June 2017

IRISgroup

A comparative analysis of seven world leading biotech clusters

English summary

Content

1. Background and approach

1.1. Background

The biotech sector is unique in many ways. First, many biotechnological inventions de rive from research at universities and university hospitals, and the biotech sector depends on highly qualified employees educated in strong research environments.

Second, drug development is extremely expensive and the risk of failure is high. Private investors are unlikely to invest in the early phases of drug development. Thus, public funds are often necessary to test ideas, proof of concepts and early innovations. However, a solid investment environment that can carry start-ups from idea to market is essential to establish a diverse and strong biotech cluster.

Third, it is important to create a strong and coherent ecosystem for biotech innovation with the right mix of entrepreneurs, pharma companies, skilled technology transfer offices, entrepreneurial universities, advisors and mentors, investors and incubators.

This short paper presents key findings from a benchmarking analysis of seven world leading biotech clusters – Basel, Boston, Cambridge, Copenhagen, Munich, Paris, and Stockholm-Uppsala.

The focus is on so-called "red biotech" (see definition in appendix).

The paper is a summary in English of a comprehensive study that IRIS Group completed and published early 2017. The aim was to compare the Copenhagen biotech sector with other leading biotech clusters – focusing on the entire value chain from research to growth in existing biotech companies.

The entire analysis is available in Danish at www.irisgroup.dk.

1.2. Methodological approach

First, we did a bibliometric analysis in which we compared research production and quality. Moreover, we developed a model to identify and benchmark research strengths.

Second, we gathered key information from universities, hospitals, and cluster organisations in each region. We asked for hard data such as number of spinouts, but also detailed information on the functioning of the regional biotech ecosystem, framework conditions etc. We also used the BCIQ BioCentury Online Intelligence database to collect data on venture investments in the regions. Valid data was not available for all variables in all regions. For specifications on our methodological approach, please see appendix.

Finally, we studied national and regional framework conditions relevant to the biotech sector in each region/country, such as proof of concept grants, seed investments, resources at technology transfer offices and national funding opportunities.

1.3. Contributors

The analysis was financed by a group of stakeholders including the Novo Nordisk Foundation, the Danish Growth Fund, the Danish Ministry of Business and Growth, the Danish Ministry for Higher Education and Science, the Capital Region of Denmark, and the City of Copenhagen.

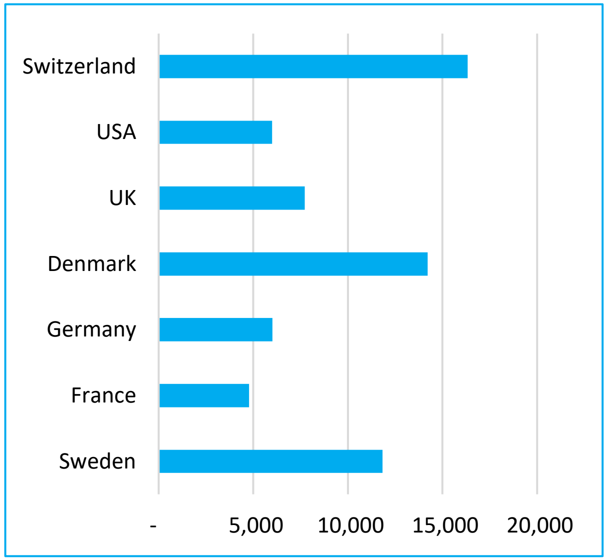
2. Performance

2.1. Research production

To make a solid comparison of biotech clusters, a first step is to compare the production of biotech related university research in each region.

In Scopus – the world's largest database for international research articles – all biotech related subfields were identified and included in a bibliometric analysis[1].

Figure 2.1. Number of biotech publications per million population (country based)

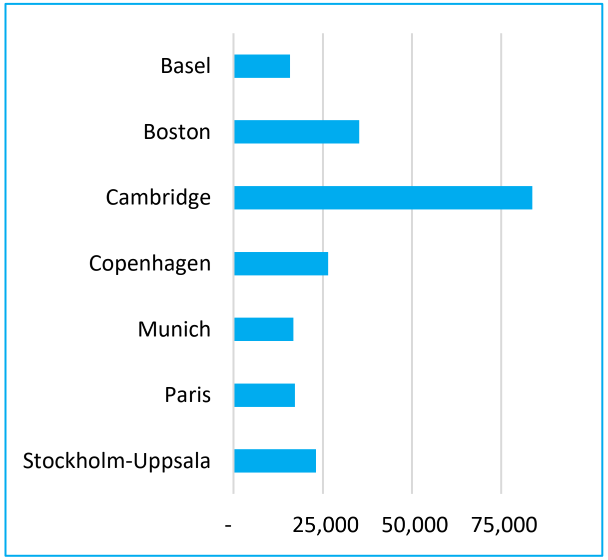


Source: IRIS Group based on Scival/Scopus.

