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Do Firms Benefit from being Present in Multiple Technology Clusters? An Assessment of the Technological Performance of Biopharmaceutical Firms

CATHERINE LECOCQ*, BART LETEN*†, JEROEN KUSTERS‡ and BART VAN LOOY*§¶

**Department of Managerial Economics, Strategy and Innovation, Faculty of Business and Economics, K.U. Leuven, Naamsestraat 69, B-3000 Leuven, Belgium. Emails: Catherine.Lecocq@econ.kuleuven.be, Bart.Leten@econ.kuleuven.be and Bart.VanLooy@econ.kuleuven.be*

†Vlerick Leuven–Gent Management School, Reep 1, B-9000 Gent, Belgium

‡Deloitte Consulting (Belgium), Berkenlaan 8c, B-1831 Diegem, Belgium. Email: jkusters@deloitte.com

§Expertisecentrum O&O Monitoring (ECOOM), Waaistraat 6, B-3000 Leuven, Belgium

¶School of Management and Governance, University of Twente, Twente, the Netherlands

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LECOCQ C., LETEN B., KUSTERS J. and VAN LOOY B. Do firms benefit from being present in multiple technology clusters? An assessment of the technological performance of biopharmaceutical firms, *Regional Studies*. Firms active in knowledge-intensive fields are increasingly organizing their research and development activities on an international scale. This paper investigates whether firms active in biotechnology can improve their technological performance by developing research and development activities in multiple technology clusters. Regions in Europe, Japan and the United States, characterized by a critical mass in terms of technological activity within biotechnology, are identified as clusters. Fixed-effect panel data analyses with fifty-nine biopharmaceutical firms (for the period 1995–2002) provide evidence for a positive, albeit diminishing (inverted 'U'-shape) relationship between the number of technology clusters in which a firm is present and its overall technological performance. This effect is distinct from a mere multi-location effect.

Cluster Innovation Biotechnology

LECOCQ C., LETEN B., KUSTERS J. and VAN LOOY B. 公司是否从其所参与的多技术集群中受益？对于生物制药公司技术性业绩的评价，区域研究。 知识密集型产业中的公司正试图在国际尺度上组织其研究与发展活动。本研究考察了生物制药产业公司能否通过在多重技术集群中发展研究与开发活动而提高其业绩。本研究将欧洲、日本以及美国地区内生物科技产业活动积聚的部分定义为集群。对59家生物制药公司进行的固定效应面板数据分析（时间跨度1995－2002）表明，公司业绩与其所在的技术集群数量之间存在着倒U形关系。这一结果与单纯的多区位效应有所不同。

集群 创新 生物科技

LECOCQ C., LETEN B., KUSTERS J. et VAN LOOY B. Les entreprises, tirent-elles profit de leur présence au sein de multiples clusters à technologies? Une évaluation de la performance technologique des entreprises biopharmaceutiques, *Regional Studies*. Les entreprises qui travaillent dans les secteurs à la pointe de la technologie organisent de plus en plus leurs activités de recherche et de développement au niveau international. Cet article examine si les entreprises actives dans le secteur de la biotechnologie sont capables d'améliorer leurs performances technologiques en développant des activités de recherche et de développement au sein de multiples clusters à technologies. Sont considérées comme clusters, les régions situées en Europe, au Japon et aux Etats-Unis qui secaractérisent par une masse critique en termes d'activité technologique au sein de la biotechnologie. Des analyses (effects fixes) à base de données de cinquante-neuf entreprises biopharmaceutiques (de 1995 à 2002) fournissent des preuves d'un rapport positif, bien qu'en baisse (à savoir, courbe en U inversée), entre le nombre des clusters technologiques au sein desquels une entreprise est présente et sa performance technologique globale. Cet effet se distingue d'un simple effet d'emplacements multiples.

Cluster Innovation Biotechnologie

LECOCQ C., LETEN B., KUSTERS J. und VAN LOOY B. Profitieren Unternehmen von einer Präsenz in mehreren Technologie-Clustern? Eine Bewertung der technologischen Leistung von biopharmazeutischen Unternehmen, *Regional Studies*. Firmen, die in wissensintensiven Gebieten aktiv sind, organisieren ihre Forschungs- und Entwicklungsarbeit zunehmend auf internationaler Ebene. In diesem Beitrag wird untersucht, ob Firmen im Bereich der Biotechnologie ihre technologische Leistung durch den

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Ausbau ihrer Forschungs- und Entwicklungsarbeit in mehreren technologischen Clustern verbessern können. Als Cluster werden Regionen in Europa, Japan und den USA identifiziert, die sich durch eine kritische Masse an technologischer Aktivität im Bereich der Biotechnologie auszeichnen. Die (Fix Effekt) analyses der panel daten von 59 biopharmazeutischen Unternehmen (im Zeitraum von 1995 bis 2002) liefern Anhaltspunkte für eine positive, wenn auch nachlassende (Form eines umgekehrten U) Beziehung zwischen der Anzahl der Technologie-Cluster, in denen ein Unternehmen vertreten ist, und der generellen technologischen Leistung dieses Unternehmens. Dieser Effekt unterscheidet sich von einem einfachen Mehrfachstandort-Effekt.

