LIFE SCIENCES IN THE NETHERLANDS: GROWTH DESPITE THE TIDE?

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Abstract

This paper examines the policy program in the Netherlands that aimed to improve the conditions for knowledge valorization in the life sciences. The Netherlands is an interesting case to study because the country hosts one of the largest numbers of newly established firms in the life sciences in the EU, while growth in this segment has remained limited due to a large share of small and vulnerable firms. The target number of newly established firms set in the program could easily be achieved and the program was able to improve the business climate for new firm establishment. However, the program could not improve conditions for growth of new firms because it could not achieve a comprehensive turn in the business climate, due to the short cycle-time of the program (4/5 years). In addition, the program did not take advantage of existing critical mass in the largest cluster or from any other competitive strength of particular clusters. However, regional competitive strength is now increasingly enhanced by regional initiatives.

Key words: life sciences, new firm formation, policy, institutional change, The Netherlands.

1. Introduction: Large Business Opportunities but also Huge Risks

Traditionally the term biotechnology was used to encompass technologies connected to recombinant DNA techniques and cell fusion (OECD, 1989). However, more recently the focus has broadened and covers: “the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge goods and services” (OECD, 2006, p. 7). Currently, the most important technological trend is genomics, including the functioning of genes and metabolism in the cell, and systems biology (MEA, 2003; Ernst & Young, 2005). Results from new genomics research combined with improvements in existing technology, like cloning, cell and tissue culturing, and genetic modification, may imply drastically new approaches in identifying and curing diseases. In addition, biotechnology in health care increasingly connects with three other generic technologies, namely informatics and computational science, e.g., in data-mining in searching of new hits and in remote diagnostics and clinical trials; new materials technology such as in new types of artificial bone and tissues; and nanotechnology, such as in bio-sensors.

The combination and integration of the above technologies open ways to entirely new applications in products, processes and services, and provide a wide range of new business opportunities. The medical challenges to fight diseases of an ageing population and the strategy of large pharmaceutical companies to introduce new drugs in the market in an era of expiring of many of their lucrative patents, as well as progress in the production of healthy food, add to these business opportunities.

Aside from clear business opportunities, newly established research firms are facing huge risks to survival and these risks are much stronger than in any other high-technology sector (Audretsch, 2001; Van Geenhuizen, 2003). For example, there is the threat of failure in research, early or later in a long and intensive development and testing time of new medicines. Then, these firms face the danger of not acquiring sufficient investment capital after initial rounds (equity gap). A large failure risk of start-ups may also be caused by customer resistance, but this applies mostly to agricultural and food applications, not to medical applications. In the context of start-ups adopting various strategies dealing with opportunities and risks (Barney, 1991) it is important to make a distinction between different business models, i.e., the product model, the tool model and the service model (BioPartner 2004; Mangematin et al., 2003). Product companies are highly innovative and undertake large R&D efforts in developing and bringing new products to market. Tool companies focus on developing platform technologies, like in functional genomics, and usually generate revenues through out-licensing and royalties. By contrast, service companies perform research on contract or offer standard or customized services to product and tool companies, and generate revenue from the start. There is also the hybrid company that typically combines activities of two or more of the previous models, particularly by adopting “safe” activities enabling to finance R&D internally, like sales of accepted products from manufacturers and routine contract research (e.g., Walsh, 1993). Another popular strategy of small firms to reduce risk is collaboration with large pharmaceutical industry, with the aim to improve financial position, to gain experience in testing and trial procedures, and to achieve access to marketing and global distribution channels (e.g., Powell, 1998; Senker and Sharp, 1997). More recently, we observe an increase of merging (acquisition) and alliances within the biotechnology sector, causing innovations increasingly to emerge in network configurations of firms (Salman and Saives, 2005).

