Strategic Management Journal
Strat. Mgmt. J., **33**: 1016–1036 (2012)
Published online EarlyView in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/smj.1956
Received 30 April 2008; *Final revision received 16 January 2012*

TECHNOLOGICAL DEVELOPMENT AT THE BOUNDARIES OF THE FIRM: A KNOWLEDGE-BASED EXAMINATION IN DRUG DEVELOPMENT

JEFFREY T. MACHER[1]* and CHRISTOPHER BOERNER[2]
[1] *McDonough School of Business, Georgetown University, Washington, D.C., U.S.A.*
[2] *Seattle Genetics, Incorporated, Bothell, Washington, U.S.A.*

This paper examines how the knowledge-based view (KBV) can be applied to firm boundary decisions and the performance implications of those decisions. At the center of the paper is a theoretical and empirical examination of how firms most efficiently organize for technological development. We find that distinct organization approaches are advantaged in the speed of technological development depending on the structure of technological development problems and the depth of firms' technological area experience. We make theoretical and empirical contributions to KBV research that examines knowledge development and transfer. Drug development in the pharmaceutical industry serves as our empirical setting. Copyright © 2012 John Wiley & Sons, Ltd.

INTRODUCTION

The knowledge-based view (KBV) of the firm emphasizes the role of knowledge in determining organization and performance. Knowledge develops within firms from experiential learning facilitated by organizational routines and problem-solving activities, and creates values from its effective application (Grant, 1996). This perspective predominantly emphasizes the virtues of hierarchies in both limiting and facilitating knowledge transfer, despite their inefficiencies for certain kinds of knowledge-related activities (Nickerson and Zenger, 2004). Relatively underexplored in the KBV literature is an examination of how knowledge development and transfer differs between organizational modes and by firms with different experience levels; but just such a theoretical and empirical examination is necessary to realize a comprehensive knowledge-based theory of the firm.

In this paper, we comparatively examine the organization and speed of technological development within and between firms, which entails significant knowledge development and transfer. The speed (i.e., time-to-market) with which new technologies and products can be developed and introduced is a primary arena of competition in many high technology industries (Brown and Eisenhardt, 1995). Firms with faster development speed are often rewarded with first-mover advantages that help establish market and technological leadership positions, preempt scarce geographic and technological resources, and create indelible switching costs (Lieberman and Montgomery, 1988). We use the pharmaceutical industry as our empirical setting, which places considerable emphasis on drug development completion time. Case study evidence suggests that when nearly identical drug products are brought to market three to six months apart, the product appearing first achieves the largest market share and maintains

Keywords: knowledge-based view (KBV); problem solving; firm boundaries; learning economies; pharmaceutical industry
*Correspondence to: Jeffrey T. Macher, McDonough School of Business, Georgetown University, Washington, DC 20057, U.S.A. E-mail: jtm4@georgetown.edu

this advantage indefinitely (Wiggins, 1981). Even when drug products do not face significant competition, development completion time remains important as the majority of economic returns are reaped between regulatory approval and patent expiration (Grabowski and Vernon, 1990).

Following previous research (Nickerson and Zenger, 2004), we assume that firms' primary objectives in technological development are to create valuable knowledge. But because this knowledge does not typically exist, firms must instead solve particular problems that yield valuable knowledge. Our problem-solving approach to knowledge development is particularly germane in research and development (R&D) intensive environments, given the inherent uncertainties and complexities (Fleming and Sorenson, 2004). Depending on problem characteristics, particular organizational modes are argued superior for problem solving relative to other modes (Macher, 2006; Nickerson and Zenger, 2004). We add to this research by examining the interactive effects that technological area experience and problem characteristics have on problem-solving organization and speed in technological development.

We make several contributions to the KBV literature. We find that problem structure influences firms' organizational decisions and subsequent performance. Firms improve performance from outsourcing well-structured technological development problems—given the benefits of specialized knowledge development resources available within markets and the ease of knowledge transfer—and from insourcing ill-structured technological development problems—given the benefits of knowledge integration resources within firms and the difficulty of knowledge transfer. We also find that technological area experience plays a dual role in knowledge development and transfer. It not only improves knowledge development within firms via experiential learning by doing (Argote, 1999) but also facilitates knowledge transfer between firms via improved supplier selection, monitoring, and communication (Mayer and Salomon, 2006). We also find that problem structure, technological area experience, and organization choice interact to impact performance. While technological area experience improves performance regardless of organizational approach, the difficulties associated with solving ill-structured problems are lessened within firm boundaries vis-à-vis between firm boundaries.

We therefore add to empirical research that examines the performance implications of alternative organizational modes (Poppo and Zenger, 1998), and find support for the importance of organizational alignment in firms' knowledge development and transfer activities. We also examine pharmaceutical drug development—an area of research that has received more limited scholarly attention (Azoulay, 2004), especially in comparison to pharmaceutical drug discovery (Henderson and Cockburn, 1994,1996). Drug development costs nevertheless typically exceed drug discovery costs and are often cited as a primary rationale for pharmaceutical industry mergers. Understanding the organization and performance implications of knowledge development and transfer in R&D is of critical strategic importance to managers in this industry, as well as other similarly knowledge-intensive industries.

The next section provides a review of the KBV organization and performance literature, and develops comparative hypotheses from it. The following section sets the empirical context, highlighting the evolving organization of R&D activities in the pharmaceuticals industry. We then describe the data and variables, present the econometric and robustness results, and discuss the main findings and limitations. The final section makes concluding comments.

HYPOTHESES DEVELOPMENT

The KBV of the firm conceptualizes organizations as institutions for developing and integrating knowledge. Knowledge develops within firms from experiential learning facilitated by internal rules, organizational routines, and problem-solving approaches. Knowledge transfers within and across firms, allowing for value creation (Grant, 1996). The KBV has predominantly underscored the benefits of hierarchies due to their abilities to not only avoid knowledge transfer by exercising authority (Conner, 1991; Conner and Prahalad, 1996) but also promote knowledge transfer by facilitating communication (Grant, 1996; Kogut and Zander, 1992, 1996). At least two knowledge-related issues that are potentially important to boundary decisions and performance remain relatively underexplored within the KBV: first, the role that markets play in developing knowledge; and second, the role that firm technological area

DOI: 10.1002/smj

experience plays in both developing and transferring knowledge. An approach that discriminately compares the efficiency of knowledge development and transfer across different organizational modes, as well as considers the effects of heterogeneous firm-level experience on these activities, is nevertheless required to realize a comprehensive knowledge-based theory of the firm.

We build on Nickerson and Zenger (2004) and Macher (2006), who propose a knowledge-based theory of the firm based on the problem solving and solution search efficiencies of alternative organization modes. Problems represent systems that correspond to decisions that potentially interact in non-simple ways (Simon, 1962). Problems are accompanied by sets of potential solutions termed 'landscapes,' each of which relates to unique combinations of decisions made (Hsieh, Nickerson, and Zenger, 2007). Kauffman's NK framework is typically used to conceptualize solution landscapes, whereby N represents the number of knowledge sets applicable to a problem and K represents the degree of interdependence among knowledge sets. Given a particular N and K, firms attempt to efficiently search the landscape for high value solutions by combining (potentially dispersed) knowledge resources. Theoretical and empirical discriminating alignment arguments are made between problems, which vary according to their structure and complexity, and organizational modes, which vary according to their abilities to effectively support solution search. We add to this research by examining the interdependent effect of technological area experience on problem structure, and thereby solution search. Firms with more technological area experience can improve performance not only via experiential learning by doing (Argote, 1999) but also via improved supplier selection, monitoring, and communication (Mayer and Salomon, 2006). Technological area experience is, therefore, likely to have organization and performance implications that depend in part on the structure of technological development problems.

In our approach, we emphasize firms' 'knowledge production' activities (i.e., the development and transfer of knowledge) related to R&D. Our view of R&D is inclusive—from the discovery of new technologies through their development and commercialization into new products. The efficiency of firms in these R&D activities typically entails the development of and/or access to different knowledge sets within and across boundaries. In many industries, technological development is characterized by unstructured problem solving and an inability to predict success or performance *ex ante*. Technological development is, thus, a process of solution search utilizing different knowledge sets (Ethiraj and Levinthal, 2004) that can be described generally as a trial-and-error exercise in which particular knowledge set parameters are altered, learned about, and improved upon. Depending on the problems presented, technological development ranges from relatively well structured (i.e., straightforward), given the known interactions among knowledge sets, to relatively ill structured (i.e., difficult), given the unexpected or unknown knowledge set interactions.

The structure of technological development problems that firms face thus suggest that particular organizational approaches are more efficient in developing and/or transferring knowledge. But experience also provides certain problem-solving advantages, which subsequently affects how firms organize technological development and the performance achieved. Moreover, internal and external incentives that reward and encourage knowledge development and transfer are often necessary for efficient technological development. We hypothesize that firms determine in a discriminating way how best to organize technological development by simultaneously considering integration demands and efficiency requirements. As we compare the performance of knowledge-based assets both between and within firms, our approach represents an ideal setting in which to theoretically and empirically add to the KBV.

