paradigms also have a normative effect on technological innovations. A technological paradigm seldom dominates other paradigms across all dimensions of merit and, as a result, technological specifications alone fail to explain whether relevant actors will assess an innovation favorably (Anderson and Tushman, 1990; Wade, 1995; Martin and Mitchell, 1998). The establishment of certain technological paradigms in a product category increases the uncertainty associated with the assessment of an innovation that is based on a different paradigm.

Endorsements of innovations by the scientific community reinforce the validity of the underlying knowledge. Repeated endorsements of innovations by the scientific community hinder the assessment of an innovation that builds on different knowledge. Endorsements of drugs by the scientific community increase the uncertainty that FDA officers face when assessing a subsequent new drug based on a different mechanism of action. FDA officers need more time to assess a new drug when the scientific community has repeatedly endorsed drugs based on other mechanisms of action. Thus:

Hypothesis 1a: *Prior publications in top scientific journals about drugs building on different mechanisms of action than the focal drug increase the time for the regulatory approval of that drug.*

I argue that the inertia stemming from prior endorsements has a greater impact on the assessment of a subsequent innovation that deviates from existing paradigms by pioneering novel knowledge than on the assessment of a subsequent innovation that builds on existing knowledge. Scientific endorsements of innovations building on existing knowledge constitute a greater hindrance to the assessment of an innovation based on novel knowledge for three reasons.

First, the more innovations based on existing knowledge are endorsed by the scientific community, the more they become cognitively available to regulators, which can interfere with their understanding of an innovation that pioneers novel knowledge. Endorsements of an

innovation by a professional community establish a cognitive basis for its legitimacy (DiMaggio and Powell, 1983). Professional communities, the scientific community most notably, play an important role in the theorization of novelty, by distilling the main properties and areas of application of innovations (Strang and Meyer, 1993). What regulators understand about innovations that exploit existing knowledge affects their expectations about the performance of an innovation that pioneers novel knowledge. Even if the pioneering innovation outperforms prior innovations, its assessment will require a longer time because it is likely to involve a revision of the very criteria that guide the assessment.

Second, the more innovations based on existing knowledge are endorsed by the scientific community, the more they become cognitively available to other relevant actors as well and, as a result, the more challenging it is for regulators to justify the approval of an innovation that pioneers novel knowledge. Because the decisions made by regulatory agencies are subject to public scrutiny (McCaffrey, 1982; Olson, 1999; Carpenter, 2004b), regulators need time not only to understand the innovation but also to articulate the reasons justifying their assessment. Decision makers are more likely to support an innovation that has a ready rationale they can use to explain the adequacy of that novelty to outside parties (Davis and Greve, 1997). The more prior innovations building on existing knowledge receive scientific endorsements, the more they become cognitively available to other institutional actors interested in regulatory decisions, such as the media and interest groups. When existing knowledge has become largely established as appropriate for the creation of innovations in a product category, explaining the decision to support an innovation based on novel knowledge is more challenging.

Third, the more innovations based on existing knowledge are endorsed the higher the potential reputational damage associated with the regulatory support of an innovation that

pioneers novel knowledge. Long periods of time elapse before the implications associated with the application of novel knowledge are fully understood (Merton, 1968). Hence, regulators face some risk that evidence available subsequent to the approval of the pioneering innovation reveals that such certification was not a good decision. Negative evidence about an innovation available *post* approval can tarnish the reputation of regulators and result in loss of autonomy (Olson, 1999; Carpenter, 2004a). The more the scientific community endorses innovations that build on existing knowledge, the greater the relative uncertainty inherent in the assessment of an innovation that pioneers novel knowledge. Although the application of novel knowledge may result in significant performance improvement in a certain dimension of merit, there is also a chance that deficiencies in other dimensions of merit might be discovered.

The introduction by Forest Laboratories of memantine, a drug for the treatment of moderate to severe cases of Alzheimer's disease provides an illustration of the influence of prior innovations on the assessment of an innovation that pioneers novel knowledge. Previous drugs used to treat Alzheimer's disease were cholinesterase inhibitors designed to offset the loss of the cholinergic function and slow the decline of memory. This mechanism of action requires that intact cholinergic neurons be present. Because fewer intact cholinergic neurons remain as Alzheimer's disease progresses, cholinesterase inhibitors become less effective. Hence, cholinesterase inhibitors targeted population with mild to moderate dementia. Memantine pioneered the use of a new mechanism of action that enabled the treatment of moderate to severe cases of the disorder. Although memantine represented a potential therapeutic improvement, the prevalence of cholinesterase inhibitors hindered its assessment by the FDA. All treatments previously approved by the FDA had to show improvement on patients' cognitive function but, because memantine targeted more severe occurrences of dementia, evaluation of the new drug in

that regard was more difficult. As a representative from the Division of Neuropharmacological Drug Product of the FDA observed in the opening remarks during the meeting of the Advisory Committee evaluating that drug:

“The sponsor has and, of course, in discussions with us, adopted a similar approach for the patients with moderate to severe disease, and so we want to first ask the committee whether or not you think that that's an appropriate way to proceed in this population, again a new population with which we have little experience from a regulatory point of view. Some have maintained that it's not important or it's inappropriate to measure cognitive function in these patients who are very severely impaired. (...) So we've never used them and never relied upon these particular measures of cognitive functioning or global functioning and we'd like to know whether or not the committee thinks that those are appropriate measures to use in this population” (FDA, 2003).

As the example above suggests, the prevalence of technological paradigms in a product category represents an obstacle to the assessment of an innovation that pioneers novel knowledge. Criteria that are relevant to innovations based on existing paradigms may not be applicable to the assessment of the pioneering innovation. Endorsements by the scientific community of innovations based on existing paradigms influence the regulatory assessment of a subsequent innovation pioneering novel knowledge because they hinder regulators' ability to understand that innovation, increase the importance of developing a rationale in support of the pioneering innovation, and enhance the reputational concerns associated with regulators' decision. The greater the level of endorsements received by drugs building on existing mechanisms of action, the more time FDA regulators need to assess a new drug that pioneers a new mechanism. Following the arguments developed above, I hypothesize that:

Hypothesis 1b: *The effect of prior publications in top scientific journals about drugs building on different mechanisms of action than the focal drug on the time for the regulatory approval of that drug is greater when that drug pioneers a new mechanism than when that drug builds on an existing mechanism.*

Overcoming Inertia Stemming from Prior Endorsements

Above I discussed that endorsements hinder the assessment of a subsequent innovation that builds on different knowledge. In this section I discuss that endorsements of the focal innovation mitigate the influence of prior endorsements.

