# Clusters in the biopharmaceutical industry: toward a new method of analysis

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**Clusters are groups of co-located and interconnected firms and institutions linked by commonalities in their strategies and complementarities in their activities and resources. There are several reasons for the geographical clustering of firms in the biopharmaceutical industry. This review unpacks some advantages and disadvantages of cluster participation, and proposes a new method to enable managers and researchers to identify clusters in the biopharmaceutical industry.**

## Introduction

Clusters are groups of co-located and interconnected firms and institutions linked by commonalities in their strategies and complementarities in their activities and resources [1]. What are the advantages and disadvantages of locating in a cluster of firms and institutions for biopharmaceutical firms? This is a crucial question for managers and scholars alike, because cluster membership tends to be a salient feature of firms in this industry, and research has shown that cluster participation is linked to firm performance [2,3]. Herein, we unpack some advantages and disadvantages of cluster participation, and propose a simple new method for managers and researchers to identify clusters in the biopharmaceutical industry.

The importance of agglomeration has been noted by scholars across several disciplines and areas, including economic geography, management and organization science [3–5]. In his seminal work, Marshall argued that agglomeration economies exist in many industries owing to industry specialization, labor pooling and the spillover of knowledge between firms and institutions [6]. Importantly, firms in industries where important inputs include industry R&D, university research and skilled labor are more likely to cluster than firms in industries where knowledge spillovers from such sources are less important [7]. The biopharmaceutical industry consists of firms that develop and/or manufacture drugs for human therapeutics and/or diagnostic purposes, and that have at least one product that can only be produced by biotechnological methods; that is, techniques and technologies that use the principles of genetics, immunology and molecular, cellular and structural biology to discover and develop new products [8]. In this paper we show that the biopharmaceutical industry tends to be highly geographically concentrated, similar to the high geographic concentration found in the biotechnology industry [9,10].

There are several reasons for the high geographical concentration in the biopharmaceutical industry. First, clusters play an important part in drug development because of the fragmented nature of knowledge in drug development and the complementary resources and inter-firm activity required by the development process. In the biopharmaceutical industry, innovation depends on tight relationships between suppliers, customers and partners. With the introduction of biotechnology and increased complexity of the tools required, drug development has shifted from being an activity of a single large pharmaceutical firm to a collective and collaborative activity involving different actors, such as dedicated biotechnology firms, large pharmaceutical firms, contract research organizations (CROs), public research laboratories, universities and regulatory institutions. Drug development consists of a less regulated phase of basic and preclinical research for new technology and compounds, as well as a highly regulated chain of clinical trials for developing a therapeutic compound for a specific medical indication or need. This 'basic' versus 'applied' research distinction allows firms to focus and specialize in different parts of the value chain. Yet, specialization also increases the interdependency between firms and other institutions; efficient and effective drug development requires interaction within and between phases [11].

Second, at a more fine-grained level, researchers have shown that clusters foster cooperation; knowledge flows between firms,

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and other institutions are less costly, more reliable and easier to coordinate [12]. However, it is not only vertical interactions between players in the industry (i.e. interactions between upstream suppliers and downstream buyers in a value chain) that impact drug development; the spillover of knowledge and information between competing firms also has a significant effect. In clusters, knowledge spills over more easily to competitors because of employee membership of professional associations, informal social relationships between scientists, sharing of scientific talent or laboratory equipment, university collaborations and market exchange of information [10]. In particular, the personal relationships between scientists can lead to spillover of valuable tacit knowledge or skills, not just explicit product information, scientific studies, engineering documents and process specifications. Thus, Michael Porter reasoned early on that, by providing access to tacit knowledge, clusters offer firms the potential for differentiating from nonclustered competitors – enhancing their competitive advantage [1].