Problem structure

Problem structure represents the level of understanding of the K interactions among N knowledge sets for a given problem. Differences in levels of understanding result from characteristics of the problem domain on the one hand, and the availability of problem-solving mechanisms on the other (Fernandes and Simon, 1999; Simon, 1973). Given this level of understanding, problems vary on a continuum from relatively ill structured to relatively well structured. Well-structured problems are those with well-defined initial states (N and K are unequivocal) and explicit problem-solving approaches, whereas

DOI: 10.1002/smj

ill-structured problems have poorly defined initial states (N and K are equivocal) and ambiguous problem-solving approaches. Well-structured problems also have well understood knowledge set interactions, while ill-structured problems have unexpected and/or unknown knowledge set interactions (Levinthal, 1997).

Firms' understanding of the relevant knowledge sets and their interdependencies therefore determine the extent to which problems are considered well structured or ill structured, and subsequently shape the ease (or difficulty) of solution search. Well-structured problems have well understood knowledge set interactions, making solution search simpler in comparison to ill-structured problems. Well-documented and/or formalized processes are available or can more easily be put into place as knowledge sets interact in known or predictable ways. Moreover, solution search can be subdivided, with activities conducted and decisions made independently from each other using multiple actors examining particular knowledge sets relevant to problem solving. By contrast, ill-structured problems have unexpected and sometimes unknown knowledge set interactions, making solution search much more difficult. These types of problems cannot easily be subdivided due to the unknown extent of knowledge set interdependencies. These characteristics suggest that well-structured problems entail more data-intensive activities—given the formalized processes available for solution search—whereas ill-structured problems entail more knowledge-intensive activities—given the presence of tacit knowledge and expected novelty of solution search (Azoulay, 2004).

The distinction between ill- and well-structured problems suggests that particular organizational approaches should realize solution search advantages. As well-structured problems have more formalized problem-solving processes in place, outsourcing should provide certain efficiencies in comparison to insourcing due to the more specialized expertise (Hammond and Miller, 1985), high powered incentives, and decentralized decision making (Williamson, 1991) present. Markets face more acute competitive pressures that reduce organizational slack and increase incentives to operate efficiently (D'Aveni and Ravenscraft, 1994). Because knowledge set interdependencies are well understood for well-structured problems, (specialized) firms can operate independently in examining alternatives and finding solutions. Insourcing is comparatively disadvantaged for well-structured problems, in comparison to markets. Internal organization facilitates knowledge transfer, either through additional control or improved coordination. But well-structured problems already have formalized problem-solving processes in place, and neither require nor benefit from authority- or consensus-based problem-solving approaches (Nickerson and Zenger, 2004). The low powered incentives, generic knowledge sets, and bureaucracy that exist, slow the speed and reduce the efficiency of solution search in comparison to markets. Simply put, internal organization adds additional costs to well-structured problem solving with less than commensurate benefits.

By contrast, ill-structured problems have more ambiguous problem-solving approaches. Because limited information exists on whether and how knowledge sets interact within a technological domain, ill-structured problems require and benefit from approaches that guide problem solving and prioritize solution search. The control and coordination offered via insourcing encourages knowledge development and facilitates knowledge transfer in ways that outsourcing cannot easily replicate (Macher, 2006). Insourcing offers superior control, given the low powered incentives and dispute resolution mechanisms in place (Williamson, 1991). Defining R&D goals and research agendas are also comparatively easier via insourcing (Armour and Teece, 1980), as decisions are based upon convergent expectations (Malmgren, 1961) and adaptation can take place in a sequential fashion as events unfold and new information is revealed. Insourcing also offers comparatively better coordination, given the firm-specific communication codes, information channels, and heuristics in place (Grant, 1996; Kogut and Zander, 1992, 1996; Monteverde, 1995). As ill-structured problems often entail tacit knowledge development (Zucker, Darby, and Armstrong, 2002), insourcing is also comparatively better at codifying, transferring, and integrating this type of knowledge (Kogut and Zander, 1996; Monteverde, 1995). Outsourcing is relatively less efficient in solving ill-structured problems, given its limited protection against knowledge appropriation and weak support for knowledge sharing (Nickerson and Zenger, 2004). Given the control and coordination mechanisms of insourcing better support the adaptive, sequential, and interrelated changes necessary in

DOI: 10.1002/smj

solution search, it is more efficient that outsourcing in solving ill-structured problems.

The structure of technological development problems is, thus, expected to have comparative organization and performance implications. Technological development that entails well-structured problem solving is more explicit and unequivocal and likely entails more data-intensive activities (Azoulay, 2004), with minimal performance questions or concerns. But because markets face more high powered incentives and greater competitive pressures than internal organization, technological development performance should realize superior benefits between firms than within firms. Technological development that entails ill-structured problems is more ambiguous and equivocal and entails more knowledge-intensive activities (Azoulay, 2004), and subsequently creates performance difficulties between firms both administratively and contractually. But because internal organization is better able to adapt to changing circumstances as information unfolds and is revealed, the adverse performance effects from ill-structured problems should be more effectively reduced within firms than between firms. Firms should, therefore, realize performance benefits from outsourcing when solving well-structured technological development problems and from insourcing when solving ill-structured technological development problems. The following set of hypotheses is examined:

Hypothesis 1a: Firms are more likely to insource (outsource) technological development that entails ill-structured (well-structured) problems.

Hypothesis 1b: Firms that insource (outsource) technological development that entails ill-structured problems complete development faster (slower) than firms who outsource (insource) such technological development, ceteris paribus.

Technological area experience

The KBV argues that knowledge develops within the firm from experiential learning. Firms are described as routine-based and history-dependent systems that adapt incrementally to past experiences. Experience provides informational advantages via legitimacy (March, 1988) or past success (Baum, Li, and Usher, 2000), and reduces uncertainty via learning by doing (Argote, 1999). Experience also develops internal routines (Nelson and Winter, 1982), expertise (Leonard-Barton, 1992), and mechanisms (Grant, 1996) that improve problem solving and facilitate knowledge integration within and outside the firm. By contrast, firms with less experience are less likely to have detailed information filters, routines, and heuristics in place for efficient problem solving.

Because experience impacts knowledge production activities, it has performance implications. Less experienced firms possess more limited explicit and tacit knowledge within a particular domain and have less developed problem-solving mechanisms in place, in comparison to more experienced firms. Given an internal development approach, less experienced firms are expected to face greater performance challenges than their more experienced counterparts. But less experienced firms within a domain also face greater performance challenges when outsourcing in comparison to more experienced firms. The knowledge integration challenges related to selecting, managing, and communicating with partner firms are especially acute for less experienced firms in comparison to more experienced firms.

More experienced firms have a better understanding of the relevant knowledge sets and their interdependencies and more competent problem-solving approaches in place in comparison to less experienced firms. Because these mechanisms can be drawn on in future internal efforts, more experienced firms enjoy learning-by-doing performance advantages (Argote, 1999). At the same time, experience also improves firms' abilities to manage knowledge development and transfer activities across firm boundaries. Experience helps develop skills that are effective in evaluating potential partner firms and monitoring their performance (Mayer and Salomon, 2006), as well as absorbing the information developed from these partners (Cohen and Levinthal, 1990). As firms build problem-solving skills from the routines, expertise, and mechanisms in place, they learn from the previous mistakes made and successes achieved (Mitchell, Shaver, and Yeung, 1994). The experiential benefits available can be drawn on in subsequent internal or outsourced technological development activities going forward.

Firms with more technological area experience, thus, have greater organizational options in technological development. On the one hand, experienced firms can effectively insource technological development, given their inherent understanding and

DOI: 10.1002/smj

developed capabilities (Argote, 1999). On the other hand, experienced firms can effectively outsource technological development, given their existing knowledge and underlying expertise (Parmigiani, 2007; Parmigiani and Mitchell, 2009). While we are agnostic as to the more 'efficient' organizational approach with greater experience, we do expect more experienced firms will achieve superior performance in comparison to less experienced firms—regardless of whether technological development is insourced or outsourced. We examine the following hypothesis:

Hypothesis 2: Firms with more technological area experience complete development faster than firms with less technological area experience, ceteris paribus.

Problem structure and technological area experience

While we argue that experience enhances both insourced and outsourced performance, we suggest that it improves ill-structured problem solving particularly. Firms with more experience have a better understanding of the knowledge set interdependencies within a domain and more developed problem-solving approaches in place in comparison to less experienced firms. Both of these experiential factors are beneficial in effectively managing ill-structured problem solving. Experience also improves knowledge development and integration activities within and across technological areas and firms—both of which are relatively common occurrences with ill-structured problem solving. Finally, more experienced firms are better at selecting and monitoring partner firms capable of managing ill-structured problems and then absorbing the explicit and/or tacit information developed, if technological development is outsourced.

Given the comparative development of our first hypothesis, we do not theorize directly that ill-structured problems decrease technological development performance more than well-structured problems. But we nevertheless suggest that this argument makes sense as ill-structured problems entail greater effort and (time) commitment given the ambiguity and tacit information present, while well-structured problems entail less effort and commitment given the formal problem-solving approaches available. With this argument in mind, we hypothesize that experience reduces the magnitude of the deleterious effect of ill-structured problems on technological development performance. In other words, the negative performance effect of ill-structured problems on technological development diminishes in firms' levels of technological area experience. We further hypothesize that these results hold for either insourced or outsourced technological development. The following hypothesis is examined:

Hypothesis 3: The negative effect of ill-structured problems on technological development completion speed is moderated by firms' technological area experience, ceteris paribus.

