Science and Public Policy, 46(1), 2019, 136–147
doi: 10.1093/scipol/scy044
Advance Access Publication Date: 4 July 2018
Article

OXFORD

Policies and patenting to stimulate the biotechnology sector: Evidence from The Netherlands

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Abstract

Evidence-based results of innovation policies stimulating the use of academic patents and thereby contributing to the development of economic sectors are scarce. This article describes the effects of a policy instrument (BioPartner programme) to commercialise scientific research during the emerging stage of the biotechnology sector in the Netherlands. From the year 2000, this instrument provided funding for the reimbursement of academic biotechnology patent applications and assistance with the creation of spin-offs. We studied general trends in biotechnology patent applications in the time period between 1990 and 2009 and quantified the appropriation of academic biotechnology patents by the industry. Biotechnology patent classification codes and the PATSTAT database of the European Patent Organisation were used to define and identify all Dutch biotechnology patent applications. Matching the data from these applications with the names of some 65,000 potential Dutch academic inventors and 3,400 Dutch academic patents, we found a net contribution of the policy instrument of approximately 20 per cent of all Dutch biotechnology patent applications. However, the policy instrument did not result in an increase in the overall number of biotechnology patent applications or their use in the sector. Our data suggest that BioPartner contributed to improve the 'business culture using biotechnology patents' at universities.

Key words: innovation policy; biotechnology; patent application trends; spin-offs

1. Introduction

1.1 General

Patents are often used as one of the output indicators to measure the output of scientific research and can make major contributions to future innovations (OECD 2013; Tijssen 2001, 2011). The impact of policies on patenting for the commercialisation of scientific knowledge can depend on national patent rules and regulations (Geuna and Rossi 2011), effectiveness of university–industry technology transfer (TT) (Siegel et al. 2007) and other elements of innovation systems (Etzkowitz 2008). Quantitative data about the effects of policies on TT including the exploitation of patents are scarce or limited to a specific sector for a short period (Chatterjee and Rohrbaugh 2014). Policies regulating public funding of biotechnology research were found to be only one of the many factors that positively affected the strength of the biotechnology industry (Senker et al. 2000). A comparison between dedicated biotechnology instruments in public policies and general policy instruments in 14 EU member states showed that the first category of instruments did not contribute to better country commercialisation performance (Enzing et al. 2004). An EU wide study indicated a lack of internationally comparable and suitable quantitative and qualitative input and output data describing the performance of biotechnology innovation systems (Reiss et al. 2003).

Annually, the biopharmaceutical sector invests billions of euros into medicine development with an average duration of R&D projects of 12 years (Pronker et al. 2011). In this competitive sector, patents are crucial to secure investments and R&D collaborations for the development of the pipelines of companies, thus enabling product development (Fernald et al. 2014). After the enactment of the Bayh–Dole Act in the USA, some 150 medicines based upon university patents were approved by the FDA (McDevitt et al. 2014). The birth and growth of the biotechnology sector in the USA started with the successful exploitation of university patents by a number of spin-off

companies (Zucker et al. 1998), but the long-term effects of the impact of policies on and the appropriation and use of university patents at the emergent state of the biotechnology sector have not been studied empirically (Patzelt and Brenner 2008). With this research, we wish to bridge this knowledge gap and contribute to existing literature by testing hypotheses about whether policies and patenting have contributed to the development of the biotechnology sector. Thereto, we studied the effects of the BioPartner programme in the Netherlands and this article addresses following research questions: Can we identify academic biotechnology patent applications? Can we quantify the contribution of this policy instrument and measure the appropriation of academic biotechnology patent applications by companies in the sector? Does such a dedicated policy instrument lead to a sustainable 'business culture using biotechnology patents' at universities, and can we ascertain whether the developments in the number of academic biotechnology patent applications would not have occurred without a dedicated policy instrument?

1.2 The innovation system and the biotechnology sector in the Netherlands

Here, we refer to an assessment of the OECD of the innovation system and give a short description of the biotechnology sector. The high quality of scientific research and the high rate of patenting were regarded as positive features of the innovation system (OECD 2005). On the contrary, the low level of private R&D, the less than optimal interaction between industry and academia, the insufficient innovative entrepreneurial activity, and the limited ability for research commercialisation were described as negative features. Before 2000, the role and position of universities as serious actors in the innovation system in the Netherlands was relatively weak. The budgets from the Ministry of Education, Culture and Science (MECS) did not provide funding for research commercialisation, TT, or spin-off development. The Ministry of Economic Affairs (MEA) used a number of instruments to enhance the growth of start-ups and spin-off companies.