Forecasting studies have indicated a large growth of economic sectors on the basis of application of life sciences. For example, global markets of sectors in which life sciences constitute a major part of the new technology were estimated to amount over 2000 billion Euro in 2010, including 820 billion in the pharmaceutical sector (EC, 2002). Against this background, the government of the Netherlands realized at the end of the 1990s that - despite an affluent new knowledge production and well-developed infrastructure for clinical trials - new entrepreneurship in the life sciences was lagging behind, due to serious institutional obstacles in the sector and a rather modest entrepreneurial culture in general and particular at universities. Note that scientists in the Netherlands are not very willing to leave their (comfortable) academic positions to get fully engaged in business activity (Enzing et al., 2005). In addition, universities did and do not receive a budget from the Ministry of Education, Culture and Science intended to develop the activity of knowledge valorization, particularly of enhancing spin-off development. In this sense, the position of universities as actors in the innovation system in the Netherlands has been and is relatively weak. On the other hand, since the mid 1990s the Ministry of Economic Affairs has implemented various tools to enhance the emergence and growth of high-technology start-ups, among others at universities. The dedicated action program for the life sciences fits into this broader policy effort as a sector-based initiative (MEA, 2000; MEA, 2001). The action program employed a twofold aim, that is (1) to increase the economic utilization of (academic) life sciences knowledge through newly established firms (i.e. a total of 75), among others by (2) improving the business culture for new firm formation, particularly at universities.

This paper examines whether the above aim could be reached and whether various aspects of the policy were realistic. It starts with a discussion of the support program and with an analysis of potentials of the sector and of the actual size and spatial distribution of the segment of small, dedicated firms. This is followed by the focal analysis, i.e., of growth of this segment and changes in its structure (firm size, business model), and of underlying institutional aspects, the last mainly on the basis of an evaluation study by national policymakers and the design of a follow-up policy (MEA, 2006). The conclusion provides a set of learning experiences from the Netherlands' case study.

2. Action Plan Life Sciences

The Action Plan Life Sciences employed the principle of differentiating financial support to start-ups according to the stages of establishment and early growth, and included five lines in a comprehensive approach (Table 1). The aim was to support the establishment of 75 biotechnology firms in the years from 2000 to 2004, with a total budget of 45 million Euro. Of course, these are modest numbers, also if the budgets of two additional support programs are taken into account, but it needs to be realized that the Netherlands economy is relatively small (a GDP in 2005 of $ 595 billion) and that the country has just the size of some of the large biotechnology regions in the world, like the Boston area and the San Francisco-Bay area. However, a research initiative in the field of genomics (Strategic Action Plan Genomics) aimed at building a strong national research infrastructure was granted a budget of 189 million Euro for the years 2002-2007.

To implement the Action Plan Life Sciences, an intermediary organization was established, named BioPartner. BioPartner was also founded as a learning organization to scan the market and technology environment of biotechnology; to monitor the outcomes of its program lines and instruments, like characteristics of new entrants (product pipeline, business strategy, financial expectations).

Table 1 Program lines of Action Plan Life Sciences

Program lines	Details
1. First Stage Grant (pre-seed fund) *11 million Euro*	To stimulate researchers to apply for a patent and undertake applied research. It serves salary needs of researchers, costs of patenting, etc. up to 250.000 Euro for a maximum of 2.5 years.
2. Facilities Support (facility fund) *5 million Euro*	To provide loans to universities (research organizations) for pre-financing advanced life sciences facilities to enable start-ups to use these facilities against a reasonable price.
3. Start-up ventures (seed fund) *11 million Euro*	To provide investment capital on the condition that private parties also invest substantially (50% matching). The fund invests up to a maximum of 227.000 Euro and possibly another 227.000 in a subsequent financing round.
4. BioPartner	To provide laboratory, offices, R&D and pilot plant facilities and

Incubators) *11 million Euro*	shared services in university-linked incubators, and to facilitate easy access to universities and other companies (in *six* different places).
5. BioPartner Network *7 million Euro*	To facilitate and stimulate entrepreneurship through advice, information, scouting, training programs, and creating networks, e.g. founding of special chairs at the university and master classes.

Source: adapted from MEA (2000) and BioPartner (2005).

The policy may be qualified as follows:

- *Comprehensive*: a range of conditions underlying entrepreneurship are addressed, including public relations, entrepreneurial skills, accommodation and research facilities, seed capital, etc.
- *Network-oriented*: networks are addressed in two ways, i.e., as a tissue underlying biotechnology business in general and as a means for small start-ups to gain resources.
- *Stage-based in terms of company growth*: the financial incentives are differentiated for the pre-seed stage and seed-stage.
- *Cluster-based*: academic hospitals and medical schools are seen as anchors for new company starts and this holds for six larger and small clusters.
- *Strong self-learning*: the organisation monitors the external environment as well as the impacts from own instruments, and adjusts instruments if necessary.

Note that the cycle-time of the Action Plan Life Sciences was quite short, that is four/five years, and that the action plan was followed by a set of somewhat adapted program lines within a generic technology policy (named Technopartner).