It is imperative for managers to understand the advantages and disadvantages associated with the location of firms within clusters. Location is a long-term decision with potentially strong implications for the financial performance of a company. To understand these implications we should first identify the cluster boundaries in the biopharmaceutical industry, which in turn indicate the types of 'member' firms (competitors and potential partners) and other institutions. To date, there is no common understanding of how cluster boundaries should be identified. Previous studies mainly used metropolitan statistical areas (MSAs) to identify cluster boundaries [2,3,10,13]. This approach is conceptually problematic because clusters defined according to MSA do not necessarily provide accurate information on the clusters in a specific industry. A cluster might consist of more than one MSA, or one MSA might be too large to capture knowledge spillovers that can occur because of clustering.

In the remainder of this article we outline the advantages and disadvantages of firm membership in geographical clusters, introduce a new method for identifying cluster participation and conclude with a brief reflection across the subject.

## Advantages of geographical cluster membership

Previous work has outlined several advantages of cluster membership [1,9,14,15]. Herein, we categorize and explain the advantages of clusters according to their contribution to generic business-level strategies of cost leadership and differentiation [16,17]. The factors that enable a firm to reduce unit production costs serve a cost leadership strategy, whereas factors that enable the firm to innovate and create unique, premium-priced services and products serve a differentiation strategy. These generic strategies are not mutually exclusive [18]. In dynamic industries such as the biopharmaceutical industry firms can achieve the best effects by pursuing both strategies simultaneously [19].

### *Seeking cost advantages*

Clusters offer several cost advantages for firms. First, firms in clusters could benefit from the investments made by governments, public institutions and other organizations to foster the development of a specific industry in a region. The biotechnology industry is heavily dependent upon public funding of basic scientific research, which gives rise to spin-off activity in regions close to universities, research hospitals and public research laboratories. For example, some US$770 million of public research funding flows annually through the Boston biotechnology cluster and at least US$1 billion is channeled through the San Francisco and San Diego clusters [20]. Public spending or private investment by companies in training programs, special infrastructure, quality centers or laboratories can contribute to overall productivity of a firm [1,21]. For example, under the BioRegio Program, Baden-Württemberg's biotechnology region, the 'Rhine-Neckar-Triangle', received public funding of ~€25 million in the period 1997–2002 [19]. Until 2006 the firms funded had created approximately 1000 qualified jobs and had acquired private investments of >€500 million [22].

Second, co-location of firms can incur lower coordination and transaction costs. Coordination costs arise from the operational interdependence of the partners' activities, which need to perform different activities jointly, whereas transaction costs arise from opportunistic behavior of one or more partners, and include the costs of negotiating, monitoring and enforcing contracts [23]. Transaction costs are reduced because of the proximity of buyers and sellers, lower search costs for finding potential buyers and sellers, easier communication, increased trust and more-specialized labor [1,15,21]. Moreover, clusters offer abundant specialized suppliers, lowering the cost of shipments and the need for an in-house inventory, while improving support services for operations in the industry and learning through feedback between firms. In addition, there is a reduced risk that suppliers in the cluster overprice their products because it is in their interest to retain an impeccable reputation among buyers in the cluster [1].

Third, clusters foster the development of a local labor market for specialized skills making it less costly for firms to search for talent and coordinate their hiring and other HR policies [1,4,6,15]. Because clusters can signal job opportunities and provide a well-connected network for rapid career development they typically attract skilled labor [1,10,24]. For the biopharmaceutical industry, specialized labor with expertise in scientific disciplines such as microbiology, genetics, biochemical engineering, biochemistry, as well as entrepreneurial and management skills, is crucial and, here, clusters can benefit the supply [9]. A survey of biotechnology firms located in California showed that the most important factor determining location is the availability of qualified labor in the geographical area [8].

Fourth, clusters provide easier and less costly access to specialized and complementary knowledge [4,6,15,21]. Because extensive technical, market and operational knowledge can accumulate among individuals, firms and institutions in clusters, member firms might face lower search costs in obtaining access to such knowledge than nonmember firms. In addition, R&D by firms and universities creates knowledge spillover for other firms to exploit [25,26], potentially leading to reduction of in-house R&D spending and higher innovation output from cluster members. Owing to this effect, in knowledge-intensive industries such as biopharmaceuticals small firms with limited R&D spending appears highly innovative [26,27]. The presence of universities in an area creates a kind of 'intellectual commons' for the benefit of cluster members [26]. For example, student placement agreements between the university and firms foster the sharing of scientific knowledge

[28]. Finally, increased trust between firms lowers the costs of identifying, accessing and transferring knowledge [29]. In particular, a local business culture, work ethic and professional standards support the sharing of tacit knowledge between firms [21].