EMPIRICAL SETTING

There are two main R&D activities related to bringing new drug compounds to market in the pharmaceutical industry. The first set of activities (drug discovery) involves the initial screening and extraction of a compound with desired therapeutic properties. Once a compound has been discovered, a second set of activities (drug development) involving extensive laboratory, animal, and human testing, clinical trials, and regulatory oversight begins. Food and Drug Administration (FDA) drug development regulations leave most of the key clinical trial decisions in the hands of sponsoring firms (OTA, 1993). Rather than provide a blueprint for drug development, FDA specifies a series of hurdles that pharmaceutical firms must clear in order to gain regulatory approval. The most imperative of these to FDA regulators are ensuring that sponsor firms develop accurate drug profiles (i.e., basic activity, dose response, mechanism of action, etc.); prove drug safety and effectiveness; and demonstrate consistent manufacturability while preserving drug composition and stability.

Close linkages had historically existed between drug discovery and drug development. Drug discovery was effectively a quasi-random screening process in which a large number of natural and chemically derived compounds were tested in laboratory and animal models. Scientists lacked a well-developed corpus of knowledge regarding the biological underpinnings of specific diseases, and were, therefore, forced to rely more on observation than established theory. Advances in several scientific fields have provided a better understanding of

DOI: 10.1002/smj

the 'mechanisms of action' of many drug compounds related to specific diseases, and thereby have facilitated the discovery process by allowing more careful screening, selection, and testing (Henderson and Cockburn, 1996). The rise of biotechnology has also created new drug research and discovery opportunities (Malerba and Orsenigo, 2001).

The combined effects of these scientific and technological advances are two-fold. First, these advances have given rise to what is now known as 'rational drug design,' or the application of established biomedical knowledge to the design and testing of new drug compounds (Malerba and Orsenigo, 2001)—the net effect of which has reduced the degree of uncertainty involved with drug research. Second, these advances have helped decouple the organizational capabilities that underlie drug discovery from those in drug development (Arora and Gambardella, 1994) and subsequently led to increases in the number of specialized R&D firms pursuing commercial opportunities. Some firms focus on basic research and contract with other firms that possess downstream clinical, regulatory, and marketing capabilities needed to bring drug compounds to market (Spilker, 1989). The increasingly specialized nature of development has also given rise to a large and growing number of contract research organizations (CROs) (Azoulay, 2004; Macher and Boerner, 2006). While outsourcing development to CROs is not new, it initially was used sparingly. Recent evidence suggests development activity is increasingly outsourced (McGee, 2005) and global (Thiers, Sinskey, and Berndt, 2008). CROs offer services from discovery to development and post-approval marketing, and their capabilities rival those of traditional pharmaceutical firms (Miller and Pryce, 1999). CROs have, thus, become an important R&D component, especially for smaller pharmaceutical firms focused on discovery with more limited internal development resources.

Drug development is often ill structured, requiring that pharmaceutical firms integrate local and external expertise and information across a variety of functional areas (Mathieu, 1997). This R&D activity is fundamentally a trial-and-error exercise, whereby information obtained in one stage is examined to determine how best to proceed in subsequent stages in terms of resource allocation over multiple years and across organizations (Spilker, 1989). Because development approaches vary significantly by therapeutic characteristics, therapeutic area experience provides advantages: in establishing relationships with scientific, medical, and regulatory personnel involved in clinical trials; in facilitating understanding and the codification of tacit study designs; and in setting reasonable clinical endpoints, among others.

Most pharmaceutical firms, nevertheless, rely in part on the knowledge and capabilities of other organizations in addition to their own internal expertise. Establishing ties with academic institutions and CROs allow pharmaceutical firms to not only gain access to specialized knowledge but also to better monitor scientific and technological breakthroughs. The importance of access to internal and external knowledge sources is heightened by the inability and/or unwillingness of the FDA to provide detailed guidelines to pharmaceutical firms on key aspects of drug development (Woodcock, 1997), which is confounding in light of the strategic importance of and resources committed to this R&D activity. Drug development performance determines whether a drug compound will be approved, how quickly it can get to market, and the indications for which it can be marketed. First-mover advantages and intense post-patent generic competition give pharmaceutical firms strong incentives to shorten this development window. The importance of fast and efficient drug development is also reflected in the time and resources pharmaceutical firms commit to these activities. Drug development accounts for roughly 50 percent of the time required and 60 percent of R&D expended in bringing a drug compound to market (PhRMA, 1999), both of which have increased over time from additional regulatory requirements, increased development scope, and more complex drug compounds and technologies.

EMPIRICAL ANALYSIS

Data

Data for this paper were obtained from several sources. Drug development completion data were obtained from the Center for the Study of Drug Development at Tufts University and FDA Freedom of Information Act requests. Firm-level data were obtained from *Scrips Pharmaceutical League Tables*, Compustat, and Security and Exchange Commission filings. Data on pharma-

DOI: 10.1002/smj

ceutical-related sales and R&D expenditures were available for most of the firms in the sample. Drug-level data were obtained from FDA FOIA requests, *Scrips Pharma Projects,* and pharmaceutical industry experts. *Scrips Pharma Projects* is a proprietary database containing project-level information on drug products approved or under development. *Scrips Pharmaceutical League Tables* and *Scrips Pharma Projects* are published by PJB Publishers, a provider of business information for the pharmaceutical industry. CRO data were obtained from *CROCAS*, a proprietary database of CRO information produced by DataEdge (now part of Fast-Track Systems), a professional services and market research firm to the pharmaceutical industry.

Measures

Dependent variable

Organization: How firms organize drug development activity is expected to have significant performance effects. The variable *internal development* indicates whether the drug compound was insourced (coded 1) by the pharmaceutical firm or outsourced (coded 0) in part or in total to CROs.

Performance: Superior performance is ultimately measured through firms' competitive standing as demonstrated in revenue, profitability, market share, or market value. The use of such measures to explore drug development performance is somewhat problematic. As drug development is an inherently long process, it is difficult to determine the effect of any one development phase on the performance measures above. Moreover, performance measures are sometimes misleading in the pharmaceutical industry since they are often skewed toward a small number of 'blockbuster' drugs that dominate firms' portfolios. Similar to Cockburn and Henderson (2001) and Danzon, Nicholson, and Pereira (2005), we explore drug development performance. Whereas these authors examine drug development success (i.e., regulatory approval of drug compounds in clinical development stages), our data allow us to examine drug development completion time (i.e., the calendar time drug compounds are under clinical trials).

Our dataset represents investigational new drug (IND) submission and new drug application (NDA) submission and approval times for a random sample of pharmaceutical drug products approved by the FDA from 1981 to 1995. These data provide the exact calendar dates when an IND application was submitted by the pharmaceutical firm to the FDA, when the corresponding NDA was submitted by the pharmaceutical firm to the FDA, and when the NDA was approved by the FDA. We base our performance measure on the logged calendar time between IND submission and NDA submission (*IND time*) as it is under the direct control of pharmaceutical firms, whereas the time between NDA submission and NDA approval (*NDA time*) is determined mainly by internal FDA actions. Pharmaceutical firms have strong incentives to submit INDs expeditiously, as completion speed generally trumps all other considerations.

Independent variables

Problem structure: Problem structure is a measure of the degree to which clinical knowledge and information of a particular drug compound is disseminated across firms in the industry. PJB Publishers codes this variable for each drug compound relative to the number of other drug compounds under development or approved within the same drug indication (a subset of a therapeutic area). With less preexisting knowledge and information regarding the therapeutic characteristics of new drug compounds, firms' understanding of the knowledge sets and interactions applicable to a new drug compound are more limited. These firms must expend extra effort profiling and exploring potential clinical effects. As more similar drug compounds (i.e., within the same drug indication) either enter development or are approved, however, industry understanding of the relevant knowledge sets and their interactions improve from the additional information available. Pharmaceutical firms can subsequently leverage this information by altering clinical approaches or utilizing scientific and regulatory connections. *Problem structure* is coded for the focal drug compound as 2 if there are no other drug compounds under development or approved in the same drug indication; 1 if there are one to three drug compounds under development or approved in the same drug indication; and 0 if there are four or more drug compounds under development or approved in the same drug indication. We test the robustness of this measure using an alternative specification in the empirical analysis.

Technological area experience: A review of the pharmacoeconomics literature and discussions

DOI: 10.1002/smj

with industry experts highlight the importance of technological area experience to drug development performance. Drug development has a standard taxonomy with which drug compounds can be assigned into technological areas via therapeutic areas (e.g., cardiovascular, gastrointestinal, respiratory, etc.). Because clinical approaches vary by the therapeutic characteristics of drug compounds, prior therapeutic area experience is an important determinant of development performance. As firms gain therapeutic area experience, they develop expertise and problem-solving approaches that can be drawn on in similar and subsequent development efforts. *TA experience* uses this taxonomy and is determined by:

$$TA\ experience_{i,j,t} = \delta \cdot TA\ experience_{i,j,t-1} + TA\ activity_{i,j,t}$$

where *TA experience*$_{i,j,t}$ represents the cumulative success of prior drug development efforts by pharmaceutical firm i in therapeutic area j at time t, and *TA activity*$_{i,j,t}$ represents a count of successful drug development projects for pharmaceutical firm i in therapeutic area j in time t. The depreciation factor (δ) allows recent experience to be weighed more heavily than past experience and is consistent with organizational forgetting (Benkard, 1999). We depreciate *TA experience* by 20 percent per period, but vary it from 10 to 40 percent and confirm that no changes to the empirical results are found.

