OUTSOURCING, EXTERNAL COLLABORATION, AND INNOVATION AMONG U.S. FIRMS IN THE BIOPHARMACEUTICAL INDUSTRY

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ABSTRACT

This paper examines the outsourcing patterns of U.S. firms in the biopharmaceutical industry. Data from an exploratory survey of 86 companies suggest that the outsourcing of strategic activities such as applied research and formulary development has started to decline among firms of all sizes, though noncore activities such as manufacturing and clinical trials continue to be outsourced at an accelerating pace. The data suggest that there is no correlation between outsourcing and innovation performance, but that external collaboration supports innovation in positive ways. The results also show that medium-sized firms tend to manage their external partners more efficiently than smaller or larger firms – especially with respect to innovation-oriented collaboration. Medium-sized companies are found to be the most innovative in terms of patents and new product introductions, despite lower levels of research-intensity than those observed for smaller and larger firms. The paper concludes with a brief discussion of the implications of the survey findings for technology analysis and strategic management.

Key words: biopharmaceutical industry, external collaboration, innovation, outsourcing, firm size.

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Introduction

Much of the recent literature on the innovation performance of the biopharmaceutical sector has focused on large firms or multinational corporations (e.g., Boasson et al., 2005; Lane and Probert, 2007; Tapon and Thong, 1999). This is a logical focus because major drug companies have long dominated biopharmaceutical activity in terms of employment, output, and research spending (for a recent overview, see Mittra, 2007). According to Booth and Zemmel (2004), however, large firms have recently been losing their share of new compounds in development to smaller pharmaceutical companies and specialized biotechnology players. Many of these small and medium-sized enterprises (SMEs) are positioned at the front end of product cycles that require enormous levels of research and development (R&D), as well as cutting-edge human capital. These SMEs must exhibit technological or research leadership in order to survive, as few small companies have the financial resources to withstand lengthy periods of innovation dormancy. Although the organization of the discovery function is well documented for large firms, this is not the case for SMEs operating in niche markets (often very high risk). A central goal of this paper is to compare SMEs with their larger counterparts across key dimensions of the product development process, including internal R&D, external collaboration, and outsourcing. A further goal is to compare the characteristics of exporters versus nonexporters. Foreign markets are often required to recoup earlier investments in new drug formulations, rendering an exporter versus nonexporter comparison potentially instructive.

Our interest in the SME component of the biopharmaceutical sector stems from three factors. First, SMEs have recently been capturing a growing share of the market for new drugs (Booth and Zemmel, 2004). Many of these firms operate in specialized markets where the distinction between pharmaceutical activity and biotechnology is blurred (hence our use of the term *biopharmaceuticals*). Second, the imperative to develop external sources of innovation support is arguably stronger for SMEs than for larger firms, if only because SMEs contain limited in-house resources for drug discovery. Third, R&D productivity in the biopharmaceutical industry has been falling steadily since the 1970s (Buxton and Easton, 2003). If SMEs are to survive or grow, then they will presumably need to generate better R&D returns than their larger counterparts.

Set against this backdrop, three interlinked questions are addressed in the empirical sections which follow. First, are innovation or export-participation rates sensitive to firm size? Second, do firms of different sizes exhibit different approaches toward external collaboration or outsourcing? And third, to what extent does location within an established biopharmaceutical cluster make a difference to firm-level innovation performance? Data for the inquiry come from a sample of 86 companies that participated in an exploratory survey in the winter of 2006. Supplementary data come from follow-up telephone interviews with a sub-sample of 20 respondents.

Our paper is organized as follows. The next section provides a research context for the study, along with an overview of current theoretical perspectives with regard to outsourcing and external collaboration. Next, we describe the survey methodology, and give a synopsis of the main characteristics of the sample. We then examine the sources of external innovation support for the survey firms and assess the contribution of these linkages to the product development process. Following this section, we describe the geography of these external linkages by type and review the role of cluster membership in supporting company

growth. The paper concludes with a brief discussion of the implications of the survey results for the strategic management of the innovation function.

From the outset, however, it should be conceded that we are not attempting to contribute to ongoing theoretical debates regarding the motives behind outsourcing or external collaboration (see Howells et al., 2008). Instead, our focus is empirical, exploratory, and descriptive. Even so, some of our findings will be of interest to R&D managers and/or students of industrial organization. In particular, we find that R&D outsourcing is no longer as popular as it once was – regardless of firm size.