### *Seeking differentiation advantages*

Competition in the biopharmaceutical industry is mainly driven by the ability of a firm to learn continuously and to innovate new products, processes and services [30]. Clusters are important for the ability of a company to create new knowledge and innovate [1], making cluster members potentially more innovative than nonmembers [31].

According to Miller [32], two main differentiation strategies are based on product innovation and/or intensive marketing and image management. Clusters contribute to firm differentiation in three ways. First, cluster membership allows firms to gain access to a wide variety of knowledge through spillovers from other firms and institutions, including competitors [7,25,33]. Innovation depends on the integration of different types and forms of knowledge [34] and firms can build an advantage by locating close to the source of technology development [26]. Co-location eases firms' identification and imitation of superior solutions within the cluster [21]. Key sources of knowledge for biopharmaceutical firms include university and industrial R&D, firms in related industries and networks of business service firms [26]. DeCarolis and Deeds [3] identified clusters as a so-called 'knowledge-flow' channel and empirically found that the location of a firm in a geographic area, as a result of various knowledge flows, positively impacts firm performance in the biotechnology industry. For example, the biotechnology cluster around Cambridge, UK provides a valuable knowledge-flow channel for biopharmaceutical firms with its globally recognized university and hospital research facilities including: the MRC Laboratory of Molecular Biology at Addenbrooke Hospital; Cambridge University Institute of Biotechnology, Department of Genetics and Centre for Protein Engineering; the Babraham Institute; the Sanger Institute; and >50 firms operating in this industry [20].

Second, scholars have argued that clusters tend to speed up innovation among member firms compared with noncluster firms [1]. Owing to trust, business culture and other effects discussed earlier, suppliers, customers and competitors become more closely involved in the innovation process of a firm, ensuring more-efficient and -effective knowledge creation geared toward customer needs. For example, a biopharmaceutical firm conducting clinical trials can benefit from its proximity to a hospital. Here, it should also be noted that customers can be an important source of tacit knowledge [26] that enhances both the speed and the likelihood of successful innovation. Conversely, tacit knowledge sharing between firms needs proximity [35] and thus noncluster members cannot benefit from such knowledge to the same degree.

Third, clusters enhance the reputation of member firms [1] allowing them to create a unique and superior image for their products and services. Investors such as venture capitalists and 'business angels' also gravitate toward active geographical clusters populated by innovative firms, universities, promising research projects, entrepreneurially minded scientists and unique expertise. For example, Powell *et al.* [36] found that venture capitalists invest most in co-located firms to benefit from increased collaboration and knowledge exchange, and eventually increased return on investment. Capital and management advice is crucial for firms to pursue differentiation strategies through innovation and image building.

## Disadvantages of cluster membership

Notwithstanding these advantages, managers should make prudent decisions about their cluster membership. Firms in a cluster can face several sources of so-called 'agglomeration diseconomies' because of unintended knowledge spillovers and other effects. Extensive spillover of valuable and rare knowledge to competitors can quickly erode the sources of a firm's competitive advantage. Given that intense knowledge spillover in a cluster is considered a source of advantage, several firms might seek to join the cluster, leading to further knowledge spillover between firms and erosion of advantages for the leading firms in the cluster. The total impact of these two opposing forces might be contingent on the cost or differentiation advantages for firms, means of knowledge protection (including trade secrets or patents), industry fragmentation, R&D investment levels, degree of innovation among member firms, similarities and differences in knowledge, and the maturity of the industry. According to Shaver and Flyer [37], firms that possess strategically relevant knowledge and other resources might choose not to co-locate with other firms, because of knowledge spillover, whereas, firms with the weakest technologies and pools of talented employees might choose to co-locate in clusters precisely for that reason. Shaver and Flyer [37] found evidence that cluster members have survival disadvantages owing to an adverse selection with respect to the types of firm that agglomerate (for a similar study, see Ref. [38]).