Interaction: We argue that firm experience within a particular technological area moderates ill-structured problem-solving performance in drug development. The interaction of *TA experience* and *problem structure* is therefore included in our empirical analysis.

Control variables

We include several firm- and drug-level control variables. Firm age and size may influence drug development organization and performance. The liability of newness suggests that older firms benefit from accumulated experience, whereas the liability of senescence suggests firms ossify as they age (Carroll and Hannan, 2000). *Firm age* measures the logged number of years since firm founding or entry into the pharmaceutical industry. Larger firms may face a degree of institutional insulation and bureaucratization that decreases responsiveness to changing industry conditions (Haveman, 1993); but, larger firms also possess resource endowments and enjoy market power and positional advantages that improve their abilities to adapt to changing conditions (Baum and Oliver, 1991). Two variables control for firm size. *Firm size (pharma sales)* represents the log of firm pharmaceutical revenue in the year prior to the start of drug development, while *firm size (pharma R&D)* represents the log of firm pharmaceutical R&D expenditures in the year prior to the start of drug development.

We also control for the general experience that pharmaceutical firms gain as a result of prior drug development experience across all therapeutic areas. As pharmaceutical firms undertake more drug development activity, they develop a stock of general skills that can be drawn on for early stage testing and profiling of new drug compounds, irrespective of therapeutic area. General experience also improves understanding of common regulatory and administrative issues that span therapeutic areas and fortifies relationships with important constituents, including clinicians, patient populations, and regulators (Danzon *et al.*, 2005). To the extent that general experience builds on knowledge acquired over time and becomes organizationally embedded, it may represent a source of competitive advantage. *General experience* is defined as:

$$GEN\ experience_{i,t} = \delta \cdot GEN\ experience_{i,t-1} + GEN\ activity_{i,t}$$

where *GEN experience*$_{i,t}$ and *GEN activity*$_{i,t}$ are defined similarly to the therapeutic area experience variables, but over all other therapeutic categories. We utilize a 20 percent depreciation factor (δ) per period.

Two variables control for other types of firm knowledge potentially relevant to drug development organization and performance. *Research centers* measures the number of established connections between the pharmaceutical firm and any major research medical centers (defined as one of the top 100 research institutions in terms of research funding provided by the National Institutes of Health). This variable is a count of the number of previously approved drug compounds within a therapeutic area that utilized at least one

DOI: 10.1002/smj

major research medical center, and helps control for pharmaceutical firms' access to external sources of information (Gambardella, 1995; Mathieu, 1997). These institutions keep abreast of advances in medical technologies and provide functional expertise necessary to design and execute the battery of clinical tasks required. Associations with these organizations allow firms to monitor changes in medical technologies that may affect development or alter the criteria with which it is evaluated by the FDA. The variable *Clinical patents* measures the logged number of clinical patents held by the pharmaceutical firm in the five years prior to the start of development. This variable controls for pharmaceutical firms' knowledge stocks by separating the effects of technological area experience from some other knowledge-based measure that may also explain performance.

Three variables capture drug compound-related information. *Internal discovery* indicates whether the drug compound under development was discovered in-house (coded 1) or licensed in (coded 0) by the pharmaceutical firm. It is more likely easier for pharmaceutical firms to outsource the development of drug compounds that were discovered in-house than drug compounds that were licensed in, given firms' internal understanding of drug compounds' underlying scientific and pharmacokinetic properties. *Market size* serves as a proxy for the market size for which the drug compound is commercially targeted. PJB Publishers rates drug market size on a five-point scale based on worldwide sales: (1) < $500 MM; (2) $500 MM–$2,000 MM; (3) $2,000 MM–$5,000 MM; (4) $5,000 MM–$10,000 MM; and (5) > $10,000 MM. Drug compounds targeted to larger patient populations usually entail additional testing than those targeted to smaller patient populations. Dranove and Meltzer (1994) suggest that drug compounds categorized by the FDA as high priority are given greater attention by FDA reviewers and are subject to expedited review after NDA submission, while standard drug compounds receive no such consideration. *Drug priority* is coded 1 if the focal drug compound has a FDA priority rating, and 0 otherwise.

CRO variables: Two variables examine heterogeneity in CRO capabilities in the empirical robustness analysis. *CRO TA experience* measures the number of other drug development projects in the same therapeutic area as the focal drug compound that the CRO used for outsourced drug development has previously completed. *CRO functional areas* represents the number of functional areas with at least 10 employees that the CRO used for outsourced drug development has in operation. These variables examine whether CROs with more therapeutic area experience or CROs offering a wider range of drug development services (i.e., supplier scope economies) affect performance (Macher and Boerner, 2006).

Summary statistics

Table 1 provides summary and correlation statistics. The sample includes 82 drug products by 38 pharmaceutical firms that entered clinical trials and were eventually approved by the FDA. There is considerable variation among firms in logged IND time (i.e., calendar time from IND submission to NDA submission) and logged NDA time (i.e., calendar time from NDA submission to NDA approval). Pharmaceutical firms in the sample have completed slightly more than one drug development project in a given therapeutic area and more than six across all therapeutic areas on average, but with significant heterogeneity present. Nearly two-thirds of the pharmaceutical firms outsource some amount of drug development activity. Significant heterogeneity is present in drug development problem structure.

Table 1 also indicates significant pair-wise correlations between several of the dependent and independent variables. In particular, *IND time* is positively correlated with *problem structure* and negatively correlated with *TA experience*. The firm size measures are highly correlated with each other and variance inflation factor tests confirm multicolinearity, suggesting additional considerations in the econometric analyses are required. Since variables based on assets or employees more directly influence integration decisions, we utilize *pharma sales* as our primary measure of firm size. No significant changes to the econometric results are found using *pharma R&D* as the firm size measure.

Econometric model

We argue that firms improve performance by aligning problems, which differ in their attributes, with organizational modes, which vary in their abilities to support knowledge development and transfer (Macher, 2006; Nickerson and Zenger, 2004). If

DOI: 10.1002/smj

Table 1. Summary and correlation statistics

	(1) IND time	(2) NDA time	(3) Internal develop-ment	(4) Problem structure	(5) TA experi-ence	(6) Firm age	(7) Firm size (pharma sales)	(8) Firm size (pharma R&D)	(9) General experi-ence	(10) Clinical patents	(11) Research centers	(12) Internal discovery	(13) Market size	(14) Drug priority	(15) CRO TA experience	(16) CRO functional are as
Mean	3.84	3.17	0.31	1.14	1.17	4.03	6.68	4.78	6.57	3.32	0.78	0.67	2.88	0.46	10.28	2.05
Std dev	0.62	0.64	0.47	0.47	1.66	0.79	1.53	1.07	4.26	1.41	1.39	0.47	1.10	0.50	12.62	2.30
Min	1.36	0.83	0.00	0.00	0.00	1.79	0.00	0.10	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00
Max	4.75	4.50	1.00	2.00	7.00	4.93	8.09	5.91	18.00	5.14	5.00	1.00	5.00	1.00	37.00	8.00
(1)	1.00															
(2)	**−0.28**	1.00														
(3)	−0.03	−0.15	1.00													
(4)	**0.40**	−0.12	**0.25**	1.00												
(5)	**−0.28**	−0.02	−0.07	**−0.29**	1.00											
(6)	0.08	0.13	**−0.24**	**−0.24**	**0.24**	1.00										
(7)	−0.19	0.01	−0.04	**−0.32**	**0.27**	**0.45**	1.00									
(8)	−0.20	0.06	−0.08	**−0.36**	**0.34**	**0.55**	**0.90**	1.00								
(9)	**−0.48**	−0.01	−0.02	**−0.31**	**0.46**	**0.31**	**0.41**	**0.49**	1.00							
(10)	**−0.59**	0.08	0.18	**−0.32**	**0.31**	0.17	**0.40**	**0.38**	**0.32**	1.00						
(11)	**−0.26**	−0.13	**0.26**	−0.09	0.20	0.06	**0.25**	**0.26**	**0.26**	**0.47**	1.00					
(12)	−0.07	−0.02	−0.03	0.05	0.01	−0.20	0.08	0.06	−0.11	−0.02	0.06	1.00				
(13)	0.10	**0.23**	0.12	−0.06	0.10	0.09	0.19	**0.27**	0.06	0.00	−0.01	−0.03	1.00			
(14)	0.05	**−0.29**	−0.06	0.11	−0.18	−0.20	−0.16	−0.14	−0.07	−0.04	0.11	0.21	**−0.23**	1.00		
(15)	**−0.33**	−0.02	**−0.56**	**−0.42**	0.07	−0.02	0.07	0.10	0.19	−0.04	−0.06	0.02	−0.05	0.03	1.00	
(16)	**−0.24**	−0.07	**−0.61**	**−0.35**	0.08	0.12	0.07	0.10	0.07	−0.04	−0.10	0.00	−0.13	−0.04	**0.90**	1.00

Bold indicates pair-wise correlation significance at 0.05 level.