In the 1990s of the last century multinational corporations (e.g. DSM, Unilever, Nutricia, AkzoOrganon, Solvay, Abbott, and Philips) dominated the biotechnology sector in the Netherlands, while some small- and medium-sized enterprises (SMEs) (e.g. RijksZwaan, Nunhems, Pacques, Norit) played an important role in the sectors of plant breeding and environmental technology (Van der Giessen 2014). Most Dutch companies are operational in three subsectors (i.e. medical, food, and industrial biotechnology). Given the potential contribution of €595 billion from the life sciences and health (LSH) sector to the GDP in the Netherlands (European Commission 2002), this sector has been earmarked as a top sector by the government since 1998. At that time, entrepreneurship in the LSH sector in general and at universities in particular was poorly developed (Enzing et al. 2005).

Therefore, the government decided to implement a policy instrument to stimulate the growth of this sector This policy instrument contained the BioPartner programme with the objective of commercialising academic knowledge through the creation of seventy-five new life science companies and stimulating a more 'entrepreneurial business culture' at universities (Ministry of Economic Affairs 2000). The first stage grant of this programme (some 25 per cent of the total budget of 45 million euros) provided salaries for university biotechnology scientists and funding for the reimbursement of biotechnology patent applications (up to 250,000 euros, with a maximum of 2.5 years) to consortia of companies and universities (Van Geenhuizen, 2008). Between 2000 and 2004, the BioPartner organisation also facilitated further support for the commercialisation of academic life science research (e.g. master classes, business plan development, access to finance, incubator programmes, use of equipment).

2. Theory and hypotheses

With the invention of recombinant DNA in the 1970s, modern biotechnology has become an enabling technology in many industrial processes in the sectors like chemistry, nutrition, pharma, and plant breeding (Zucker et al. 1998). In these sectors, the numbers of biotechnology patent applications have been used as one of the indicators to measure the average commercial country performance, including the Netherlands (Enzing et al. 2004). In light of the objectives of the BioPartner programme, we shall focus our research on the transfer or appropriation of academic patents from the original academic inventor to a company. Commercialisation of research in the life sciences usually follows a pathway from discovery, to an invention disclosure at a technology transfer office (TTO) followed by the filing, licensing, or sales of academic biotechnology patents (Fig. 1).

Here, we define academic biotechnology patent applications as those applications in which at least one of the inventors has a university position at the date of the filing (Lissoni 2012) and is working in the discipline of biotechnology or life sciences. The Netherlands Patent Act does not provide for a 'professor's privilege'. Therefore, patent applications based upon publically-funded academic research are proprietary assets of a university (Lissoni et al. 2009). Academic (biotechnology) patent applications can be filed and appropriated by universities (Lissoni 2013), licensed or assigned to start-ups (Åstebro et al. 2012) or university spin-offs (Lehoux et al. 2014), SMEs (Andries and Faems 2013), and multinational corporations and technology institutes (Pugatch et al. 2012).

'Scientists' patent awareness' has been defined as the phenomenon that scientists are informed about the possibility to use patents for TT (Nerkar and Shane 2003) and 'a business culture using biotechnology patents' as scientists' motivation to file a patent application in order to commercialise their research (Di Gregorio and Shane 2003). Scientists may either contact their university TTO, a research funding organisation or a third party during the decision making process for the filing of a patent application.

In the Netherlands, the financial budgets for scientific research as proposed by the MECS and MEA (indicated with the numbers 1 and 2, see Fig. 1) have to be approved by the government and will then be administrated via research funding agencies, such as the Royal Dutch Academy for Sciences (KNAW) and the Netherlands Research Council (NWO). Some of the commercially-viable results of academic research at the faculties of science, engineering, and medicine might eventually lead to patentable inventions (Van Dongen et al. 2017b). Within the theoretical framework of Fig. 1, we examine the relationships between the research funding by BioPartner on the filings of academic biotechnology patent applications (indicated with number 3, see Fig. 1) by (a) university spin-offs, or their appropriation into the biotechnology patent portfolio of (b) SMEs and multinational companies or (c) technology institutes (all indicated in red colour, see Fig. 1). The linear flow model of TT in this framework oversimplifies a more complex reality because public–private partnerships between university scientists and the business sector might influence the intellectual property (IP) output.