Cluster Innovation Biotechnologie

LECOCQ C., LETEN B., KUSTERS J. y VAN LOOY B. ¿Se benefician las empresas de estar presentes en varias aglomeraciones de tecnología? Una valoración del rendimiento tecnológico de empresas biofarmacéuticas, *Regional Studies*. Las empresas que son activas en campos que requieren un alto nivel de conocimientos específicos organizan sus actividades de investigación y desarrollo cada vez más a nivel internacional. En este artículo investigamos si las empresas activas en biotecnología pueden mejorar su rendimiento tecnológico al fomentar actividades de investigación y desarrollo en varias aglomeraciones de tecnología. Identificamos como aglomeraciones las regiones en Europa, Japón y los Estados Unidos que se caracterizan por una masa crítica en términos de actividad tecnológica en biotecnología. Los análisis (efecto fijo) de los datos de un panel de 59 empresas biofarmacéuticas (para el periodo de 1995 a 2002) demuestran una relación positiva, aunque decreciente (en forma de 'U' invertida) entre el número de aglomeraciones tecnológicas en las que una empresa está presente y su rendimiento tecnológico general. Este efecto es distinto al de un simple efecto de varias ubicaciones.

Aglomeración Innovación Biotecnología

JEL classifications: O30, R12, R30

INTRODUCTION

Corporate activities, especially in knowledge-intensive industries, display a tendency to cluster geographically (AUDRETSCH and FELDMAN, 1996; FELDMAN and FLORIDA, 1994). According to MARSHALL (1920), a presence in clusters enhances the innovative capacity of firms through the presence of localized knowledge spillovers, and the access to a pool of highly skilled labour and specialized suppliers that agglomerate in such regions. Innovation dynamics in clusters are further stimulated by the presence of local competition and peer pressure among firms (PORTER, 1990). Empirical studies stemming from the economic geography literature indeed provide evidence that firms located in clusters are more innovative than counterparts located elsewhere (BAPTISTA and SWANN, 1998; BATEN *et al.*, 2007; BEAUDRY and BRESCHI, 2003; DEEDS *et al.*, 1999; VAN GEENHUIZEN and REYER-GONZALES, 2007). At the same time, little is known about the relationship between presence in *multiple* clusters and the overall technological performance of firms. Exploring this relationship is relevant because firms increasingly organize research and development (R&D) activities on an international scale whereby knowledge from different regions is being accessed (GASSMANN and VON ZEDTWITZ, 1999; KUEMMERLE, 1999; GRANSTRAND, 1999). The present paper engages in such an analysis by means of a panel data set of fifty-nine biopharmaceutical firms (for the period 1995–2002). Its focus is on the relationship between the technological performance of consolidated firms (that is, the parent firm and its subsidiaries) and the number of technology clusters in which they engage in technological activities. Clusters are identified as regions within the United States, Europe and Japan with a critical mass of technological activities in the field of biotechnology. Whereas previous economic geography studies controlled only to a limited extent[1] for the heterogeneity of firms in terms of innovative efforts and capabilities, this study uses fixed-effect panel data techniques and includes controls for time-varying firm differences in R&D expenditures and past experience. This allows one to distinguish the presence of clusters from other firm-specific characteristics (BEUGELSDIJK, 2007). The analyses provide evidence of an inverted 'U'-shape relationship between the number of technology clusters in which a firm is present and its overall technological performance. This effect is distinct from a mere multi-location effect.

The paper is organized as follows. First, an overview of prior research on clusters and firm performance is provided, resulting in hypotheses on the relationship between the presence in clusters and firm's technological performance. Next, the data sources and variables used in this study are presented, followed by the empirical results. Conclusions, limitations and directions for further research are discussed in the final section.

INDUSTRY AND TECHNOLOGY CLUSTERS

The clustering of industrial activity in well-defined and relatively small geographical areas has been observed for a long time by economic geographers and regional scholars (for example, MARSHALL, 1920; KRUGMAN, 1991; PORTER, 1990). Famous examples of industrial clusters include Detroit's car manufacturing industry, the entertainment industry of Hollywood and the fashion industry in northern Italy. Clustering remains a striking feature of national and regional economies, despite the availability of better transportation and communication infrastructure and the presence of global markets from which capital, talent and technology can be sourced (PORTER, 1998, 2000). Following the success of Silicon Valley in California and Route 128 in Boston (SAXENIAN, 1994), there has been a wide interest of researchers and policy-makers in the innovative and economic potential of technology clusters. Unlike industry-focused clusters, where inter-firm connections are predominantly vertical, technology clusters exhibit a more lateral structure consisting of direct and indirect competitors developing diversified applications of the same core technology within different markets or industries (ST. JOHN and POUDER, 2006). Value dynamics in technology clusters or 'technology districts' build on unique technological resources – the technological infrastructure – which support firms' innovation activities (FELDMAN and FLORIDA, 1994; STORPER, 1992). Sources of knowledge in technology clusters are diverse, ranging from universities and public research institutes to firms, suppliers and customers.

MARSHALL (1920) highlighted three incentives for firms to cluster geographically: (1) broader access to specialized, highly skilled labour; (2) access to specialized suppliers; and (3) the presence of inter-organizational knowledge spillovers among similar firms.[2] The broad concept of knowledge spillovers is probably the most frequently invoked source of agglomeration economies (HEAD *et al.*, 1995) and has been widely investigated in the literature (for example, DÖRING and SCHNELLENBACH, 2006; BRESCHI and LISSONI, 2001). Knowledge spillovers arise through labour mobility (ALMEIDA and KOGUT, 1999) and exchange processes involving competitors, suppliers, customers and providers of professional services (VON HIPPEL, 1988; ROSENKOPF and ALMEIDA, 2003). They allow firms to achieve similar R&D results faster and/or with fewer resources. Empirical work has shown the existence and geographically bounded nature of knowledge spillovers (JAFFE *et al.*, 1993; ALMEIDA and KOGUT, 1999; VARGA, 2000; RODRÍGUEZ-POSE and CRESCENZI, 2008). Spillovers are more local to the extent that the relevant knowledge base is tacit (POLANYI, 1966; NONAKA, 1994; VON HIPPEL, 1994). This is particularly true for emerging, complex technologies like biotechnology. PORTER (1990, 1998) provided two additional reasons why firms located in clusters are more innovative than firms located outside clusters. First, opportunities for innovation (both new buyer needs and new technological opportunities) are more visible in clusters. Next, competitive and/or peer pressure among local firms stimulates firms to be more innovative and increases the efficiency of their operations.

