Measuring Competence?
Exploring Firm Effects in Pharmaceutical Research.

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Introduction

There has recently been a revival of interest in the "resource based view of the firm." Those working within this tradition have drawn inspiration from the work of authors such as Selznick (1957) and Penrose (1959), and have suggested that inimitable firm heterogeneity, or the possession of unique "competencies" or "capabilities" may be an important source of enduring strategic advantage (Lippman and Rumelt, 1982; Wernerfelt, 1984; Barney, 1986; Rumelt, 1991; Peteraf, 1993; Amit and Schoemaker, 1993; Dosi and Teece, 1993). This perspective promises to be an important complement to the strategic management field's more recent focus on industry structure as a determinant of competitive advantage (Porter, 1980).

However despite the renewed theoretical interest in these ideas, empirical work in the area is still at a preliminary stage. Several studies have shown that heterogeneous firm effects account for a high proportion of the variance of profit rates across firms (Cool and Schendel, 1988; Hansen and Wernerfelt, 1989; Rumelt, 1991), and at the same time an important stream of research has confirmed that idiosyncratic firm capabilities both shape diversification strategy and drive the performance of diversified firms (Hitt and Ireland, 1985; Montgomery and Wernerfelt, 1988). But in general this work has been forced to rely on measures of competence constructed at such an aggregate level that they cannot capture the richness of the constructs of the theoretical literature. Studies of the evolution of capability at individual firms have greatly enriched our understanding of the nature of particular competencies (Burgelman, 1994; Iansiti, 1993; Leonard-Barton, 1992), but by and large these insights have not been incorporated into studies of aggregate firm behavior or systematic studies of competition. With some notable exceptions (see, for example, work by Clark and Fujimoto, 1991; Kogut and Kim, 1991; and Mitchell, 1989, 1992) relatively little empirical work has attempted to combine the richness of measures of competence derived from field work with large scale statistical studies of competition.

This paper explores the role of "competence" in pharmaceutical research. In "Scale, Scope and Spillovers: The Determinants of Research Productivity in Drug Discovery" (Henderson and Cockburn (1993), hereafter "Scale, Scope and Spillovers") we drew upon detailed qualitative and quantitative data obtained from ten major pharmaceutical firms at the program level to show that large firms were at a significant advantage in the management of research through their ability to exploit economies of scope. But this paper raised a number of puzzling questions. In the first place, we found that a large proportion of the variance in research productivity across firms could be attributed to firm fixed effects. In the second place, our results suggested that despite the fact that differences in the

structure of the research portfolio had very significant effects on research productivity, variations in portfolio structure across firms were both large and persistent. Both findings are consistent with the existence of exactly the kinds of firm specific, enduring sources of heterogeneity that are highlighted by the resource based view of the firm.

Here we build on these results to explore the nature of firm effects and the role of "competence" in pharmaceutical research. While the possession of an unusually productive research effort is only one amongst several possible sources of advantage in the industry,[1] focusing on research as a first step in understanding the role of competence in pharmaceutical competition has a number of advantages. Successful research efforts typically take many years to build and often rely on idiosyncratic search routines that may be very difficult to transfer across organizations (Nelson, 1991). Thus a substantial body of theoretical work suggests that idiosyncratic research capabilities are likely to be a particularly important source of strategically significant "competence" in science and technology driven industries (Dierickx and Cool, 1989).

We draw on detailed qualitative data about the history of research at each of the ten firms in our sample to construct a variety of measures of "competence." These variables account for much of the firm effect identified in our previous work, in both firm level and research program level data. "Architectural competence", as captured by our indicators of the firm's ability to knowledge integratively, is positively associated with research productivity. Firms which maintain links to the wider scientific community through the use of publication in the open literature as a criterion for promotion, and firms which manage the allocation of key research resources through collaborative rather than dictatorial processes are significantly more productive in drug discovery. This result is robust to controls for variation in technological opportunity and in "component competence", or possession of skills or assets specific to particular local activities within the firm. We conclude that focussing on "architectural" or "integrative" characteristics of organizations can offer valuable insights into the source of enduring differences in firm performance.

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[1] While productive research may be a critically important factor in the quest for competitive advantage in the pharmaceutical industry, promising new drug candidates need to be tested in humans, to satisfy a long and complex regulatory process and to capture share in an increasingly competitive market. Successful pharmaceutical firms may thus be able to sustain themselves through the development of unique competencies in clinical testing, in sales or marketing or in their ability to work effectively with regulatory authorities. (Hirsch, 1975; Cool and Schendel, 1988).

We begin with a brief review of the literature as background to the development of some hypotheses. Section 2 describes the estimation methodology and Section 3 the data and the construction of the variables used in the quantitative analysis. Section 4 describes the results and the paper closes with a discussion of their implications and of some directions for further research.

II. Literature Review and Hypothesis Development

For an organizational "competence" to be a source of competitive advantage it must meet three conditions: it must be heterogeneously distributed within an industry, it must be impossible to buy or sell in the available factor markets at less than its true marginal value, and it must be difficult or costly to replicate (Barney, 1986; Wernerfelt, 1986; Peteraf, 1993). While a wide variety of possible sources of heterogeneity fit these criteria, several authors have suggested that unique capabilities in research and development are particularly plausible sources of competitively important competence (Dierickx and Cool, 1989; Nelson, 1991), and several studies have confirmed that there are significant and persistent differences across firms in their ability to conduct research and to develop new products (Henderson, 1993; Clark and Fujimoto, 1991; Leonard-Barton, 1992; Tabrizi and Eisenhardt, 1994).

To structure our empirical analysis, we draw on the literature to distinguish between two broad classes of capability that might act as sources of idiosyncratic firm advantage in pharmaceutical research: "component competence" or the local abilities and knowledge that are fundamental to day to day problem solving and "architectural competence" or the ability to *use* these component competencies -- to integrate them effectively and to develop fresh component competencies as they are required. Under "component competence" we mean to include what others have called "resources" (Amit and Shoemaker, 1993) and "knowledge and skills" or "technical systems" (Leonard-Barton, 1992; Teece, Pisano and Shuen, 1992), while by using the term "architectural competence" we mean to include what others have called "capabilities" (Amit and Schoemaker, 1993) "integrative capabilities" (Lawrence and Lorsch, 1967) "dynamic capabilities" (Teece, Pisano & Shuen, 1992), "implicit/social" or "collective" knowledge (Spender, 1994) "organizational architecture" (Nelson, 1991); "combinative capabilities" (Kogut and Zander; 1992), "managerial systems" and "values and norms" (Leonard-Barton, 1992) and "invisible assets" (Itami, 1987).

Component Competence

A number of researchers have suggested that locally embedded knowledge and skills may be a

"competence" for the firm and a source of enduring competitive advantage. For example Leonard Barton (1992) suggests that the tacit knowledge developed by skilled engineers with a particular production process over an extended period of time may become a source of advantage for the firm. Similarly Teece, Pisano and Shuen (1992) suggest that local capabilities such as proprietary design rules may become so deeply embedded in the knowledge of local groups within the firm that they become strategically important capabilities.

Within the context of pharmaceutical research, there are two dimensions along which firms might develop strategically important local competencies. In the first place, firms may acquire unique disciplinary expertise. Modern drug discovery requires the input of scientists skilled in a very wide range of disciplines, including molecular biology, physiology, biochemistry, analytic and medicinal chemistry, crystallography and pharmacology. As Peteraff (1993) points out, the employment of a Nobel prize winning chemist is unlikely, in itself, to be a significant source of competitive advantage since these kinds of highly skilled individuals are likely to be both mobile and able to command a wage that reflects their value to the firm. But to the degree that expertise in any one of these disciplines builds on a foundation of experience that is largely tacit, excellence in say, pharmacology, may be a source of enduring competitive advantage. Our qualitative analysis leads us to believe that disciplinary groups embedded within particular firms develop deeply embedded, taken for granted knowledge or unique modes of working together that make the group particularly effective and that cannot be easily codified. For example, one of the roots of Merck's recent success may be a legacy of superb medicinal chemistry that dates back to Max Tishler's leadership at the firm.[2] Thus we hypothesize:

H1: Drug discovery productivity is an increasing function of firm specific expertise in particular disciplinary areas.