3. Life Sciences in the Netherlands: Potentials, Size and Spatial Pattern

With regard to innovation output, the Netherlands holds an intermediate position in the European Union. Output as a result of research at universities, in large firms and small dedicated firms can be measured by the number of patent applications in the field, and can be seen as an indicator for a potential to be commercialized in the near future. As a percentage of the national total the Netherlands was in 7th position in the EU for the years 1996 to 1998, but felt back to a lower position in 2002 to 2004 (Table 2). The previous indicator reflects the level of specialization within a country. The next indicator shows the importance in the global playing field. In the EU, the Netherlands is in 4th position, following Germany at a large distance, and United Kingdom and France at a shorter distance. The overall impression is that based on numbers of biotechnology patents, particularly the world share in 2004, the Netherlands has a reasonably good position. However, patent position is only part of the story, the entrepreneurial climate, and integrative and relational ability in a country is the other part (e.g. Swan et al. 2007).

Table 2 Biotechnology patents (highest ranking countries in EU) a)

Country	1996-1998, Share (%) in national total	2002-2004, Share (%) in national total	2004, Share (%) of country in world total
Belgium	13.3	9.2	1.0
Denmark	12.7	12.8	1.8
UK	9.5	6.7	4.2

Ireland	7.2	4.3	0.2
France	7.1	5.2	4.0
Spain	6.2	6.9	1.0
Netherlands	6.0	4.4	1.9
Switzerland	5.4	5.5	1.1
Austria	4.5	4.6	0.6
Italy	4.5	3.5	1.2
Germany	3.9	5.1	10.0

a) Patent applications filed under the Patent Co-operation Treaty (EPO)
Source: OECD Science, Technology and Industry Scoreboard (2007).

The specific development of the life science sector in the Netherlands in comparison with other European countries is shown in Table 3. The Netherlands is in place five with regard to the number of firms and in place six/seven if this number is 'corrected' for the size of the economy, but the average size of the firms is the smallest among the top-ten countries and half the size of the average for the EU (22.9 versus 44.6). In addition, the Netherlands does not belong to countries with the more robust public biotechnology firm pipeline. In this respect, United Kingdom, Switzerland and Denmark are leading. What might have influenced this situation as a factor specific for the Netherlands - and different from for example, Switzerland - is that no large domestic pharmaceutical industry has been acting as a driving force, pushing small life science firms forward into next growth stages. This is a limiting factor because the growth particularly of medical life science firms is partly shaped by relations with downstream industry that provides demand (Senker and van Zwanenberg, 2001).

Table 3. Life sciences in Europe (10 highest ranking countries) (2004) a)

Country	Firms	Firms/ billion GDP ($)	Employment	Average employment per firm	Product pipeline b) (medical)
Germany	538	0.193	16.094	29.9	39
UK	457	0.208	21.134	46.2	211
France	233	0.110	9.142	39.2	36
Sweden	138	0.390	3.942	28.6	25
Netherlands	124	0.208	2.837	22.9	6
Denmark	117	0.461	18.461	157.8	50
Switzerland	90	0.246	4.990	55.4	109
Belgium	84	0.230	3.654	43.5	8
Spain	81	0.072	2.201	27.2	n.a.
Finland	66	0.342	2.160	32.7	7
Europe	2163	0.161	96.459	44.6	523

a) Use of a somewhat different definition compared with BioPartner (Table 4-6) that is, established biotechnology companies are also included.
b) Product pipeline gives the number of products in four stages (preclinical and Phase 1 to Phase III) for public firms only.

Source: Adapted from Critical 1/EuropaBio, 2006, except for product pipeline (Ernst & Young, 2006).

The domestic pharmaceutical industry in the Netherlands is either focused on generics production or on bulk compounds without a strong interest in life sciences, or it is has moved parts of R&D abroad (van Geenhuizen and van der Knaap, 1997). Aside from this, the domestic life sciences industry itself is not yet sufficiently strong to adopt such a role. It is only recently, that two domestic, medium-sized pharmaceutical companies attempt to adopt such a role, i.e. DSM Biologicals with a focus on healthcare and food, and AKZO Pharma with a focus on particular drugs research. These circumstances have hampered the development of a bioscience *megacentre*, capturing major parts of the healthcare value chain (from exploration through examination to exploitation) in the Netherlands.