While clusters are often associated with positive effects on firm performance, potential disadvantages can be noticed as well. First, resources (for example, labour, real estate, professional services) might be significantly more expensive in clusters due to congestion effects (BEAUDRY and BRESCHI, 2003). Second, cluster membership might lead to an inward orientation whereby relevant developments situated outside the cluster are neglected (PORTER, 1998). Firms located in clusters might also be confronted with higher levels of unintended (outward) knowledge spillovers, affecting the firm's competitive advantage in a negative way (SHAVER and FLYER, 2000). While such disadvantages might occur, they are not directly relevant for the research questions addressed in this paper as the focus is on the firm's technological performance (as opposed to the overall competitive position of the firm or the efficiency implications of being present in clusters).

CLUSTERS AND FIRM PERFORMANCE

The capacity of firms to innovate is not limited to the boundaries of the firm but increasingly depends on external resources that agglomerate in specific places (FELDMAN and FLORIDA, 1994; STORPER, 1992). If knowledge spillovers are an essential characteristic of clusters, the beneficial effects from being present in a cluster should manifest themselves in the first place on the innovative output of firms rather than on the firm's financial or growth performance (BAPTISTA and SWANN, 1998). Studies in the economic geography literature have investigated whether firms (plant level) located in an industrial or technology cluster are more innovative than firms outside clusters.[3] These studies can be classified in two groups based on the methodologies used to measure clusters.

A first set of studies investigated whether firms located in industrial clusters are more innovative. The concentration of industrial activity in a region is measured by sector-level employment data. BAPTISTA and SWANN (1998) found a positive effect of own-sector employment in the region on the likelihood of manufacturing firms in the United Kingdom to innovate. In contrast, BEAUDRY and BRESCHI (2003) found no effect of own-sector employment on firms' innovative performance for a sample of UK and Italian firms. Only the concentration of innovative firms (and the size of their accumulated knowledge base) in the own industry had a positive impact on the technological performance of firms. Similar results were found by BATEN *et al.* (2007) for firms trading in the state of Baden (Germany) around 1900. These findings suggest that for firms' innovative performance the presence of critical mass in terms of knowledge creation activities in a region is more important than the overall industrial activity per se.

A second set of studies classified regions in clusters and non-clusters based on the amount of technological activity observed in the region, and examined whether firms located in technology clusters are more innovative than firms located elsewhere. DEEDS *et al.* (1999) classified eight regions in the United States (metropolitan statistical area (MSA) level) that host the largest number of biotechnology firms as clusters and found that biotechnology firms located in clusters are more innovative than firms located outside the clusters. For the Netherlands, VAN GEENHUIZEN and REYER-GONZALES (2007) defined clusters as regions with at least one knowledge institute and ten young entrepreneurial biotechnology firms. Their analyses showed no significant effect from cluster location on the innovativeness of biotechnology firms. However, when only the largest and oldest biotechnology cluster in the Netherlands – the Leiden region – is considered, cluster presence had a significant positive effect on firm performance. These results, again, suggest that a critical mass of technological activity is needed before positive cluster effects can be observed at the level of the firm.

The aforementioned economic geography studies use cross-sectional data at the level of single plants to investigate whether clusters are supportive of firms' innovation activities. While the results indicate that firms in clusters are more innovative than firms located elsewhere, they do not provide evidence whether firms can improve their technological performance by extending their presence within multiple clusters. This research question is addressed in this paper. More specifically, the relationship between the number of technology clusters in which a firm is present and its overall technological performance is studied. Exploring this relationship is relevant because firms increasingly organize R&D activities within multiple units – located in different regions – to benefit from agglomeration externalities (GASSMANN and VON ZEDTWITZ, 1999; KUEMMERLE, 1999; GRANSTRAND, 1999; CANTWELL and PISCITELLO, 2005). In so doing, R&D location choices are not confined to national borders, but increasingly take place on a global scale. As such, empirical analyses assessing the impact of cluster presence should not be limited to one particular country or region, but should consider technology clusters on a more global scale. Likewise, at the firm level, studying the impact of cluster presence requires taking into account the location of all firms' R&D facilities (headquarters and subsidiaries).

In this paper, such an analysis is performed by means of a panel data set consisting of the technological activities of fifty-nine biopharmaceutical firms (1995–2002). In line with economic geography studies, locations of firms' R&D activities (including the presence of clusters) are analysed at the regional level. Technology clusters are defined as worldwide-leading regions in technology development. The models in this study control for firm-level heterogeneity in innovative efforts and capabilities by employing fixed-effects panel data techniques and including time-varying, firm-level control variables (R&D expenditures and innovation experience). This allows one to distinguish clearly between the presence in clusters and other, firm-specific, characteristics (BEUGELSDIJK, 2007).

A positive effect on a firm's overall technological performance is expected from being present in multiple clusters as this coincides with increased access to the state-of-the-art knowledge available within each of these regions. At the same time, the more one is already involved in different clusters, the smaller the additional effects in terms of access to new, relevant knowledge might become. In addition, the costs of coordinating multiple R&D units and leveraging and integrating knowledge from multiple locations will increase with the number of locations in which a firm is present. Building on the aforementioned research, it is expected that location benefits will principally stem from being present in technology clusters with a critical mass of relevant knowledge. Therefore, the effects of cluster membership on the overall technological performance of firms should be distinctive from a mere multiple location effect. Taken together, these arguments lead to the following set of hypotheses:

Hypothesis 1: Firms improve their technological performance when extending their presence in technology clusters.