Research Context

For firms operating in the life-sciences domain, including large companies, external linkages to tap specialized knowledge have become increasingly common in recent years (Howells et al., 2008; Lane and Probert, 2007). Although outsourcing to achieve cost-containment has been taking place for several decades, recent evidence suggests that many firms now outsource to access new knowledge, expertise, or technology (Lewin and Peeters, 2006). According to Yasuda (2005), the resource-based theory of external linkage development explains much of the recent outsourcing behavior of high-technology firms – notably in terms of collaborator selection. In knowledge-based sectors such as biopharmaceuticals, however, the role of firm size in the outsourcing decision has not been systematically explored. Intuitively, for example, one might expect SMEs to outsource a larger proportion of their *innovation budgets* than larger firms – if only because the latter sometimes invest billions of dollars per year on in-house R&D. This said, there is a paucity of empirical evidence to confirm or reject this suspicion.

From an economic perspective, outsourcing entails a *cost-driven* switch from internal to external input supply – and thus reflects an efficiency imperative. When a biopharmaceutical company outsources R&D, for example, the goal is typically to capitalize on the superior efficiency of external vendors with respect to specialized aspects of the drug development process – leaving in-house personnel to focus on more critical segments of the R&D function (e.g., exploratory research on promising compounds). External collaboration is also cost-driven, but only in the sense that individual collaborators do not possess the internal resources to work entirely on their own within a specific therapeutic domain. The decision to collaborate is powered by a need to access the human capital resources of complementary firms, some of whom may also be competitors (see Rothaermel and Boeker, 2008). It is important to differentiate between these two strategies from the outset, as outsourcing is driven primarily by the need for cost-containment, whereas collaboration is more strongly motivated by the need to access knowledge that cannot be readily generated via in-house investment.

For both *outsourcing* and *collaboration,* however, a source of ongoing and protracted debate concerns the question of whether such external linkages need to be forged within geographically restricted areas (e.g.. to promote speedy interaction) -- or whether long-distance relationships can be developed to exploit the best possible sources of innovation support (e.g., internet-assisted). The 'being there' school of thought that surged in the aftermath of Gertler's (1995) work on the machine tool industry now seems to have morphed toward a more hedged position, in that spatial proximity between network participants is now seen as a bonus – but long-distance relationships can work too (especially if distant suppliers or partners rank among the world's best). Although we have no interest in exploring

the 'death of geography' perspective (see Johnson *et* al., 2006), some of our data suggest that the 'being there' effect has not entirely disappeared. Contrary to our initial expectations, however, the proximity factor appears to be of only minor importance to SMEs.

The role of geographically clustered production in promoting innovation has been a topic of similar debate in recent years, with no clear resolution in sight as far as we can tell. The various theoretical arguments are compelling (e.g., Porter, 1998), but the empirical evidence is mixed (see St John and Pouder, 2006). As Watts et al (2006) observed, cluster membership is a useful but insufficient factor in the stimulation of successful innovation among industrial firms. Perhaps paradoxically, we find that large firms in the biopharmaceutical industry are more likely than smaller firms to perceive cluster membership as being important to the drug-development process. This finding has been reinforced by recent empirical evidence from Boasson et al (2007), who noted that larger U.S. biopharmaceutical companies tend to rank the importance of urbanization or agglomeration economies more strongly than their smaller counterparts. We return to this point later in the paper.

Several attributes of the biopharmaceutical industry should be flagged from the outset, as this segment of the U.S. manufacturing sector is unusual in at least three respects. First, many firms in this sector are classified as manufacturers under the North American Industrial Classification System (NAICS), but many do not actually manufacture drugs or anything else. For example, approximately 50 percent of the SMEs in our sample are research laboratories that develop new drug formulations that are then manufactured by larger companies. Second, some of these SMEs allocate as much as 100% of their annual revenues toward applied R&D, which means that operational funding comes from accumulated cash reserves, government grants, or investment injections from larger firms. A third and related point is that some of the most innovative and R&D-intensive firms in this industry sell knowledge rather than products – suggesting a case of NAICS classification error.