Endorsements of an innovation by the scientific community increase the confidence of regulators in the quality of that innovation. Because a technological paradigm rarely dominates other paradigms across all dimensions of merit, the assessment of an innovation based on a different type of knowledge entails a tradeoff between different performance dimensions, which adds a layer of uncertainty to the assessment of that innovation (Nelson and Winter, 1982; Dosi, 1988). Besides reducing uncertainty about the focal innovation, endorsements also mitigate the effects of prior endorsements by helping regulators situate the focal innovation against the backdrop of prior innovations building on other types of knowledge.

Scientific endorsements of an innovation establish a cognitive basis for its legitimacy (DiMaggio and Powell, 1983; Strang and Meyer, 1993). The more certain types of innovations become cognitively available to regulators, the more time they need to understand a different type of innovation. However, endorsements of the focal innovation by the scientific community reduce the distance between what regulators know about that innovation and what they know about prior innovations building on other types of knowledge. Further, the support that an innovation elicits from relevant institutional actors is also contingent on the availability of a rationale in support of that innovation (Davis and Greve, 1997). Scientific endorsements of the focal innovation provide regulators with elements to articulate their support of that innovation and, hence, attenuate the effect of prior endorsements.

Finally, scientific endorsements of an innovation reduce the likelihood that evidence available subsequent to the regulatory approval of that innovation will indicate that regulators

did not make a good decision. Reputational damage following a bad decision is less severe when decision makers can share the blame for the mistake with other groups of decision makers (Scharfstein and Stein, 1990). Prior endorsements of innovations building on certain types of knowledge increase regulators' reputational concern when assessing an innovation based on a different type of knowledge but endorsements of the focal innovation diminish the potential reputational damage. Even if facts known after regulatory approval reveal deficiencies associated with the use of that different type of knowledge, the reputational costs that regulators will experience will be lower if another constituent, who is in a privileged position to assess the knowledge underlying innovations, also failed to anticipate those deficiencies. Hence:

Hypothesis 2a: *Publications in top scientific journals about a new drug contribute to decreasing the effect of prior publications about drugs building on other mechanisms of action on the time for the regulatory approval of that drug.*

Endorsements conferred by the scientific community to an innovation that pioneers novel knowledge are particularly important to mitigate the influence of the endorsements of prior innovations. Regulators' understanding of innovations based on existing technological paradigms and the availability of a rationale in support of previous innovations obfuscate the assessment of the pioneering innovation. The firm sponsoring that innovation can partly mitigate the effects stemming from prior endorsements by establishing the validity of that innovation and of the knowledge on which it builds. Because endorsements are particularly important in situations characterized by higher uncertainty, scientific endorsements of the focal innovation have a greater effect as a neutralizer of the influence of prior endorsements when the focal innovation pioneers novel knowledge.

The efforts of the firm sponsoring memantine, a drug for the treatment of moderate to severe dementia of the Alzheimer's type, to highlight the fact that the drug had been endorsed by a prestigious medical journal, illustrate the importance of scientific endorsements in overcoming

the inertial effects stemming from prior endorsements. As illustrated earlier, the dominance of cholinesterase inhibitors hindered the assessment of memantine by the FDA although this pioneering drug was potentially more efficacious than pre-existing drugs. During the meeting of the FDA's Advisory Board in September of 2003, the Executive Vice President of Forest Laboratories, the firm sponsoring memantine, drew the attention of the FDA's Advisory Committee to the fact that studies on the new drug had been published in the prestigious *New England Journal of Medicine* and to the greater salience of the new therapy following that publication:

“This is the study that was published by Dr. Reisberg, et al., in the *New England Journal of Medicine*. As an aside, I should state that since that study was published, we've been receiving over 1,000 calls per month in our Professional Affairs Office in St. Louis inquiring as to the availability of the drug” (FDA, 2003).

The arguments above lead to the following prediction:

Hypothesis 2b: *Publications in top scientific journals about a new drug contribute more to decreasing the effect of prior publications about drugs based on other mechanisms of action on the time for the regulatory approval of that drug when that drug pioneers a new mechanism.*

METHODS

To examine the effects of inertia on the assessment of technological innovations I collected data on new pharmaceutical drugs introduced between 1980 and 2004. I gathered primary data from a Freedom of Information Act request submitted to the FDA. The FDA provided the name of the sponsoring firm and the therapeutic use for all new drugs approved between 1980 and 2004, and the approval time for those approved between 1983 and 2004. My analysis focuses on new drug applications classified by the FDA as new molecular entities, which are *de facto* new drugs, while applications classified as incrementally modified drugs refine pre-existing drugs. In the empirical analysis I estimate the FDA approval time of new

drugs submitted to the FDA in 1983 or later, and approved by the end of 2004. I used the years prior to 1983 to compute lagged variables.

I made several attempts to control for drugs still under FDA review by the end of 2004 and for drugs that the FDA did not approve. I requested data on all new drug applications submitted between 1980 and 2004, including those still under review by the end of 2004 as well as those rejected. However, the FDA did not furnish data on these two categories of drugs and informed that the agency “does not release data on all NDAs submitted, as requested (...) but only on those submitted and approved” (FDA, 2004; emphasis in original). I ran additional analyses restricting the sample to only those drugs submitted for FDA review by 2002. With this procedure the number of right-censored observations not included in the sample reduces significantly because the average FDA approval time in the sample was 21 months. The findings I report in this paper are not sensitive to that change, increasing the confidence that the unavailability of data on drugs still under review by the end of 2004 does not affect the findings.

When the FDA does not approve a new drug, it issues a non-approval letter to the sponsoring firm. Firms have both legal and reputational incentives to disclose that news (Skinner, 1994). Following the procedure that prior studies adopted, I extensively searched the *Lexis-Nexis* database for news on the voluntary announcement of non-approval letters (Bosch and Lee, 1994; Sharma and Lacey, 2004). I was able to identify over eighty such events. However, among these cases there were only nine new molecular entities. The remaining cases referred to incremental modifications of existing drugs. This evidence suggests that the FDA eventually approves the vast majority of new molecular entities, which increases the confidence that the unavailability of detailed data on rejections does not bias the findings of this study.

To identify the mechanisms of action underlying pharmaceutical drugs I triangulated information provided by the pharmacological databases *Micromedex*, *Mosby's Drug Consult* and *Drug Facts and Comparisons*, and subjected my classification to external validation by an expert in pharmacology and medicinal chemistry. To identify the introduction of a new mechanism of action in a therapeutic class I gathered information on all drugs introduced in that class, even prior to the start of the study period, to avoid left-censoring observations. To ensure reliability in this extensive data collection, I limited my analysis to the eighteen therapeutic classes listed in Table 1. To my knowledge, no study has examined such a broad range of therapeutic classes in detail. Prior empirical studies relying on detailed information about pharmaceutical drugs focused on a single class, such as cholesterol-reducing drugs (e.g. Afuah, 2002) or antiulcerants (e.g. Berndt, Pindyck and Azoulay, 2003).