Some scholars also argue that very strong clusters might negatively affect the survival of new firms because of congestion of firms in one area and extreme competition for resources and personnel [2,15]. This was typical for information technology firms in Silicon Valley, USA during the late 1990s. Congestion and competition might force a rapid increase in firm costs for labor, land, services and products [9], reducing the profit margins for cluster members. For example, the congestion in the biotechnology clusters of Oxford, UK and Boston, USA resulted in rising labor and real-estate costs [20,39]. In the Boston area some of the small biotech companies even moved some of their operations to more-peripheral locations to find less expensive lab and office space [39]. Folta *et al.* [2] investigated 806 US biotechnology firms founded between 1973 and 1998 and found that the advantages of cluster membership decrease as the number of firms in the cluster increases.

## Methods for identifying clusters

Although it is clearly important to take clusters into consideration when formulating strategies for biopharmaceutical firms, it is difficult to identity cluster boundaries [21]. The notion of spatial scale used in previous literature is arbitrary, extending from a street to whole nations. It is not possible to define a specific geographical scale once and for all, and different scales can be used according to the type of phenomenon under investigation [21]. For example, if institutions or cultural and linguistic aspects are the focus, the nation state could be a good proxy for defining clusters; but if the focus is knowledge spillovers associated with social interactions and informal ties, then ‘small places’ such as cities, urban neighborhoods and city blocks might offer a better proxy [21]. Such diversity in methods produces inconsistent results in prior research [15,40]. For example, several empirical studies investigated the impact of geographic agglomeration on knowledge spillovers, innovation and growth [7,25,26]. In the literature, cluster boundaries are defined with different proxies, such as states, districts, provinces, MSAs and specific regions in countries such as UK Central Statistical Office regions [9,15,31,41]. Eisingerich *et al.* [42], for example, used countries to define clusters. Yet, measuring the effect of agglomeration at this level could be misleading because countries are not homogeneous and strong agglomeration patterns could exist within a nation [15].

Some authors have chosen ‘state boundaries’ to define clusters [7,37]. Feldman [26] used states and included a geographic concentration measure as a control variable to account for the degree to which manufacturing activity is concentrated within states. This allowed for controls of potential sources of aggregation bias. Prevezer [9] also used the individual state to define clusters, although she discussed the problem that clusters might not be confined within state borders. Audretsch and Feldman [7] argue that states provide a superior number of data sources and the most relevant unit of policy making. Although states have their own tax regimes, utility pricing and policies toward emerging industries, which provide some justification for their use in cluster analysis, they are also somewhat artificial for the analysis of spatial phenomena. Previous literature mostly used MSAs to identify cluster boundaries [2,3,10,13]. Feldman and Audretsch [33] used either the consolidated metropolitan statistical areas (CMSAs) or the MSAs. However, defined according to MSA, clusters do not necessarily provide accurate information on members and interactions in a specific industry. A cluster might consist of several MSAs, or one MSA might simply be too large to capture knowledge spillovers. For example, the biotechnology cluster of Basel, Switzerland includes the Basel metropolitan region as well as parts of neighboring areas of Alsace, France and South Baden, Germany. To obtain a comparative view, Jaffe *et al.* [25] included three different geographic levels (country, state and CMSA/MSA) in their analysis of patents and citations by firms in the same region.

Complementing predefined cluster boundaries, some authors [43] have argued in favor of an algorithm to identify the geographic regions that constitute the clusters. Watts and Mitchell [43] used journey-to-work data and defined the regions using the Intramax method – a hierarchical clustering algorithm maximizing the proportion of the total interaction within a region while minimizing cross-boundary movements between regions. Although their view of ‘region’ does not entirely fit our definition of ‘clusters’, their algorithm is similar to the new method we propose.