This said, several important changes have taken place in the organization of the biopharmaceutical sector since the 1980s (which is when economic geographers first started to explore this industry). First, the industry has become increasingly concentrated from a spatial standpoint – with most firms belonging to clusters of similar firms in related industries (see Rosiello and Orsenigo, 2008). Second, strategic alliances have become critically important to firms in this industry (see Xia and Roper, 2008). Indeed, locational clustering and external partnering are now well recognized as being important factors in overcoming innovation barriers, especially among smaller firms (Aharonson, Baum, and Plunket, 2008; Ebers and Powell, 2007; Greis, Dibner, and Bean, 1995). Since the 1980s, then, the innovation thrust among biopharmaceutical companies has become increasingly conditioned by external linkages (alliances), spatial clustering, and a general trend toward the integration of biotechnology with pharmaceutical activity.

Our study was framed with respect to three general expectations that were distilled from the recent literature, including: (1) external collaborative activity was expected to play a positive role in the innovation performance of the survey firms, most notably SMEs; (2) we anticipated that SMEs would be more prone to outsourcing than larger firms; and (3) location within a biotechnology cluster was envisioned as a competitive asset for all firms (regardless of size). This latter expectation was based on the fact that the

biopharmaceutical industry as a whole has become increasingly dependent on the biotechnology sector for the development of new drug formulations (Rothaermel and Boeker, 2008; Sen, 2007).

Survey Methodology

In a preliminary effort to explore the business characteristics of firms in this industry, self-administered questionnaires were mailed to the Chief Executive Officers (CEOs) or R&D Directors of 390 companies in November 2006. The sampling frame for the project was developed from the database of the North American Biotechnology Directory (May 2006). SMEs were defined as firms with less than 500 employees (small firms were defined as having 1-100 employees, whereas medium-sized firms were allocated to the 101-500 employee class).

From a total sampling base of 862 U.S. based companies, a random sub-sample of 390 companies (45%) was selected for the study and questionnaires were then mailed. Our research budget was limited, in that we could not afford to randomly sample more than 45% of the population. The survey instrument was pre-tested with a pilot study of 20 firms during April and May 2006. The results and feedback from the pilot study were used to design the final survey instrument. A cover letter and 4-page survey instrument was then distributed to the 390 R&D Directors or CEOs in November, 2006. A return postage-paid envelope was included in the survey package. Follow-up telephone calls and faxes were made to the companies during December, 2006. By the end of December, 2006, 60 usable responses were received (yielding an initial response rate of 15.4%). Second requests were mailed in January 2007 to the companies that had not responded. Follow-up telephone calls and faxes were made through the end of January 2007, and 26 additional completed surveys were received (giving a final response rate of 22.0%).

Although response rates of 20% or lower are common in survey research that focuses on business establishments, our 22% participation level was disappointing in light of the potential salience of the study to the target firms. Nevertheless, t-tests comparing early (n = 60) versus late respondents (n = 26) failed to uncover statistically significant differences between the two groups in terms of critical variables such as R&D-intensity, patent counts, levels of R&D outsourcing, and new product introductions. This said, we openly concede that a 22% response rate is insufficient to offer conclusive findings. Instead, our results should be treated as suggestive only.

Our survey instrument included questions which were both quantitative and qualitative in nature. Quantitative measurements of the variables ranged from categorical (yes/no), ordinal (5 point Likert scales) to interval (percent of total revenue, etc). The survey was divided into three sections. The first section solicited information on company ownership type, revenue, employment size, R&D-intensity, export activity, and growth characteristics. The second section asked about innovation and biotech collaboration. The third section asked about outsourcing strategies for research, product development, manufacturing, marketing, and distribution (a copy of the survey instrument can be obtained from the authors upon request).

To determine firm-level innovation performance, several measures were employed. These included the percentage of revenue used toward R&D, patent approvals received, and new product introductions over the past seven years. The study also measured the extent of innovation through collaboration with external partners.

Another critical measure was the extent of outsourcing of R&D and the impact on innovation. The survey instrument also included a section on export activity (e.g., growth rates, target markets, export-intensity levels). Here, our goal was to test for the presence of an inverted-U relationship between export-orientation and firm size. Borrowing from Dunning's (1979) model of foreign market entry (i.e., the eclectic paradigm), we expected the inverted-U to resemble a logistics curve (i.e. modest levels of export-intensity among small firms, high levels among medium-sized firms, and better than modest levels among large firms). Exports are not especially important to large biopharmaceutical firms because such firms tend to serve foreign markets via direct investment (i.e., subsidiary plants abroad). For SMEs, however, export participation often signals early product acceptance at the international level. Within the SME category, then, we expected to find significant organizational and/or performance differences between exporters versus nonexporters.