Based on the bibliometric analysis, figure 2.1-2.3 present three different indicators of biotech research performance. Figure 2.1 shows the number of biotech research articles at *national* level relative to population size in the seven countries. The smaller countries (Switzerland, Denmark, and Sweden) have the largest production of biotech publications per million population.

In figure 2.2, the number of biotech research articles at *regional* level is calculated relative to population size in the seven regions, which paints a different picture with Cambridge in top.

Figure 2.2. Number of biotech publications per million population (region based)

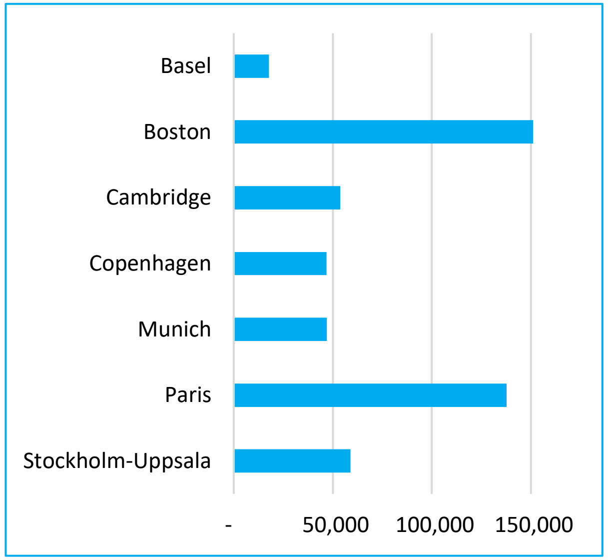


Source: IRIS Group based on Scival/Scopus.

If we look at the total number of articles produced (not taking population size into consideration), Boston and Paris are the leading regions. See figure 2.3.

In absolute numbers Cambridge, Copenhagen, Munich, and Stockholm-Uppsala have approx. the same scientific foundation to create new biotech companies – in quantitative terms.

Figure 2.3. Total number of biotech publications (region based)



Source: IRIS Group based on Scival/Scopus.

[1] In Scopus research production is divided into 334 scientific subfields. 95 subfields were identified as biotech related.

2.2. Research quality

The *quality* of the research is, of course, also important for the development of a strong biotech cluster. Top quality, groundbreaking research is likely to pave the way for new drugs, technologies etc. Research quality also affects talents – the better research quality in a region, the better students and PhDs are available for biotech companies.

Bibliometrically, research quality can be measured in several ways. We have used different indicators all showing a similar picture: Boston and Cambridge are the two regions with the best biotechnological research.

Table 2.1 compares the regions on one of the key indicators, namely the amount of scientific papers that globally are among the 10 per cent most cited within their field of biotech research. Underscored numbers in bold indicate top-2 for each research area.

Cambridge is ranked in top-2 in all six research areas, while Boston is in top-2 in five areas. Basel shares top-2 with Cambridge when it comes to research in pharmacology, toxicology, and pharmaceutics.

The four remaining regions are not ranked in top-2. However, the total scores for Copenhagen and Munich are a bit higher than for Paris and Stockholm-Uppsala.

Table 2.1. Amount of scientific papers among the 10 per cent most cited (2011-2015)

	Basel	Boston	Cambridge	Copenhagen	Munich	Paris	Stockholm-Uppsala
Chemistry and Chemical Engineering	18,9	**29,1**	**26,7**	19,3	16,9	14,3	18,1
Biochemistry, Genetics and Molecular Biology	21,1	**24,9**	**26,9**	20,5	19,6	17,5	18,1
Immunology and Microbiology	20,9	**24,2**	**23,6**	19,7	21,8	19,0	18,5
Medicine	22,0	**24,0**	**27,3**	20,9	19,4	18,7	20,0
Pharmacology, Toxicology and Pharmaceutics	**24,1**	20,7	**26,4**	18,2	17,4	17,0	16,5
Neuroscience	20,3	**21,8**	**23,1**	15,2	17,9	16,1	16,2
Total	21,2	**24,1**	**25,7**	19,0	18,8	17,1	17.9

Source: IRIS Group based on Scival/Scopus

To get an overall picture of research strongholds, we conducted a model combining measures for research production and quality. The model enabled us to estimate strongholds in each region among the 95 biotech-related subfields that we identified in Scopus.