## Toward an alternative method

Although some empirical studies of clusters in the biotechnology industry are available, to our knowledge there is no study on clusters in the biopharmaceutical industry (a subfield of the biotechnology industry [44]). Taking into account the limitations of the previous methods discussed, we introduce a new method to identify the

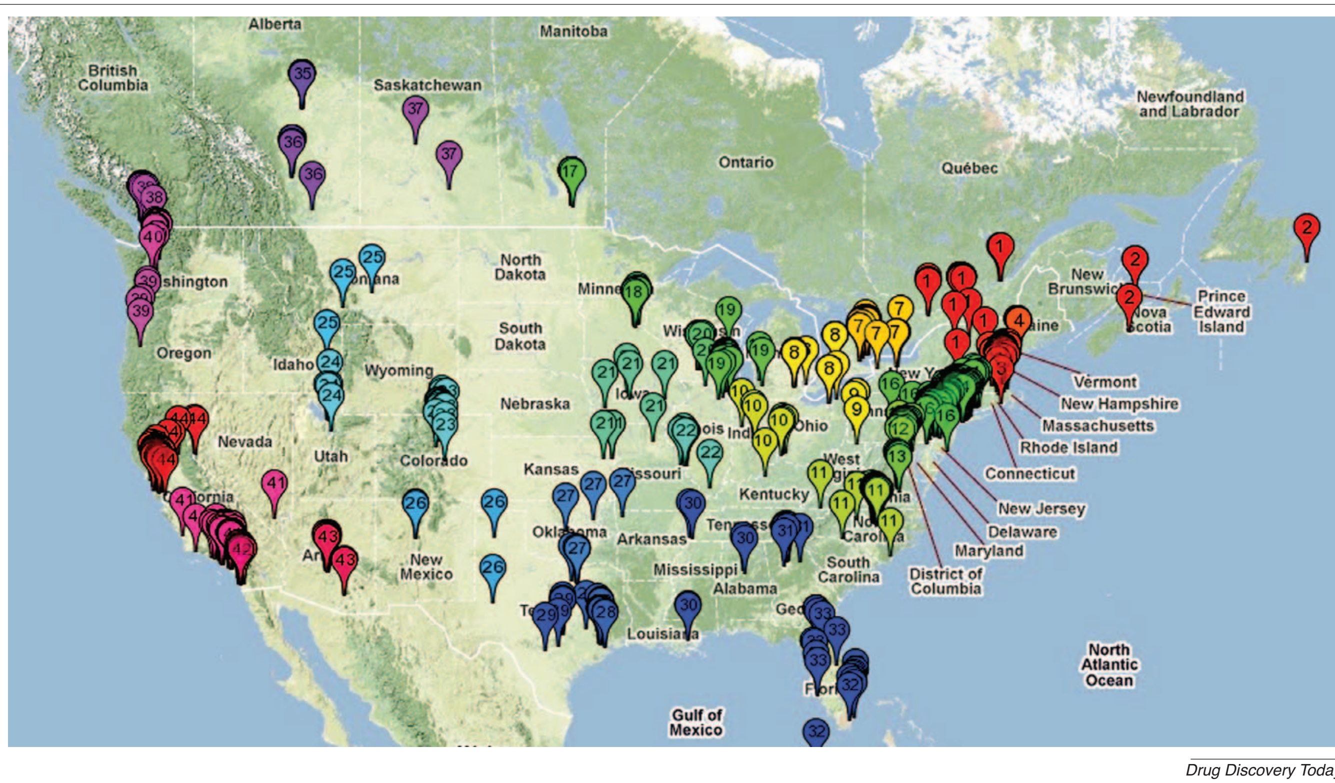


**FIG. 1**

The biopharmaceutical clusters in the USA. Each marker on the map corresponds to a firm. Firms in the same cluster are colored and numbered identically. Different colors (numbers) indicate different clusters.

clusters in the biopharmaceutical industry. The method finds a configuration in which the distance between the firms in a cluster is minimized while the distance between the clusters is maximized. Our method has two advantages: first, it is flexible and can be used to determine clusters on different levels (e.g. state, country or worldwide) – predefined boundaries, such as MSAs, cannot be used globally because there is no worldwide unit of area that can account for comparable clusters; second, with longitudinal data, we can observe the evolution of clusters over time – it is not limited to static boundaries, for example provided by MSAs.