Between 2000 and 2004, the BioPartner programme provided financing to consortia of universities and companies in order to

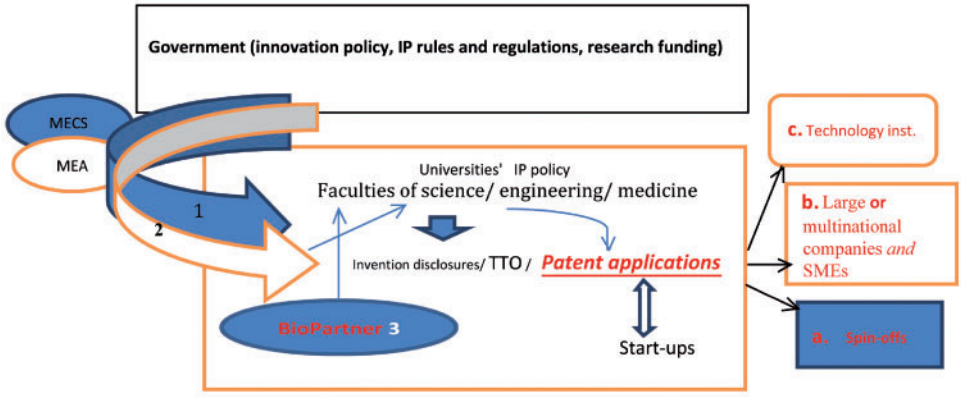

Figure 1. Theoretical framework on transfer of academic biotechnology patents in the Netherlands. Research funding by (1) MECS = Ministry of Education, Culture and Science, (2) MEA = Ministry of Economic Affairs, and (3) BioPartner. Adapted from Panagopoulos and Carayannis (2013), Van Looij et al. (2011), Geuna and Rossi (2011) and Greenhaulg and Rogers (2010).

reimburse the costs for filing biotechnology patent applications. Therefore, we use this feature of this policy instrument as a measure of TT in life science research. The time required to translate scientific results into patentable technologies differs per discipline and economic sector. For patents in the biotechnology sector, we take 6 years as the default time span (OECD 2007). The year 2000 has been chosen as a dividing line since biotechnology patent applications filed after that year can be correlated with the start of the BioPartner programme. Next, we have to distinguish four categories of patent applications in this research:

1. All biotechnology patent applications filed by Dutch organisations (companies, universities, etc.)
2. Academic biotechnology patent applications financed by the BioPartner programme
3. Academic biotechnology patent applications without funding from the BioPartner programme
4. Academic patent applications in all disciplines and sectors (as a control)

Research commercialisation can be measured by the transfer of academic patents to companies via a TTO (Siegel et al. 2007), so we expect that **H1.a**: The BioPartner programme will contribute to a significant increase in the number of academic biotechnology patent applications filed by or licensed to Dutch biotechnology companies. In line with literature about the relationships between academic patenting, spin-off creation and academic entrepreneurship (Lehoux et al. 2014; Lissoni 2013; Lissoni et al. 2009; Shane 2004), we also expect that **H1.b**: the BioPartner programme will contribute to a significant number of academic biotechnology patent applications filed by university spin-offs that started after the year 2000. Referring to effects of changes in patent laws on university patenting (Geuna and Rossi 2011; Mowery et al. 2001) and literature on the commercialisation of biotechnology research by 'star scientists' in spin-offs (Di Gregorio and Shane 2003; Nerkar and Shane 2003; Zucker et al. 2002), we hypothesise that **H2:** the BioPartner programme will contribute to an increased 'patent awareness' amongst scientists and a sustainable 'business culture using biotechnology patents' at universities.

A number of governments in the European Union, including the Netherlands, have introduced policies for research commercialisation, e.g. incubators in the ecosystems around universities in the last decade (Fini et al. 2011; OECD 2013). At the same time university boards have given more priority to research commercialisation and patenting (Van Looij et al. 2011) and non-monetary incentives for scientists stimulating them to disclose their inventions at university TTOs have become more common (Panagopoulos and Carayannis 2013). Considering these other policy developments, we expect that **H3:** the numbers of Dutch academic biotechnology patent applications filed after the year 2000 may have to be corrected, as these numbers could also be correlated with other factors than the BioPartner programme.