The number of strongholds depends on the criteria applied. We did four different calculations with diverse threshold values to determine which research areas to include as regional strongholds.

In table 2.2 on the next page, the numbers of strongholds are listed for each of the seven regions.

Table 2.2. Calculated number of scientific strongholds

Region	Number of strongholds (min-max value)
Basel	0-3
Boston	17-48
Cambridge	8-19
Copenhagen	8-16
Munich	1-3
Paris	1-5
Stockholm-Uppsala	2-9

Source: IRIS Group based on Scival/Scopus

Boston has between 17-48 scientific strongholds (depending on the criteria applied) followed by Cambridge and Copenhagen.

It should be emphasised that the model includes both quantitative and qualitative measures to calculate the number of scientific strongholds in each region.

2.3. Spinouts from public research

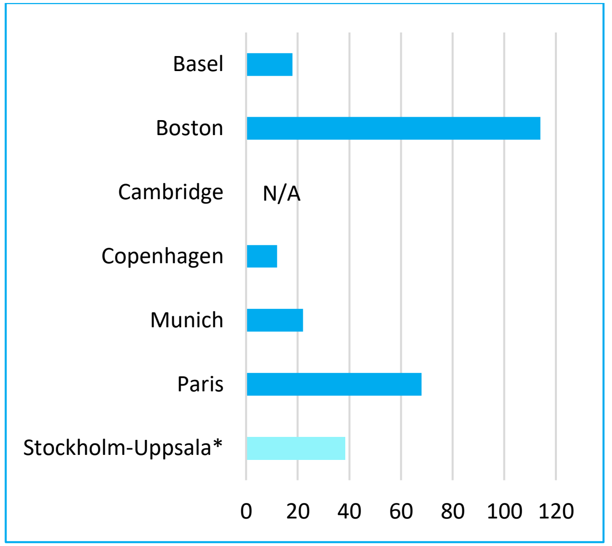
Figure 2.4 shows the total number of red biotech spinouts from universities and university hospitals[2] between 2009-2015.

In Boston, universities and hospitals spun out almost twice as many red biotech companies as in Paris, which is the second largest producer of spinouts.

The number of spinouts in Stockholm-Uppsala is estimated. In Sweden, researchers own IPR from their research, and are thus not obligated to make use of technology transfer offices (TTOs) at the universities when creating new companies. Only data on companies created in collaboration with TTOs was available. The estimated number of spinouts in Stockholm-Uppsala is based on interviews with key stakeholders in the region[3].

Unfortunately, data on spinouts in Cambridge was not available.

Figure 2.4. Number of red biotech spinouts from universities and university hospitals (2009-2015)



*Source: Data is collected from universities and university hospitals in each region. *The number for Stockholm-Uppsala is estimated.*

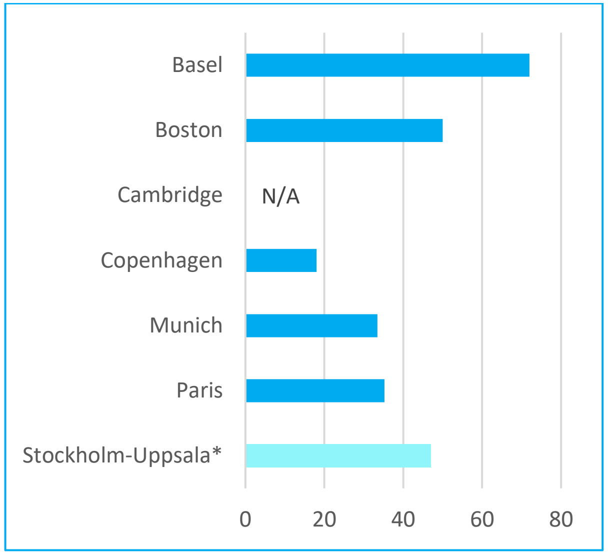
If we look at spinout production relative to research production, a different picture appears.