***** Insert table 1 about here *****

I used the *Web of Science* to gather data on the scientific publications about pharmaceutical drugs and on the scientific publications by authors affiliated with the respective sponsoring firm, totaling more than 1,200,000 academic references. I used the FDA's publication *Approved Drug Products with Therapeutic Equivalence Evaluations*, also known as the *Orange Book*, to collect data on the patents protecting the drugs. I obtained detailed information on these patents using the U.S. Patent and Trademark Office database. Finally, I used the *Securities Data Company's* database, as well as *Lexis-Nexis* and historic information displayed on the companies' website, whenever available, to gather information on the merger and acquisition activity of pharmaceutical firms and adjusted my measures accordingly.

Dependent variable

Time to Regulatory Approval. The dependent variable is the number of months elapsed between the submission of a new drug application and its approval by the FDA.

Independent variables

Top Publications on Drug (H2a, H2b). This variable refers to publications about a new drug in top scientific journals. I used the count of publications on a new drug until the year preceding the submission of the respective application for FDA approval. To measure this variable, I considered journals listed by the Institute for Scientific Information (ISI) under the category Medicine – General and Internal. This category comprises medical journals that are more likely to be salient both to FDA regulators and to other audiences interested in the approval of new drugs. I defined as top journals those with the highest impact factor, as published by the ISI. The results reported in the paper relate to measures considering journals with impact factor beyond the category mean plus two standard deviations. As I discuss later, models with alternative measures produced similar results. To test Hypothesis 2a I interacted this variable with the variable *Top Publications on Other Mechanisms*. To test Hypothesis 2b I split this interaction into two groups, one with drugs pioneering a new mechanism of action and another with drugs applying existing mechanisms.

Top Publications on Other Mechanisms (H1a, H1b, H2a, H2b). To measure the accumulated scientific endorsements of drugs building on other mechanisms of action, I used the count of publications in top journals about drugs building on each mechanism existing in a given therapeutic class. I considered all mechanisms in the therapeutic class other than the mechanism underlying the focal drug. I summed publications on each of the drugs based on the same mechanism, following the procedure described above for the variable *Top Publications on Drug*. The final measure is the average of that count across the mechanisms existing in the respective

therapeutic class. To test Hypothesis 1b, I split this measure into two groups, one with drugs introducing a new mechanism of action and another with drugs applying existing mechanisms. To test Hypotheses 2a and 2b I interacted this variable with the variable *Top Publications on Drug*.

Control variables

Empirical tests of the effects of endorsements present researchers with the challenge of accounting for unobserved heterogeneity across firms that correlate with both firms' ability to elicit endorsements and the outcome that endorsements are thought to influence. In my study I examine the effects of endorsements on the assessment of innovations and observe several innovations sponsored by the same firm. As I discuss later, I adopt a model specification that takes into account potential unobservable heterogeneity across firms. Moreover, my arguments relate to the effects of prior endorsements on the approval of a new drug introduced subsequently. Whereas it is possible that unobserved heterogeneity across drugs correlates with the amount of publications about these drugs in top scientific journals, it is unlikely that it correlates with the amount of scientific publications on drugs introduced previously, especially when those prior drugs were based on a different type of knowledge. Yet, I gathered data on various aspects of the drugs, the sponsoring firms and the respective therapeutic classes to address potential unobserved heterogeneity.

Drug Heterogeneity. To control for the possibility that drugs for the treatment of rare diseases are more likely to draw the attention of the scientific community and experience shorter approval times, I used the *Dummy Orphan Drug*, set to one when the new drug was designated as an orphan drug and to zero otherwise. To control for the likely effect of variation across drugs in the amount of publicly available knowledge I included the variable *Total Publications on Drug* with

the sum of all publications on a new drug in scientific journals listed by the *Web of Science* available in the year preceding the observation year.

Further, I used data on the patents protecting new drugs to control for heterogeneity across drugs in technological quality. Prior studies used patent information to construct indicators about the quality and importance of innovations (Griliches, 1990; Trajtenberg, 1990; Patel and Pavit, 1995; Podolny and Stuart, 1995; Ahuja, 2000). The variable *Development Time*, with the number of years elapsed between the grant of the patent protecting a new drug and the submission of the respective application for FDA approval, accounts for the time spent on the development of a potential new drug. In cases where several patents protected a new drug, I considered the earliest patent. The variable *Patent Forward Cites*, which contains the average number of cites received by the patents protecting a new drug until the year preceding the observation year, captures the likely effect of the perception of the technological value of a new drug. The variables *Patent Backward Cites*, containing the average number of cites to prior patents, and *Patent Number of Claims*, containing the average number of claims in those patents, capture the effects related to the scope of the knowledge on which the patents build and to the scope of the patents, respectively. Variables with the sum rather than the average across patents produced similar results.

To account for the possibility that the use of a new mechanism of action affects both firms' propensity to seek scientific endorsement and the time for the regulatory approval of a new drug, I added the *Dummy New Mechanism of Action*, set to one when the new drug was based on a new mechanism of action and to zero otherwise. Finally, the variable *Number of Drugs Building on Mechanism* accounts for the likely influence of the number of drugs already building on the same mechanism.

Firm Heterogeneity. I used a variety of firm-level controls to capture the effects of firms' scientific, technological and commercial quality. The variables *Firm's Total Publications* and *Firm's Publications in Top Journals* control for heterogeneity across firms in their ability to publish scientific papers and to elicit scientific endorsements. These variables contain the count of publications by authors affiliated with the sponsoring firm in all scientific journals and in top scientific journals, respectively. The number of patents possessed by a firm is a signal of its technological capabilities (Stuart, Hoang and Hybels, 1999). The variable *Firm's Patents*, which contains the number of patents in technological class 514 (drug, bio-affecting and body treating compositions) granted to the firm in the previous three years, accounts for heterogeneity across firms in their technological capabilities. An alternative measure considering patents in all technological classes produced similar results. The variable *Firm's Best-Selling Drugs*, which contains the yearly average of new drugs sponsored by a firm that were listed as one of the Top 200 Best-Selling Drugs in the previous three years, controls for variation across firms in the ability to create commercially successful drugs. The variable *Firm's FDA-Approved Drugs*, with the count of new drugs introduced by the sponsoring firm that the FDA approved in the previous three years, captures firms' ability to create new drugs that receive FDA approval.

Therapeutic Class Heterogeneity. The variables *Total Publications Therapeutic Class* and *Total Publications Mechanism of Action*, which contain, respectively, the number of scientific publications on all drugs targeting a therapeutic class and on all drugs building on the underlying mechanism of action, control for the likely effect of total information available. The variable *Top Publications Mechanism of Action* accounts for the likely effect of prior endorsements of drugs building on the same mechanism of action. The variable *Number of Mechanisms of Action*

controls for the influence of the number of mechanisms in a therapeutic class. Finally, dummies for therapeutic classes capture effects specific to drugs addressing the same medical condition.