3. Methodology and data resources

For the quantification of the patent related contribution of the BioPartner programme to the Dutch biotechnology sector, we identified the four categories of patent applications described in the previous section. Applications are the files for which applicants have decided to request a patent from the patent granting organisations. They are a direct measure for the explicit interest of innovating companies and other organisations to assert their patent rights on the biotechnology market. Filings can be regarded as a preliminary patent application activity indicating the potential interest of innovating organisations from all over the world in the biotechnology market. The data collection was carried out with PATSTAT—also known as the worldwide statistical database[1] of the European Patent Office (EPO). The analysis for this study was conducted by using the International and Cooperative Patent Classification codes for biotechnology patents[2] (Appendix) in order to identify and quantify the numbers of all Dutch biotechnology patent applications with a Dutch origin (companies, universities, spin-offs, inventors, etc.). The time period that we investigated ranged from 1995 till 2009.

Secondly, we used a methodology adopted from the Fraunhofer Institute (Dornbusch et al. 2013) to identify all academic patent applications, including biotechnology applications. With the assistance of human resource departments of universities and available personnel data from the databases of the Royal Netherlands Academy of Arts and Sciences,[3] we had collected the first names, surnames, and scientific disciplines of some 65,280 tenured scientists with employment contracts at Dutch universities between 1990 and 2009. Next, we matched the names of these tenured scientists

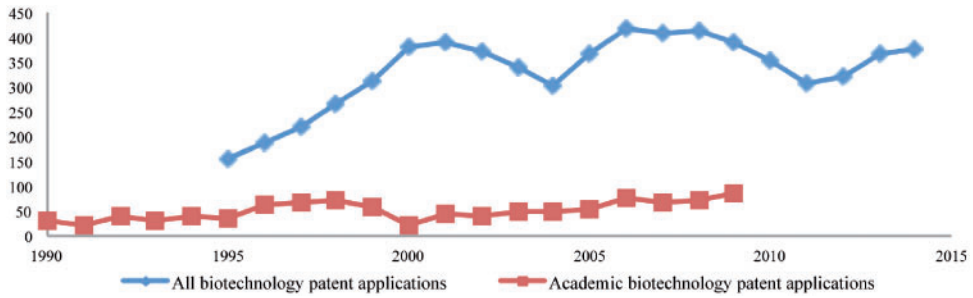

Figure 2. Overall numbers of biotechnology patent applications filed by Dutch organisations.

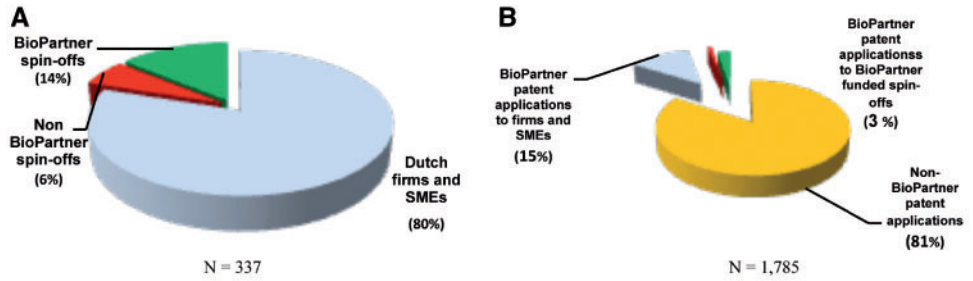

Figure 3. BioPartner funded patent applications (A) and all Dutch biotechnology patent applications (B).

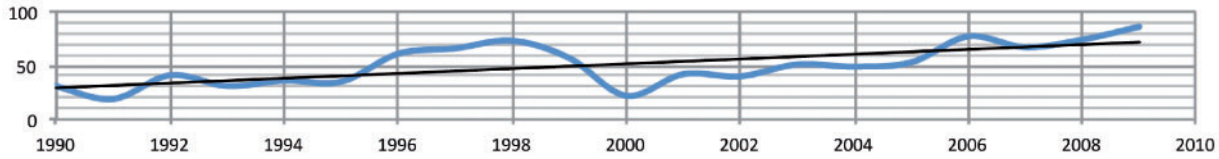

Figure 4. Number of annual academic biotechnology patent applications in the Netherlands. Significant at level P = 0.05.

working at Dutch universities with the names of inventors mentioned in patent applications and then used two algorithms to control for homology effects (Van Dongen et al. 2014). All identified academic patent applications can then be combined with the biotechnology patent classification codes (see Appendix) to yield the relevant academic biotechnology patent applications. Our study thus considers all national and international biotechnology patent applications filed by Dutch organisations at the Netherlands Patent Office (=NL), European patent applications at the EPO (=EP) and the World Intellectual Property Organisation [under the Patent Cooperation Treaty at the WIPO (=PCT)].