Export Characteristics of the Survey Firms

Our analysis begins with an overview of the characteristics of exporters versus non-exporters, disaggregated across the three size-classes of firms mentioned earlier (i.e., small, medium, and large). Five sets of statistically significant contrasts are evident from the data shown in Table 1. First, there is a direct relationship between firm size and export propensity (Chi-square = 9.21; p = 0.010). However, ANOVA tests for export-intensity revealed that medium-sized firms are significantly more export-oriented than their larger and smaller counterparts (p = 0.032). On average, medium-sized firms earned around 30% of their 2005 sales from export markets, compared to 25% among larger companies and 15% among smaller firms. Experimental scatterplots (not shown here) suggest that the inverted-U relationship mentioned earlier is in place for this industry. The data also point to a direct relationship between export propensity and company age (ANOVA p = 0.047), as well as between firm size and age (ANOVA p = 0.002). Although these findings are not especially remarkable, they do provide an important empirical context that we rejoin later in the paper.

A second feature of Table 1 is that small firms exhibit significantly higher levels of R&D-intensity than larger firms (ANOVA p = 0.002). This is notably the case among small firms that are export active. The latter allocated an average of 57% of their 2005 sales to R&D, compared to around 20% for larger firms. In terms of R&D productivity, however, it would seem that medium-sized firms enjoy a competitive edge. Over the last 7 years, medium-sized firms introduced an average of 10 patents per annum (74.3 in total) – compared to less than 3 per annum among large firms and slightly more than 3 per annum among small firms. Although the ANOVA p-value falls short of 0.05 in this case (p = 0.081), a crisper picture emerges when innovation is scaled as the percentage of 2005 sales represented by products that were developed and commercialized over the last 7 years. Here, medium-sized firms lead the pack by a considerable margin (ANOVA p = 0.011). Among medium-sized firms in the export class, for example, recently developed products accounted for 18% of 2005 sales – compared to 10% among large companies and 5% among smaller firms (ANOVA p = 0.032). Within the small firm class, moreover, it is noteworthy that exporters enjoy a significant innovation advantage over their nonexporting counterparts.

Table 1. Size of firm by export-involvement, age, R&D-intensity, patent counts, and new product introductions: cross tabulation, ANOVA and t-tests. *

Size of firm		Small	Medium	Large	All
( ) = % of column [ ] = export-intensity					
Exports	**Yes**	23 (46) [15.3]	13 (72) [34.6]	15 (83) [24.5]	51 (59) [26.1]
	No	27 (54)	5 (28)	3 (17)	35 (41)
	Total	50 (100)	18 (100)	18 (100)	86 (100)
Chi-square = 9.21 (p = 0.010): ANOVA p-value for export-intensity = 0.032					
Age (years)					**ANOVA**
	Exporters	19.2	23.6	39.2	0.047*
	Non-exporters	11.4	21.3	36.1	0.054
	All	13.6	23.2	38.7	0.037*
	T-test by column:	0.042*	0.097	0.162	
R&D-intensity (%)					**ANOVA**
	Exporters	57.3	22.3	21.7	0.019*
	Non-exporters	40.1	19.6	26.8	0.039*
	All	50.1	20.8	23.0	0.002*
	T-test by column:	0.058	0.137	0.119	
Patent counts					**ANOVA**
	Exporters	22.8	74.7	16.9	0.081
	Non-exporters	11.7	71.2	15.8	0.075
	All	14.4	74.3	16.7	0.073
	T-test by column:	0.026*	0.192	0.216	
New products					**ANOVA**
	Exporters	4.7	18.2	10.3	0.032*
	Non-exporters	1.8	16.9	9.7	0.047*
	All	2.5	17.1	10.1	0.011*
	T-test by column:	0.042*	0.236	0.269	

* Significant group differences at p = 0.05 or less.

This said, no clear correlations were uncovered between R&D-intensity and either of the two innovation measures. This was the case for the sample as a whole, as well as within each of the three size-classes of firms (i.e., Pearson's r-values were statistically insignificant). Research &Development is obviously an important contributor to innovation; otherwise firms would not allocate such a fat proportion of their operating budgets to this activity. Nevertheless, there is no direct or linear association between innovation and research spending (i.e., innovation returns are unpredictable).