DOI: 10.1002/smj

P_O represents the expected performance of outsourced development and P_I the expected performance of insourced development, firms should outsource when $P_O > P_I$ and insource when $P_I > P_O$. Firms that do not appropriately align problem characteristics with problem-solving organizational approaches are presumed to suffer performance consequences.

Biased and inconsistent estimates result when examining drug development performance with ordinary least squares (OLS) regression models, however, because pharmaceutical firms do not choose organization randomly (Hamilton and Nickerson, 2003). These organizational decisions are instead made systematically by pharmaceutical firms to maximize expected performance. Unobserved factors that influence both the organization decision and performance outcome create self-selection biases, and normative implications drawn from these analyses are problematic. We correct for this misspecification through the addition of a selection equation using two stage censored regression techniques (Heckman, 1979), which differentiate insourced from outsourced drug development using a vector of exogenous variables. *Drug priority* serves as a choice-specific instrument for identification purposes that is associated with development organization, but has no effect on development performance. Drug priority influences pharmaceutical firms' development organizational decisions because higher priority drug products are potentially subject to FDA expedited review. Pharmaceutical firms, thus, have high powered incentives to complete drug development quickly, which is suggestive of a tapered integration (i.e., partial outsourcing) organizational approach given the potential efficiency benefits that result. But FDA expedited review occurs after NDA submission, which is after the time window that we examine (i.e., from IND submission to NDA submission). While drug priority likely reduces calendar time between NDA submission and NDA approval, it has no such effect on calendar time between IND submission and NDA submission.

In our empirical estimation, we utilize the logged calendar time from IND submission to NDA completion. Variables that lead to shorter (longer) drug development completion times have negative (positive) coefficients. We also adjust standard errors for robustness and within-firm clustering (by pharmaceutical firm). One final econometric issue is the bias built into the sample of drug compounds that we examine. There are three main 'end' states associated with drug applications: (1) approved; (2) not approved; and (3) still in progress. Due to data availability, our sample consists of FDA-approved drug compounds, and as such does not contain drug compounds falling into categories (2) and (3). The interpretation of our results should therefore be qualified as those factors that drive drug development completion speed, conditional on approval.

First stage selection results

Table 2 presents the organizational decision probit estimation results. Outsourced development serves as the comparison group. The results are presented for the full model only given space constraints, although simpler models are entirely consistent. Firm-level control measures for age (logged years since founding), size (logged pharmaceutical sales revenue), general drug development experience, and knowledge stocks (logged clinical patents and research centers); drug-level control measures for discovery method, market size, and priority; and independent measures of interest (problem structure, technological area experience and their interaction) are included.

The probit estimation results indicate that pharmaceutical firm age increases the likelihood of outsourcing drug development ($p < 0.01$), while pharmaceutical firm size has no statistically significant effect on pharmaceutical firms' drug development organizational decisions. Pharmaceutical firms with greater access to external knowledge—as exhibited in the number of academic research center connections ($p < 0.01$)—are more likely to insource drug development. Pharmaceutical firms are also more likely to outsource drug development for priority drugs ($p < 0.10$), which supports our market-based argument regarding high powered incentives and efficiency.

In terms of hypothesis testing, drug development that entails ill-structured problems is more likely to be insourced ($p < 0.01$), providing strong support for Hypothesis 1a. This result suggests that pharmaceutical firms recognize the difficulties that ill-structured technological development problems present, and the control and coordination benefits that internal organization provides. Pharmaceutical firms with different levels of technological area experience do not differ from each other in terms of development organizational approach.

DOI: 10.1002/smj

Table 2. Empirical results

	Selection	Outsourced Performance			Insourced Performance		
		Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Problem structure	1.20***		1.14**	1.25**		0.37***	0.34**
	(0.40)		(0.56)	(0.62)		(0.11)	(0.12)
TA experience	0.03		−0.06**	−0.05*		−0.03***	−0.03***
	(0.05)		(0.03)	(0.03)		(0.01)	(0.01)
Problem structure X TA experience	−0.10			−0.12			−0.08*
	(0.28)			(0.13)			(0.04)
Firm age	−0.68**	0.37**	−0.20	−0.22	0.15	0.15**	0.12*
	(0.26)	(0.14)	(0.27)	(0.27)	(0.12)	(0.07)	(0.06)
Firm size (pharma sales)	0.03	−0.09	0.07	0.08	0.02	0.03	0.04*
	(0.14)	(0.11)	(0.07)	(0.07)	(0.05)	(0.03)	(0.02)
General experience	−0.01	−0.07*	−0.02	0.09	−0.06	0.00	0.11
	(0.40)	(0.03)	(0.05)	(0.11)	(0.06)	(0.02)	(0.06)
Clinical patents	0.27	−0.15	0.09	0.11	−0.14**	−0.09**	−0.09**
	(0.17)	(0.13)	(0.21)	(0.22)	(0.06)	(0.04)	(0.04)
Research centers	0.30***	−0.03	0.13	0.15*	−0.01	0.02	0.02
	(0.11)	(0.08)	(0.08)	(0.08)	(0.03)	(0.02)	(0.02)
Internal discovery	−0.32	−0.14	−0.50**	−0.49**	0.13	−0.05	−0.06
	(0.44)	(0.14)	(0.22)	(0.22)	(0.13)	(0.07)	(0.08)
Market size	0.27*	0.04	0.17	0.20	0.01	0.02	0.01
	(0.16)	(0.12)	(0.14)	(0.15)	(0.06)	(0.06)	(0.06)
Drug priority	−0.64*						
	(0.34)						
Mill's ratio		−0.06	0.75*	0.80*	0.50*	0.51***	0.54***
		(0.13)	(0.41)	(0.42)	(0.26)	(0.17)	(0.22)
Constant	−1.15	3.52***	1.49	1.15	3.76***	3.06***	3.22***
	(1.23)	(0.77)	(1.40)	(1.56)	(0.33)	(0.24)	(0.28)
Observations	82	56	56	56	26	26	26
Log-likelihood	−37.7						
Wald statistic	24.4***	5.7***	16.2***	14.4***	2.1*	4.4***	9.9***
R-squared	0.26	0.25	0.52	0.52	0.53	0.67	0.72
Estimation	PROBIT	OLS	OLS	OLS	OLS	OLS	OLS

*** $p < 0.01$ ** $p < 0.05$ * $p < 0.10$.
Standard errors are robust and clustered (by pharmaceutical firm).
Outsourced development is comparison group.

This result is relatively unsurprising. More experienced firms appear able to effectively insource technological development—given their inherent understanding and developed capabilities—or effectively outsource technological development—given their existing knowledge and underlying expertise. While technological area experience is not a statistically significant determinant of drug development organizational approach, it is an important factor of drug development performance which we discuss below.

Second stage performance results

Table 2 also presents the Heckman-corrected OLS estimation performance results, with logged calendar time from IND submission to NDA submission as the dependent variable. The results are displayed conditional on whether drug development was outsourced (left half of table) or insourced (right half of table). Model 1 establishes a baseline that includes firm-level control measures for age, size, general experience, and knowledge stocks; and drug-level measures for discovery method and market size. Model 2 adds problem structure and technological area experience to Model 1, while Model 3 adds the interaction term to Model 2. We focus our discussion on the Model 3 results.

The statistical significance of the *Mills ratio* indicates unobserved characteristics that underlie drug development organizational decisions also influence performance. There are comparative performance advantages for pharmaceutical firms in

DOI: 10.1002/smj

organizing drug development activity, which suggest that the influence of organization on performance is driven in part by an endogenous selection process (Hamilton and Nickerson, 2003).

Several control variables have statistically significant effects on drug development performance. Older pharmaceutical firms have longer completion times when drug development is insourced ($p < 0.10$)—a result consistent with the liability of senescence. Pharmaceutical firms with larger clinical patent stocks have shorter drug development times when development is insourced ($p < 0.05$). Large internal 'knowledge stocks' thus appear to be effective in improving drug development performance, but conditional on the organizational approach taken. More internal clinical patents appear to offer additional information relevant to drug development. Performance benefits and spillovers accrue to pharmaceutical firms from these internal 'knowledge stocks' when drug development is insourced. But any benefits and/or spillovers provided from these resources appear lost (or not put to good use) when firms outsource drug development. Pharmaceutical firms that outsource the development of internally discovered drug compounds have shorter drug development times ($p < 0.05$), while firms that insource the development of these drug compounds do not realize performance benefits. These results suggest discriminating performance differences from the organizational approach taken. In particular, 'virtual' firms that outsource R&D activity in both upstream (e.g., drug discovery) and downstream (e.g., drug development) directions and essentially function as a nexus of contracts appear to face greater knowledge development and transfer difficulties in comparison to firms that maintain (at least) some internal R&D posture.