Thirdly, all academic biotechnology patent applications have been categorised by their university of origin of the invention and the patent applicant. As biotechnology patent applicants, Dutch universities, technology institutes, multinational corporations, SMEs, university spin-offs, individual inventors, and foreign organisations (with headquartered outside of the Netherlands) have been taken into consideration.

Finally, all identified academic biotechnology patent applications were matched again with the names of existing Dutch dedicated biotechnology companies and also with the names of the new university spin-offs which had been created with the assistance of the BioPartner programme.[4] To analyse the data, the following software and databases were used: Espacenet, Epoque, PATSTAT, Google (Patents and Scholar). In the years between 2013 and 2016, we held some thirty-five semi-structured interviews with research funding organisations, university TTO personnel at ten universities, BioPartner spin-offs, SMEs and large (multinational) companies in the Dutch biotechnology sector. During these interviews, both quantitative and qualitative data were collected to validate our findings about the appropriation, ownership, licensing and exploitation of academic biotechnology patents.

4. Results

4.1. Overall numbers of biotechnology patent applications

Key findings from a longitudinal analysis of biotechnology patent applications filed between 1995 and 2009 are shown in Figs 2–4. Figure 2 shows the development of the overall numbers of NL, EP, and PCT biotechnology patent applications filed by Dutch organisations. In this time period, the overall number of biotechnology patent applications filed by Dutch organisations increased, but we observe a decrease between the years 2000 and 2004, when the BioPartner programme was operational. In this period, a total number of 1,785 biotechnology patent applications were filed by Dutch organisations (companies, universities, etc.). More than 200 biotechnology patent applications were filed based upon academic research that took place at the universities involved in this study (see also Section 5). In the subsectors of medical (red) biotechnology, Akzo Nobel and Crucell were important patent applicants, while DSM, Unilever were important applicants in industrial (white)

Table 1. Top 10 Dutch biotechnology patent applicants.

Organisation applications	Numbers of patent applications in 2000	Organisation applications	Numbers of patent in 2000
1. DSM	48	1. Philips	81
2. AKZO Nobel	39	2. DSM	72
3. Crucell	26	3. Unilever	37
4. Unilever	21	4. Crucell	36
5. DLO[a]	16	5. Synthon	24
6. University Leiden (incl. Medical Centre)	13	6. TNO	24
7. TNO[a]	12	7. Syngenta	19
8. University Utrecht (incl. Medical Centre)	10	8. Univ. Leiden and Medical Centre	18
9. Wageningen University	9	9. University Utrecht and Medical Centre	11
10. Syngenta	4	10. Wageningen University and Res. Centre	10

Note: There is a potential overlap in numbers of patent applications due to classification in more than one patent classification code and filing via multiple application procedures.

[a]Wageningen Research Foundation (DLO) and Netherlands Organisation for Applied Scientific Research (TNO).

biotechnology, and Syngenta, Wageningen University (and the technology institute abbreviated DLO) were important patent applicants in the green, agricultural sector and in food biotechnology. Table 1 shows the top ten Dutch organisations that filed biotechnology patent applications via national or international application procedures (NL or EP and PCT, using the European Patent Convention or the Patent Cooperation Treaty).