Overall, however, two general conclusions can be drawn from Table 1. First, firms that serve export markets tend to be more innovative than their counterparts that focus solely on domestic customers. This is especially the case for small firms. Second, and perhaps more important, medium-sized firms outperform their smaller and larger counterparts in terms of export-intensity, patent counts, and new product introductions. As a group, the medium-sized firms are the least R&D-intensive – suggesting stronger research productivity relative to larger and smaller firms. Indeed, the superior innovation performance of medium-sized firms surely goes some way toward explaining why so many of the world's biggest pharmaceutical companies have become increasingly interested in acquiring these innovators (Sen, 2007).

Outsourcing

Keeping these findings in mind, Table 2 compares our three size-classes of firms with respect to several dimensions of outsourcing. These dimensions include R&D, formulary development, clinical trials, product development, marketing, distribution, and manufacturing. Respondents were asked to estimate the outsourced proportion of their total budgets for each of these dimensions. The data are for two time periods (1995 and 2005).

For the combined sample, outsourcing levels for 3 of the 7 dimensions increased over the study period. In the case of clinical trials, for instance, outsourcing levels increased from an average of 45.8% in 1995 to 55.9% in 2005 (a 22% increase). Clinical trials have become increasingly expensive, time-consuming, and fraught with legal and regulatory complexities because they involve human subject experimentation and extensive statistical testing. It is no surprise that most biopharmaceutical companies outsource on this dimension as much as possible (to constrain costs), and that the outsourcing trend is systematically upward (especially for SMEs). Data presented elsewhere show that cost-minimization is the key driver in this respect (see Sen, 2007), as few biopharmaceutical companies want to internalize this particular activity. The marketing and distribution dimensions also show upward trends with respect to outsourcing, and again this is primarily cost-driven.

In contrast, scientific or knowledge-based activities that pertain to the discovery or development of new drugs appear to be migrating back toward the in-house domain. In the case of research, for example, outsourcing levels dropped from a 1995 average of 38.7% to a 2005 average of 28.4% (a 26% decrease). Similar declines can be seen for formulary development and product development. At first blush, then, it would seem that outsourcing levels have been falling across knowledge or science-intensive fields, in line with recent evidence reported by Boasson et al (2007) for large U.S. pharmaceutical companies.

With regard to outsourcing patterns by firm size, Table 2 again suggests that medium-sized firms occupy a distinct category. On average, such firms currently outsource less than 10% of their current research spending (the sample mean is 28%). Ten years ago, such firms only outsourced an average of 13% of research spending (the 1995 sample mean was 38%). Both now and in the recent past, then, medium-sized firms stand out as being different from the pack with regard to the outsourcing of knowledge-intensive activities. Although the ANOVA tests are not statistically significant in this regard, the general pattern would seem fairly clear. Specifically, the medium-sized firms are different from the population as a whole.

Table 2. Outsourcing trends by company size.

	Sample Mean %	Firm Size			ANOVA
		Small %	Medium %	Large %	
Research: Current	28.4	35.4	9.3	25.4	.112
10 years ago	38.7	48.1	13.4	31.7	.147
Clinical Trial: Current	55.9	63.0	31.3	56.0	.128
10 years ago	45.8	50.5	29.3	56.0	.458
Formulary Development: Current	49.9	61.8	17.6	55.0	.132
10 years ago	51.4	75.6	6.5	44.0	.033
Product Development: Current	27.5	30.6	14.6	33.8	.345
10 years ago	36.2	47.6	8.8	37.0	.100
Manufacturing/Production: Current	37.6	47.3	9.8	44.0	.032
10 years ago	47.2	65.0	13.2	36.2	.029
Marketing/Sales: Current	41.5	41.5	*	*	-
10 years ago	25.8	30.3	8.7	35.0	.407
Distribution: Current	57.6	73.9	21.2	*	.030
10 years ago	37.2	55.0	16.5	31.3	.391

* There are no firms in that size category reporting data.