I avoided double-counting when computing measures based on publication counts. For example, I subtracted the count of publications on the focal drug when counting the publications on the respective mechanism of action and subtracted the number of publications on the focal mechanism of action when counting the publications on the therapeutic class.

To control for the effect of the passage of the Prescription Drug User Fee Act, which intended to expedite the FDA review process, I added a dummy variable set to one if the new drug application was submitted after 1992, when the act was passed, and to zero otherwise. Finally, year dummies based on the year of submission of the application capture effects specific to drugs submitted in the same year.

Table 2 reports descriptive statistics and the correlation matrix for the variables.

***** Insert table 2 about here *****

Model estimation and econometric issues

I used the accelerated event-time method to analyze the effects of scientific endorsements on the time for the regulatory approval of new drugs. This method assumes that event times follow a parametric baseline distribution that would hold if all independent variables were zero and then estimates effects of covariates as exponentially multiplicative accelerations or decelerations of the baseline distribution (Wooldridge, 2002). I used the Weibull parameterization, which prior studies used to estimate FDA approval times (Dranove and Meltzer, 1994; Carpenter, 2004b). Prior studies used a similar method to examine the timing of firms' entry into emerging technological areas (Mitchell, 1989) and the duration of

interorganizational alliances (Dussauge, Garrette and Mitchell, 2000). In this specification, event times are modeled as follows:

$$\ln(t_i) = \beta X_i + z_i ,$$

where t_i represents the event-time of observation i , X_i is a vector of covariates associated with observation i , β is a vector of coefficients and z_i is the corresponding error term scaled by a variance-related factor.

I ran models using shared frailty which captures the effect of any potential heterogeneity between drugs sponsored by different firms by adding a group (firm) effect that follows the Gamma distribution with a mean of one and variance θ (Hougaard, 1986).

RESULTS

Table 3 presents the results of the accelerated event-time regressions. I ran models on all 217 new drugs protected by patents that were submitted for FDA approval in 1983 or later and approved by the end of 2004, and that were intended for use in the therapeutic classes listed in Table 1.

***** Insert table 3 about here *****

Consistent with prior analyses of FDA approval times (Dranove and Meltzer, 1994), the results reveal that hazard rates of FDA approval increase monotonically with time elapsed since the submission of the new drug application. The estimate of the shape parameter of the Weibull distribution is significantly greater than one (p-level < 0.001) in all models. The results also show that the specification captures significant variation across firms. The estimate of the frailty parameter θ , which measures the variability of the frailty across firms, is statistically greater than zero (p-level < 0.001).

Model 1 of Table 3 contains control variables, while model 2 introduces *Top Publications on Drug*. Consistent with prior research on endorsements, the results reveal that the endorsements substantiated in publications about a new drug in top scientific journals contribute to reducing the time for the FDA approval of that drug. The coefficient on this variable is negative and significant (p-level < 0.01).

Model 3 tests whether scientific endorsements influence the FDA assessment of new drugs introduced subsequently. The findings show that prior endorsements of drugs building on other mechanisms of action hinder that assessment. The coefficient on the variable *Top Publications on Other Mechanisms* is positive and significant (p-level < 0.001). FDA officers need more time to review a new drug when the scientific community has repeatedly endorsed drugs building on mechanisms of action different than the mechanism underlying that drug. Hypothesis 1a is supported.

Model 4 examines whether prior endorsements have a greater effect on the FDA assessment of a subsequent new drug that pioneers a new mechanism of action than on the FDA assessment of a subsequent new drug that applies a mechanism that already existed in the respective therapeutic class. As predicted, prior endorsements of drugs building on other mechanisms are a greater hindrance to the assessment of a drug that pioneers a new mechanism. The coefficient on *Top Publications on Other Mechanisms* is negative and significant (p-level < 0.001) in both cases. However, the coefficient is greater for drugs pioneering a new mechanism than for drugs applying existing mechanisms (p-level < 0.02). Hypothesis 1b is supported.

Model 5 checks whether endorsements of the focal drug partly offset the effects that prior endorsements have on the assessment of that drug by the FDA. The results reveal that, although prior endorsements of drugs applying other mechanisms hinder the assessment of the focal drug

and retard its FDA approval, endorsements of the focal drug by the scientific community mitigate that effect. The coefficient on the interaction between the amount of top publications on prior drugs building on other mechanisms with the amount of top publications on the focal drug is negative and significant (p-level < 0.001). The coefficient on the amount of top publications on drugs building on other mechanisms remains positive and significant (p-level < 0.001). The coefficient on *Top Publications on Drug* remains negative but becomes only marginally significant (p-level < 0.10). This suggests that the influence of endorsements of a new drug on its assessment by the FDA occurs primarily as a counterpoint to prior endorsements of drugs applying other mechanisms. Hypothesis 2a is supported.

Model 6 analyzes whether endorsements of the focal drug diminish the effect of prior endorsements more when that drug pioneers a new mechanism of action. The findings exhibit a pattern that is consistent with the prediction. Whereas endorsements of the focal drug contribute to mitigating the influence of prior endorsements of drugs applying other mechanisms, this effect is more pronounced when the focal drug pioneers a new mechanism. The coefficient on the interaction between the amount of top publications on prior drugs building on other mechanisms and the amount of top publications on the focal drug is negative and significant both when the focal drug applies an existing mechanism and when it pioneers a new mechanism. However, the difference in the coefficient across the two groups is significant (p-level < 0.01), showing that top publications on the focal drug contribute more towards diminishing the effects of prior endorsements when that drug pioneers a new mechanism. Hypothesis 2b is supported.

Several control variables were significant in the full model (model 6). The use of a new mechanism of action can result in significant improvements in drug efficacy and safety, and FDA officers have an interest in accelerating the market availability of potentially superior

drugs, but prior endorsements of drugs building on existing mechanisms obfuscate the assessment of a drug pioneering a new mechanism. The findings in models 1-3 show that a new drug building on a new mechanism of action does not experience faster regulatory approval, despite the potential superiority of that drug. However, as the results in models 4-6 show, that drug experiences faster approval once the analysis incorporates the influence of prior endorsements of existing mechanisms. This further supports the argument that one of the main obstacles to the assessment of an innovation pioneering novel knowledge is the consolidation of existing knowledge as appropriate to create new products in the respective category.