In terms of hypothesis testing, we argue that insourced drug development provides performance advantages vis-à-vis outsourced drug development for ill-structured problems (Hypothesis 1b). Our results indicate problem structure increases drug development times for both outsourced ($p < 0.05$) and insourced ($p < 0.05$) drug development. Given our comparative approach, we determine if Hypothesis 1b is supported by examining the economic significance of these results. We next argue that technological area experience shortens drug development completion time (Hypothesis 2), and find support for this hypothesis for both outsourced ($p < 0.10$) and insourced drug development ($p < 0.01$). Our results, thus, support the argument that technological area experience is an important determinant of drug development performance, irrespective of organizational approach. Firms' experience within a particular technological area not only develops useful knowledge internally via experiential learning-by-doing (Argote, 1999) but also improves knowledge integration capabilities externally through improved supplier selection, monitoring, and communication (Mayer and Salomon, 2006). Experienced firms can effectively keep technological development internal—given their inherent understanding and developed capabilities (Argote, 1999)—or can effectively outsource technological development—given their existing knowledge and underlying expertise (Parmigiani, 2007; Parmigiani and Mitchell, 2009). The interactions between problems structure and technological area experience are also noteworthy. The effect of problem structure on drug development completion time is moderated by pharmaceutical firms' therapeutic area experience for insourced drug development ($p < 0.10$), but not for outsourced drug development. These results provide partial support for Hypothesis 3.

Economic significance

An examination of economic significance better illustrates our empirical findings and hypotheses support. Figure 1 plots average *IND time* for ill-structured and well-structured problems across the range of therapeutic area experience levels, using simulations of coefficient parameters, preset values for explanatory variables, and calculated expected values. The CLARIFY suite of Stata commands for interpreting statistical results is used to generate the simulation results and accompanying figures (King, Tomz, and Wittenberg, 2000). Figure 1 sets *problem structure* equal to 0 (i.e., well structured) and to 2 (i.e., ill structured) and varies TA experience across its range for both the insourced and outsourced estimations. The interaction term *problem structure X TA experience* is similarly varied, depending on initial conditions of the direct effects. All other variables are set at their mean levels.

Figure 1 indicates that well-structured development problems are completed faster via outsourced development than insourced development, while ill-structured development problems are completed faster via insourced development than outsourced

DOI: 10.1002/smj

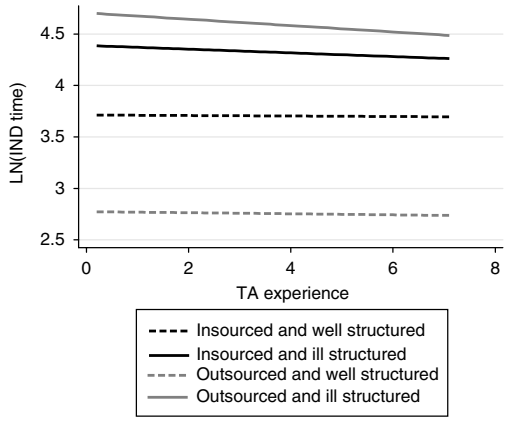

Figure 1. Technological development completion speed

development. As problems move from well structured to ill structured, development completion times increase for both organizational approaches. Figure 1 also indicates as technological area experience increases, completion times for both insourced and outsourced development approaches decrease. Note that these results are found for well-structured (less so) and ill-structured (more so) problems. Experience therefore provides not only learning-by-doing benefits that aid in knowledge development and problem solving but also supplier selection, monitoring, and communication benefits that facilitate knowledge transfer and problem solving. Figure 1 also indicates that technological development is more efficient on average via outsourcing when it entails well-structured problems and more efficient on average via insourcing when it entails ill-structured problem solving. In sum, performance penalties result when technological development entails well-structured problem solving within rather than between firms and when technological development entails ill-structured problem solving between rather than within firms.

Robustness results

Table 3 presents several robustness tests of our empirical estimation.[1] Model 1 addresses concerns regarding the coding of *problem structure*. This variable is measured according to the number of other drug compounds under development and/or approved in the same drug indication as the drug compound under development using particular thresholds and on a three-point scale. We recode *problem structure* as 1 if there are no other drug compounds under development or approved in the same drug indication, and 0 otherwise, which represents a more rigid threshold. The Model 1 results indicate that the coefficient estimates and standard errors are nearly identical in comparison to our baseline.

Model 2 addresses concerns regarding the OLS estimation approach by replacing it with event history analysis, given that we examine the calendar time from start to completion of drug development. In this specification, we model drug development as a stochastic process, defining the transition rate $r(t)$ from development start to completion for pharmaceutical firm i at time t as:

$$r_i(t) = \lim_{t' \to t} \frac{Pr(t \leq t' | T \geq t')}{t' \to t}$$

We specify the transition (or hazard) rate as a function of time t and a vector of covariates Z that represents our independent variables. This estimation approach takes the general form $r_i(t) = f(t, Z_{it})$. We utilize a Heckman-corrected Cox proportional hazards model that makes no assumptions about the baseline hazard. Given our event history analysis, shorter (longer) drug development completion times have positive (negative) coefficients in the Cox proportional hazards model. The Model 2 results indicate that the coefficient estimates and standard errors are comparable in terms of statistical significance—albeit opposite in sign—to our baseline model.

Models 3 and 4 address concerns that particular CRO characteristics impact drug development completion times. Model 3 includes CRO therapeutic area experience, while Model 4 includes the number of functional areas (e.g., clinical, data management, laboratory, medical, quality assurance, regulatory) in which the CRO has 10 or more employees and represents a functionally related scope economies measure. As these measures are highly correlated with each other and only observed when drug development is outsourced, the results are presented separately and only for outsourced development. Model 3 indicates that CROs with more therapeutic area experience have shorter drug development completion

[1] We also tested for multicolinearity concerns associated with our firm size measures by replacing pharmaceutical sales with pharmaceutical R&D. We confirm but do not report that coefficient estimates and standard errors are nearly identical in comparison to our baseline model, and no improvement in explanatory power was found.

DOI: 10.1002/smj

Table 3. Robustness results

	Outsourced Development				Insourced Development	
	Model 1	Model 2	Model 3	Model 4	Model 1	Model 2
Problem structure	1.24*	−1.19**	0.93*	0.91*	0.34**	−2.91***
	(0.68)	(0.49)	(0.55)	(0.51)	(0.13)	(0.92)
TA experience	−0.05*	0.09*	−0.05*	−0.06**	−0.03***	0.25***
	(0.03)	(0.05)	(0.03)	(0.03)	(0.01)	(0.10)
Problem structure X TA experience	−0.04	0.43	−0.09	−0.08	−0.07*	0.43*
	(0.10)	(0.29)	(0.12)	(0.12)	(0.04)	(0.25)
Firm age	−0.21	0.01	−0.23	−0.13	0.27***	−1.10**
	(0.28)	(0.44)	(0.24)	(0.22)	(0.07)	(0.52)
Firm size (pharma sales)	0.10	−0.08	0.08	0.07	0.04	−0.11
	(0.08)	(0.15)	(0.05)	(0.06)	(0.02)	(0.12)
General experience	0.02	−0.45*	0.06	0.06	0.09	0.48
	(0.08)	(0.24)	(0.10)	(0.10)	(0.06)	(0.38)
Clinical patents	0.09	0.64**	0.06	0.05	−0.15***	0.78**
	(0.22)	(0.30)	(0.20)	(0.19)	(0.04)	(0.36)
Research centers	0.17*	−0.35*	0.15**	0.13*	−0.03	0.03
	(0.09)	(0.18)	(0.07)	(0.07)	(0.03)	(0.17)
Internal discovery	−0.50**	0.61**	−0.47**	−0.44**	0.00	−0.23
	(0.22)	(0.29)	(0.23)	(0.21)	(0.08)	(0.48)
Market size	0.22	−0.37*	0.20	0.15	−0.04	−0.61
	(0.16)	(0.20)	(0.14)	(0.13)	(0.06)	(0.38)
Mill's ratio	0.72*	−0.79*			0.62***	−0.51**
	(0.40)	(0.47)			(0.17)	(0.25)
CRO experience			−0.02**			
			(0.01)			
CRO functional areas				−0.09**		
				(0.03)		
Constant	1.65		2.17	2.17	3.32***	
	(1.49)		(1.35)	(1.28)	(0.24)	
Observations	56	813	56	56	26	252
Wald statistic	12.2***	70.7***	25.6***	26.7***	13.2***	193.1***
Log-likelihood		−142.7				−43.9
R-squared	0.51		0.55	0.55	0.69	
Estimation	OLS	Cox	OLS	OLS	OLS	Cox

*** $p < 0.01$ ** $p < 0.05$ * $p < 0.10$.
Standard errors are robust and clustered (by pharmaceutical firm).

times ($p < 0.05$), while Model 4 indicates that CROs with more functional scale have shorter drug development completion times ($p < 0.05$). The coefficient estimates and standard errors are relatively stable in these models in comparison to our baseline model. *TA experience* maintains its level of statistical significance ($p < 0.10$), while *problem structure* is marginally significant ($p < 0.10$).

Discussion

Our empirical results confirm that experience is an important determinant of technological development performance. Experience provides informational advantages and uncertainty reductions that improve performance. More experienced firms have superior learning-by-doing and problem-solving approaches (Grant, 1996), and are more effective at selecting and monitoring partner firms (Mayer and Salomon, 2006; Parmigiani, 2007; Parmigiani and Mitchell, 2009) and absorbing relevant knowledge (Cohen and Levinthal, 1990). Experience thus helps firms build capabilities that provide performance benefits in developing knowledge within and integrating knowledge across organizational boundaries. Technological area experience provides firms some amount of organizational flexibility, moreover, given its positive and interdependent effect on development performance.