There are seven steps in the method:

i. Identify the industry.
ii. List all the firms in the industry.
iii. Collect unique data on the geolocations (headquarter addresses) of the firms in the sample.
iv. On the basis of headquarter addresses, use the Google Maps algorithm to generate the exact geocode (longitude and latitude) of firm location.
v. Calculate the point-to-point distance between companies using geocodes.
vi. Conduct a cluster analysis using the point-to-point distance matrix of companies as an input.
vii. Approximate the area of each cluster as a rectangle, with the borders of the rectangle defined by the geocodes of the outermost firms in a cluster.

We applied the method to obtain precise information on existing worldwide clusters in the biopharmaceutical industry in 2003. First, we developed a list of all public and private biopharmaceutical firms worldwide using the Bloomberg® database and the BioScan® database, respectively. We recorded all firms belonging to the industry segment 'pharmaceuticals, biotechnology and life sciences' (GICS: 3520) of the healthcare sector (GICS: 35) according to Standard and Poor's Global Industry Classification Standard (GICS). This resulted in a list of 2084 firms. On the basis of headquarter addresses, we used the Google Maps algorithm to generate the exact geocodes (longitude and latitude) of firm locations. Firms without a clear address, identifiable geocode or identifiable founding year were removed from the clustering sample, resulting in a list of 1777 firms. On the basis of the geocodes we grouped all firms into five regions to account for the regional circumstances of cluster formation: Africa (2), the Americas (1024), Asia (282), Australia–New Zealand (75) and Europe–Middle East (394). Next, we ran a hierarchical clustering algorithm (Ward's linkage method) using the point-to-point