A new drug sponsored by a firm with a greater record of scientific publications experiences faster FDA approval. Firms that participate more actively in the scientific community gain access to relevant external knowledge which is likely to translate into better drugs that, in turn, experience faster approval. On the other hand, a new drug sponsored by a firm with a stronger record of commercial success experiences longer FDA approval time, which suggests that the firm's prior demonstrations of commercial quality encourage regulators to subject the innovation to deeper scrutiny. The availability of information on a therapeutic class reduces FDA approval times. The results also reveal that the availability of information on a mechanism of action contributes to extending approval times, probably because it results in regulators' deeper understanding of the limitations associated with that mechanism.

Sensitivity tests

To make sure that the results reported in Table 3 showing the effect of scientific endorsements on regulatory approval are not restricted to the therapeutic classes studied, I ran additional models considering the 544 new drugs submitted for FDA approval in 1983 or later.

This additional analysis confirmed the effects of endorsements of the focal drug as a facilitator of the FDA review of that drug.

The FDA assigns priority review status to new drugs that represent a greater therapeutic advance. I ran models controlling for the review status of drugs to capture the likely influence of FDA's perception of the therapeutic quality of new drugs. Because scientific endorsements of a new drug are likely to affect regulators' perception of therapeutic quality, the addition of the information on priority review status makes the test of the impact of scientific endorsements overly conservative. Sensitivity analyses showed the same pattern of results.

The variables measuring scientific endorsements considered all publications available in the year preceding the observation year. Additional models measuring scientific endorsements based on papers published in the previous five years produced similar results. Further, the use of an alternative criterion for the definition of top journals, considering journals with impact factor above the mean and one standard deviation, led to comparable results.

The specification of an inverse Gaussian instead of a Gamma distribution to model the frailty did not affect the findings. Finally, although the results reported in Table 3 suggest that the hazard of FDA approval increases monotonically during the course of regulatory review (a characteristic of the data that the Weibull specification takes into account), the findings are robust to alternative distributions. I obtained similar results when using a log-normal specification (Carpenter, 2004b). The results are also robust to the use of the Gamma distribution, which makes additional assumptions about event times, and to the use of the Cox specification, which makes fewer assumptions about the functional form of hazard rates.

DISCUSSION AND CONCLUSION

This paper sought to examine the existence of inertia in the assessment of technological innovations by outside parties. Innovations in a technological area follow an ordered pattern: most of the time innovations refine or recombine existing knowledge and occasionally an innovation discontinues that trend by introducing novel knowledge (Nelson and Winter, 1982; Van den Belt and Rip, 1987; Dosi, 1988; Anderson and Tushman, 1990). Prior research showed that one important reason underlying that regularity is firms' inertia favoring the exploitation of existing knowledge and hindering the exploration of novel knowledge (Tushman and Anderson, 1986; Mitchell, 1989; Henderson and Clark, 1990). More recently, scholars have investigated factors that affect the balance between exploitation and exploration by aggravating or attenuating firms' internal inertial pressures (Benner and Tushman, 2002; He and Wong, 2004; Jansen, Van Den Bosch and Volberda, 2006). While highlighting the importance of firm-level inertia, prior literature overlooked the influence of externally-driven inertia on technological innovations. Firms' success in innovation presupposes the ability to convince relevant outside parties about the merits of the innovations they introduce. Hence, a firm that overcomes its own inertia towards the exploitation of existing knowledge and generates an innovation based on novel knowledge still needs to demonstrate the merits of that innovation to outside parties. I focused empirically on the review of new drugs by the FDA to investigate how the types of innovations introduced previously affect the assessment of a subsequent innovation.

Although regulatory structures are established by legal mandate to mitigate the uncertainty involved in the assessment of particularly complex innovations, such as new drugs, regulators also face uncertainty when evaluating innovations. Consistent with the argument that outside parties resort to social references to assuage the uncertainty they face when evaluating

the prospects of a new organization, this study shows that endorsements of an innovation by the scientific community facilitate its assessment by outside parties. Publications about a new drug in top medical journals contribute to accelerating the FDA approval of that drug. This paper focused on the effects of endorsements of prior innovations on the assessment of innovations introduced subsequently.

The findings of this study reveal that endorsements of specific innovations by the scientific community increase the hurdles for the assessment of a subsequent innovation that is based on a different type of knowledge. Prior publications in top scientific journals about drugs building on certain mechanisms of action result in extended times for the FDA approval of a new drug based on a different mechanism. Hence, scientific endorsements have not only a direct effect on the assessment of the innovation receiving those endorsements, as the arguments developed in prior research on third-party endorsements suggest, but also a long-lasting influence on the assessment of other innovations introduced subsequently, as this study shows.

Because outside parties experience greater uncertainty when assessing an innovation based on novel knowledge, the assessment of that innovation is most affected by the inertial effects of prior endorsements. The impact of prior publications in top scientific journals on the time for the FDA approval of a new drug is greater when that drug applies a new mechanism of action. The results show that endorsements are an important mechanism to which the firm sponsoring an innovation can resort to diminish the inertial effects stemming from the endorsements of prior innovations. Publications about a new drug in top scientific journals mitigate the effects of top publications about prior drugs building on other mechanisms, especially when the new drug pioneers a new mechanism.

Two issues regarding the interpretation of these findings are worth mentioning. The first issue refers to unobserved heterogeneity across the recipients of endorsements that happen to correlate with both firms' ability to elicit endorsements and the outcome that endorsements are thought to influence, which presents a challenge to the inference of causality (Stuart, Hoang and Hybels, 1999). I engaged in extensive data collection in order to control for heterogeneity across drugs, sponsoring firms and therapeutic classes in the empirical analysis. Moreover, this investigation is about the effects of the endorsements of prior innovations on the assessment of an innovation introduced subsequently. Although one can never rule out the possibility that residual unobserved heterogeneity across drugs correlates with the ability of the sponsoring firms to elicit endorsements, it is difficult to construct a cogent explanation of how that unobserved heterogeneity correlates with the endorsements of drugs introduced previously.

The second issue relates to alternative explanations for the influence of scientific publications on the assessment of innovations. Perhaps the most compelling alternative explanation is that publications in premier scientific journals influence the assessment of an innovation by increasing the amount of information available to outside parties assessing that innovation. As discussed earlier, publications in top scientific journals, besides disseminating scientific discoveries, lend an aura of scientific legitimacy to the research portrayed in those publications (Ziman, 1968; Zuckerman and Merton, 1971; Merton, 1973; Rindova et al., 2005). Moreover, the analysis controls for the influence of the mere availability of information with variables that contain the total count of publications in all scientific journals, regardless of their level of academic prestige. The inertial effects that this paper shows emanate from publication in top scientific journals and not from all publications available. Actually, the mere availability of information in a product category seems to facilitate the assessment of a subsequent innovation

in that category, perhaps by increasing regulators' knowledge of the technical problems that innovations in that category are expected to address. However, consistent with the theory that this paper develops, publications in top scientific journals hinder the assessment of a subsequent innovation building on different knowledge. This strengthens the evidence that the effects of publications in top scientific journals on the assessment of innovations are not merely informational.