Hypothesis 2: Firms extending their presence in technology clusters will gain additional benefits in terms of technological performance, albeit of a diminishing nature (inverted 'U'-shape relationship).

Hypothesis 3: The relationship between cluster membership and overall technological performance is distinct from a mere multi-location effect.

DATA AND METHODOLOGY

Panel data on the technological activities of fifty-nine biopharmaceutical firms with parent firms located in the United States, Europe and Japan were collected to study the relationship between the location of R&D activities in multiple clusters and regions and the overall technological performance of firms. Patent data were used to create indicators of firms' technological activities (location and performance) and to identify biotechnology clusters within the United States, Europe and Japan. The use of patent data has several advantages (PAVITT, 1985; GRILICHES, 1990). They are easy to access, cover long time series, and contain detailed information on the technological content, owners and inventors of patented inventions. This allows one to mark out biotechnology patents, construct indicators of the technological performance of firms and regions, and identify the locations where inventions took place. At the same time, patent indicators also have some deficits: not all inventions are patented, patent propensities vary across industries and firms, and patented inventions vary in technical and economic value (MANSFIELD, 1986; GAMBARDELLA *et al.*, 2008). One can lessen these problems by restricting patent analyses to technologies with high propensities to patent such as biotechnology (ARUNDEL and KABLA, 1998), and by weighting patent counts (technological performance indicator) by the number of forward citations received (HALL *et al.*, 2005; TRAJTENBERG, 1990; HARHOFF *et al.*, 1999). Despite their shortcomings, there is simply no other indicator that provides the same level of detail on firms' technological activities as patents do (GRILICHES, 1990). Further, studies have found a strong correlation between patent counts and other technology indicators (for example, new product announcements and expert opinions) on the level of firms (HAGEDOORN and CLOODT, 2003; NARIN and NOMA, 1987) and regions (ACS *et al.*, 2002), establishing patents as a valid indicator of novel technological activity.

In this study, patent indicators are based on data from the European Patent Office (EPO). Patent application data rather than patent grants are used because of the extensive time periods observed between application and granting decisions at the EPO (especially for biotechnology).[4] The geographic location of inventions is identified via inventor address information (LECOCQ *et al.*, 2008). Allocation based on inventor addresses is the most commonly used approach in patent studies since – especially for large firms – allocation based on assignee addresses might signal the location of corporate headquarters rather than the research laboratory where the invention took place (DEYLE and GRUPP, 2005; KHAN and DERNIS, 2006). The use of inventor addresses may however also introduce some bias since inventors may not live in the same region in which they work. LANDONI *et al.* (2008) performed a validation exercise where both allocation methods (inventor and applicant addresses) are compared with the real R&D locations of inventions. This work confirmed the superiority of the inventor's address criterion for patent statistics at a fine-grained geographical level.

Sample of biopharmaceutical firms

Parent firms with a large biotechnology patent portfolio are identified from a data set with all EPO patent applications in the field of biotechnology (time period 1978–2001). This data set is the result of a study by GLÄNZEL *et al.* (2004) that delineates technological activity in the field of biotechnology.[5] The selected firms are active in different sectors: mostly in biotechnology, the pharmaceutical or chemical industry, but the list of parent firms also includes producers of consumer products, energy concerns and breweries. For consistency in the sample, only the biopharmaceutical firms (seventy-five largest patenting firms) were retained. Due to missing data on firm R&D expenditures or incomplete information on the group structure of parent firms, the list of firms was further reduced to fifty-nine biopharmaceutical firms. All these firms have headquarters in the United States, Japan or Europe (EU-15 and Switzerland). Appendix A contains a complete list of the firms under study.

For this sample of fifty-nine biopharmaceutical firms, patent data were collected at the consolidated parent level, that is, comprising headquarters and all majority-owned (share more than 50%) subsidiaries of the parent firm. This consolidation process implied the mapping of all changes in the group structure of the parent firms due to acquisitions, mergers, greenfield investments and spin-offs during the period 1995–2002. For this purpose, yearly lists of subsidiaries included in annual reports were used, as well as yearly 10-K reports filed with the Securities and Exchange Commission (SEC) in the United States and, for Japanese firms, information on foreign subsidiaries published by Toyo Keizai in the yearly Directories of Japanese Overseas Investments. Using consolidated patent data is important to obtain a complete picture of firms' technological activities as a significant part of large firms' patents are not filed under the parent firm name (LETEN *et al.*, 2007). Firm financial data are also collected at the consolidated firm level via corporate annual reports, Worldscope and Compustat financial databases.

Biotechnology clusters

Biotechnology is a knowledge-intensive technology field, which from its origin has developed within a limited number of regions, such as California and the Boston area in the United States, and Cambridge in the UK. To identify biotechnology clusters worldwide, the aforementioned data set with all EPO patent applications in the field of biotechnology is used (GLÄNZEL *et al.*, 2004). The data set shows that, for the period 1990–1999, almost all patenting activity in the domain of biotechnology (94%) takes place in the United States, Europe (EU-15 and Switzerland) and Japan. No other region has sufficient patent applications to qualify as a cluster.

In this study, the focus is on regions in the United States, Europe and Japan. It is important to select a spatial level of analysis which is comparable across continents in terms of size (population). Regions are therefore defined at the level of the following national subdivisions: European NUTS-1 regions ($n = 73$), US states ($n = 50$), and Japanese prefectures ($n = 47$).[6] Cluster boundaries do not necessarily coincide with the boundaries of such administrative regions. Clusters may well spread over more than one region (for example, the tri-state cluster in the US states of New York, New Jersey and Pennsylvania; and the cluster covering the prefectures of Tokyo and Kanagawa). Alternatively, regions may enclose more than one cluster (for example, the triangle San Francisco–

San Jose–Sacramento, better known as Silicon Valley, and the region between Los Angeles and San Diego in the state of California). Despite these concerns, an analysis of regions coinciding with the boundaries of the administrative subdivisions was chosen as they provide comparable regional units of analysis.