With regard to spatial patterns within countries, the literature indicates that the research-intensive life sciences industry (particularly in the medical field) is more than any other high-technology industry clustered around public scientific institutes as knowledge and facility providers, like universities, research hospitals and laboratories, and (mainly in the US) venture financing (e.g. Audretsch, 2001; Cooke, 2001, 2004a; Powell et al., 2002). In the 1980s and early 1990s, the idea of advantages from a clustered location for innovativeness and growth, including knowledge spillovers from the local university (academic hospital), was widely accepted. However, later empirical studies revealed overall weak relationships of the clustered firms with local knowledge institutes or revealed mixed evidence (e.g., Lawton Smith, 2004). For example, for the US Bagchi-Sen et al., (2004) reports a continued importance of proximity to university research but - with regard to factors affecting business performance - a relatively low importance of collaboration with knowledge institutes compared with in-house conditions towards product development. These results may gave rise to the idea that close proximity to knowledge institutes merely matters in the incubation stage of new firms. In later stages, relationships with local knowledge institutes may weaken when the firms enter global relationships and markets (van Geenhuizen, 2008).

The largest single cluster in the Netherlands is in the region of Leiden, midway Amsterdam and The Hague in the Western part of the country (Randstad). In measuring the size of clusters, official industrial statistics cannot be used because the companies are dispersed over different sectors in such statistics. Therefore, we made use of sector reports on life-sciences in which most companies are listed (BioPartner, 2001-2005). With approximately 30 dedicated life-science firms (note 1) Leiden is larger than other clusters, like Amsterdam and Groningen (between 15 and 20 firms) (Table 4). The cluster of Leiden at large encompasses around 45 firms when foreign subsidiaries, pharmaceutical industry, medical devices and consultancy firms are included.

The knowledge institutes in Leiden today include various faculties of the University of Leiden and its medical school and research hospital, two Higher Educational Institutes, an institute of applied sciences in prevention and health (TNO), and two national research centres of which one in genomics. Note that the relatively small size of the Leiden cluster, from an international perspective, should be seen in the context of the polycentric system of cities in which Leiden is located (Randstad). Thus, within a short distance from Leiden, one finds the life science clusters of Amsterdam (30 km), Utrecht (40 km), Delft (35 km) and Rotterdam (45 km). If defined as a *system* or *network* of clusters, the number of dedicated life science firms amounts to 80 (Table 4), but this is still small compared to various centres in the world. Already in 2000, the number of dedicated biotechnology firms amounted to 141 in Boston, 152 in San Francisco and Silicon Valley, 120 in Munich (Germany), and 94 in San Diego (Cooke, 2004a). Only Cambridge (UK) hosts a smaller amount of companies, i.e. 54.

Table 4 Approximate size of life-sciences clusters in The Netherlands (end 2005)

Location	Nr of firms	Details
Leiden	30	Within a distance of 5 km from knowledge institutes. Focus: *general and medical.*
Randstad: Amsterdam, Leiden, Delft, Rotterdam, Utrecht as a *network*	80	A distance of 20-40 km in-between the clusters (65 km. max.). Focus: *general and medical.*
The Netherlands	165	Max. distance of about 300 km (Groningen – Maastricht). Focus: *general and medical,* and *agro/food* (mainly in Wageningen).

a) Dedicated life-sciences firms.
Source: Adapted from BioPartner 2005.

Contrary to many assumptions on benefits from a clustered location, a recent study indicates that a location in a cluster in the Netherlands has no positive influence on innovativeness and growth. However, there are signs that a clustered location merely in Leiden has a positive influence on innovativeness (van Geenhuizen and Reyes-Gonzalez, 2007). Apparently, the largest cluster provides various beneficial qualities. Unique for Leiden, due to its older age as a cluster and its larger size, are the availability of a pool of specialized workers, the presence of specialized services, and accumulated knowledge concerning start-up processes and global networking (van Geenhuizen, 2008).

4. Dynamics and Structure of the Sector

This study - because it is limited in scope – does not allow to perform a formal *ex-post* evaluation of the Action Plan Life Sciences that is methodologically sound. Thus, causal relations between the policy and actual developments cannot be established because it is unknown how the sector would have developed without the policy. Also, with the exception of the number of newly established firms, it is impossible to identify to what extent goals have been reached because most of them were stated in a qualitative way. In addition, only a few reference cases of policies (policy lines) in other countries are available for comparison. The article examines whether the previously indicated aims could be reached and whether various aspects of the policy itself were realistic. The remaining section focuses on changes in *size* and *structure* of the segment of dedicated life sciences firms.