DOI: 10.1002/smj

Technological development problem structure has a notable effect on organization and performance. Ill-structured problems require greater control and/or coordination to efficiently solve, as the knowledge sets interactions are less understood. Firms that insource these problem types outperform those firms that outsource, given hierarchical efficiencies. Well-structured problems require less control and/or coordination to efficiently solve, as knowledge set interactions are well understood. Firms that outsource these problem types outperform those firms that insource, given market-based efficiencies. These results support KBV arguments that firms improve performance by discriminatingly aligning knowledge attributes and organization (Macher, 2006; Nickerson and Zenger, 2004).

Importantly, our empirical results suggest that internal organization provides certain performance benefits above and beyond the benefits provided by firms' technological area experience. Holding firm experience constant, insourcing fosters control and facilitates communication in ways that outsourcing has difficulty matching. Although more experienced firms possess superior knowledge development and integration capabilities and can solve technological development problems more quickly than less experienced firms, insourcing provides superior problem-solving features (especially for ill-structured problems) vis-à-vis outsourcing. Knowledge development and transfer related to ill-structured problems is, thus, more efficient within rather than across firm boundaries. Our empirical results, therefore, suggest that technological development performance is conditioned by the interplay among the attributes of the technology, the choice of organization, and the depth of technological area experience.

An important question is: why do some pharmaceutical firms take potentially less efficient organizational approaches in their technological development activities? We believe, and our interviews with industry practitioners confirm, there are several reasons. First, some pharmaceutical firms are not strategic in their organizational approaches toward technological development. Instead of considering the drug product portfolio currently and potentially under development in the near-future, some firms quasi-randomly and somewhat myopically assign internal development resources (when available) to the next drug compound, irrespective of its particular problem-solving requirements. Our findings suggest that pharmaceutical firms must balance their drug development portfolios (Wheelwright and Clark, 1992), and maintain some amount of development resource slack according to the problem-solving requirements of the drug compounds currently in or soon to be under development in the foreseeable future. Second, our analysis suggests that firms with more technological area experience are provided greater flexibilities in their organizational decisions, given their superior problem-solving approaches and partner selection, monitoring, and communication capabilities. What might at first glance appear to be mistakes are quite possibly rational outsourcing decisions, given the performance benefits of technological area experience. Third, CROs differ in terms of experience and capability. Pharmaceutical firms can and do improve development performance by selecting CRO partner firms with more experience or development scope.

Our analysis has obvious implications for firms competing in the pharmaceutical industry. As pharmaceutical firms allocate significant resources to drug discovery and drug development, how well they organize these R&D activities has a substantial impact on whether and when drug compounds achieve commercialization and, if so, the size of economic returns. We also believe our results have important implications beyond pharmaceuticals, and are relevant to managers and firms engaged in the production of technological knowledge both within and outside of firm boundaries. Relevant general industry examples are likely to include those where outsourcing particular R&D activities is a viable strategic alternative; where technological area experience increases knowledge and improves capabilities in R&D; and where technological sophistication varies across products and within firms. Relevant industry examples are likely to include, but not be limited to, chemicals, consumer electronics, semiconductors, and software.

Certain limitations and caveats in our empirical analyses and results are noteworthy. First, we examine a single and somewhat idiosyncratic industry, as well as a narrow set of development activities. While our narrow focus potentially limits generalizability, it nevertheless allows for greater precision in our measures and a more direct link between these factors and firm performance differences. Second, due to data limitations we examine only FDA-approved drug compounds. A more complete and more informative picture

DOI: 10.1002/smj

would consider successes and failures. Our approach nevertheless represents one of the few drug development completion time studies (Abrantes-Metz, Adams, and Metz, 2004), but is subject to the qualification that this is but one of several important measures in the industry. Third, due to sample size we are unable to utilize therapeutic area fixed effects. Particular conditions that relate directly to individual therapeutic areas or disease groups might influence firms' outsourcing decisions and subsequent development performance. Fourth, we do not control for the breadth and depth of pharmaceutical firm-CRO partnerships. While we question whether partnerships achieve the same level of success as internal organization, relationship breadth and depth likely impact performance. Fifth, as firms are unlikely to choose drug development organization randomly, we similarly recognize that they are unlikely to choose CRO partners randomly. Instead, a myriad of (potentially confounding) CRO factors—including but not limited to (general regulatory and particular therapeutic area) experience, extant capabilities, geographic proximity, availability, prior relationships, and costs—likely influence the CRO selection process. While we cannot control for such selection bias, its effect on our performance results is somewhat difficult to determine. Some CRO factors (e.g., experience, capabilities) should clearly shorten development completion times and bias pharmaceutical firms toward greater outsourcing, whereas other CRO factors (e.g., proximity, relationships) could potentially lengthen development completion times while still biasing pharmaceutical firms toward greater outsourcing.

One final comment centers on the relationship between drug discovery and drug development. Drug discovery capabilities differ fundamentally from those required for drug development, but important feedback loops between these two R&D activities remain. Drug discovery is more reliant on pharmaceutical knowledge, but remains in part an empirical process with close ties to drug development. Moreover, the speed and efficiency with which drug compounds move through development depend in part on the 'quality' of the drug compounds coming out of discovery. In other words, superior development performance may at least partially reflect pharmaceutical firm expertise in discovering better candidate compounds. What is required from a research standpoint is isolating the influence of the skills in discovery from those in development. While we control for whether a drug compound was discovered in-house or licensed in, this is an imperfect measure since it may be the case that some pharmaceutical firms are more skilled at selecting candidate compounds for licensing in than are other firms. Our empirical results provide some evidence that performance penalties exist for those firms that simultaneously license-in drug compounds and outsource their development. Outsourcing development can be problematic in general, as firms or their partners respond to changes and adapt autonomously in ways that are sensible in isolation but suboptimal for the R&D effort in total. Outsourcing R&D activity in both upstream and downstream directions appears to create managerial challenges that increase more than linearly as firms must integrate knowledge development activities that take place across multiple entities. Whether so-called virtual firms can survive and prosper by outsourcing everything is an empirical question (Chesbrough and Teece, 1996). Our results nevertheless suggest that keeping at least one R&D activity internal provides firms with a greater amount of control and coordination in adapting R&D processes to changes that arise (Teece, 1996; Williamson, 1991). We raise this important issue here, but leave it to future research.

CONCLUSION

This paper utilizes the KBV to examine technological development at the boundaries of the firm. Firms' 'knowledge production' activities in R&D are highlighted and examined from a problem-solving perspective. Several theoretical contributions to existing KBV research are put forth, and a comparative examination of the organization and speed of knowledge development and transfer within and between firms is conducted. Performance implications among the structure of technological development problems, the depth of technological area experience, and the choice of organization are found, which adds to the KBV research that examines boundary decisions.

The structure of technological development problems is found to have important performance effects in firms' technological development activities. Problem structure—the level of understanding of knowledge set interactions within a tech-

DOI: 10.1002/smj

nological area—influences the ways firms organize as well as the speed and efficiency with which they find solutions. Technological area experience also has a significant effect on firm performance. Technological area experience improves knowledge development within firms through experiential learning-by-doing, but also improves knowledge transfer between firms by facilitating and improving partner selection, monitoring, and communication. Arguably the most interesting finding, however, is the interplay found among the structure of problems, the choice of organization, and the depth of technological area experience. While technological area experience improves performance regardless of firms' organizational approaches, the difficulties associated with developing and integrating knowledge across firm boundaries rather than within firm boundaries become especially acute with ill-structured technological development problems. We, therefore, argue that technological area experience and problem structure are important and interdependent determinants of organization and performance in firms' technological development activities.

Using the pharmaceutical industry as the empirical setting and drug development completion speed as our performance measure, we add to the empirical KBV research that examines the performance implications of alternative organizational modes and provide support for the importance of organizational alignment in firms' knowledge development and integration activities. Because technological development is a process characterized by unstructured problem-solving approaches in many industries, our analysis has important implications for firms competing in these industries. As firms allocate significant resources to R&D and technological development, how they organize these activities and build experience influence whether and when new products will reach the market and provide economic return.

ACKNOWLEDGEMENTS

This research was supported in part by Georgetown University's Center for Business and Public Policy (CBPP). We acknowledge the helpful comments of John Mayo, Will Mitchell, David Mowery, and Todd Zenger. The authors are solely responsible for any errors or omissions.

REFERENCES

Abrantes-Metz RM, Adams CP, Metz A. 2004. Pharmaceutical development phases: a duration analysis. FTC Bureau of Economics Working paper no. 274. Federal Trade Commission, Washington, D.C.

Argote L. 1999. *Organizational Learning: Creating, Retaining and Transferring Knowledge*. Kluwer Academic: Boston, MA.

Armour HO, Teece DJ. 1980. Vertical integration and technological innovation. *Review of Economics and Statistics* **62**(3): 470–474.

Arora A, Gambardella A. 1994. The changing technology of technological change: general and abstract knowledge and the division of innovative labor. *Research Policy* **23**(5): 523–532.

Azoulay P. 2004. Capturing knowledge within and across firm boundaries: evidence from clinical development. *American Economics Review* **94**(5): 1591–1612.