The BioPartner programme contributed to the start of some ninety university life science spin-offs[5] and provided funding to file 337 biotechnology patent applications by ninety-two companies in the period between 2000 and 2004 (see Fig. 3A). These 337 biotechnology patent applications represent a significant contribution of 19 per cent of the total number of biotechnology patent applications, while some 80 per cent of these applications were filed by Dutch (multinational) firms and SMEs that were already operational in the biotechnology sector before 2000. After the process of matching the names of tenured university scientists with the names of the inventors in the 337 biotechnology patent applications financed by the first stage grant of the BioPartner programme, we found that only twenty-four of the ninety new university spin-offs—which received support from BioPartner—had filed forty-seven academic biotechnology patent applications (14 per cent). Ten spin-off companies, operational in the life sciences sector before the start of BioPartner in 2000 (e.g. Crucell, Pamgene, Pepscan, Keygene), filed another twenty-two BioPartner funded biotechnology patent applications during the programme (6 per cent). Here, we observe that the BioPartner programme contributed to (337/1,785=) 19 per cent of all biotechnology patent applications filed by Dutch organisations, while (47/1,785=) 3 per cent was filed by twenty-four new university spin-offs starting in the years when this programme was operational (see Fig. 3B). Based upon these results, we cannot accept the hypotheses 1.a. and 1.b stating that the BioPartner policy instrument would contribute to a significant increase in the number of academic biotechnology patent applications filed by companies (1.a) and spin-offs (1.b) thus contributing to research commercialisation in the biotechnology sector.

4.2. BioPartner's effect on transfer of academic biotechnology patent applications

A quantitative analysis shows that some hundred Dutch companies, universities and technology institutes filed approximately 3,450 academic patent applications between the years 2000 and 2009, out of which 565 were classified as biotechnology patent applications. In a general comparison between the number of academic biotechnology patent applications filed by universities, technology institutes, and companies prior to (1990–9) and since the start (2000–9) of the BioPartner programme, we found an overall increase of 26 per cent. Table 2 shows that since the year 2000 (266/565), 47 per cent of all academic biotechnology patent applications have been filed by Dutch companies (including university spin-offs). Here, we find that Dutch universities—in the time period between 2000 and 2009—filed almost four times as many biotechnology patent applications compared with the time period before the year 2000.

Figure 4 shows a small, but significant, increase in numbers of annual academic biotechnology patent applications between the years 1990 and 2009. Taking into consideration that the total numbers of all Dutch biotechnology patent applications decreased (see Fig. 2), whereas the academic biotechnology patent applications increased during the BioPartner programme and continued to increase after its closure (Fig. 4), we have to validate these findings in interviews with TTO staff and entrepreneurs in university spin-offs (in Section 4.3). In summary, we found that the potential commercialisation of academic research in the biotechnology sector within the national boundaries of the Netherlands, enabled by the use of academic biotechnology patent applications, increased significantly.

4.3. Origin, appropriation, and use of academic biotechnology patent applications

Sections 4.1 and 4.2 described the effects of the BioPartner programme on the numbers of biotechnology patent applications and the transfer of academic biotechnology patent applications to companies in the Dutch biotechnology sector. A policy instrument like the BioPartner programme might also have an additional effect on the origin of academic biotechnology patent applications and TT distribution patterns to organisations in the biotechnology sector (e.g. Dutch multinational companies, SMEs, academic inventors, university TTOs, spin-offs, foreign organisations). Figure 5 shows the numbers of the academic biotechnology applications that have been filed before (1990–9, in blue colour) and since the start of the BioPartner programme (2000–9, in red colour). In this figure the numbers of the applications have been categorised in relationship with the name of the university of origin (defined as the university where the research has taken place on the basis of which the biotechnology invention has been patented). Since the start of the BioPartner programme in 2000,

Table 2. Numbers of academic biotechnology patent applications categorised by applicants and time period.

Patent applicants	1990–9 (=*A*)	2000–9 (=*B*)	Change rate (%) (=*B*/*A*)
Dutch universities	45	176	+391
Dutch technology institutes[a]	49	61	+124
Dutch companies and SMEs (including university spin-offs)	247	266	+107
Foreign companies (with headquarters outside of The Netherlands)	108	62	−57
Total	449	565	+26

[a]Netherlands Organisation for Applied Scientific Research (TNO) and Wageningen Research Foundation (DLO).