As a point of general clarification, it should be noted that all of our 86 outsourcers in 2005 were outsourcers in 1995. Further, the patterns shown in Table 2 were not influenced by clusters of outliers (i.e., skewed distributions). For example, all of our 86 respondents outsourced some of their research spending in both 1995 and 2005 – and all 86 reported a moderate or substantial decrease in their external R&D spending over the study period. The same comments apply to most of the other dimensions listed in Table 2. In short, these trends appear to be systemic.

On this note, Table 3 offers a number of clues regarding the patterns shown in Table 2. Here, firms were asked to estimate their outsourcing-related savings over the study period (aggregated across all of the outsourcing categories).[1] Close to 37% of our respondents stated that outsourcing did not result in cost savings – even though cost-reduction was the strategic driver in the first place. Again, however, medium-sized firms stand out as being different. For example, 54.6% of these firms achieved outsourcing-related cost savings in the range of 6-15% over the study period, compared to 15.4% among large firms and 22.2% among small firms. Though not statistically significant,

[1] The survey instrument asked firms to estimate cost-savings across all of the outsourcing categories, as well as provide an overall estimate for outsourcing as a whole. Unfortunately, estimates for individual categories had too many missing responses to warrant tabulation here. In general, however, the available data suggest that savings have been lowest for knowledge-based activities such as R&D and highest for production (manufacturing), distribution, marketing, and clinical trial activities.

Table 3. Financial Benefits of Outsourcing by Firm Size: Savings Realized.*

Size of Savings	Total Sample %	Size of Firm		
		Small %	Medium %	Large %
None	36.7	33.3	36.4	46.2
1 – 5%	20.0	25.0	9.1	15.4
6 – 10%	21.7	19.4	45.5	7.7
11 – 15%	5.0	2.8	9.1	7.7
16 – 20%	3.3	2.8	-	7.7
>20%	13.3	16.7	-	15.4

* Aggregate estimates for all the main outsourcing categories

there is at least a shade of evidence from Table 3 that medium-sized firms are more adept at managing the outsourcing relationship than larger or smaller firms. More broadly, the fact that over one third of the firms across all three size categories did not achieve cost savings goes some way toward explaining why so many of the outsourcing dimensions listed in Table 2 show a downward trend.

Given the importance of cost reduction as the strategic or tactical driver of the outsourcing thrust, it is no surprise that neither of our two innovation metrics were found to correlate significantly with any of the outsourcing dimensions for 1995 or 2005. We mention this only because outsourcing has been associated with an innovation dampening effect by some scholars (e.g., Dankbar, 2005), or even an innovation retardation effect by others (e.g. Boasson et al, 2007). We find no evidence of an innovation impact in one direction or the other. During the early days of our study, however, we did expect innovation to respond positively to levels of external collaboration (innovation partnerships). Our findings in this regard are presented in the following section.

Table 4. External collaboration and company size.

	Small	Medium	Large	All
Patent Collaboration				
Yes	22 (56%)	8 (53%)	8 (73%)	38 (58%)
No	17 (44%)	7 (47%)	3 (27%)	27 (42%)
Total	*39 (100%)*	*15 (100%)*	*11 (100%)*	*65 (100%)*
Chi-square = 1.152 (p = .562)				
Product Collaboration				
Yes	15 (62%)	11 (73%)	9 (82%)	35 (70%)
No	9 (38%)	4 (27%)	2 (18%)	15 (30%)
Total	*24 (100%)*	*15 (100%)*	*11 (100%)*	*50 (100%)*
Chi-square = 1.454 (p = .483)				

External Collaboration and Innovation

Most of the survey firms (58%) collaborate with external partners regarding patent applications, while 70% collaborate to design, develop, and/or commercialize new products (Table 4). Fully 65% of the survey firms indicated that they collaborate with complementary firms to access specialized expertise. Although the incidence of external collaboration does not vary significantly by firm size, there is a general tendency for collaborators across all size classes to exhibit better innovation performance than non-collaborators (Table 5). Medium-sized firms again outperform their smaller and larger counterparts in both the collaborator and non-collaborator categories, but collaborators exhibit a clear innovation advantage across all size classes. Among small firms, for example, collaborators introduced an average of 4.8 new products over the last 7 years, compared to 1.7 among non-collaborators (t-test p = 0.041).

Table 5. External collaboration by firm size and innovation performance.