In figure 2.5 on the next page, the number of red biotech spinouts is shown relative to published scientific articles within biotech research.

[2] We define spinouts as: a registered company that has received initial funding for the development of a new product or service based on technology developed at a university or a university hospital.

[3] The TTOs in Stockholm-Uppsala reported 19 spinouts between 2009-2015. The key stakeholders, whom we interviewed, estimated that only about half of the spinouts in the region were created in collaboration with a TTO. Thus, we have doubled the number of spinouts reported by the TTOs.

Figure 2.5. Number of red biotech spinouts per 100,000 scientific article (2009-2015)



Source: IRIS Group based on Scival/Scopus. *Spinout data is collected from universities and university hospitals in each region. *The number for Stockholm-Uppsala is estimated.*

The figure reveals that Basel spun out most companies from 2009-2015 compared to research output, followed by Boston. As shown in section 2.2, the research quality in these regions is high making up favourable conditions for spinouts.

2.4. Red biotech companies

To get a picture of the size of the biotech clusters, table 2.3 provides the number of red biotech companies in five of the seven regions, including growth in numbers from 2005-2015.

The total number of red biotech companies has increased in all regions. The most prominent increase has taken place in Stockholm-Uppsala. Two of Sweden's largest life science companies Pharmacia and Astra merged with international partners in the late 1990's and moved their activities out of the region. New biotech companies were established and many of the lost life science jobs were recreated. Thus, many red biotech companies in Stockholm-Uppsala are relatively young and small.

Table 2.4 shows the number of full time employees (FTE) in red biotech companies and bio pharma, respectively. Bio pharma includes the big

Table 2.3. Number of red biotech companies (2005-2015)

	2005	2010	2015	2005-2015
Boston	420*	470	570	37%
Cambridge	225	260	310	38%
Copenhagen	71	92	85	20%
Munich	90	140	150	66%
Stockholm-Uppsala	130	190	230	76%

*Source: Data is collected from biotech clusters in each region. Data was not available for Basle and Paris. *Data indicates the number of companies in 2007.*

Table 2.4. Number of FTE in red biotech companies and bio pharma in total (2005-2015)

	2005	2010	2015	Growth 2005-2015	Bio pharma in total (2015)	Number of citizens
Boston	20,000*	22,500	27,400	35%	49,000	4.6m
Cambridge	4,500	7,000	9,000	100%	N/A	0.6m
Copenhagen	2,039	2,544	3,203	57%	23,400	1.8m
München	2,100	2,500	3,250	55%	Approx. 25,000	2.8m
Stockholm-Uppsala	3,700	4,500	4,950	34%	9,500	2.5m

*Source: Data is collected from biotech clusters in each region. Data was not available for Basle and Paris. *Data indicates the number of FTE in 2007.*

pharma companies like GlaxoSmithKline, Roche, and Novo Nordisk. The last column shows the population size in each region.

The two largest biotech clusters are found in Boston and Cambridge. The high number of companies and spinouts in Boston are, of course, a main explanation for the many biotech jobs in the region, but the biotech cluster in Boston is also older than the other clusters making it home for bigger and more market-ready companies.

Copenhagen and Munich are characterised by a strong position within big pharma.

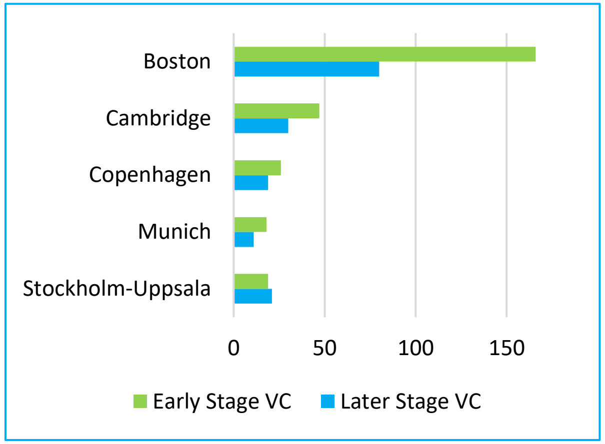
2.5. Venture investments

The number and size of venture investments in each region are indicators of the amount of growth companies and their market potentials.

Figure 2.6 shows number of early and later stage venture investments registered in the international database Pitchbook between 2006-2015.