By investigating the influence of inertia in the assessment of technological innovations, this study expands our understanding of technological evolution. The creation of technological innovations is usually considered from an evolutionary perspective of variation, selection and retention (Nelson and Winter, 1982; Anderson and Tushman, 1990). Prior studies showed that the embedding of innovations in organizational routines engenders firm-level inertia that contributes to the retention of certain technological paradigms and increases the rates of variation within that paradigm, while inhibiting the emergence of innovations based on novel knowledge. This study shows that inertia also exists in the selection environment. Outside parties such as governmental agencies, regulatory structures and professional communities play a key role in assessing innovations (e.g. Garud and Rappa, 1994; Wade, 1995; Hargadon and Douglas, 2001). The embedding of innovations in the wider institutional context creates externally-driven inertia that hinders the assessment of innovations based on knowledge different than the knowledge underlying innovations introduced previously.

Firms engaged in technological innovation, anticipating the hurdles that an innovation based on novel knowledge faces in the assessment by outside parties, may prioritize the exploitation of existing knowledge. Hence, the inertial effects in the selection environment reinforce firms' incentives to exploit existing knowledge. But when a firm creates an innovation

based on novel knowledge, it has stronger incentives to elicit the endorsement of that innovation by the scientific community in order to overcome the inertial effects emanating from the endorsements of prior innovations. Scientific endorsements of the innovation pioneering novel knowledge, while facilitating its assessment by outside parties, can also mitigate the uncertainty that rival firms experience when evaluating the prospects of the emerging technology. When a firm draws on novel knowledge it has potentially greater chances to appropriate more value from that discovery, given the greater difficulty of competitors to assimilate novel knowledge. However, it is precisely in this case that the sponsoring firm has greater incentives to elicit endorsements to facilitate the assessment of that innovation by outside parties, which may eventually enhance the salience of the novel knowledge to rival firms.

Endorsements of an innovation by a relevant institutional constituent, besides mitigating the uncertainty faced by outside parties assessing that innovation, can also mitigate the uncertainty faced by rival firms and attract competition for the exploitation of the emerging technological opportunity. Although prior studies emphasized the benefits of third-party endorsements, we know substantively less about the impact of endorsements on subsequent competition between firms. Endorsements of a start-up company by prominent investment banks can attract competition for the exploitation of the business opportunity underlying the new venture. Likewise, endorsements of an innovation by the scientific community can attract competition for the exploitation of the knowledge underlying that innovation. Future studies can examine the extent to which endorsements attract competition for the opportunity underlying the new venture or the innovation that receives endorsement.

Prior studies made an important contribution by showing the importance of third-party endorsements in promoting order in the market for new technologies. The market for new

technologies could fail if outside parties were unable to overcome the uncertainty inherent in the assessment of start-up companies dedicated to the discovery of new technologies. Endorsements of a new biotechnology firm by prominent exchange partners enable potential investors and other resource providers to mitigate uncertainty about the prospects of that firm and, as a result, facilitate the functioning of markets for new technologies (Stuart, Hoang and Hybels, 1999; Higgins and Gulati, 2003; Hsu, 2004). This study adds to that literature by uncovering the effects of endorsements on the assessment of technological innovations. Endorsements of an innovation by a relevant institutional constituent have both an immediate effect on the assessment of that innovation by another important outside party and a long-lasting influence on the assessment of subsequent innovations. At the same time that endorsements facilitate the assessment of the focal innovation, they hinder the assessment of subsequent innovations building on a different type of knowledge. Future research can examine the consequences of endorsements that new organizations receive on the types of organizations founded subsequently and on the assessment of these companies by outside parties. For instance, endorsements of start-up firms displaying certain characteristics can hinder the subsequent market evaluation of start-up firms exhibiting different attributes and, as a result, encourage the founding of subsequent companies with similar characteristics.

This paper contributes to expanding our knowledge of sociology of technology (Tushman and Nelson, 1990) by examining the influence of scientific endorsements on the regulatory approval of new products. Prior research showed the influence of the scientific community on technological innovations as an important source of knowledge on which private firms draw to create innovations (e.g. Arora and Gambardella, 1990; Rosenberg, 1990; Powell, Koput and Smith-Doerr, 1996). This study shows that the scientific community, besides having a cognitive

function as provider of knowledge that can be critical to firms' ability to generate innovations, also has an important normative function in the assessment of the technological innovations that firms generate. By showing the effects of scientific publications on the introduction of innovations building on different types of knowledge, this paper highlights the influence of the scientific community on competition between technological paradigms.

This paper focused on the assessment of specific technological innovations by outside parties but inertia may also affect the market evaluation of firms' innovation strategies. The prevalence of certain technological paradigms in a product category, besides affecting the assessment of a specific innovation based on novel knowledge, is likely to also influence how financial markets value the strategies of firms that focus on exploration of novel knowledge. Endorsements of innovations by professional communities, prominent exchange partners and regulatory structures help reinforce the dominance of the technological paradigms on which those innovations build, which, in turn, is likely to make capital markets to respond less favorably to the strategy of a firm whose innovative efforts focus primarily on a new paradigm. Future research in this direction can expand our understanding of how environmental conditions reinforce firms' internal pressures to exploit existing knowledge. Moreover, in complement to recent work on firms' attempt to overcome internal inertial pressures when creating technological innovations (Benner and Tushman, 2002; Jansen, Van Den Bosch and Volberda, 2006), future work can elucidate the extent to which firms can behave strategically to overcome external inertial pressures that affect the assessment of the innovations they generate.

As discussed earlier, inertia in the assessment of innovations contributes to reinforcing the regularity observed in technological evolution. Prior literature showed that organizational evolution shows a similar pattern, with long periods of stability in which organizations

implement small-scale changes punctuated by occasional bursts of fundamental change (Romanelli and Tushman, 1994). An avenue for future research is to investigate the extent to which externally-driven inertia affects organizational evolution. Organizations face structural inertia when undertaking organizational change, especially when those changes occur in core organizational features (e.g. Hannan and Freeman, 1984; Singh, House and Tucker, 1986; Amburgey, Kelly and Barnett, 1993). This internal inertia hinders organizations' ability to undertake adaptive change that is expected to increase their fitness with the environment (Levinthal, 1991). But, besides structural inertia affecting organizations' ability to effectively implement change, inertia in the selection environment can also affect organizations' propensity to undertake organizational change. Even when an organization successfully implements a change that potentially increases its efficiency, it might not enjoy enhanced survival prospects if outside parties that play a key role in determining organizational fit fail to perceive the benefits of that change. Future studies can refine our understanding of inertia in selection environments by examining, for instance, how endorsements of prior organizational changes influence the response of relevant resource providers to the implementation of subsequent changes by other organizations in the same population.