Compared with the late 1990s, there has been a clear increase in the number of entrants in the years of the effective policy. In 1998-2004 this amounted to 144.4%, bringing the total population of dedicated life-science firms at almost 160 firms (Table 5). In the years before the launch of the policy, the average annual growth of entrants was 11.5 whereas growth turned out to be almost twice as large in the years of the effective policy, i.e. 22. The launch of the program in 2000 was expected to result in the creation of 75 new firms. After five years, a total of 102 new firms could be established, thereby surpassing the initial expectations. When taking into account that the program was largely implemented in years of a macro-economic downturn, as reflected in a decrease in the overall level of new entrants in the Netherlands economy, the quantitative results are even more surprising (Table 5).

Table 5 Population and entrants of dedicated life-science firms

Years	Population (index	New entrants per year	New entrants per year all

	numbers)	(index numbers) (a)	sectors (index numbers)
1998	57 (100.0)	9 (100.0)	71.463 (100.00
1999	74 (129.8)	14 (155.6)	77.797 (108.9)
2000	97 (170.2)	24 (266.7)	88.014 (123.2)
2001	118 (207.0)	21 (233.3)	80.269 (112.3)
2002	126 (221.1)	18 (200.0)	68.961 (96.5)
2003	138 (242.1)	17 (188.9)	68.947 (96.5)
2004	157 (275.4)	22 (244.4)	76.252 (106.7)

Source: BioPartner, 2001-2005; MEA, 2003; EIM, 2006.

The increase of the population of firms in the years 2000 to 2004 (61.9%) was coupled with a stronger increase of employment (112%) and turnover (164%) (Table 6). Nevertheless, the growth of the sector manifested itself mainly in the small segment. This development is confirmed by figures on the size-structure. A large majority of dedicated life-science companies employs less than 10 fte and the share of this segment has increased between 2000 and 2004 from 65% to 73% (Table 7).

Table 6 Size-indicators and financial performance of dedicated life-science firms

Indicators	Period/Year	Outcome
Firms		
Population of firms	2004	157
Total increase of population (%)	2000-2004	+ 61.9%
Nr of new entrants	2000-2004	109 (22 on average) a)
Employment		
Size of employment	End of 2004	about 2.150 fte
Total increase of employment (%)	2000 – 2004	+112%
Financial performance and R&D		
Turnover	2004	190 million Euro
Total increase of turnover (%)	2001-2004	+164%
Net result (loss)	2004	- 75 million
R&D expenditure	2004	118 million
Total increase of R&D expenditure	2000-2004	+115%

a) Due to definitional issues, the sum over five years is slightly more than the number of entrants of each individual year as recorded in annual reports.
Source: Adapted from BioPartner, 2005.

This observation, together with a net result of a loss of 75 million Euro in 2004, points clearly to an early stage of the sector, dominated by relatively small and highly vulnerable firms. At the same time, there has been a shift in business models, on the one side to product companies (from 11% to 27%) introducing a higher level of innovativeness (and risk-taking) and on the other side to hybrid companies (from 49% to 57%) as a risk-aversive strategy, the latter leading to an overall majority of firms employing a hybrid strategy (Table 7).

Table 7 Size and business models among dedicated life science firms

Type of result	Period/Year	Outcome

Size structure <10 fte 11-25 fte 26-50 fte > 50 fte *Change in structure* Share of firms < 10 fte	 } End of 2004 2000 - 2004	 73% 14% 6% 7% from 65% to 73%
Business model structure Service Tool Product Hybrid *Change in structure* Service Product Hybrid	 } End of 2004 2000 - 2004 idem idem	 8% 8% 27% 57% from 33% to 8% from 11% to 27% from 49% to 57%

Source: Adapted from BioPartner, 2005.

Of course, there are various success stories in terms of size and innovation in 2005, like *Crucell* (210 jobs after 11 years, including predecessor *Introgene*, and even much larger after the acquisition of *Berna Biotech* in Switzerland), *Octoplus* (90 jobs after 9 years), *Pepscan* (20 jobs after 6 years) and *Galapagos* (70 jobs after 5 years, including a site in Belgium) (BioPartner, 2005), but this does not change the nature of the sector.