The amount of biotechnological R&D activities in a region is measured by the number of EPO patents in that region during the period 1990–1999. Patent applications are allocated to regions based on inventor addresses. When a patent contains multiple inventors in different regions, the patent is fully counted in each region. Table 1 shows the fifty regions with the highest technological performance in the field of biotechnology. A region is defined as a biotechnology cluster if it contains at least 2.5% of the total number of EPO patent applications in the field of biotechnology. Twelve regions satisfy this condition. Together they account for 50% of biotechnology patents worldwide. Most biotechnology clusters are located in the United States, with a clear supremacy of the state of California, which accounts for almost 15% of all biotechnology patents. Other US regions with a substantial amount of activity in biotechnology are Massachusetts, Maryland, Pennsylvania, New York and New Jersey. Europe has three top regions: the region of Paris (France); the region of Cambridge–Bedfordshire–Hertfordshire–Essex (that is, East Anglia; UK); and the region of Munich (Bayern, Germany). For Japan, Tokyo, Kanagawa and Osaka count as the three top regions in biotechnology.

Firm variables and model

Dependent variable. The dependent variable in this study is the technological performance of firms in biotechnology. This is measured by the number of biotechnology patent applications of a firm in a certain year, weighted by the number of forward patent citations received over a fixed four-year time window.[7] The 'weighting' is done to account for variation in the technological and economic importance of patented inventions (ALBERT *et al.*, 1991; HARHOFF *et al.*, 1999; TRAJTENBERG, 1990; HALL *et al.*, 2005).[8]

The dependent variable is a count variable with only non-negative integer values. In this case, non-linear count data models are preferred to standard linear regression models as the former explicitly take into account the non-negativity and discreteness of the dependent variable (CAMERON and TRIVEDI, 1998). Negative binomial models used in the study allow for over-dispersion in the dependent variable. To control for the presence of unobserved firm-specific effects (which may correlate with and bias the effect of explanatory variables in the models if not controlled for), fixed-effects panel data estimators are used. This estimation technique removes (time-constant) unobserved firm-specific factors by time-demeaning all variables (dependent and explanatory) before performing regressions (WOOLDRIDGE, 2001).

Presence in technology clusters. To identify the regions in which firms are present, inventor address information on the biotechnology patents of the firms is used. More specifically, a firm is considered to engage in biotechnology R&D activities in a region if the firm owns patents with at least two inventors residing in that region during the last two years. Given the fact that R&D collaboration is quite widespread in the field of biotechnology (LECOCQ and VAN LOOY, 2009),[9] it was decided to consider presence in a region only on the firm's fully owned patents, thus reflecting the number of regions (clusters and other regions) in which a firm is present through its fully owned or single parent patents. For co-owned patents, that is, patents with multiple assignees from different parent organizations, it is not possible to identify to which assignee an inventor belongs. Therefore, using inventor address information on such patents may pick up not only a firm's own R&D locations, but also the R&D locations of co-assignees. It should be noted that the R&D location variable, even after correcting for co-assigneeship, might contain additional locations through the location of co-inventors not belonging to the firm. This is, for instance, the case when a firm engages in collaboration with a university or other organization, while retaining full ownership of the intellectual property. The location variable will then be overestimated, however, only to the extent that the firm is collaborating with at least two inventors located outside the firm's own region. Despite this shortcoming, patent data are the best available public source to map systematically the biotechnology R&D locations of global firms. Other sources of information such as corporate annual reports also show some limitations: they often do not specify the exact location (region) of firm facilities and the type of activities (for example, research, production, administration, sales) undertaken at different locations. Corporate annual reports also do not provide information on the type of research activities (biotechnology versus other research fields) in R&D establishments. This is however important information as the locations where firms engage in biotechnology R&D activities are studied.

Three indicators related to the location of the biotechnology R&D activities of a firm are created: (1) 'clusters', reflecting the number of R&D biotechnology clusters in which a firm is present; (2) 'other regions', reflecting the number of other regions, not defined as clusters, in which a firm undertakes R&D activities; and (3) 'countries', reflecting the number of countries in which a firm is present.[10] To test for non-linear relationships between the R&D location variables and the firm's overall technological performance, both linear and squared terms of the location variables are included in the empirical models. Applying fixed-effect panel data models require that there is enough