Baum JAC, Li SX, Usher JM. 2000. Making the next move: how experiential and vicarious learning shape the locations of chains' acquisitions. *Administrative Science Quarterly* **45**: 766–801.

Baum JAC, Oliver C. 1991. Institutional linkages and organizational mortality. *Administrative Science Quarterly* **36**: 187–218.

Benkard LC. 1999. Learning and forgetting: the dynamics of aircraft production. *American Economic Review* **90**(4): 1034–1054.

Brown SL, Eisenhardt KM. 1995. Product development: past research, present findings, and future directions. *Academy of Management Review* **20**(2): 343–378.

Carroll GR, Hannan MT. 2000. *The Demography of Corporations and Industries*. Princeton University Press: Princeton, NJ.

Chesbrough HW, Teece DJ. 1996. When is virtual virtuous? Organizing for innovation. *Harvard Business Review* **74**(1): 65–73.

Cockburn IM, Henderson RM. 2001. Scale and scope in drug development: unpacking the advantage of size in pharmaceutical research. *Journal of Health Economics* **20**: 1033–1057.

Cohen WM, Levinthal DA. 1990. Absorptive capacity: a new perspective on learning and innovation. *Administrative Science Quarterly* **35**(1): 128–152.

Conner KR. 1991. A historical comparison of resource-based theory and five schools of thought within industrial organization economics: do we have a new theory of the firm? *Journal of Management* **17**(1): 121–154.

Conner KR, Prahalad CK. 1996. A resource-based theory of the firm: knowledge vs. opportunism. *Organization Science* **7**(5): 477–501.

D'Aveni RA, Ravenscraft DJ. 1994. Economies of integration versus bureaucracy costs: does vertical integration improve performance? *Academy of Management Journal* **37**(5): 1167–1206.

Danzon PM, Nicholson S, Pereira NS. 2005. Productivity in pharmaceutical-biotechnology R&D: the role of experience and alliances. *Journal of Health Economics* **24**(2): 317–339.

Dranove D, Meltzer D. 1994. Do important drugs reach the market sooner? *RAND Journal of Economics* **25**: 402–423.

Ethiraj SK, Levinthal D. 2004. Bounded rationality and the search for organizational architecture: an evolutionary perspective on the design of organizations and their evolvability. *Administrative Science Quarterly* **49**: 404–437.

Fernandes R, Simon HA. 1999. A study of how individuals solve complex and ill-structured problems. *Policy Sciences* **32**(3): 225–245.

Fleming L, Sorenson O. 2004. Science as a map in technological search. *Strategic Management Journal*, August–September Special Issue **25**: 909–928.

Gambardella A. 1995. *Science and Innovation: The U.S. Pharmaceutical Industry During the 1980s*. Cambridge University Press: Cambridge, UK.

Grabowski H, Vernon M. 1990. A new look at the returns and risks to pharmaceutical R&D. *Management Science* **36**(7): 804–882.

Grant RM. 1996. Toward a knowledge-based theory of the firm. *Strategic Management Journal*, Winter Special Issue **17**: 109–122.

Hamilton BH, Nickerson JA. 2003. Correcting for endogeneity in strategic management research. *Strategic Organization* **1**(1): 53–80.

Hammond TH, Miller G. 1985. A social choice perspective on expertise and authority in bureaucracy. *American Journal of Political Science* **29**: 1–28.

Haveman HA. 1993. Follow the leader: mimetic isomorphism and entry into new markets. *Administrative Science Quarterly* **38**: 564–592.

Heckman JJ. 1979. Sample selection bias as a specification error. *Econometrica* **47**(1): 153–162.

Henderson R, Cockburn I. 1994. Measuring competence? Exploring firm effects in pharmaceutical research. *Strategic Management Journal*, Winter Special Issue **15**: 63–84.

Henderson R, Cockburn I. 1996. Scale, scope and spillovers: the determinants of research productivity in drug discovery. *RAND Journal of Economics* **27**(1): 32–59.

Hsieh C, Nickerson JA, Zenger TR. 2007. Opportunity discovery, problem solving and a theory of the entrepreneurial firm. *Journal of Management Studies* **44**(7): 1255–1277.

King G, Tomz M, Wittenberg J. 2000. Making the most of statistical analyses: improving interpretation and presentation. *American Journal of Political Science 44* **44**(2): 347–361.

Kogut B, Zander U. 1992. Knowledge of the firm, combinative capabilities, and the replication of technology. *Organization Science* **3**(3): 383–397.

Kogut B, Zander U. 1996. What firms Do? Coordination, identity and learning. *Organization Science* **7**(5): 502–518.

Leonard-Barton D. 1992. Core capabilities and core rigidities: a paradox in managing new product development. *Strategic Management Journal*, Summer Special Issue **13**: 111–125.

Levinthal D. 1997. Adaptation on rugged landscapes. *Management Science* **43**(7): 934–950.

Lieberman MB, Montgomery DB. 1988. First-mover advantages. *Strategic Management Journal*, Summer Special Issue **9**: 41–58.

Macher JT. 2006. Technological development and the boundaries of the firm: a knowledge-based examination in semiconductor manufacturing. *Management Science* **52**(6): 826–843.

Macher JT, Boerner CS. 2006. Experience and scale and scope economies: trade-offs and performance in drug development. *Strategic Management Journal* **27**(9): 845–865.

Malerba F, Orsenigo L. 2001. Innovation and market structure in the dynamics of the pharmaceutical industry and biotechnology: towards a history-friendly model. *Industrial and Corporate Change* **11**(4): 667–703.

Malmgren HB. 1961. Information, expectations and the theory of the firm. *Quarterly Journal of Economics* **75**: 399–421.

March JG. 1988. *Decisions in Organizations*. Basil Blackwell: Oxford, U.K.

Mathieu M. 1997. *New Drug Development: A Regulatory Overview* (4th edn). Parexel International Corporation: Waltham, MA.

Mayer KJ, Salomon R. 2006. Capabilities, contractual hazards and governance: integrating resource-based and transaction cost frameworks. *Academy of Management Journal* **49**(5): 942–959.

McGee P. 2005. Virtual discovery and development. *Drug Discovery & Development* **8**(11): S3–S8.

Miller KL, Pryce SL. 1999. *Better, faster, worldwide too: update on pharmaceutical contract support organizations*. Hambrecht & Quist LLC Industry Report: San Francisco, CA.

Mitchell W, Shaver JM, Yeung B. 1994. Foreign entrant survival and foreign market share: Canadian companies' experience in United States medical sector markets. *Strategic Management Journal* **15**(7): 555–567.

Monteverde K. 1995. Technical dialog as an incentive for vertical integration in the semiconductor industry. *Management Science* **41**(10): 1624–1638.

Nelson RR, Winter SG. 1982. *An Evolutionary Theory of Economic Change*. Belknap Press: Cambridge, MA.

Nickerson JA, Zenger TR. 2004. A knowledge-based theory of governance choice–a problem-solving approach. *Organization Science* **15**(6): 617–632.

OTA. 1993. *Pharmaceutical R&D: costs, risks and rewards*. Office of Technology Assessment: Washington, DC.

Parmigiani A. 2007. Why do firms both make and buy? An investigation of concurrent sourcing. *Strategic Management Journal* **28**(3): 285–311.

Parmigiani A, Mitchell W. 2009. Complementarity, capabilities, and the boundaries of the firm: the impact of within-firm and interfirm expertise on concurrent sourcing of complementary components. *Strategic Management Journal* **30**(10): 1065–1091.

PhRMA. 1999. *Industry Profile*. Pharmaceutical Manufacturers Association: Washington, DC.

Poppo L, Zenger T. 1998. Testing alternative theories of the firm: transaction cost, knowledge-based, and measurement explanations for make-or-buy decisions in

DOI: 10.1002/smj

information services. *Strategic Management Journal* **19**(9): 853–877.
Simon HA. 1962. The architecture of complexity. *Proceedings of the American Philosophical Society* **106**(6): 467–482.
Simon HA. 1973. The structure of ill-structured problems. *Artificial Intelligence* **4**: 181–191.
Spilker B. 1989. *Multinational Drug Companies: Issues in Drug Discovery and Development*. Raven Press: New York.
Teece DJ. 1996. Firm organization, industrial structure, and technological innovation. *Journal of Economic Behavior and Organization* **31**(2): 193–224.
Thiers FA, Sinskey AJ, Berndt ER. 2008. Trends in the globalization of clinical trials. *Nature Reviews* **7**: 13–14.
Wheelwright SC, Clark KB. 1992. Creating project plans to focus product development. *Harvard Business Review* **70**(2): 70–82.
Wiggins S. 1981. Product quality regulation and new drug introductions: some new evidence from the 1970s. *Review of Economics and Statistics* **63**(4): 615–619.
Williamson OE. 1991. Comparative economic organization: the analysis of discrete structural alternatives. *Administrative Science Quarterly* **36**: 269–296.
Woodcock J. 1997. An FDA perspective on the drug development process. *Food and Drug Law Journal* **52**: 145–150.
Zucker LG, Darby MR, Armstrong JS. 2002. Commercializing knowledge: university science, knowledge capture, and firm performance in biotechnology. *Management Science* **48**(1): 138–153.

DOI: 10.1002/smj