Overall, we observe that in the period 2000-2004 90 dedicated lifescience firms were established and that 19% of them could not survive or were aquired/merged within this period (Table 8). It is difficult to say whether the survival rate is high or low because the age at exit is not exactly known (it differs between 1 and 4 years). We could speculate that the survival rate is about 80% four years after establishment and this rate comes close to what Mustar et al. (2007) observe for all categories of spin-off firms in the EU six years after establishment. However, most dedicated life-science firms get confronted with the equity gap just after the first years, meaning that the survival rate might seriously fall down in the years that follow.

Table 8 Established dedicated life-science firms and exits (2000-2004)

Established firms	**Failure**	**Merged/acquired**
90	9 (10.0%)	8 (8.9%)

Source: Biopartner Sector Reports; MEA, 2005.

By considering the recent past, we may conclude that the Netherlands life-science sector (dedicated firms) has remained in an early growth stage. The sector today primarily consists of small and loss-making firms with fewer than 10 employees. This situation, of course, gives rise to some interesting questions about institutional change and about other aspects of the action plan.

5. Improvements but no Turn

The Action Plan Life Sciences had a cycle-time of four/five years. In general this is too short to achieve institutional transformation, including formal and informal institutions. The cycle-time is also considered too short compared with the time-to-market of product firms in the life sciences (MEA, 2005a). When considering institutional aspects of the action plan in more detail, the following five points need to be addressed:

(1) There was a positive change in the business climate concerning start-ups in the life sciences, particularly at universities, but there was no turn.
(2) There was no change in supply of venture capital in later stages, indicating a remaining risk-aversive attitude of investors.
(3) Pressure from strong regulation and long-lasting procedures, like in the agro-segment of life sciences has remained.
(4) The traditional policy model of equity (equality) was employed in the distribution of support over six locations, whereas regional economic policy was already in favor of the efficiency model (MEA, 2005b).
(5) A strong international orientation was missing, despite the small and open economy and increasing trend of globalization (van Geenhuizen, 2003).

Concerning the first point, the action plan was clearly able to contribute to reducing obstacles to starting up new firms in the life sciences. In terms of entrepreneurial culture, awareness has been increased and universities have adopted a more pro-active attitude with regard to valorization of life sciences knowledge (see, note 2 for the instruments used). The situation of what Swan et al. (2007) name a nation's integrative capabilities (the ability to move between basic science and clinical development) and relational capabilities (the ability to collaborate with diverse organizations) has clearly improved. However, the overall entrepreneurial climate has not yet improved in such a way that we can talk about a turn in this climate, due to the short time-span of the action plan (MEA, 2005a).

Concerning the point of financial support to start-ups, the policy was rather effective in the first stage (seed-stage) in which practical knowledge is translated into a feasible business plan. Of all applications for seed-fund in the four years of the program, 67 (52.3%) could be granted and this is more than later stage funding so far. However, it can be questioned whether solid entrepreneurship - in terms of the ambition to grow and take risks – could be introduced through this first-stage funding. The emphasis might have been somewhat too strong on gaining numbers of new firms (quantitative side) instead of gaining competitive firms (qualitative side).

Conditions affecting the supply of venture capital seem not to have changed. Thus, action line Start-up Ventures could not trigger the market, in which venture suppliers remained reluctant. Of all applications only 38 (17.0%) could be accomplished through finding matching funds. Note that this percentage will increase because various applications were still pending at the time of this study. It is difficult to say whether this result so far is a failure or success. The relatively small numbers of co-financed participations clearly stayed behind the number of granted applications of the first-stage grant, suggesting a trend of stagnation, but should also be understood in the context of the economic downturn in the years involved, facing a refraining from high-risk investments and a move to later stages. The lack of funding in early years following the start is also not a typical problem in the Netherlands (Ernst & Young, 2006). The equity gap is a hurdle in many European countries, stemming from a fundamental timing mismatch, particularly in new drugs research. As previously indicated, taking a drug candidate from discovery to product launch can last about 15 years, yet the life of a typical venture fund is about 10 years. Thus, the long road between private investment and an IPO - an initial public offering, as a popular exit option – stretches beyond the preferred time horizon of venture funds. In this context, it may be questioned whether the short cycle-time of the action plan (four/five years) could ever have improved the situation. What became clear is that even with granting the venture funds, the equity gap for individual firms could not be sufficiently closed (MEA, 2005a). Overall, the size of venture capital investment is relatively small in the Netherlands, i.e., clearly smaller than in the Nordic countries and in the large EU countries (OECD, 2006) (Table 9). It is approximately ten times smaller than in the US and one-fifth of the share in the UK and Sweden.