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Table 1**List of Therapeutic Classes Included in the Study**

Alzheimer's Disease
Ansiolitics
Antiarrhythmic Agents
Antiarthritis Drugs
Anticoagulants
Antidepressants
Antidiabetic Agents
Antiemetics
Antifungals
Antihypertensives
Antimalarials
Antineoplastics
Antiretrovirals
Antiulcerants
Cholesterol-reducing Drugs
Bronchodilators
ED
Glaucoma

Table 2

Descriptive Statistics and Correlation Matrix

Variable	Mean	S.D.	Min	Max	1	2	3	4	5	6	7
1. Time to Approval	20.79	14.96	1	71							
2. Top Publications on Drug	1.42	8.00	0	105	-0.07						
3. Top Publications on Other Mechanisms	41.97	54.86	0	333	-0.23	-0.09					
4. Top Publications on Other Mechanisms_Drug Based on New Mechanism	8.36	32.07	0	333	-0.20	0.00	0.42				
5. Top Publications on Other Mechanisms_Drug Based on Existing Mechanism	33.61	50.46	0	292	-0.12	-0.09	0.82	-0.17			
6. Top Publications on Drug * Top Publications on Other Mechanisms	1.69	19.72	0	285	-0.09	0.19	0.11	-0.02	0.13		
7. Top Publications on Drug * Top Publications on Other Mechanisms_Drug Based on New Mechanism	0.01	0.05	0	1	-0.05	0.00	-0.05	-0.02	-0.05	0.00	
8. Top Publications on Drug * Top Publications on Other Mechanisms_Drug Based on Existing Mechanism	1.68	19.72	0	285	-0.09	0.19	0.11	-0.02	0.13	1.00	-0.01
9. Dummy Orphan Drug	0.10	0.30	0	1	-0.10	0.01	-0.13	-0.03	-0.13	-0.03	-0.02
10. Total Publications on Drug	1.31	9.13	0	134	-0.05	0.46	-0.01	0.07	-0.06	0.01	-0.01
11. Development Time	7.82	3.60	0	19	0.09	-0.03	-0.11	-0.03	-0.11	-0.15	-0.02
12. Patent Forward Cites	9.16	9.27	0	52	-0.03	-0.08	-0.04	0.06	-0.08	-0.07	0.08
13. Patent Backward Cites	5.71	6.75	0	46	-0.14	-0.11	0.13	0.03	0.13	-0.02	-0.03
14. Patent Number of Claims	16.76	13.51	1	91	-0.13	-0.02	0.07	0.02	0.06	-0.02	-0.08
15. Dummy New Mechanism	0.19	0.39	0	1	-0.12	0.05	0.02	0.54	-0.32	-0.04	0.14
16. Number of Drugs Building on Mechanism	5.60	4.75	1	23	0.09	-0.03	0.00	-0.25	0.16	-0.05	-0.07
17. Firm's Total Publications (in hundreds)	8.74	9.72	0	41	-0.27	-0.08	0.26	0.24	0.13	0.04	0.07
18. Firm's Publications in Top Journals	7.56	10.77	0	61	-0.14	-0.04	0.15	0.18	0.05	0.12	0.14
19. Firm's Patents	75.87	102.53	0	506	-0.20	-0.05	0.13	0.15	0.04	0.00	0.09
20. Firm's Best-Selling Drugs	4.60	4.28	0	18	0.14	0.11	-0.02	-0.04	0.00	0.05	0.16
21. Firm's FDA-Approved Drugs	1.67	1.84	0	9	-0.06	0.03	0.05	0.06	0.02	0.06	0.20
22. Total Publications Therapeutic Class (in hundreds)	127.23	169.45	0	805	-0.22	-0.08	0.51	0.10	0.49	-0.05	-0.05
23. Total Publication Mechanism of Action (in hundreds)	20.69	32.55	0	208	0.02	-0.08	0.14	-0.17	0.26	-0.05	-0.04
24. Top Publications Mechanism of Action	0.54	1.27	0	9	-0.18	-0.06	0.05	-0.11	0.13	-0.01	-0.03
25. Number of Mechanisms of Action	6.27	3.49	0	16	-0.16	0.09	-0.07	-0.08	-0.03	-0.07	-0.04
26. Dummy User Fee Act	0.56	0.50	0	1	-0.53	-0.17	0.31	0.18	0.22	0.04	-0.08
Variable	8	9	10	11	12	13	14	15	16	17	18
9. Dummy Orphan Drug	-0.03										
10. Total Publications on Drug	0.01	-0.03									
11. Development Time	-0.15	0.07	-0.07								
12. Patent Forward Cites	-0.07	-0.08	-0.06	0.22							
13. Patent Backward Cites	-0.02	-0.11	-0.08	-0.16	-0.01						
14. Patent Number of Claims	-0.02	-0.04	-0.04	-0.14	0.25	0.19					
15. Dummy New Mechanism	-0.04	0.12	0.15	-0.04	0.10	-0.04	0.09				
16. Number of Drugs Building on Mechanism	-0.05	0.08	-0.06	0.25	-0.13	0.06	-0.19	-0.47			
17. Firm's Total Publications (in hundreds)	0.04	-0.07	-0.08	-0.19	0.10	0.02	0.04	0.11	-0.14		
18. Firm's Publications in Top Journals	0.12	-0.11	-0.06	-0.11	0.17	0.04	-0.01	0.10	-0.15	0.79	
19. Firm's Patents	0.00	-0.07	-0.06	-0.15	0.14	0.09	0.07	0.14	-0.18	0.76	0.74
20. Firm's Best-Selling Drugs	0.05	-0.01	-0.05	-0.05	0.14	-0.17	-0.02	0.05	-0.07	0.39	0.45
21. Firm's FDA-Approved Drugs	0.06	0.03	-0.05	-0.04	0.14	-0.11	-0.02	0.17	-0.16	0.43	0.46
22. Total Publications Therapeutic Class (in hundreds)	-0.05	0.12	-0.01	0.07	0.02	0.23	0.23	-0.06	0.21	0.09	-0.01
23. Total Publication Mechanism of Action (in hundreds)	-0.05	-0.09	-0.03	0.17	-0.04	0.02	-0.02	-0.31	0.60	-0.08	-0.07
24. Top Publications Mechanism of Action	-0.01	-0.09	-0.05	-0.14	0.01	0.07	0.05	-0.20	-0.04	0.05	0.03
25. Number of Mechanisms of Action	-0.07	0.33	0.05	0.14	0.06	0.14	0.03	-0.14	0.41	-0.03	-0.07
26. Dummy User Fee Act	0.04	0.01	-0.09	0.02	0.09	0.25	0.15	0.07	-0.05	0.19	0.10
Variable	19	20	21	22	23	24	25				
20. Firm's Best-Selling Drugs	0.46										
21. Firm's FDA-Approved Drugs	0.42	0.60									
22. Total Publications Therapeutic Class (in hundreds)	0.06	-0.06	0.02								
23. Total Publication Mechanism of Action (in hundreds)	-0.05	-0.01	-0.08	0.25							
24. Top Publications Mechanism of Action	0.02	-0.02	0.04	-0.09	0.24						
25. Number of Mechanisms of Action	-0.02	-0.02	-0.06	0.55	0.20	-0.22					
26. Dummy User Fee Act	0.20	-0.16	-0.03	0.36	0.18	0.14	0.20				