The second dimension along which firms may be able to develop strategically important component competence is in particular disease areas. Fundamental science plays an important role in modern pharmaceutical research (see below), but human physiology is enormously complex, and there is still much that is not known about the etiology of many diseases and the ways in which drugs affect their progress. Thus there is room for groups of disciplinary specialists working together to develop tacit or proprietary knowledge about particular disease areas. For example Eli Lilly has been a leader

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[2] Our mention of a particular company by name, both here and later in the paper, does not imply that it is or is not included in the data set.

in the field of diabetic therapy for over a hundred years, and Hoffman-La Roche developed extensive expertise in anti-anxiety drugs following its discovery of the tranquillizer Valium. Our earlier finding that the most important determinant of investment in any given disease area is the previous year's investment (Cockburn and Henderson, 1994) is also consistent with the presence of substantial "local" knowledge and ability in particular areas. Thus we hypothesize:

H2: Drug discovery productivity is an increasing function of component competence in particular disease areas.

Architectural Competence

The "architectural competence" of an organization allows it to make use of its component competencies: to integrate them together in new and flexible ways and to develop new architectural and component competencies as they are required. We include in our definition both the "architectural knowledge" defined by Henderson and Clark (1990) -- the communication channels, information filters and problem solving strategies that develop between groups within a problem solving organization -- as well as the other organizational characteristics that structure problem solving within the firm and that shape the development of new competencies: the control systems and the "culture" or dominant values of the organization. Several scholars have suggested that these types of assets may be one of the most enduring sources of competitive advantage. Leonard-Barton (1992) points to the role of both managerial systems and the values and norms of the organization in sustaining the ability to use existing skills and to respond to changes in the environment, and Nelson (1991) suggests that the "organizational architecture" and idiosyncratic search routines that sustain these types of competence develop in an evolutionary way that makes them extraordinarily difficult to replicate. Similarly Kogut and Zander (1992) and Itami (1987) suggest that unique abilities to redeploy existing knowledge may be fundamental to long term strategic advantage.

Prior research exploring the determinants of effective research organizations and of effective product and process development processes in combination with our qualitative work suggests that two forms of integrative or architectural competence may be particularly important as sources of enduring competitive advantage in pharmaceutical research: the ability to access new knowledge from outside the boundaries of the organization and the ability to integrate knowledge flexibly across disciplinary and therapeutic class boundaries within the organization.

In the sixties and early seventies, drug research was largely a matter of the large scale screening of thousands of compounds in the hopes of discovering something new. For example firms

injected hundreds of compounds into hypertensive rats in the hopes of finding something that would lower their blood pressure. Medicinal chemists modified compounds that showed signs of positive therapeutic effects in the hopes of finding something that might make an effective drug, but in general the "mechanism of action" of most drugs - the specific biochemical and molecular pathways that were responsible for their therapeutic effects - were not well understood. As long as this mode of drug discovery (popularly but misleadingly known as "random" drug discovery) was the dominant mode of research, knowledge generated outside the firm was of only limited usefulness, and there was also relatively little need to stimulate rich conversations across disciplinary or disease area boundaries within the firm (Henderson, 1994).

But as advances in biomedical science have greatly increased knowledge of both physiology and biochemistry, drug research has moved from a regime of random screening to one of so called "rational" drug design. The request "find me something (anything!) that makes the rat less depressed" has been supplemented with the request "find me something that inhibits the uptake of serotonin," and the ability to take advantage of scientific advances generated outside the firm -- within the public sector and by the competition -- as well as elsewhere within the firm, have become increasingly important to productive research.

An extensive body of research that explores the training and management of R&D professionals (Allen, 1977; Allen, Lee and Tushman, 1980; Katz, 1988) suggests that in these kinds of highly turbulent science driven environments, research performance is positively associated with the ability to span the boundaries of the firm. For example this research implies that those firms that nurture the development of "gatekeepers" - key individuals who bridge the gap between the firm and its environment and that aggressively stimulate the exchange of information between individuals - are likely to outperform those that do not. Similarly Von Hippel's research (1988) suggests that those firms that reach outside the organization for critical knowledge that is generated elsewhere perform more effectively than those that do not. We thus hypothesize:

H3: ***Firms with the ability to encourage and maintain an extensive flow of information <u>across</u> the boundaries of the firm will have significantly more productive drug discovery efforts, all other things equal.***

Successful drug discovery also requires the ability to integrate knowledge across both disciplinary and disease area boundaries <u>within</u> the firm. For example in 1981 Sankyo halted clinical studies on Compactin, the first HMG CoA reductase inhibitor discovered, in the face of evidence that the drug caused intestinal tumors in dogs. Human testing was only resumed when path breaking work

at Merck in pharmacology, physiology and biostatistics showed that the mechanisms responsible for these adverse results would not be important in humans (Minsker et al, 1983). Similarly research into the structure and function of alpha and beta receptors originally directed towards the development of superior cardiovascular drugs has since spawned an important stream of research into the workings of the central nervous system.

Recent work exploring the determinants of effective product development under these kinds of conditions suggests that high performance is associated with the use of organizational mechanisms that actively encourage the exchange of information across "component" boundaries within the firm. For example the work of Clark and Fujimoto (1991), Hauser and Clausing (1988) and Iansiti (1993) suggests that in rapidly changing environments organizations that invest in cross functional boundary spanning mechanisms that explicitly focus on the need to rethink the systemic nature of complex products and deepen the flow of information across functional boundaries significantly outperform those that do not. Similarly the work of Henderson and Clark (1990), Christensen (1993) and Iansiti (1993), suggests that in turbulent environments firms that systematically revisit the "architectural" knowledge of the organization - deeply embedded knowledge about the ways in which the components of the system should be integrated together - are likely to substantially outperform their competitors. We thus hypothesize that:

> ***H4:*** ***Firms that encourage and maintain an extensive flow of information across the boundaries between scientific disciplines and therapeutic classes <u>within</u> the firm will have significantly more productive drug discovery efforts, all other things equal.***

Prior research on the pharmaceutical industry.

These hypotheses are broadly consistent with much of the prior research that has explored the determinants of success in the pharmaceutical industry. For example Koenig (1983) found that the publication of highly cited clinical medical articles is correlated with research productivity, and Roberts and Hauptman (1986) found that new biomedical firms that maintained richer contacts outside the firm developed technologically more advanced products, while Gambardella (1992) found that firms with superior in house research programs were better positioned to exploit public science, an ability that was also correlated with research productivity. Similarly in an intriguing study of the use of language as an indicator of technological competence Sapienza (1994) suggests that pharmaceutical firms who make use of boundary spanning imagery may be more productive than those whose language is dominated by more hierarchical metaphors.

III. Specification of the Econometric Model

The strategic significance of any particular competence is ultimately a matter of its impact on the competitive standing of the firm, or of its role in determining factors such as the long term survival of the firm, sales, profitability and market share. Unfortunately the use of these measures to explore the research competencies of pharmaceutical firms is fraught with difficulty. Drug discovery is an exceedingly risky, time consuming process. On average it takes about seven years to take a promising compound from the laboratory, and for approximately 10,000 compounds synthesized, only about 10 will be advanced to clinical development, of which on average only 1 will be approved for commercial introduction (Sheck, 1984). Moreover the economic returns to new drugs are highly skewed, with a few "blockbuster" drugs dominating the portfolios of the major pharmaceutical firms (Grabowski and Vernon, 1990).