Table 1. Top biotechnology regions, 1990–1999

	Country/region	Country	Number of patents	%	Cumulative %[a]
1	California	United States	4162	15.4	15.4
2	Massachusetts	United States	1853	6.8	21.6
3	Maryland	United States	1285	4.7	25.5
4	Pennsylvania	United States	1264	4.7	29.6
5	New York	United States	1072	4.0	32.8
6	New Jersey	United States	1005	3.7	34.9
7	Tokyo	Japan	916	3.4	38.2
8	Île-de-France	France	873	3.2	41.1
9	East of England	United Kingdom	766	2.8	43.5
10	Kanagawa	Japan	724	2.7	45.2
11	Bayern	Germany	716	2.6	47.6
12	Osaka	Japan	672	2.5	49.7
13	Baden-Württemberg	Germany	654	2.4	51.7
14	Denmark	Denmark	643	2.4	53.7
15	Switzerland	Switzerland	626	2.3	55.4
16	Washington	United States	619	2.3	57.1
17	South East	United Kingdom	614	2.3	58.8
18	Hessen	Germany	607	2.2	60.3
19	West-Nederland	Netherlands	601	2.2	62.1
20	Nordrhein-Westfalen	Germany	534	2.0	63.4
21	Illinois	United States	473	1.7	64.7
22	Texas	United States	446	1.6	65.8
23	London	United Kingdom	444	1.6	66.6
24	North Carolina	United States	416	1.5	67.5
25	Indiana	United States	406	1.5	68.7
26	Ibaraki	Japan	394	1.5	69.6
27	Hyogo	Japan	394	1.5	70.1
28	Vlaams Gewest	Belgium	389	1.4	71.2
29	Connecticut	United States	385	1.4	71.9
30	Kyoto	Japan	377	1.4	72.5
31	Sverige	Sweden	376	1.4	73.5
32	Centre-Est	France	373	1.4	74.4
33	Wisconsin	United States	320	1.2	75.1
34	Saitama	Japan	317	1.2	75.5
35	Ohio	United States	308	1.1	76.2
36	Niedersachsen	Germany	283	1.0	76.8
37	Missouri	United States	280	1.0	77.4
38	Chiba	Japan	276	1.0	77.7
39	Michigan	United States	265	1.0	78.3
40	Iowa	United States	261	1.0	79.0
41	Berlin	Germany	258	1.0	79.6
42	Colorado	United States	251	0.9	80.2
43	Shizuoka	Japan	245	0.9	80.6
44	Scotland	United Kingdom	237	0.9	81.1
45	Delaware	United States	232	0.9	81.4
46	Nord-Ovest	Italy	220	0.8	82.1
47	Minnesota	United States	213	0.8	82.6
48	Est	France	213	0.8	82.9
49	Virginia	United States	211	0.8	83.1
50	Rheinland-Pfalz	Germany	210	0.8	83.4

Note: [a]Cumulative % excludes double counts due to co-patenting in multiple regions.

within-firm variation in the number of R&D locations over time. This is the case for the sample firms, as they all engaged in merger and acquisition activities, opened new laboratories and/or closed existing ones over the time period 1995–2002.

Control variables. Several (time-varying) variables that might affect the technological performance of firms are included as control variables in the analyses. First, an indicator for the size of a firm's existing technology portfolio in biotechnology is included, measured by the number of biotechnology patents applied for by the firm in the last five years. In analogy to the dependent variable, this variable is weighted by the number of forward patent citations received over a fixed four-year time window to account for differences in patent quality. Firms with large technology portfolios are more experienced in innovation, and may be better positioned to develop new technological competences (NESTA and SAVIOTTI, 2005). In previous studies, a period of five years has been considered as appropriate for assessing the validity of knowledge bases in a given

Table 2. Descriptive statistics

	Number observed	Mean	Standard deviation (SD)	Biotechnology patents	Biotechnology portfolio	Research and development	Clusters	Other regions	Countries
Weighted number of biotechnology patents	422	21.1	36.2	1					
Size of biotechnology patent portfolio (five-year, weighted)	422	106.1	131.1	0.5673	1				
Research and development expenditures (US$, thousands)	422	452.4	760.3	0.0681	0.2164	1			
Number of clusters	422	1.8	1.6	0.3082	0.5024	0.4427	1		
Number of other regions	422	2.4	2.7	0.1471	0.3253	0.5401	0.4453	1	
Number of countries	422	2.0	1.5	0.0930	0.2435	0.5579	0.4348	0.7685	1

technology (STUART and PODOLNY, 1996; AHUJA and LAMPERT, 2001; LETEN *et al.*, 2007). Second, differences in the size of firms' R&D effort are included, measured by one-year lagged R&D expenditures.[11] Firms that have more R&D resources are expected to have a higher technological performance. Third, year dummies are included in the models to control for changes over time in the propensity of firms to patent.

Descriptive statistics and correlation coefficients for the dependent and explanatory variables are reported in Table 2. The mean (yearly) number of citation-weighted patents for the firms in the sample is twenty-one, and firms' average R&D expenditures amount to US$452 million per year. The sample firms are, on average, present in 1.8 biotechnology clusters and 2.4 other regions, spread over two countries. None of the reported correlations is excessively high.

EMPIRICAL RESULTS

The results of the fixed-effects negative binomial models on the relation between cluster membership and firms' overall technological performance are presented in Table 3. Model 1 includes only the control variables. Both the lagged biotechnology patent portfolio and the R&D expenditure variable are positive and significant. In Model 2, the 'clusters' variable is introduced, which indicates the number of clusters in which a firm is involved when developing R&D activities. The cluster variable is positive and significant, indicating that firms can enhance their technological performance by extending their R&D activities in multiple technology clusters (confirming Hypothesis 1). In Model 3, the 'other regions' variable is added to the set of control variables, reflecting the number of regions, outside clusters, in which a firm develops R&D activities. This variable is not significant. The log-likelihood ratio test reveals that including the other regions variable does not add significantly to the explanatory power of the model (Chi^2 likelihood ratio (LR) test = 1.89, $p = 0.17$). Model 4 includes both the 'clusters' and 'other regions' variables. A positive and significant coefficient is found for the 'clusters' variable, while the coefficient for the 'other regions' variable remains insignificant. Together, the findings from Models 2–4 suggest that it is the presence in technology clusters, and not in other regions, that influences the technological performance of firms.