Boston attracted most venture investments followed by Cambridge. Counting both early and later stage investments, Copenhagen attracted more venture investments than Munich and Stockholm-Uppsala.

Figure 2.6. Number of early and later stage venture investments in biotech companies (2006-2015)



Source: IRIS Group and The Danish Growth Fund based on Pitchbook.

Table 2.5 presents the 50 largest venture investments in European life science companies in two periods of time, based on the international database BioCentury.

The table shows that most of the investments was placed in one of the six European countries included in this analysis. Only 25 of 100 investments were placed in other parts of Europe. When we zoom in on regions, the table reveals that many investments are placed in companies located outside of the regional clusters (Denmark is the exception). The trend between the two periods of time indicates that the six regions are getting stronger as they attracted 12 of the 50 largest investments in 2013-2016 compared to just five in 2009-2012.

Table 2.5. Europe's 50 largest venture investments in life science divided into countries and regions

	2009-2012	2013-2016	Hereof in:	2009-2012	2013-2016
Switzerland	6	10	Basel	2	2
UK	15	15	Cambridge	2	3
Denmark	1	3	Copenhagen	1	3
Germany	11	6	Munich		1
France	3	3	Paris		2
Sweden	1	1	Stockholm-Uppsala		1
Remaining countries	13	12	Remaining countries and regions	45	38
Total	**50**	**50**	**Total**	**50**	**50**

Source: IRIS Group based on BCIQ BioCentury Online Intelligence

On the regional level, life science companies in Basel, Cambridge and Copenhagen attracted most of the largest venture investments.

3. Framework conditions

Outstanding research in itself does not alone make an outstanding biotech cluster. A number of critical framework conditions are essential to foster birth of, and growth in, biotech companies.

First, a vibrant biotech cluster is characterised by a sufficient influx of capital from investors to place both seed and later stage investments in biotech companies. Second, government support (through grants and tax credits) for R&D is important for many companies. Finally, well-functioning technology transfer units and a vibrant ecosystem that is able to connect new companies with established companies, investors, and specialised service providers are important.

In the benchmarking analysis, we compared a number of these factors in the seven regions.

In this summary, we present some of the findings.

3.1. Proof of concept

Proof of concept (PoC) funding is grants dedicated to initial tests of technological or commercial perspectives for new research outcomes. Researchers can apply for PoC grants, and the grants are normally managed by the universities.

For biotech research in particular, PoC grants are an important first step towards seed investments. We have compared availability and size of PoC funding at the largest life science university in each of the following regions: Boston, Cambridge, Copenhagen, Paris, and Stockholm-Uppsala.

At Massachusetts Institute of Technology (MIT) in Boston, the Deshpande Center runs the so-called "Ignition Grants" and "Innovation Grants". "Ignition Grants" are an initial €45,000 grant provided for the financing of preliminary technological tests. If the early tests look promising, an "Innovation Grants" of up to €138,000 can be granted as follow-up funding.

University of Cambridge and Uppsala University provide a two-phased PoC funding as well. At University of Cambridge, researchers can apply for an initial PoC grant called "Path Finder" up to €22,500 and following PoC funding up to €56,000. In Uppsala, researchers have access to the government funded "Early Verification Programme" that provides PoC grants up to €30,000. In some cases, the cluster organisation in Uppsala (Uppsala Bio) provides a €200,000 grant for promising project under the so-called "Bio-X program".

At the University of Copenhagen, PoC grants are not divided into an early and later stage of PoC. Grants up to €67,000 can be awarded for all kinds of PoC-projects.

In France, PoC grants are managed by the SATT units covering all government funding to early stage business development (see section 3.2). PoC grants up to €500,000 are available.

In addition to PoC grants managed by the universities, several private funds provide grants for early verification of new research. In Denmark and Sweden, Novo Seeds provides "Pre-seed Grants" and "Explorative Pre-seed Grants" to researchers at universities and university hospitals in Scandinavia.

In Cambridge, the collaborative venture "Apollo Therapeutics" provides translational funding and drug discovery expertise for therapeutics. The venture is established between three global pharmaceutical companies (AstraZeneca, GlaxoSmithKline and Johnson & Johnson) and the TTOs at Imperial College London, University College London, and University of Cambridge.

PoC grants are available in all regions included in this analysis. However, budgets available for PoC differs with the most favourable conditions in France/Paris where researchers can receive up to €500,000 in PoC funding.