Thus as a first step towards the exploration of our hypotheses we focus on the productivity of drug discovery as measured by counts of "important" patents, where we define an "important" patent as one that was granted in two of the three major jurisdictions: Japan, Europe and the United States.[3] While patents are clearly only one possible measure of success, and later work will explore the use of Investigational New Drug applications ("INDs"), New Drug Approvals ("NDAs"), as well as sales and market share as alternative measures of research output, patents are critical to competitive advantage in the industry, and all of the firms in our sample described their patenting strategies as highly aggressive. Moreover there is considerable evidence that in science intensive industries such as pharmaceuticals, patents are closely correlated with profitability and market value (Jaffe, 1986; Cockburn and Griliches, 1988).

We hypothesize that patent counts are generated by a production function:

$$Y = f(X,\beta) \tag{1}$$

where Y is patent counts, X is a vector of inputs to the drug discovery process that includes a firm's core competencies, and β is a vector of parameters. Since the dependent variable in this relationship only takes on non-negative integer values, some type of discrete dependent variable model is dictated,

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[3] We would have preferred to have been able to use citation weighted patents as our measure of output. Unfortunately since the U.S. patent classifications do not map directly into our definitions of research programs we would have had to buy citation data directly from Derwent Publications. This proved to be prohibitively expensive.

and in the results that follow we assume that patent counts are generated by a Poisson process. We model the single parameter of the Poisson distribution function, λ, as a function of some explanatory variables, X, and parameters β in the standard fashion:

$$E[Y_{it}] = \lambda_{it} = \exp(X_{it}\beta) \tag{2}$$

to guarantee non-negativity of λ, and estimate the parameters by maximum likelihood (Hausman, Hall and Griliches, 1984).

The assumption that the dependent variable is distributed Poisson is quite strong. As our discussion in "Scale, Scope and Spillovers" suggested, as is the case in most other data of this type, the mean = variance property of the Poisson distribution is violated in our data. In the presence of such overdispersion, although the parameters β will be consistently estimated, their standard errors will typically be under-estimated, leading to spuriously high levels of significance. Overdispersion is often interpreted as evidence that the statistical model is miss-specified in the sense that there may be unobserved variables in the equation for λ,

$$E[Y_{it}] = \lambda_{it} = \exp(X_{it}\beta + \epsilon_{it}) \tag{3}$$

If ϵ follows the Gamma distribution, then it can be integrated out giving Y distributed as a negative binomial variate (Hausman, Hall, Griliches, 1984). If ϵ is not truly Gamma, however, the maximum likelihood estimates of the coefficients of the model will be inconsistent. Gourieroux, Montfort, and Trognon (1984) suggest using a quasi-generalized pseudo-maximum likelihood estimator based on the first two moments of the distribution of Y, which gives consistent estimates for ϵ drawn from a wide variety of distributions. The GMT estimator is just weighted non-linear least squares estimates of the NLLS model

$$Y_{it} = \exp(X_{it}\beta) + \epsilon_{it} \tag{4}$$

with weights derived from the relation $VAR[Y] = E[Y]\ (1+\eta^2\ E[Y])$ using initial consistent estimates of β. In previous work we have shown that our estimates of the determinants of research productivity were quite robust to these alternative estimation methods, but we continue to explore this issue in the results reported below.

In "Scale, Scope and Spillovers" we focussed on the role of the size and shape of the firm's research portfolio in shaping research productivity, including quantitative measures of firm size and scope, program size, and intra- and inter- firm spillovers in equation (1). One of the most intriguing

findings from this research was that even after controlling for all of these "visible" factors, we still found surprisingly large and persistent heterogeneities among firms in their research performance. Firm fixed effects were highly significant in our research productivity regressions, and accounted for a substantial portion of the variance explained. We also found that despite the fact that small changes in the scope and focus of the research portfolio had quite significant impacts on productivity, there was relatively little variance in scope and focus within firms over time.

In this paper we expand the set of explanatory variables, X, to include variables designed to test the hypotheses that we developed above in the hopes of "explaining" the firm effects identified in "Scale, Scope and Spillovers." Thus one useful way to think about this specification is to divide this specification into three classes: the R&D variables, R, which are entered in logs, a set of control variables, Z, (which include measures of competitive activity and measures of scope and scale), and a set of variables designed to capture heterogeneous firm competencies, C. Thus rewriting the equation in logs,

$$\log(\lambda_{it}) = \beta \log(R_{it}) + \delta Z_{it} + \gamma C_{it} \qquad (5)$$

where one can interpret the coefficient on *log(R)* directly as the elasticity of Y with respect to R&D, while the elasticities of the control variables, Z, are δZ and the elasticities of the "capabilities" variables, C, are γC.[4]

IV. The Data

We use both qualitative and quantitative data drawn from a larger study of research productivity in the pharmaceutical industry. These data were obtained from both public sources and from the internal records of ten major pharmaceutical firms. These ten include both European and American firms and between them account for approximately 28% of U.S. R&D and sales and a somewhat smaller proportion of world wide sales and research.

The Quantitative Data

The quantitative data set matches research inputs and outputs at the level of individual

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[4] Note that the choice of whether to use explanatory variables in levels or logs has important implications in this type of model. We report results in levels, but we found little difference in the results when the independent variables were entered in logs. A detailed discussion of this issue is given in our paper "Scale, Scope and Spillovers."

research programs, where a "program" is a level of aggregation somewhere between individual research projects and the level of therapeutic classes -- for example "Hypertension" as opposed to "Cardiovascular therapy" or "Compound 12345". Data was collected by research program rather than by broad therapeutic class or by individual project since we believe that analyzing the problem in this way best reflects the dynamics of pharmaceutical research. A grouping by therapeutic class is too general: "cardiovascular research," for example, includes research into widely different areas such as hypertension, cardiotonics, antiarrhythmics and hyperlipoproteinemia, while at the early stages of research firms fund programs, rather than particular projects. Moreover the use of the research program allows us to be consistent across firms since it corresponds to the level of analysis at which firms organize their internal data and make strategic budgeting decisions.

The database contains up to 30 years of data on each research program, and up to 30 programs per firm. However we do not have data from every firm for every year, and not all firms are active in all research areas. After deleting missing values, grossly problematic data and peripheral classes we are left with 4930 usable observations in our working sample, indexed by firm, research program, and year. The number of observations per firm varies from over 1000 to less than 100, with a mean of 489.8. Since we can only construct organizational variables with any confidence for years following 1975, and since because patents grants may lag applications by as much as four years in the United States and six in Japan we only use observations for the years 1975-1988. Our final dataset contains 3210 observations. Table (1a) presents some descriptive statistics for the sample. (Full details of the data collection methodology and of variable construction are given in Appendix (1).)

The Qualitative Data

Our qualitative data is drawn from both primary and secondary sources. We drew on secondary sources including the national press, reference texts, academic textbooks, medical journal articles and reports by both consultants and the Office of Technology Assessment in order to develop a preliminary understanding of the organizational and scientific history of the industry. We then conducted in depth field interviews at the ten firms participating in the study in order to construct a series of narrative histories of the development of cardiovascular drugs within each company.[5] These

[5] Since pharmaceutical technology is enormously complex, we thought it unrealistic to attempt to construct a comprehensive history of drug research at each firm. Cardiovascular drugs were chosen as the focus of the study for several reasons. The class includes both extraordinarily powerful agents whose mechanism of action - the precise biochemical means whereby the drug has a physiological effect - is well

histories were used to construct our measures of organizational structure and process.