Table 3

Weibull Accelerated Event-Time Regressions: Estimates of Influences on FDA Approval Times

(positive coefficients: longer approval times)

	(1)	(2)	(3)	(4)	(5)	(6)
Top Publications on Drug		-0.009 ** (0.004)	-0.008 ** (0.004)	-0.008 ** (0.004)	-0.005 (0.004)	-0.005 (0.004)
Top Publications on Other Mechanisms			0.004 *** (0.001)			
Top Publications on Other Mechanisms_Drug Based on New Mechanism				0.006 *** (0.001)	0.006 *** (0.001)	0.006 *** (0.001)
Top Publications on Other Mechanisms_Drug Based on Existing Mechanism				0.004 *** (0.001)	0.004 *** (0.001)	0.004 *** (0.001)
Top Publications on Drug * Top Publications on Other Mechanisms					-0.004 *** (0.001)	
Top Publications on Drug *						-1.197 ** (0.486)
Top Publications on Other Mechanisms_Drug Based on New Mechanism						-0.004 *** (0.001)
Top Pub Drug *						
Top Publications on Other Mechanisms_Drug Based on Existing Mechanism						
Drug Heterogeneity						
Dummy Orphan Drug	0.133 (0.155)	0.057 (0.155)	0.170 (0.143)	0.229 (0.145)	0.217 (0.143)	0.199 (0.142)
Total Publications on Drug	-0.008 * (0.004)	-0.004 (0.004)	-0.005 (0.004)	-0.005 (0.004)	-0.006 (0.004)	-0.006 (0.004)
Development Time	0.012 (0.011)	0.015 (0.011)	0.021 (0.011)	0.021 (0.011)	0.019 (0.011)	0.019 (0.011)
Patent Forward Cites	-0.006 (0.004)	-0.007 (0.004)	-0.004 (0.004)	-0.003 (0.004)	-0.004 (0.004)	-0.003 (0.004)
Patent Backward Cites	0.009 (0.005)	0.008 (0.005)	0.009 (0.005)	0.009 (0.005)	0.009 (0.005)	0.009 (0.005)
Patent Number of Claims	0.002 (0.003)	0.003 (0.003)	0.004 (0.003)	0.004 (0.003)	0.004 (0.003)	0.003 (0.003)
Dummy New Mechanism of Action	-0.183 (0.103)	-0.190 (0.102)	-0.140 (0.097)	-0.249 * (0.107)	-0.245 * (0.106)	-0.227 * (0.106)
Number of Drugs Building on Mechanism of Action	-0.002 (0.012)	-0.005 (0.012)	-0.001 (0.011)	-0.0002 (0.011)	-0.001 (0.011)	-0.001 (0.011)
Firm Heterogeneity						
Firm's Total Publications (in hundreds)	-0.021 * (0.009)	-0.021 * (0.009)	-0.027 ** (0.009)	-0.026 ** (0.009)	-0.027 ** (0.009)	-0.027 ** (0.009)
Firm's Publications in Top Journals	0.0003 (0.007)	-0.0002 (0.007)	0.001 (0.007)	0.002 (0.006)	0.002 (0.006)	0.003 (0.006)
Firm's Patents	0.001 (0.001)	0.001 (0.001)	0.001 (0.001)	0.001 (0.001)	0.001 (0.001)	0.001 (0.001)
Firm's Best-Selling Drugs	0.024 * (0.012)	0.028 * (0.012)	0.023 * (0.012)	0.026 * (0.012)	0.024 * (0.012)	0.025 * (0.012)
Firm's FDA-Approved Drugs	-0.024 (0.025)	-0.027 (0.024)	-0.013 (0.023)	-0.014 (0.022)	-0.010 (0.022)	-0.010 (0.022)
Therapeutic Class Heterogeneity						
Total Publications Therapeutic Class (in hundreds)	-0.0003 (0.0003)	-0.0004 (0.0003)	-0.001 ** (0.0004)	-0.001 * (0.0004)	-0.001 * (0.0004)	-0.001 * (0.0004)
Total Publication Mechanism of Action (in hundreds)	0.003 * (0.002)	0.003 * (0.002)	0.004 * (0.002)	0.004 * (0.002)	0.004 * (0.002)	0.004 * (0.002)
Top Publications Mechanism of Action	-0.051 (0.037)	-0.053 (0.037)	0.043 (0.042)	0.062 (0.044)	0.051 (0.044)	0.049 (0.043)
Number of Mechanisms of Action	0.037 (0.048)	0.034 (0.047)	0.072 (0.046)	0.068 (0.045)	0.072 (0.045)	0.071 (0.045)
Therapeutic Class Dummies	Yes	Yes	Yes	Yes	Yes	Yes
Other Controls						
Dummy User Fee Act	-1.423 *** (0.400)	-1.434 *** (0.398)	-1.806 *** (0.388)	-1.837 *** (0.389)	-1.826 *** (0.383)	-1.807 *** (0.382)
Submission Cohort Dummies	Yes	Yes	Yes	Yes	Yes	Yes
Constant	2.968 *** (0.497)	3.005 *** (0.491)	2.561 *** (0.483)	2.565 *** (0.481)	2.515 *** (0.475)	2.507 *** (0.472)
Ln(Shape Parameter)	1.224 *** (0.048)	1.242 *** (0.048)	1.290 *** (0.051)	1.310 *** (0.051)	1.333 *** (0.051)	1.340 *** (0.051)
Frailty Parameter	0.832 *** (0.229)	0.860 *** (0.234)	0.892 *** (0.241)	0.963 *** (0.254)	1.006 *** (0.260)	0.980 *** (0.254)
Number of Observations	217	217	217	217	217	217
Model loglikelihood	-125.68	-123.18	-115.49	-113.26	-110.17	-108.13
Loglikelihood chi-squared	247.11 ***	252.11 ***	267.50 ***	271.96 ***	278.15 ***	282.21 ***

* p < 0.05; ** p < 0.01; *** p < 0.001

Standard errors in parentheses. Two-tailed test for control variables, one-tailed test for independent variables.