		Small	Medium	Large
Product collaboration*	**Yes**	4.8	20.7	10.9
	No	1.7	13.6	7.8
t-test p		0.041	0.048	0.064
Patent collaboration**	**Yes**	22.2	75.6	17.1
	No	11.9	64.2	14.9
t-test p		0.024	0.078	0.073

* Average number of new product introductions over last 7 years
** Average number of patent introductions over the last 7 years

One of our survey questions asked firms to indicate the extent to which location within a cluster of biotechnology companies gave them a competitive advantage in terms of innovation, thus testing for two possible effects (see Table 6). The first effect pertains to Porter's (1990) assertion that rivalry conditions within a cluster of related firms spurs innovation as a result of competition. The second effect pertains to the potential for inter-firm collaboration, which is arguably easier when similar types of firms are located near to each other. Among large firms, 63% indicated that location within a biotechnology cluster conveyed either a very important or critically important competitive advantage. This is in stark contrast to SMEs, where approximately 50% indicated a minor or negligible role for this factor (ANOVA p = 0.030).

Looking at the geographic structure of collaborative activity, 58% of the large firms work primarily with external partners located within the same metropolitan area, compared to 46% among small firms and only 30% among medium-sized companies (Chi-square = 8.32; p = 0.043). At first glance, these findings are surprising. After all, large firms have the financial and management resources to scan globally for appropriate partners. Smaller firms might be expected to have less flexibility in this regard. Yet, in this particular sample, SMEs are more likely to operate with non-local partners than their larger counterparts.

Table 6. Perceived importance of location in a biotechnology cluster.

	Small %	Medium %	Large %	All %
Critically Important	5.7	-	27.3	8.5
Very Important	28.6	15.4	36.4	27.1
Moderate Importance	14.3	30.8	9.1	16.9
Minor Importance	25.7	23.1	27.3	25.4
Not Important	25.7	30.8	-	22.0
ANOVA p = 0.030				

One possible explanation for these patterns is that large firms tend to collaborate with small biotechnology companies and other large firms, thus underscoring the importance of being located within a biopharmaceutical cluster. Medium-sized firms tend to avoid partnering with larger companies, and seem more likely to partner with other medium-sized firms and small biotechnology players. Unfortunately, our data are too sketchy to offer reliable comparisons of the size-structure of external collaborations. Nevertheless, the fact that large firms collaborate mainly with similar types of firms located nearby suggests that these firms are better positioned to access the advantages of a clustered location than SMEs. As reported by Boasson et al. (2007), some of these advantages include knowledge spillovers between firms in related industries, access to skilled workers, and proximity to major research universities with large pharmacology or life sciences departments.

Discussion

Despite the limited size of our sample, it would appear that medium-sized firms enjoy a competitive advantage in terms of export-intensity, patents, new product introductions, innovation-related collaborative activity, and the ability to realize cost savings from outsourcing. Such firms have never outsourced basic or applied research at rates comparable with smaller or larger firms, and few seem to regard location within a biopharmaceutical cluster as being especially important. As a group, medium-sized firms are less likely to collaborate with local partners than their smaller and larger counterparts. The question thus arises: why are these firms different? Although we are not in a position to offer definitive answers, several possibilities spring to mind.

To begin with, there is now an extensive literature on the ability of SMEs to innovate more aggressively than larger firms (e.g., Christopherson and Clark, 2007; Feldman et al, 2005). Popular explanations vary from

the risk-oriented nature of SME managers to their faster decision-making, extensive participation in innovation networks, and their ability to attract young research scientists that want to be part of rapidly growing business ventures (especially those that are positioned at the front end of new product cycles). Small firms that have recently transitioned toward medium-sized status appear to be especially attractive to the industry's youngest and most promising research scientists. At this stage, however, some of the general or stylized facts reported in the recent literature on SME innovation have not been systematically tested for the biopharmaceutical sector. In this regard, we feel obliged to offer two cautionary notes. First, our innovation data do not say anything about the commercial impact or broader societal importance of recent product development activity across our three size-classes of firms. We offered innovation counts *only.* Second, our survey was not structured to probe for size-related differences in subtle aspects of business management or human capital attributes (e.g., incentive structures, hiring policies, risk-tolerance). In short, we have identified size-related differences in NPD activity and other organizational characteristics – but we have been unable to go much further.