In five of the ten firms we interviewed a wide range of individuals, from the research director and the manager of cardiovascular research to project leaders, bench chemists and pharmacologists intimately involved with particular projects. In each case, the goal of the interview was to develop a narrative history of cardiovascular drug development at each company as it was experienced by the informant. In the remaining five firms we were able to interview three to four of the most senior scientists in the company, including the chief research scientist or their equivalent, and in four of these five to interview a further three to four key individuals who had an in depth knowledge of the history of cardiovascular drug discovery development inside the firm. In every case these interviews were semi-structured, in that each respondent had been provided with a list of key questions before the interview, and each interview lasted from one to three hours. We supplemented these interviews wherever possible with internal firm documents or academic articles that documented the history that the respondents were describing, and with interviews with a number of industry experts including senior academics in the field. In all, over a hundred and ten individuals were interviewed.

This methodology has both strengths and weaknesses as a means of "measuring" competence. Perhaps its biggest weakness is that it assumes that the organizational dynamics characteristic of cardiovascular research is characteristic of the firm as a whole. Cardiovascular drugs are one of the largest and most important classes of drugs and thus central to the research program of nearly every firm in our sample, and we attempted to continually probe the validity of this assumption during our interviews, but we run some risks in applying measures of competence derived from our cardiovascular interviews to the analysis of data describing the full range of programs. Moreover it introduces a substantial element of subjective judgement into the analysis. This has its advantages -- as several authors have suggested, one might expect it to be intrinsically difficult to "measure" strategically significant organizational competencies since competencies that are easy to describe or measure may be inherently less likely to be an enduring source of competitive advantage (Barney,

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understood (such as the ACE inhibitors) and less effective agents that have been used for many years and whose mechanism of action is only dimly guessed at (drugs such as digitalis and some of the antiarrhythmic agents fall into this category). Moreover cardiovasculars are one of the largest and most rapidly growing classes of drugs, and in consequence every firm in our sample had a substantial investment in cardiovascular research. In 1978 they were around 16% of all drugs sold in the U.S. and 15% world wide, while as of 1988, cardiovascular drugs represented just over 22% (by value) of all drugs sold by in the U.S. and around 19% of all drugs sold world wide. (Decision Resources, "World Wide Pharmaceutical Industry," 1990).

1991; Nelson, 1991) and by relying on in depth field interviews to construct measures of competence one can hope to capture some of the richness and complexity that may be fundamental to the concept. But these measures are inevitably filtered through the investigators' preconceptions and beliefs, and in the case of this study this problem was compounded by the fact that severe confidentiality restrictions made it impossible to share the interview transcripts with other researchers.

Our approach does have a number of strengths. It permits the construction of detailed measures that are rooted in the experience of multiple informants. For example, rather than asking each informant, (either in person or by questionnaire), "did you use cross functional teams in 1978? In 1979? In 1980?" we asked "how was the hypertensive program organized?" "How well did that work?" "When did things change?" We believe that linking our questions about structure and process to particular scientific events in this way offers two significant advantages. Firstly we believe that it increases the accuracy of our measures. Nearly all of our respondents responded positively to the question "did you use teams?" for example, but by exploring the pattern of problem solving around particular scientific discoveries in detail we were able to gain a much richer understanding of the ways in which cross disciplinary communication was managed inside the firm. Secondly we believe that the use of a narrative history as a structuring device increased the probability of being able to traces changes in organizational structure or process over time, since in general those we interviewed had very clear memories of the timing of particular scientific events, and these dates could be used to anchor discussions of the changes in the ways in which research was organized within the firm. Thus we hope to be able to capture variation in organizational competence within as well as between firms.

Measuring Organizational Competence

We constructed a number of measures of organizational competence. Recall that we hypothesized that "competent competence" in pharmaceutical research might accrue along two dimensions. Firms might develop unique disciplinary skills, or they might develop unique competencies in particular disease areas. Since we do not have comprehensive data about the distribution of disciplinary skills within our sample firms we were unable to test formally the hypothesis that drug discovery productivity is an increasing function of firm specific expertise in particular disciplinary areas. Examining publications in the open scientific literature, however, suggests that firms do indeed differ in this respect. We can, for example, reject the hypothesis that the proportion of publications in quite broadly defined categories such as pharmacology and medicinal chemistry is constant across firms.

In order to test our second hypothesis, that drug discovery productivity is an increasing function of component competence in particular disease areas, we included KPATS, the stock of patents obtained in each program, as a dependent variable, where we calculate the stock by assuming a 20 percent "depreciation rate" for knowledge, δ. We reasoned that firms with competencies in a particular area are more likely to have obtained patents in that area historically. Notice, however, that the interpretation of the coefficient on this variable is complicated by the fact that it resembles the lagged dependent variable. Although we control for differences in scientific opportunity across programs by including therapeutic classes in our analysis, KPATS may capture other sources of unobserved heterogeneity across programs in addition to those introduced by the firm's unique competence in the field.

We constructed a number of variables in an attempt to measure architectural capabilities. In order to test our third hypothesis we included PROPUB as an explanatory variable, where PROPUB was constructed from the interview transcripts using a five point Likert scale, where the firm was coded 5 if standing in the larger scientific community was a dominant criterion for the promotion of scientific personnel and 1 if an individual's publication record and reputation in the wider community were not significant factors in promotion decisions. We constructed a variety of alternative measures of the degree to which a firm actively promoted the flow of information across its borders, including GEOG, a measure of the closeness of the firm's corporate headquarters to a research university and UNIV, a measure of the degree to which the firm was deeply involved in joint research projects with one or more major research universities. We found, however that the three measures were very highly correlated, and only PROPUB is included in the reported results.

This close correlation highlights an intriguing result of our research. Our qualitative work suggests, for example, that firms that are tightly connected to the larger scientific community invest heavily in a number of related activities: not only do they promote individuals on the basis of their standing in the larger scientific community, but they also tend to be located close to major research universities with whom they have close ties, and to invest heavily in information sources such as libraries and seminar series. This echoes Milgrom and Roberts' (1990) suggestion that organizational competencies are probably composed of several tightly linked complementary activities, and suggests that our measures are best interpreted as "symptoms" or "indicators" of the presence of architectural competence, rather than as causal variables. We return to this point in our interpretation of the results.

We constructed three additional variables to test our fourth hypothesis and to explore the

degree to which the firm was able to integrate knowledge flexibly across disciplines and disease areas within the firm: CROSS, DICTATOR and GLOBAL. Clark and Fujimoto (1991) and Tabrizi and Eisenhardt (1994) hypothesize that in complex, turbulent environments firms that make extensive use of cross functional teams will outperform those that do not. Thus CROSS is measured on a five point Likert scale, where in any given year a firm scored "5" if problem solving within the cardiovascular research programs appeared to be characterized by the frequent exchange of rich, detailed information across disciplinary or disease area boundaries and "1" if there was very little communication within the program or across programs within the firm. All of the firms in our sample manage global research activities. Since Westney (1991) has suggested that global research efforts that are organizationally fragmented will be significantly less productive that those that are managed as a coherent whole we included GLOBAL as a dependent variable, where at the extremes for any given year a value of "5" was assigned if global research was managed as a seamless whole under a single director while a value of "1" was assigned if geographically dispersed research units were managed through entirely separate organizations within the firm.

DICTATOR is also scored on a five point Likert scale, where in any given year a firm scored a "5" if resource allocation within research was entirely controlled by a single individual and a "1" if resource allocation was entirely decentralized and managed through a governing committee. Our qualitative work suggested that the use of a "Dictator" to allocate resources had both advantages and disadvantages. While it permitted the rapid transfer of resources across the firm it also tended to reduce the richness of information flow across programs since it placed a premium on the transfer of information vertically, to the central decision maker. Management by committee, on the other hand, while slow, appeared to encourage extensive and sometimes unexpected exchanges of information across programs. Thus we hypothesize that firms that do not use dictators to allocate resources will, all other things equal, be more productive than their rivals as a reflection of an architectural competence in the exchange of information across the firm.