3.2. Access to seed capital

Access to seed capital is important in order to finance new development projects (including preclinical studies) in new and young biotech companies.

The analysis shows that early stage investments are structured in different ways in the seven regions regarding the balance between: 1) soft money; 2) loans; 3) seed investors; 4) venture funds that also place investments in new biotech companies.

The different structures make it difficult to compare the regions on meaningful indicators. But conditions in Paris and Boston seem to be the most favourable among the regions analysed in this study.

In Paris, the Sociétés d'Accélération du Transfert de Technologies (SATT) units cover all early stage investments including PoC grants (as noted above) and seed investments. 14 SATT units are spread across France– with an annual budget of €85 million. Besides that, the government has established a dedicated biotech fund (InnoBio) eligible to invest up to €10 million in biotech start-ups making Paris a biotech region with favourable conditions for start-ups.

Boston is home to many venture funds that also place early investments during the seed phase.

A number of seed investors exist in all regions – typically investing up to Euro 1 mio. in the initial phase.

3.3. Support schemes for R&D

In most countries, government funded schemes exist to fuel research and development (R&D) in small and medium sized enterprises (SMEs). Some schemes are intended to increase research projects within the companies, other schemes aim to foster cooperation between businesses and research institutions.

In France, biotech companies have access to the most attractive support schemes.

In France, young research based SMEs can obtain up to €2 million to internal R&D and up to €3 million to partnerships including a research institution. The national fund BPI France has a total annual budget of €1 billion.

In USA, the SBIR and STTR programmes[4] congressionally require eligible governmental agencies to set aside a percentage of their extramural budget so that domestic small businesses can engage in R&D-projects based on university research. SMEs can obtain up to €1 million per project. The National Institutes of Health (NIH) set aside €720 million every year to R&D in life science companies.

Government funded schemes in the other countries included in this analysis provide somewhat smaller grants, and the annual budgets relative to GDP are smaller than in France.

3.4. Technology transfer at the universities

Qualified technology transfer offices (TTOs) at universities and university hospitals are an important part of a well-functioning biotech ecosystem. TTOs manage a broad scope of tasks including scouting for new research with commercial potential, supporting entrepreneurship, developing networks to the life science industry, and the management of patents and license agreements.

Thus, resources available to TTOs are critical to the amount of completed licence agreements and spinout creation. Qualified TTO-officers are, of course, essential. Officers should both have a deep insight in science and have commercial experience. Regarding biotechnological commercialisation, officers specialised in life science are important.

We have compared TTO resources available at the main universities and university hospitals in Boston, Cambridge, Copenhagen, Munich and Stockholm-Uppsala. Our analysis shows that TTOs at the selected universities in Boston, Cambridge, and Munich have most personnel employed when the size of research production is taken into consideration.

The ratio between officers dedicated to life science and other scientific fields of research are about the same across the TTOs included in this analysis. A bit more than half of the TTO officers in Copenhagen are dedicated to life science, while it is a bit less at TTOs in the other regions.

[4] Small Business Innovation and Research (SBIR) Small Business Technology Transfer (STTR).

Initiatives to accelerate spinout production exists in all the regions.

In Boston, The Deshpande Center operates a wide range of supportive mechanisms including education in entrepreneurship and PoC funding (see section 3.1). Furthermore, “Lab Central” offers all types of relevant equipment and lab facilities to test research inventions in a commercial environment.

Cambridge is home to “Judge Business School” where research and education in entrepreneurship have taken place since 1990. Also, “ideaSpace” at University of Cambridge provides office space and resources for anyone looking to start a new company in Cambridge.

3.5. Ecosystems

Companies established in strong ecosystems are more likely to grow than companies established in areas without a strong support infrastructure. Ecosystems for biotech innovation cannot be benchmarked easily, since they rest on different cultures, connections and in terms of public versus private leaderships. The framework conditions analysed above are all important parts of the ecosystem. However, the way that framework conditions and stakeholders work together is also important for the development of a cluster. Thus, it is important to consider the cohesion of the entire ecosystem.

A healthy biotech ecosystem can be characterised as a place where:

1. Researchers and start-ups have easy access to capital, advisors, incubator, knowledge, and talents.
2. Ideas and people flows easily between companies and sectors.
3. Entrepreneurs are met with the right advises and matched with the right investors.
4. There is a flourishing culture of entrepreneurship in the research environments.