Model 5 is the most complete model and includes, besides the linear terms, also the quadratic terms of the 'clusters' and the 'other regions' variables. Including quadratic terms allows one to check for non-linear relationships between the location variables and firm performance. The log-likelihood ratio test indicates that Model 5 significantly adds to Model 4 in terms of explanatory power (Chi^2 LR test = 7.43, $p = 0.02$). The 'clusters' variable has a positive and significant linear term, and a negative and significant quadratic term. This confirms Hypothesis 2: there is an inverted 'U'-shape relationship between the number of technology clusters in which a firm engages in R&D activities and the firm's total technological performance. The coefficients of the 'clusters' variables in Model 5 further indicate that biopharmaceutical firms should – ideally – be present in four biotechnology clusters. Since the average biopharmaceutical firm in the sample is present in less than two biotechnology clusters, most firms can still improve their technological performance by setting up R&D activities in additional biotechnology clusters.[12] In line with previous models, no significant effects are found for the 'other regions' variables in Model 5 (confirming Hypothesis 3).

In Model 6, an additional regression is performed to verify whether the cluster effect is distinctive from a mere R&D internationalization effect. Therefore, the linear and quadratic term of the countries variable, reflecting the number of countries in which a firm is present, are added to the initial model. The 'countries' variables are not significant, and the model does not significantly improve compared with the model containing only the control variables (Chi^2 LR test = 1.57, $p = 0.46$). This again confirms that presence in multiple technology clusters and not the mere presence in multiple locations is contributing to the firms' overall technological performance.

Table 3. Fixed-effect negative binomial regressions: weighted number of biotechnology patents acting as the dependent variable

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Biotechnology portfolio	0.0014***	0.0011***	0.0012***	0.0011***	0.0012***	0.0013***
	(0.0003)	(0.0004)	(0.0004)	(0.0004)	(0.0004)	(0.0003)
Research and development expenditures	0.0005***	0.0004***	0.0005***	0.0004***	0.0005***	0.0005***
	(0.0001)	(0.0001)	(0.0001)	(0.0001)	(0.0001)	(0.0001)
Clusters		0.0948**		0.0864**	0.2945***	
		(0.0402)		(0.0440)	(0.0924)	
Clusters^2					−0.0339**	
					(0.0132)	
Other regions			0.0325	0.0123	−0.0634	
			(0.0231)	(0.0256)	(0.0540)	
Other regions^2					0.0066	
					(0.0042)	
Countries						−0.0095
						(0.0974)
Countries^2						0.0075
						(0.0113)
Time dummies	Yes	Yes	Yes	Yes	Yes	Yes
Constant	0.2229	0.0954	0.1566	0.0802	0.0052	0.207
	(0.1541)	(0.1641)	(0.1620)	(0.1675)	(0.1879)	(0.2100)
Number of observations	422	422	422	422	422	422
Wald Chi^2	122.00***	131.01***	127.15***	132.13***	141.03***	127.85***

Notes: Standard errors are given in parentheses.

*Statistically significant at the 10% level; **statistically significant at the 5% level; and ***statistically significant at the 1% level.

CONCLUSIONS

Firms active in knowledge-intensive fields such as biotechnology are increasingly developing global research and development (R&D) activities with location choices to an important degree being determined by the presence of local technological capabilities. Studies in the economic geography literature have shown that firms located in regions where technological activities agglomerate (technology clusters) are more innovative than firms located elsewhere (BAPTISTA and SWANN, 1998; BEAUDRY and BRESCHI, 2003; DEEDS *et al.*, 1999; VAN GEENHUIZEN and REYER-GONZALES, 2007; BATEN *et al.*, 2007). However, so far, little is known about the impact of the presence in multiple clusters and regions on the technological performance of multi-location firms.

In this study, such an analysis is performed based on a panel data set of the largest biopharmaceutical firms – in terms of technological output – in biotechnology. The companies have headquarters in the United States, Europe or Japan, and engage in biotechnology R&D activities in different locations worldwide. Clusters are defined as worldwide leading regions in terms of technology development in the field of biotechnology. Over the period under study (1995–2002), most of the firms in the sample extended and/or contracted their presence in technology clusters and other regions. In the analyses, firm fixed-effect regression techniques and controls on time-varying changes in R&D efforts and past innovation experience of firms are used to account for firm-level differences in size and innovative capabilities. The findings suggest that biopharmaceutical firms can enhance their technological performance by developing R&D activities in multiple technology clusters. The results also reveal that boundaries exist in terms of the net beneficial effects of spreading R&D activities over multiple locations. When the number of clusters in which a firm is engaged becomes too large, increasing costs in terms of coordinating and integrating geographically dispersed R&D units might start to prevail over the marginal benefits from getting access to new, relevant knowledge. At the same time, the observed diminishing effects might also be caused by insufficient critical mass in terms of technological activity (economies of scale and scope) when R&D activities become dispersed.

The analyses provide evidence that the cluster effect is distinctive from a mere multi-location effect: the presence in technology clusters, and not the presence in multiple regions and countries, is contributing to a better technological performance of firms. As such, the study provides interesting insights for the R&D internationalization literature. Recently, this stream of literature started to investigate the relationship between the geographical dispersion of firms' performance. Some studies (SINGH, 2008; FURMAN *et al.*, 2005) found negative effects, while other studies (CRISCUOLO and AUTIO, 2008; IWASA and ODAGIRI, 2004; PENNER-HAHN and SHAVER, 2005; TODO and SHIMIZUTANI, 2008) reported positive effects of geographical dispersion on firms' performance. These studies did not take into account the technological characteristics of regions in which R&D activities are deployed (clusters or non-cluster regions). This may be one factor explaining the mixed results reported so far.

At the same time, the observed findings imply limitations as well. First, the sample consists of firms with large biotechnology patent portfolios and, consequently, the results only apply to this type of technology-active biopharmaceutical firms. Further research could investigate whether smaller firms in terms of biotechnology technology development activities – for example, entrepreneurial ventures – also benefit from being present in (multiple) technology clusters. Next, to retrieve the locations in which firms develop biotechnology research activities, inventor addresses on the firms' fully owned patents are used. While co-assigneeship was corrected for the derived R&D location variables might still reflect locations of co-inventors not belonging to the firm. This is notably the case when a firm engages in collaboration with a university or other organization, while retaining full ownership of the resulting inventions. Ideally, the locations where firms have R&D establishments (R&D laboratories) should be distinguished from locations where firms are present through other collaboration modes, such as R&D collaborations or sponsoring of research at universities and public laboratories. This requires conducting a firm survey since corporate annual reports do not provide sufficiently detailed information on the type and exact location of the research activities (biotechnology versus other fields) performed by firms.