One interesting question about these measures is the extent to which they vary within and between firms. Table (1b) presents ANOVA results for all four variables, decomposing their total variance into "between" and "within" components. In all cases there is a statistically significant fixed firm effect, suggesting that these variables will be of some use in accounting for firm-level differences in research productivity. However most of the variance is between rather than within firms -- while these organizational characteristics do change over time, this variation is small compared to the relatively stable differences among firms. Notice that GLOBAL hardly changes at all within firms: the

R^2 from regressing it on to firm dummies is over 0.99.

Control Variables

We constructed a variety of variables to control for other factors that might affect research productivity, including the size, shape and scope of the research portfolio and the effects of internal and external spillovers. A full description of these variables and a discussion of their significance is given in our paper "Scale, Scope and Spillovers" and is briefly summarized in the Appendix. We also constructed a variety of measures of scientific opportunity. These are described in our paper "Racing to Invest? The Dynamics of Investment in Ethical Drug Discovery" (Cockburn and Henderson, 1994). Since these measures proved generally insignificant they are not reported here, and we rely on our use of therapeutic class dummies to control for differences in opportunity across classes.

Results

Exploring the Roots of Firm Heterogeneity at the Firm level.

We focus first on the analysis of research productivity at the firm level (Table (2)). Discovery, stock of discovery, scope and scope-squared are included as control variables. A comparison of models (1) and (2) dramatically demonstrates the importance of firm effects. Introducing dummy variables for each firm into the regression substantially increases the log likelihood function and the R^2 of the model rises from 0.49 to 0.86[6]. This is in line with previous research, and lends credence to a focus on firm specific competence as a factor in competition. Notice that including firm dummies in the regression results in quite large changes in the coefficients on the control variables, confirming that some important determinants of research productivity are not being captured in the first model.

The firm dummies pick up a variety of effects. As well as the organizational effects with which this paper is concerned, they also capture factors such as systematic differences across firms in their propensity to patent, accounting practices and labor market conditions in different countries. Although at the request of the firms supplying the data we do not report the estimated coefficients on these dummies here or in the other Tables, they are jointly and separately highly significant in all of

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[6] R^2 is calculated as the squared correlation between observed values of Y and fitted values of Y from the Poisson regression.

the models estimated, and the ranking of firms according to these dummies conforms to our beliefs from our qualitative work about their relative innovative performance.

Since we cannot control for program specific competencies in these aggregate data we begin to explore these firm level effects by testing hypotheses III and IV. Model (3) introduces our measures of architectural competence. PROPUB and DICTATOR have the expected sign, but PROPUB is only marginally significant, and CROSS and GLOBAL not only have the "wrong" sign but are also significant. Including firm dummies in model (4) suggests that these rather puzzling results may be a function of specification error, since when we control for firm effects PROPUB and DICTATOR both become strongly significant with the expected signs while CROSS and GLOBAL are insignificant. In model (5) we introduce the firm's total stock of patents as an additional measure of firm heterogeneity, but it is not significant.[7] We find this unsurprising since aggregation across programs makes this a very poor measure of competence.

The standard likelihood ratio tests indicate that our measures of architectural competence are significantly related to research productivity. Comparing the fit of models (1) and (3) we see that the organizational variables explain a substantial amount of the variance in patenting at the firm level. However these variables only marginally improve the fit of the equation when firm dummies are present. This reflects the fact that the firm dummies and architectural competence variables are not orthogonal. In fact though individual correlation coefficients between the competence variables and the firm dummies are not particularly high, the two sets of variables essentially span the same space. The first three canonical correlation coefficients between PROPUB, CROSS, DICTATOR and GLOBAL and the firm dummies are greater than 0.9. Bearing this in mind, we interpret these results as suggesting that our measures of competence <u>are</u> the firm effect captured by the firm dummies, with the difference in fit between models (3) and (4) attributable to "noise" such as inter firm differences in propensity to patent.

Thus the firm level analysis suggests that heterogeneity across firms plays a significant role in determining variation in research productivity, and provides significant support for our third and

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[7] One potential problem with these results is that the Poisson assumption may be inappropriate. Alternative estimation techniques for count data yield essentially similar results, though the standard errors are much larger when we allow for overdispersion, and there are quite large changes in some of the coefficients. However we are not overly concerned by these results since we have so few observations at this level of aggregation, and the desirable properties of these more general estimators are only obtained asymptotically. We return to this issue in our analysis of the much larger sample of program level data.

fourth hypotheses. Two of our measures of architectural capability are significant and all have the expected sign, suggesting that the ability to integrate knowledge across and within the boundaries of the firm is an important determinants of heterogeneous competence.

Exploring Firm Heterogeneity at the Program Level

The results of Table (2) suggest that there are significant and persistent differences in firm productivity, and that these differences may be partly driven by variations in organizational process. However a number of important effects cannot be adequately controlled for in firm level data, particularly variation in the mix of technological areas in which the firm is investing and the effects of knowledge spillovers. Controlling for "composition" effects is important since scientific opportunity varies considerably across programs, and all other things equal firms that invest in outstandingly fruitful areas will be more productive than those that do not. Similarly, in "Scale, Scope and Spillovers" we showed that internal and external spillovers of knowledge across research programs have important implications for productivity. Moreover it is very difficult to operationalize the notion of local competence at an aggregate level in a multiproduct firm. Thus we move next to the analysis of program level data (Table (3)).

The results in Table (3) confirm the importance of controlling for therapeutic class effects and spillovers -- these variables are strongly significant in all the regressions. Including firm dummies in the regression (model (2)) significantly increases both the log likelihood function and the proportion of variance explained, but they are much less important than in the aggregate data. Some part of the firm effect identified in Table (2) appears to be a composition effect: in the absence of therapeutic class dummies, fixed firm effects pick up variation in research productivity across firms arising from their differential specialization in different technological areas. (Note that as in the firm data, because firm dummies, therapeutic class dummies, and other variables in the regression are correlated, we cannot unambiguously partition R-squared into X% = FIRM, Y% = CLASS etc.)

Model (3) includes our measure of local competence, KPATS, the stock of patents previously obtained in each program. KPATS has a very significant effect on productivity, increasing the proportion of variance explained from 50% to 68% and significantly increasing the likelihood function. This result gives strong support for our second hypothesis: "local" competence appears have a very significant impact on research productivity. But while this result is encouraging it must be interpreted with care since KPATS is close to the lagged dependent variable and as such captures a wide variety of unobserved local heterogeneity, including variations in scientific opportunity which

are not captured by the fixed therapeutic class effects and differences in local propensities to patent.

Model (4) introduces our measures of architectural competence. As was the case in the aggregate analysis, omitting firm dummies gives puzzling results. CROSS and GLOBAL have the "wrong" signs and PROPUB is only marginally significant. In model (5), our preferred model, all four variables have the expected sign although again only PROPUB and DICTATOR are significant.

Notice that as in Table (2), our measures of architectural competence only marginally improve the overall fit of the equation in the presence of other controls for firm heterogeneity. It is not that these variables are unimportant -- in model (4) where they are included in the regression by themselves, they significantly improve the fit of the model. The problem is that a large proportion of the firm effect captured by the firm dummies is precisely the same phenomena that we are modelling with our architectural competence variables. As the ANOVA results above indicate, firm dummies account for much of the variation in the architectural competence variables and canonical correlation analysis indicates that the two sets of variables are very closely associated in a multivariate sense. Thus it is very difficult to separate out their contributions to the explanatory power of the regression.