Based on desk research and interviews with key stakeholders in Cambridge, Copenhagen, Munich, and Stockholm-Uppsala, our analysis furthermore, points to the following conditions essential for a thriving biotech ecosystem:

- A strong cluster organisation able to connect and lead the cluster, or other mechanisms fostering cohesion and cluster development.
- Availability and quality of physical facilities for stakeholders to meet.
- Physical concentration of the cluster, especially proximity between large and new companies.
- A strong network of advisors and mentors capable of guiding start-ups and match them with relevant investors.
- Big pharma engagement in the cluster.

The analysis shows that these points are essential to foster new biotech start-ups, and to stimulate growth in the existing life science sector.

All regions included in this analysis have a well-developed ecosystem. However, none of the ecosystems are similar in the way the points above are balanced.

Munich has an influential cluster organisation called “BioM” with 15 employees dedicated to create and enhance networks for researchers and companies in the life science sector, and to help and guide emerging companies. The cluster organisations “One Nucleus” in Cambridge and “Uppsala BIO” in Uppsala are also characterised as agenda setting and unifying organisations. Both have approx. 10 employees.

In Copenhagen, smaller cluster organisations exist. Moreover, the universities coordinate a network (“Copenhagen Spinout”) with the industry and the investment environment that cooperates on issues related to fostering spinouts in the life science area (including a mentor network).

The physical concentration of the clusters in Cambridge and Munich is another positive factor. In Munich, 80 life science companies employ 50 per cent of the cluster, and are located no longer than

2 km from “Campus Grosshadern” that houses Ludwig Maximillian University (LMU), an innovation park, incubators, and the Max Planch Institutes for Biochemistry and Neurobiology. Technical University of Munich (TUM) and the hospital are located close too.

Big pharma companies’ engagement in the cluster is particularly dedicated in Cambridge, Copenhagen and Basel. Cambridge is home to global enterprises like Astra Zeneca, Pfizer, Roche, Upjohn, and Eli Lilly. In Denmark, Novo Nordisk, Lundbeck, and Leo Pharma are leading and have established private funds (Novo Seeds and Lundbeck Emerge) to support young life science companies.

Appendix

Definitions and delimitations

The focus in the analysis is primarily on so-called "red biotech" (including biotech used in new drugs, vaccines, in vitro diagnostics, and technologies used in the development of new drugs) – as opposed to "white biotech" (enzymes and microorganisms used for industrial processes), "green biotech" (the use of plant ingredients) and "blue biotech" (the use of marine organisms and their derivatives)".

We used the following definition for red biotech companies:

Companies whose predominant activity involves the application of biotechnology techniques to develop new goods or services within drug development, vaccines, in vitro diagnostics, as well as new technologies to be used in the development of new drugs. This excludes: Medtech, industrial biotech, environmental biotech, and agricultural biotech. Pharmaceuticals companies (Big Pharma) whose existing products are predominantly based on conventional chemistry or other non-biotechnological techniques.

Table A.1 shows population and geographical delimitation for each region included in the analysis.

Table A.1. Regions included in the analysis

	Basel	Boston	Cambridge	Copenhagen	Munich	Paris	Stockholm-Uppsala
Population (million)	1.1	4.6	0.6	1.8	2.8	8.0	2.5
Geographical delimitation	Aagau Basel-Landschaft Basel-Stadt	Arlington Belmont Boston Brookline Cambridge Chestnut Hill Lexington Medford Newton Waltham Watertown Woburn	Cambridgeshire	The Capital Region of Denmark	Dachau Erding Ebersberg Freising Fürstenfeld-bruck Landsberg A. Lech München Landkreis München Kreisfrie Stadt Starnberg	Essonne Hauts-de Seine Paris Seine-Saint-Denis Val-de-Marne	Stockholm län Uppsala län

Source: Eurostat & U.S. Census Bureau.

Data sources

The analysis is based on the following data sources:

- Survey among key stakeholders in cluster organisations, universities, and university hospitals.
- Interviews with key stakeholders in cluster organisations.
- Desk research on framework conditions etc.
- International databases in order to gather information on scientific publications, venture investments and other statistics (see source under individual table/figure).

For more information on data sources please find the full report at www.irisgroup.dk (only available in Danish) or contact IRIS Group.