This said, an issue of more general interest concerns the trend toward reduced outsourcing on the R&D front. Recall that R&D outsourcing is not typically practiced with a view to capturing superior research findings relative to in-house alternatives. Instead, the goal is more commonly to cut costs. As noted earlier, however, close to one third of the survey firms failed to realize outsourcing-related cost savings over the study period. Not surprisingly, these are the firms that have recently cut their external R&D budgets the most. But failure to achieve cost savings is only part of the story. We interviewed 20 firms by telephone to probe this issue further, and two common themes emerged. First, external research is not always reliable. Several firms noted that they did not fully trust the findings reported by their external vendors, and that much time and effort had to be expended on verification procedures (in-house checking). In all of these cases, flaws were uncovered that needed to be corrected -- sometimes at considerable expense. Second, even in cases where external findings were deemed reliable, such findings were often delivered later than expected – causing unacceptable product development delays. For these reasons, many outsourcers have become increasingly selective in their allocation of external contracts. Our follow-up inquiries suggest that R&D outsourcing peaked in the late 1990s, but has since dropped to a level that more accurately reflects the techno-market competence of the contract R&D supplier-base. In short, the days of >30% R&D outsourcing are probably over.

Most of our survey participants indicated that cost reduction was the primary driver across all of our outsourcing categories, whereas external collaboration was more commonly practiced to access specialized expertise (i.e., new or complementary knowledge). Outsourcing has been a successful business strategy for most firms, especially with regard to clinical trials, marketing, distribution, and manufacturing (for comparable evidence from the UK, see Howells et al., 2008). In strategic areas such as R&D, however, few firms reported significant cost savings over the study period. As noted earlier, all of the R&D outsourcers in 1995 had cut their R&D outsourcing budgets by 2005. From a product development perspective, external collaboration appears to be a successful strategy – notably for medium-sized firms. From a theoretical standpoint, then, our data suggest that the transactions cost perspective explains most of the outsourcing thrust. In contrast, external collaboration is more commonly designed to support new

product development by tapping outside sources of complementary expertise. Here, the resource-based theory of external linkage development appears to offer stronger insights (see Yasuda, 2005).

Summary and Conclusions

External *collaboration* to support product innovation is common in the U.S. biopharmaceutical industry and is likely to persist or even expand in light of the need for most firms to exploit the specialized expertise of complementary producers. The *outsourcing* of noncore functions such as clinical trials or marketing is also likely to increase over time, though the same cannot be said for strategic areas such as R&D or formulary development. Medium-sized firms are the innovation leaders, as evidenced by recent rates of new product development. Such firms appear to manage their external collaborations and outsourcing relationships more efficiently than their larger and smaller counterparts. Medium-sized firms are also among the most non-locally oriented in terms of external partner selection, with few firms in this size-class indicating an important technological or business role for location within a bio-pharmaceutical cluster. Medium-sized firms are also the most export-intensive, though we suspect that average levels of export-orientation among these firms will decline as they transition toward large firm status (i.e., the inverted-U mentioned at the start of the paper).

At this stage, however, it should be conceded that some of our survey results raise more questions than answers. For example, it is not clear why large firms tend to view location within a biopharmaceutical cluster as being important from a business performance perspective. Perhaps these firms are equating cluster location with wider agglomeration or urbanization economies rather than the presence of similar types of firms? At this point, we simply do not know. In a similar vein, we are unable to explain why medium-sized firms stand out as being so radically different from the crowd. Qualitative research based on personal interviews would be appropriate to probe for possible explanations.

We suspect that the days of substantial R&D outsourcing are destined to wane in light of poor results over the last 10 years. All 20 of our interviewees noted that specialized aspects of their R&D outsourcing ventures were initially viewed with enthusiasm (major cost savings were envisioned), but that outcomes were not impressive from either a cost or quality standpoint. In short, we do not believe that R&D outsourcing in the 2000s will ever again match the levels that were recorded in the 1990s unless the quality of the external supplier-base improves dramatically. This does not mean that R&D outsourcing will stop. Rather, the intent is to suggest that outsourcers will become increasingly selective in the future, subcontracting only to those vendors that have a track record of good results.

Finally, it would seem that most of the collaborators in our sample had forged strategic alliances with at least one biotechnology company over the study period. Although we are only at the preliminary stages of a follow-up study based on personal interviews, our early follow-up results suggest that these biotechnology partners are very young (less than 10 years old), very small (less than 10 employees), and research-intensive. At this stage, however, we do not know very much about the nature or durability of these alliances.

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