In Table (4) we explore the validity of the Poisson specification. The first column includes model (5) from Table (3) for comparison. Model (6) reports the Negative Binomial results, and models (7) and (8) the Non Linear Least Squares and GMT models respectively. The results suggest that our initial conclusions are quite robust. Although these data are clearly overdispersed, with the exception of the NLLS specification the results are quite similar across models. The consistent and efficient GMT estimator gives particularly encouraging results. PROPUB and GLOBAL are highly significant, with a positive impact on research productivity, while DICTATOR is also highly significant and as expected has a negative effect.

Collinearity between the architectural competence variables, the firm dummies and some of the control variables -- particularly SIZE and SCOPE -- is such that we hesitate to place too much weight on the relative magnitudes of these coefficients. But the estimated effects of PROPUB and DICTATOR are quite robust to changes in the set of explanatory variables included in the model, and we think that they are capturing important aspects of firm heterogeneity.

Conclusions and Directions for Further Research

Conclusions

Our results provide considerable support for the importance of "competence" as a source of advantage in research productivity. Idiosyncratic firm effects account for a very substantial fraction of

the variance in research productivity across the firms in our sample, and we find support for all three of the four hypotheses that we can explore with these data. Research productivity certainly increases with historical success, and to the degree that cumulative success is a reasonable proxy for the kinds of "local competence" identified in the literature, our results suggest that differences in local capabilities may play an important role in shaping enduring differences between firms. We also find that two of the measures that we constructed to measure architectural competence are significantly correlated with research productivity. Firms in which publication records are an important criteria for promotion appear to be more productive than their rivals, as are firms which use committees to allocated resources rather than relying on a single "dictator."

Our results suggest that a focus on "architectural" or "integrative" or "combinative" capabilities as a source of enduring competitive advantage may provide useful insights into the sources of enduring differences in firm performance, but they have challenging implications on two fronts.

In the first place, they highlight the methodological problems inherent in attempting to measure "organizational competence." A comparison of the results of our analysis conducted at the firm level with that conducted at the program level suggests that a significant fraction of any firm effect in research productivity identified at the aggregate level may simply reflect a failure to control for the structure of the research portfolio. To the degree that firms in a wide variety of seemingly homogeneous industries also differ in the composition of their research or product portfolios any interpretation of heterogeneity at the firm level in terms of competence must be treated with caution.

Similarly, despite the fact that we have been able to collect unusually detailed data, we cannot convincingly separate the effects of local competence in a particular field from other sources of unobserved heterogeneity. Our results suggest that there are important, long lived sources of heterogeneity in research productivity across programs. While this finding is consistent with the presence of important local capabilities, there are other possible explanations: for example the result may just reflect differences in the nature of the work being undertaken across programs or in local propensities to patent. Our qualitative work leads us to believe that there are indeed important local capabilities, but their presence is hard to prove convincingly in these data.

Our measures of architectural competence are also subject to problems of interpretation. Recall, for example, that PROPUB is closely correlated with several other measures of the degree to which the firm is linked to its wider scientific context, particularly to indicators of its geographical location and of its degree of involvement with academic science. Similarly our variable DICTATOR proxies for a complex set of organizational behaviors. These variables may be measures of symptoms

as much as they are measures of causes: firms that can manage the organizational strains inherent in using a committee to allocate research resources have typically developed a repertoire of behaviors that together support a rich flow of information within the firm. Firms that promote leading scientists on the basis of their publication records are also likely to be located close to important centers of medical research and to be deeply involved with the academic medical establishment.

In the second place, our analysis highlights the importance of exploring the *sources* of organizational competence and their implications for the strategic choices made by the firm. One of our most interesting results is that small changes in the ways in which research is managed inside the firm appear to have major implications for its productivity. Our estimated coefficients imply, for example, that the research efforts of firms which score the highest on the use of publication records as an important criteria in promotion are 38% more productive those at the bottom end of the scale, all else equal. Similarly, firms that allocate resources through a process of consensus appear to be as much as 55% more productive than those which use a "dictator". These effects may be confounded with other unobserved determinants of research productivity, and thus their magnitudes may be miss-estimated, but nonetheless we find them surprisingly large. Given the apparently large payoff to changing the organization and management of this crucial function, it is puzzling that there are such large and persistent differences across firms in these dimensions.

There are a number of possible explanations for this observation. The first is that the capabilities we have measured are fundamentally inimitable, in the sense described by Peteraf (1993). Although there might be widespread agreement within the firm that moving to a resource allocation system based around internal peer review is inherently desirable, it might still be difficult to do, partly because such a system must be supported by a complex set of organizational routines that are difficult to replicate and observe (Milgrom and Roberts, 1990).

The second is that the failure to adopt efficient techniques for managing research reflects agency problems in the firms which would have benefited from these changes. Several of the firms in our sample were very successful in the early sixties, and it may be the case that well known difficulties in monitoring the productivity of research (Holmstrom, 1989) together with failures in the market for corporate control permitted them to continue running inefficient research organizations. A third possibility is that our measures reflect the quality of the scientists recruited by our sample companies, rather than any fundamental difference in the quality of the information flow within the organization. To the degree that world class scientists insist on being able to publish in the open literature, and on control of their own research budgets through peer reviewed committees, it may be

the case that our measures describe the conditions necessary to recruit the best possible scientists. Research within the tradition of human resource management, for example, has begun to explore the differential effects of organizational mechanisms such as teams on performance, and has insisted on the importance of controlling for heterogeneous labor quality in such an analysis (Greenan, Guellec, Broussaudier and Miotti, 1993; Ichniovski, Shaw and Prennushi, 1993). Lastly, of course, it may simply be the case that our measure of innovative output is not capturing all of the relevant dimensions of innovative success. Firms that are less productive in generating "important patents" may, in fact, still be strategically or economically very successful. We are actively pursing these questions in our ongoing research.

To the degree that our results are generalizable beyond the pharmaceutical industry to other research intensive settings, they support the view that the ability to integrate knowledge both across the boundaries of the firm and across disciplines and product areas within the firm is an important source of strategic advantage. While our analysis offers insight into the organizational determinants of research productivity, it also raises a number of intriguing questions. Attempts to quantify the nature and effects of organizational competence empirically offer a fruitful avenue for further research.

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Table (1a): Descriptive Statistics: Selected variables at the research program level.

Variable	Regression Sample, 1975-1988. N=3120			
	Mean	Std. Dev.	Minimum	Maximum
Discovery, 1986$m	1.06	2.31	-3.61	20.18
Stock of Discovery	2.987	6.42	-2.21	55.19
SCOPE: Number of programs with discovery > $500k, 1986$.	10.47	4.66	2.00	19.00
SIZE: Total research spending this year	33.54	22.96	4.970	>120
News in own patents	0.44	3.24	-13.60	20.49
News in competitors' patents	9.00	19.62	-91.84	128.3
News in competitors' patents in related programs	26.66	40.59	-106.6	168.2
KPATS: Stock of own patents	7.76	12.02	0.00	98.18
PROPUB: Publication plays a key role in promotion	3.15	1.49	1.00	5.00
CROSS: Firm sustains a rich information flow across boundaries	2.97	1.28	1.00	5.00
DICTATOR: Single individual makes resource decisions	2.42	1.63	1.00	5.00
GLOBAL: World wide research managed as an integrated whole	3.00	1.54	1.00	5.00

Table (1b) - ANOVA results

Variable N=120	Between Firm Mean Square d.f. = 9	Within Firm Mean Square d.f.=110	F-ratio	R^2
DICTATOR	20.78	1.26	16.46	0.57
PROPUB	21.38	0.53	40.18	0.77
CROSS	8.27	1.08	7.67	0.39
GLOBAL	28.60	0.01	2201.88	0.99

Table (2): Determinants of patent output at the FIRM level.
Poisson Regression. Dependent variable = Total Firm Patents, 120 observations.