Table 9 Biotechnology venture capital investment (2003) (US and the top ten EU)

Country	Venture capital investment (% of GDP)
United States	0.031
Denmark	0.024
Norway	0.022
UK	0.016
Sweden	0.015
Switzerland	0.009
Finland	0.008
France	0.007
Germany	0.005
Belgium	0.005
Netherlands	0.003

Source: Adapted from OECD 2006.

However, there are recent signs that venture capital firms active in the Netherlands are willing to take some more risk, meaning that they select the most promising ventures and withdraw from them somewhat earlier compared with the common pattern (Personal Communication, 2006). Thus, the situation of a general risk-aversive culture on the side of venture capitalists seems slightly improving. In addition, in the follow-up policy since 2005, venture funds investing in risky firms were given the opportunity to receive a loan and this has already doubled the amount of available venture capital in the first year (MEA, 2006).

With regard to the next point, pressure from long-lasting and complicated procedures and tight regulation (the last influenced by a powerful ethical lobby against transgenic breeding and genetic modification of plant varieties) changes have been minor. This situation has pushed some start-ups to leave the country (e.g., Enzing et al., 2005), and seems to have contributed to a rather poor position of the Netherlands in Europe in the area of trait field trials of new GM plant varieties (comparable with patents), for example, 6 for the Netherlands as compared with, for example, 120 for Spain, 42 for France, 24 for Germany, and 17 for Sweden (in 2002-2004) (OECD, 2006). The follow-up policy since 2005 addresses various important improvements in this respect, like shortening the time for application for permits and licences (to the average European time as maximum) and reducing and simplifying the laws concerned (MEA, 2006).

The fourth point – the distribution of six incubators over the country - reflects an old institutional model in (regional) economic policy in the Netherlands, namely the one following the idea of equity, in which each candidate receives the same support. Thus, the cluster of Leiden - where opportunities appeared to be better than elsewhere - was not ‘favored’ in the action plan. The alternative model, i.e. efficiency in terms of strengthening what is already strong in a frame of increasing international competition, like adopted in the latest regional-economic policy document (MEA, 2005b), was not at stake. As a result, the action plan might have missed a chance to create the critical mass needed in a strongly competitive market and might even have caused duplication between clusters. In a situation of, for example, three large incubators and a strong specialization of each of them, critical mass might have been created more quickly and the competitive power and image towards foreign biotechnology actors might have been stronger. Overall, it is plausible that policies addressing a certain degree of *competition* between regions and giving priority to the best performing ones, like in Germany on the basis of the *BioRegio* policy and later contests of R&D cooperation, lead to better results (Cooke, 2002; Eickelpasch and Fritsch, 2005). In fact, some of the incubators in the Netherlands faced difficulties in finding tenants, caused by the relatively high (market-conform) prices and supply of cheap laboratory room by the knowledge institutes in their own buildings (MEA, 2005a). Note that an alternative development path would have been to start with a virtual network organization connecting various local biotechnology research and coordinating emerging initiatives of technology transfer at the universities, with finding entrepreneurs as a second step (LIFEscience, 2006). This model was employed in Flanders in Belgium, where the Flanders Interuniversity Institute for Biotechnology (VIB) was established already in 1995, connecting and coordinating initiatives at the four Flemish Universities (VIB, 2006).

The final point, the lack of a strong international orientation, has prevented a clear positioning of the Netherlands’ life sciences abroad and may have contributed to missing chances for cooperation by small firms. As previously indicated, it is typical for the Netherlands - at least in the medical/pharmaceutical segment - that corporate partnering is often immediately in a global playing field due to missing domestic partners. This situation seems somewhat changing today due to a greater ambition of some domestic firms to cooperate with small ones. Nevertheless, a budget to create better opportunities for collaboration abroad, including support in connecting, checking and negotiation of the best time and terms for collaboration, could have helped. This issue has been explicitly addressed in the follow-up policy in a new action line (MEA, 2006). Thus, small firms are now stimulated to participate in large fairs, exhibitions, and fairs abroad, and in individual partnering and matchmaking activities abroad.

Most recently, the need to prevent fragmentation of initiatives and research in medical life sciences was recognized as is witnessed by the establishment of the national Top Institute Pharma (TI Pharma) and its location in Leiden. This institute aims to achieve leadership in areas critical for the international competitiveness of the Netherlands’ pharmaceutical and biotechnology industry, among others by connecting and merging results from fragmented disciplines, programmes and locations (www.tipharma.nl).