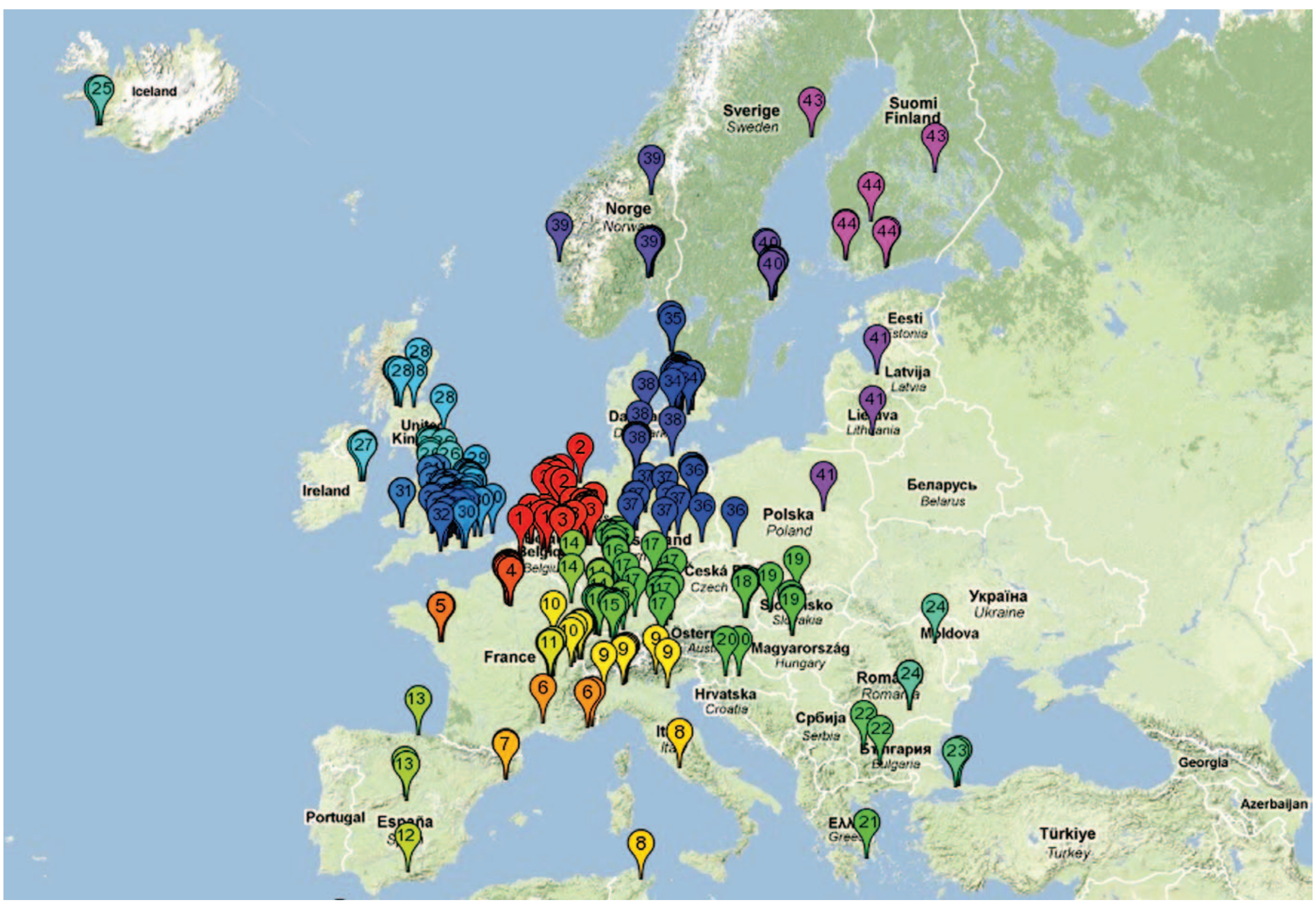


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**FIG. 2**

The biopharmaceutical clusters in Europe. Each marker on the map corresponds to a firm. Firms in the same cluster are colored and numbered identically. Different colors (numbers) indicate different clusters.
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distance matrix of firms existing in 2003 as input. On the basis of the results of the clustering algorithm, the firms in each region were grouped into a defined number of clusters (Africa 2, Americas 45, Asia 31, Australia–New Zealand 7, Europe–Middle East 50). The area of each cluster was approximated as a rectangle, with the borders of the rectangle defined by the geocodes of the outermost firms in the respective cluster. Identifying the cluster boundaries in this manner is crucial to calculate different cluster features, such as cluster density. The resulting clusters for the USA and Europe can be seen in Figs. 1 and 2, respectively. Different colors (numbers) indicate different clusters.

## Concluding remarks

In this paper, we have reviewed the relevant literature on clusters, identified the advantages and disadvantages of clusters for biopharmaceutical and other firms, briefly reviewed the methods used in previous studies to identify cluster boundaries and proposed a new method. Owing to the effect of knowledge spillover, firms located in clusters are expected to realize higher rates of innovation. However, managers of biopharmaceutical firms should also consider the disadvantages and contingencies of cluster membership. Conversely, knowledge spillover from the firm to other cluster members could weaken the firm's sources of competitive advantage.

Managers should keep in mind that the ability of the firm to benefit from knowledge spillovers might be contingent on specific factors, such as the proximity between technologies developed or used by firms in the cluster [45]; industry structure (e.g. bargaining power of suppliers, or monopolistic competition versus pure monopoly); the business culture in the cluster; and the diversity of firm strategy (e.g. see Ref. [27]). In addition, innovation is contingent on different interrelated factors that seem less dependent on cluster membership, such as demand conditions, related and supporting industries, and firm structure and strategy [1]. Therefore, when choosing locations for their firms, we advise managers to investigate cluster boundaries and cluster characteristics first, and afterwards find the appropriate cluster that supports the goals, technologies and capabilities of the firm. The method we propose in this paper allows us to identify clusters in the biopharmaceutical industry, using a sample of worldwide firms. A limitation of this alternative method is that, based on the clustering algorithm, it only considers distance measures between firms to identify clusters. If the sample is worldwide the resulting clusters might be located on the boundaries between different countries that make individual member firms subject to various taxation, regulatory and other policy-related regimes.



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