	(1)	(2)	(3)	(4)	(5)
Firm dummies		Sig.		Sig.	Sig.
PROPUB: Publication plays a key role in promotion.			0.033 (0.017)	0.132** (0.034)	0.113** (0.036)
CROSS: Firm sustains a rich info. flow across boundaries.			-0.151** (0.015)	-0.032 (0.031)	-0.021 (0.032)
DICTATOR: Single indiv. makes key resource decisions.			-0.112** (0.015)	-0.096** (0.020)	-0.091** (0.020)
GLOBAL: Worldwide research managed as an integrated whole.			-0.037** (0.012)	1.250 (1.047)	1.271 (1.048)
Stock of own patents					0.001 (0.000)
Intercept	1.356** (0.344)	1.249** (0.368)	1.549** (0.364)	-1.258 (2.118)	-0.834 (2.133)
Dum78	1.459** (0.351)	1.171** (0.375)	1.733** (0.369)	1.549** (0.389)	0.988 (0.516)
Ln(SIZE): Total Firm Research	-0.222** (0.050)	-0.022 (0.069)	0.151* (0.059)	0.006 (0.071)	0.033 (0.073)
Ln(Total Firm Stock of Research)	0.860** (0.048)	0.967** (0.084)	0.435** (0.055)	0.853** (0.095)	0.784** (0.103)
SCOPE: No. programs >500K '86$	0.255** (0.019)	-0.009 (0.026)	0.256** (0.025)	-0.017 (0.029)	-0.023 (0.030)
SCOPE * SCOPE	-0.014** (0.001)	-0.002* (0.001)	-0.013** (0.001)	-0.001 (0.001)	-0.001 (0.001)
Time	-0.049* (0.019)	-0.082** (0.022)	0.002 (0.020)	-0.059** (0.022)	-0.077** (0.025)
Time * Dum78	-0.086** (0.020)	-0.069** (0.022)	-0.101** (0.021)	-0.088** (0.022)	-0.058* (0.028)
Log-likelihood	-1195	-623	-974	-608	-607
Pseudo R-squared	0.490	0.859	0.655	0.862	0.863

Notes to Tables (2) through (4)

Standard errors in parentheses.

ln(variable) is set=0 when variable=0, and an appropriately coded dummy variable is included in the regression.

** Significant at the 1% level.

* Significant at the 5% level.

Table (3): Determinants of patent output at the research program level.
Poisson Regression. Dependent variable = Patents, 3210 observations.

	(1)	(2)	(3)	(4)	(5)
Therapeutic class dummies	Sig.	Sig.	Sig.	Sig.	Sig.
Firm dummies		Sig.			Sig.
Stock own pats in this program			0.039** (0.001)		0.034** (0.001)
PROPUB: Publication plays a key role in promotion.				0.027* (0.017)	0.081** (0.032)
CROSS: Firm sustains a rich info. flow across boundaries.				-0.169** (0.016)	0.030 (0.029)
DICTATOR: Single ind. makes resource decisions.				-0.111** (0.014)	-0.115** (0.018)
GLOBAL: W. wide research managed as integrated whole.				-0.059** (0.011)	1.531 (1.046)
Intercept	-2.263** (0.144)	-1.517** (0.179)	-1.346** (0.143)	-1.928** (0.167)	-4.059* (2.094)
Dum78	0.184** (0.062)	0.085 (0.071)	-0.216** (0.063)	0.106 (0.067)	-1.289* (0.074)
Ln(Discovery)	0.046** (0.011)	0.046** (0.011)	-0.016 (0.011)	0.072** (0.011)	-0.012 (0.011)
Ln(Stock of Discovery)	0.075** (0.011)	0.089** (0.011)	0.022** (0.010)	0.055** (0.010)	0.038** (0.010)
Ln(SIZE): Total research spending by firm.	0.461** (0.031)	0.229** (0.063)	0.271** (0.032)	0.534** (0.041)	0.219** (0.069)
SCOPE: Number of programs > 500K '86$	0.208** (0.019)	-0.027 (0.026)	0.164** (0.019)	0.209** (0.024)	-0.018 (0.029)

SCOPE * SCOPE	-0.012** (0.001)	-0.001 (0.001)	-0.009 (0.001)	-0.012** (0.001)	-0.002 (0.001)
News in patents in related programs	0.033** (0.004)	0.020** (0.004)	0.031** (0.004)	0.031** (0.004)	0.023** (0.004)
News in competitors' patents in this program	0.009** (0.001)	0.009** (0.001)	0.004** (0.001)	0.009** (0.001)	0.004** (0.001)
News in competitors' patents in related programs	0.001* (0.001)	0.001* (0.001)	0.003* (0.001)	0.001* (0.001)	0.003* (0.001)
Time	0.037* (0.020)	0.029 (0.021)	0.050** (0.020)	0.050** (0.020)	-0.034 (0.022)
Time * Dum78	-0.115** (0.021)	-0.771** (0.022)	0.004 (0.021)	-0.087** (0.021)	-0.005 (0.023)
Log-likelihood	-6388	-5811	-5366	-6085	-5208
Pseudo R Squared	0.383	0.503	0.682	0.446	0.693

Table (4): Determinants of patent output at the research program level. Exploring Econometric Issues. Dependent variable = Patents, 3210 observations.

	(5) Poisson	(6) Neg.Bin.	(7) NLLS	(8) GMT
Therapeutic class dummies	Sig.	Sig.	Sig.	Sig.
Firm dummies	Sig.	Sig.	Sig.	Sig.
Stock own pats in this program	0.034** (0.001)	0.049** (0.002)	0.029** (0.002)	0.046** (0.003)
PROPUB: Publication plays a key role in promotion.	0.081** (0.032)	0.124** (0.046)	-0.006 (0.062)	0.399** (0.074)
CROSS: Firm sustains a rich info. flow across boundaries.	0.030 (0.029)	0.033 (0.042)	0.009 (0.062)	0.007 (0.047)
DICTATOR: Single ind. makes resource decisions.	-0.115** (0.018)	-0.117** (0.026)	-0.064* (0.035)	-0.137** (0.033)
GLOBAL: W. wide research managed as integrated whole.	1.531 (1.046)	1.615* (1.059)	0.999 (1.011)	2.572** (0.531)
Intercept	-4.059* (2.094)	-4.345* (2.124)	-2.693 (2.035)	-6.472** (1.113)
Dum78	-1.289* (0.074)	-0.055 (0.114)	-0.392** (0.170)	0.103 (0.165)
Ln(Discovery)	-0.012 (0.011)	0.022 (0.016)	-0.046* (0.020)	0.053** (0.021)
Ln(Stock of Discovery)	0.038** (0.010)	0.034* (0.015)	0.044* (0.022)	0.064** (0.017)
Ln(SIZE): Total research spending by firm.	0.219** (0.069)	0.190* (0.107)	0.234* (0.144)	0.216* (0.134)

SCOPE: Number of programs > 500K '86$	-0.018 (0.029)	-0.073* (0.044)	0.025 (0.074)	-0.218** (0.040)
SCOPE * SCOPE	-0.002 (0.001)	0.001 (0.002)	-0.003 (0.003)	0.006** (0.002)
News in patents in related programs	0.023** (0.004)	0.032** (0.007)	0.011 (0.007)	0.029** (0.009)
News in competitors' patents in this program	0.004** (0.001)	0.008** (0.001)	0.001 (0.002)	0.003 (0.001)
News in competitors' patents in related programs	0.003* (0.001)	0.002* (0.001)	0.003* (0.001)	0.004** (0.001)
Time	-0.034 (0.022)	-0.033 (0.035)	-0.083* (0.045)	0.023 (0.054)
Time * Dum78	-0.005 (0.023)	-0.007 (0.036)	0.057 (0.049)	-0.076 (0.055)
Log-likelihood Alpha	-5208	-4721 2.367	-7020	-4576

Appendix: Data Sources and Construction

The data set used in this study is based on detailed data on R&D inputs and outputs at the research program level for ten ethical pharmaceutical manufacturers.