Overall, given the above circumstances, it may be speculated that the landscape of the Netherlands life sciences could have been different if there had been a focus in the beginning on two/three larger clusters or networks of clusters selected upon *competitive* initiatives and co-ordination from the beginning. More importantly, the size structure might have been more favorable with a smaller amount of small and vulnerable firms due to a stronger impulse per cluster. The same might be true if a stronger impulse was given to a smaller number of firms through a tighter selection and a longer period of financial support than 4/5 years while using the same budget as in the original program.

On the other hand, the Action Plan Life Sciences has helped to establish and improve the breeding ground for highly professional initiatives in regions that have adopted life sciences as a spearhead in economic development. This holds true, for example, for the region of Leiden in cooperation with Delft in the Province of South-Holland, benefiting from a long-standing experience, a strong knowledge infrastructure, and presence of various grown-up life science firms, and for the region of Maastricht in Limburg, the Southernmost province. This region benefits from the operating base of DSM, the world largest supplier to the life sciences industry, and from cross-border cooperation opportunities with universities and academic hospitals in Hasselt, Liege (Belgium) and Aachen (Germany).

6. Conclusion

This paper presented the results of a critical examination of the Netherlands' policy to enhance entrepreneurship in the life sciences, implemented in 2000 to 2004, and some new lines in the follow-up policy. It can be concluded that the aim of the life sciences policy, i.e., to improve the climate for the establishment of dedicated firms and to establish 75 of such firms, was achieved but that a basic turn could not be realized. The increase of the number of newly established firms exceeded the aim and was impressive compared with other EU countries, but it has led to a large segment of small and vulnerable firms, many of them suffering from an equity gap. It seems reasonable to ascribe this development to the following factors: a relatively short cycle time of the policy (4/5 years), missed chances by the policy to benefit from some unique circumstances in the largest cluster (Leiden) and from a selection of the best regions based on competition, a weak international orientation of the policy, and various disadvantages in procedures and regulation, the last falling beyond the competence of the program. A somewhat too strong focus of the policy on numbers of firms (in stead of competitive strength) may have added to the outcomes. In fact, the previous insights are the experiences from which lessons can be drawn by other small and open economies facing a relatively weak entrepreneurial culture.

Given the situation of a relatively large population of small firms facing some intrinsic weaknesses, it is uncertain whether the sector will be able to move to a mature stage including the emergence of medium-sized and larger companies. Alternatively, the sector may face a shakeout among small and vulnerable firms or face small firms remaining small and decreasing their R&D effort. The Action Plan Life Sciences ended in 2004 and was taken over by a generic program in which most of the above learning experiences as well as the problem of equity gap were explicitly addressed and attempted to be solved. The question remains whether a national policy can substantially help preventing the equity gap, in the way suggested in the previous section or by reducing the timing mismatch through a model in which a public support fund is responsible for the first (five) years and market parties for the following years within their time-horizon. Such a policy or any other financial support policy (like fiscal measures) may perform better if there is a *selection* procedure of most promising firms. Here lies a field of research, i.e., of success and failure factors of life-sciences start-ups in survival and growth, and of ways to predict success from characteristics at an early age. Another research line would be to identify how the adoption of the hybrid business model may help to avoid the equity gap. The hybrid model may be adopted in the first years to build a solid business after which the firm moves to a higher level of innovativeness (product model). Overall, a close examination of small life science firms in the Netherlands drawing on a longitudinal panel design is necessary in order to study how these firms take hurdles in moving into next growth stages, for what reasons they fail and in what respects support policies need to be adapted. Results from such a study may also help to clarify whether the policy in the Netherlands has led to outcomes that stay behind or just fit into a more general slow and incremental pattern of life sciences development outside the megacentres. The monitoring preferably also takes a broader scope than merely dynamics of the firms. By including labor market impacts, other indirect impacts in the regional economy, and improvements in health- and medical care and in agriculture, policies to enhance the sector will gain a larger legitimacy and support.

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Notes

Note 1. Dedicated life science firms are newly established, entrepreneurial firms in life sciences, excluding diversified firms, foreign subsidiaries, consultancy and medical devices firms.

Note 2. For example, the organization of master classes, the initiation of professor chairs at universities in biotechnology business, and the appointment of several scouts to track and trace promising research.

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