Within this study, the focus was on regional technological capabilities within the same field (biotechnology); as such, a natural extension of the research reported here implies an examination of 'Jacobs' externalities as well. Regions differ not only in terms of biotechnology capabilities, but also with respect to the presence of technological activities within other, related and unrelated, fields. Studying the impact of technological variety in regions on the technological performance of firms, as well as the number of regions needed to access such variety, is an interesting avenue for further research. Closely related, one could study the relative importance of field-specific regional capabilities (Marshall–Arrow–Romer externalities (MAR)) and technological variety (Jacobs externalities) in regions for the technological performance of firms. A final suggestion for further research implies the micro-dynamics underlying the observed positive performance effects from presence in multiple technology clusters. While the findings of this study are interesting within the framework of R&D location decisions, identifying the most effective mechanisms (for example, collaboration with local firms and/or research institutes, technology acquisition, researcher mobility, the establishment of fully owned research laboratories) through which firms can benefit from agglomeration externalities in technology clusters might be highly relevant to ensure that firms yield results once location decisions have been made. The authors do hope the analyses and findings inspire colleagues in the fields of economic geography and R&D internationalization to engage in such endeavours.

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APPENDIX A

Table A1. Biopharmaceutical firms

Abbott Laboratories	Innogenetics
Affymetrix, Inc.	Invitrogen
Ajinomoto	Isis Pharmaceuticals, Inc.
Amgen	Johnson & Johnson
Applera	Kyowa Hakko Kogyo
Astrazeneca	Lonza Ag
Aventis	Martek Biosciences
Beckman Coulter	Maxygen, Inc.
Becton Dickinson & Co.	Merck Co.
Biogen Idec	Merck Kgaa
Boehringer Ingelheim	Millennium Pharmaceuticals
Bristol Myers Squibb	Mochida Pharmaceutical
Cell Genesys, Inc.	Myriad Genetics, Inc.
Chiron	Nanogen, Inc.
Diversa Corp.	Novartis
Eli Lilly	Novo Nordisk As
Fujisawa Pharmaceutical	Pfizer
Gen Probe, Inc.	Regeneron Pharmaceuticals
Genelabs	Ribozyme Pharmaceuticals
Genencor	Schering
Genentech, Inc.	Schering Plough
Genzyme	Scios, Inc.
Geron Corp.	Seikagaku
Gilead Sciences	Sequenom, Inc.
Heska Ag	Shionogi
Human Genome Sciences	Solexa
Hybridon	Tanox, Inc.
Icos Corp.	Transgene
Idexx Laboratories	Wyeth
Incyte Corp.	

NOTES

1. Prior studies used cross-sectional data analysis techniques, and did not control for differences in firms' innovation efforts (absolute level of R&D expenses) when studying the impact of cluster membership on firms' technological performance.
2. MARSHALL (1920), ARROW (1962) and ROMER (1986) (henceforth MAR) suggested that knowledge spillovers mainly arise among firms in the same industry. On the contrary, JACOBS (1969) believed that the most important

knowledge spillovers occur across industries. Empirical results on the relative importance of both types of knowledge externalities are mixed (for example, GLAESER *et al.*, 1992; FELDMAN and AUDRETSCH, 1999; HENDERSON *et al.*, 1995; BEAUDRY and SCHIFFAUEROVA, 2009; FRENKEN *et al.*, 2007).

3. Other studies (e.g. HILL and NAROFF, 1984; SWANN and PREVEZER, 1996; and HENDRY and BROWN, 2006) have studied the impact of cluster location on the financial performance and growth of firms.
4. It was calculated that for EPO biotechnology patents applied for in 1995 and granted by 2006, only 40% of the patents were granted within six years after application.
5. GLÄNZEL *et al.* (2004) defined and validated a search key to retrieve all EPO patents in the biotechnology domain in the period 1978–2001.
6. The NUTS (Nomenclature des Unités Territoriales Statistiques) classification, established by Eurostat, provides a breakdown of European countries into regions, primarily based on institutional divisions currently in force in the country. The average population size for NUTS-1 regions in Europe ($n = 73$) is 5.3 million. The United States of America consist of fifty sub-national entities called states, having their own state government with substantial state responsibilities. The average population in the US states is 5.5 million. The prefectures of Japan consist of forty-seven sub-national jurisdictions with their own governor and parliament. The average size of prefectures is 2.7 million inhabitants.
7. Forward patent citations are calculated on the EPO patent citation database described by WEBB *et al.* (2005). They are calculated for all citing EPO patents and national patents with EPO patent equivalents.
8. In addition to citation-weighted patent counts, the number of triadic patents was also used as an alternative measure to control for differences in the quality of patents. Triadic patents are patents simultaneously applied at the patent offices of the United States, Europe and Japan. Analyses with triadic patents lead to similar results as the analyses presented in Table 3.
9. In Europe, 12% of biotechnology patents have multiple assignees (LECOCQ and VAN LOOY, 2009).
10. Analogous to the cluster and other regions variables, only countries from Europe (EU-15 and Switzerland), the United States and Japan were counted.
11. Firm-level R&D expenses specifically related to biotechnology activities are not available.
12. Only in 7.35% of the observations (firm-year), firms develop biotechnology activities in more than four technology clusters.

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