Inputs

Our data on inputs to the drug research process are taken from the internal records of participating companies, and consist primarily of annual expenditures on exploratory research and research by research program. Several issues arise in dealing with these data.

(a) Research vs. Development

We define resources devoted to research (or "discovery," in the terminology of the industry) as all pre-clinical expenditures within a therapeutic class, and development as all expenses incurred after a compound has been identified as a development candidate. We attributed exploratory research to a particular program wherever possible, but exploratory research that could not be so assigned was included in overhead. Clinical grants are included in the figures for development, and grants to external researchers for exploratory research are included in the total for research. In some cases, the companies supplied us with data already broken down by research versus development by research program. In others, we had to classify budget line items for projects/programs into the appropriate category. This was done based on the description of each item in the original sources, and the location of items within the structure of the company's reporting procedure.

(b) Overhead

In order to maintain as much consistency in the data collection process as possible, we tried to include appropriate overhead charges directly related to research activities, such as computing, R&D administration and finance etc., but to exclude charges relating to allocation of central office overhead etc. The overhead also includes some expenditures on discipline-based exploratory research such as "molecular biology" which appeared not to be oriented towards specific therapies. Overhead was allocated across therapeutic classes according to their fraction of total spending.

(c) Licensing

We treat up-front, lump sum payments in respect of in-licensing of compounds, or participation in joint programs with other pharmaceutical companies, universities or research institutes, as expenditure on research. Royalty fees and contingent payments are excluded. Though increasing over time, expenditures on licensing are a vanishingly small fraction of research spending in this sample.

Outputs

In this paper we use "important" patent grants as our measure of research output. We count patents by year of application, where we define "importance" by the fact that the patent was granted in two of the three major markets: the USA, Japan, and the European Community. These data were provided by Derwent Publications Inc, who used their proprietary classification and search software to produce counts of "important" patents to us broken down by therapeutic class for 29 US, European, and Japanese pharmaceutical manufacturers for the 1961 to 1990. These firms were chosen to include the ten firms that have given us data together with 19 other firms chosen on the basis of their absolute R&D expenditures, R&D intensity, and national "home base" to try to get a representative, rather than exhaustive, assessment of world-wide patenting

activity. The 19 firms have been consistently in the top 40 world wide pharmaceutical firms in terms of R&D dollars and sales.

Note that many of these patents will be "defensive" patents in that firms may patent compounds they do not intend to develop in the short term but that may have competitive value in the longer term, and that we were not able to exclude process patents. Alternative measures of "importance" such as citation weighting and more detailed international filing data proved prohibitively expensive to construct.

Classification

Classification of inputs and outputs by therapeutic class is important because this drives our measure of spillovers. There are essentially two choices: to define programs by physiological mechanisms, e.g. "prostaglandin metabolism", or by "indications" or disease states, e.g. "arthritis". We have chosen to classify on the basis of indication, largely because this corresponds well to the internal divisions used by the companies in our sample (which is conceptually correct), but also because classification by mechanism is much more difficult (a practical concern.) We classified both inputs and outputs according to a scheme which closely follows the IMS Worldwide classes. This scheme contains two tiers of aggregation: a detailed "research program" level, and a more aggregated "therapeutic class" level which groups related programs. For example, the therapeutic class "cardiovascular" includes the research programs "anti-hypertensives", "cardiotonics", "antithrombolytics", "diuretics" etc.

There are some problems with this procedure. Firstly, some projects and compounds are simply very difficult to classify. A particular drug may be indicated for several quite distinct therapies: consider serotonin, which has quite different physiological actions on either side of the blood-brain barrier. As a neurotransmitter it is believed to play important roles in mediating motor functions. As a systemic hormone it has a variety of effects on smooth muscle, for example it functions as a vasoconstrictor. Some companies report expenditures in areas which are very difficult to assign to particular therapeutic classes: a company doing research using rDNA technology might charge expenditure to an accounting category listed as "Gene Therapy/Molecular Biology" which is actually specific research performed on e.g. cystic fibrosis, but we were forced to include these expenditures in "overhead". Secondly, our two-tier classification scheme may not catch all important relationships between different therapeutic areas. We believe that we are undercounting, rather than overcounting spillovers in this respect. Thirdly, where firms supplied us with "pre-digested" data, they may have used substantively different conventions in classifying projects. One firm may subsume antiviral research under a wider class of anti-infectives, while another may report antivirals separately. Not surprisingly there are major changes within companies in internal divisional structures, reporting formats, and so forth, which may also introduce classification errors. After working very carefully with these data, we recognize the potential for significant miss-assignment of outputs to inputs, but we believe that such errors that remain are not serious. Using patents (as opposed to INDs or NDAs) as the output measure should reduce our vulnerability to this problem, since we observe relatively large numbers, and a few miss-classifications are unlikely to seriously affect our results.

Matching

Data series on inputs and outputs for each firm were matched at the research program level. This procedure appears to successfully match outputs and inputs unambiguously for the great majority of programs. In a very few cases, however, we ended up with research programs where patents, INDs or NDAs were filed, but where there were no recorded expenditures. Of these the majority were obviously coding errors or reflected dilemmas previously encountered in the classification process, and appropriate corrections were made. In other cases, it was clear that these reflected "spillovers" -- research done ostensibly in, for example, hypertension, may generate knowledge about the autonomic nervous system which prompts patenting of compounds which

may be useful in treating secretory disorders (e.g. ulcers.) In such cases we set "own" inputs for the program equal to zero, and included these observations in the data base.

Deflation

Since our data sources span many years, it is important to measure expenditures in constant dollar terms. We used the biomedical research and development price index constructed by James Schuttinga at the National Institutes of Health. The index is calculated using weights that reflect the pattern of NIH expenditures on inputs for biomedical research, and thus in large measure reflects changes in the costs of conducting research at academic institutions. However since the firms in our sample compete directly with academic research laboratories for scientific talent we believe that this index is likely to the most appropriate publicly available index, and our results proved to be very robust to the use of alternate indices. In a later paper we intend to exploit the information that some companies were able to give us on R&D inputs in units of labor hours to construct an index specifically for research costs in the pharmaceutical industry.

Construction of stock variables

Annual flows of research and expenditures were capitalized following the procedure described by Hall et al. (The R&D Masterfile: Documentation, NBER Technical WP #72). In brief, we first assume a depreciation rate for "knowledge capital", δ, here equal to 20%. (This is consistent with previous studies, and as argued above is not going to be very important in terms of its impact on the regression results since no matter what number we chose, if the flow series is reasonably smooth we would still find it difficult to identify δ separately from the estimated coefficient on the stock variable.) We then calculate a starting stock for each class within firm based on the first observation on the annual flow: assuming that real expenditures have been growing since minus infinity at a rate g, we divide the first observed year's flow by $\delta+g$. Each year, the end-of-year stock is set equal to the beginning-of-year stock net of depreciation, plus that year's flow. For the cases where the annual flow was missing "within" a series of observations, we set it equal to zero. In almost all instances, these missing values occur after the expenditure flows have been declining towards zero: we are reasonably that these are "real" zeros and not missing data which should be interpolated. We used the same procedure to accumulate "stocks" of patents, based on the flow variables described above.