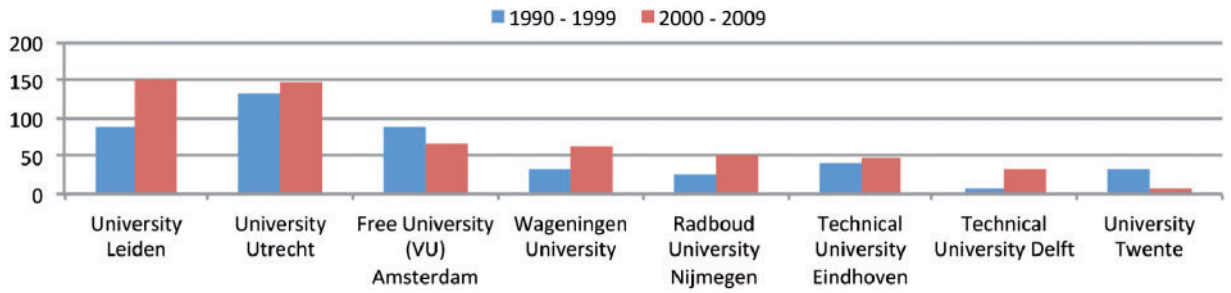

Figure 5. Numbers of academic biotechnology patent applications, categorised by their university of origin before (1990–9) (*N* = 449) and since the start of the BioPartner programme (2000–9) (*N* = 565).

it is clear that all universities, except the University Twente, have contributed to more academic biotechnology patent applications. We also see that—the scientists at—the universities and medical centres of Leiden (e.g. G.J. van Ommen) and Utrecht (e.g. J.G.J. van de Winkel) were involved in more than 50 per cent of the academic biotechnology patent applications.

Figure 6A and B show the changes in the distribution of academic biotechnology patent applications by their applicants in a time period between 1990 and 2009. Combining the data of Fig. 6A and B with the figures in the last column of Table 1, we found three major developments in the filing and appropriation of academic biotechnology patent applications that occurred since the year 2000: (1) an *increase* of 63 per cent by Dutch multinational corporations (e.g. Philips, Akzo, DSM, Unilever and Nutricia), (2) an *increase* of 150 per cent by university spin-offs (especially at the universities Leiden, Utrecht, and Nijmegen), and (3) a *decrease* of 57 per cent by foreign companies (defined as companies with headquarters located outside The Netherlands). In turn, this increased patent awareness plus the higher level of services of personnel of the growing university TTOs might have led to higher levels of filing and appropriation of academic biotechnology patent applications by universities. A different contributing factor could be that the collaboration between universities and companies in the biotechnology sector was stimulated by top sector policies and public–private partnerships.[6]

The Technology Foundation STW is a division of the Netherlands Research Council (NWO) which is responsible for the funding of scientific research at universities. STW applies a policy to file patent applications in case companies in the so-called STW user committees have expressed their interest in the commercialisation of the research results. From a legal point of view, these patent applications have been filed by and therefore belong to STW, but they should be considered as a result of scientific research which has been place at universities, usually executed by PhD students. STW's policy implies that within a certain amount of time either the university or the company will become the legitimate owner of the patent (Idsardi, pers. comm., 2015). Figure 7 shows the number of academic biotechnology patent applications that the universities and STW filed between 1990 and 2009. Here, we found large differences in the number of applications, which can be explained by the patent policies of universities and STW. For example, the University of Leiden filed and appropriated most patent applications as a result of the fact that their TTO applies an IP ownership and licensing policy comparable with most of the universities in the USA. More than 60 per cent of the 'Leiden' biotechnology patent applications—once granted—were licensed as research tools to companies or used in public–private partnerships (Smailes, pers. comm., 2014).

Since the universities of Leiden and Utrecht had filed most of these academic biotechnology patent applications, we found it interesting to compare the differences of their patent policies in relationship to spin-off support and the impact on the number of spin-offs. Eight university spin-offs appropriated biotechnology patent applications based upon research at Leiden University vs. nineteen spin-offs which appropriated patent applications based upon research at Utrecht University (Fallaux, pers. comm., 2013). Nowadays, the patent policies of most universities allow them either to file patent applications as a co-applicant with industrial partners or to encourage the latter to do so as sole applicant (KNAW 2014). In either situation the academic inventors have the right to be mentioned in the mentioned in the patent application.

We collected and analysed data from thirty-five interviews with Dutch companies, research funding organisations, university TTOs and spin-offs to measure the impact and validate the quantitative results of the BioPartner programme. The interviews were semi-structured, took about 30 min to 1 h and were organised on location or by telephone. Interviewees could give four possible answers for each question stating that they either (1) yes or agree (positive response), (2) no or disagree (negative response), (3) question is not appropriate for my organisation (N.A) or (4) have no answer. Table 3 shows the percentages of positive responses by all interviewees of different categories of organisations, when asked about the use of academic biotechnology patents enabled by the BioPartner programme and the effects of this programme. For example, if only

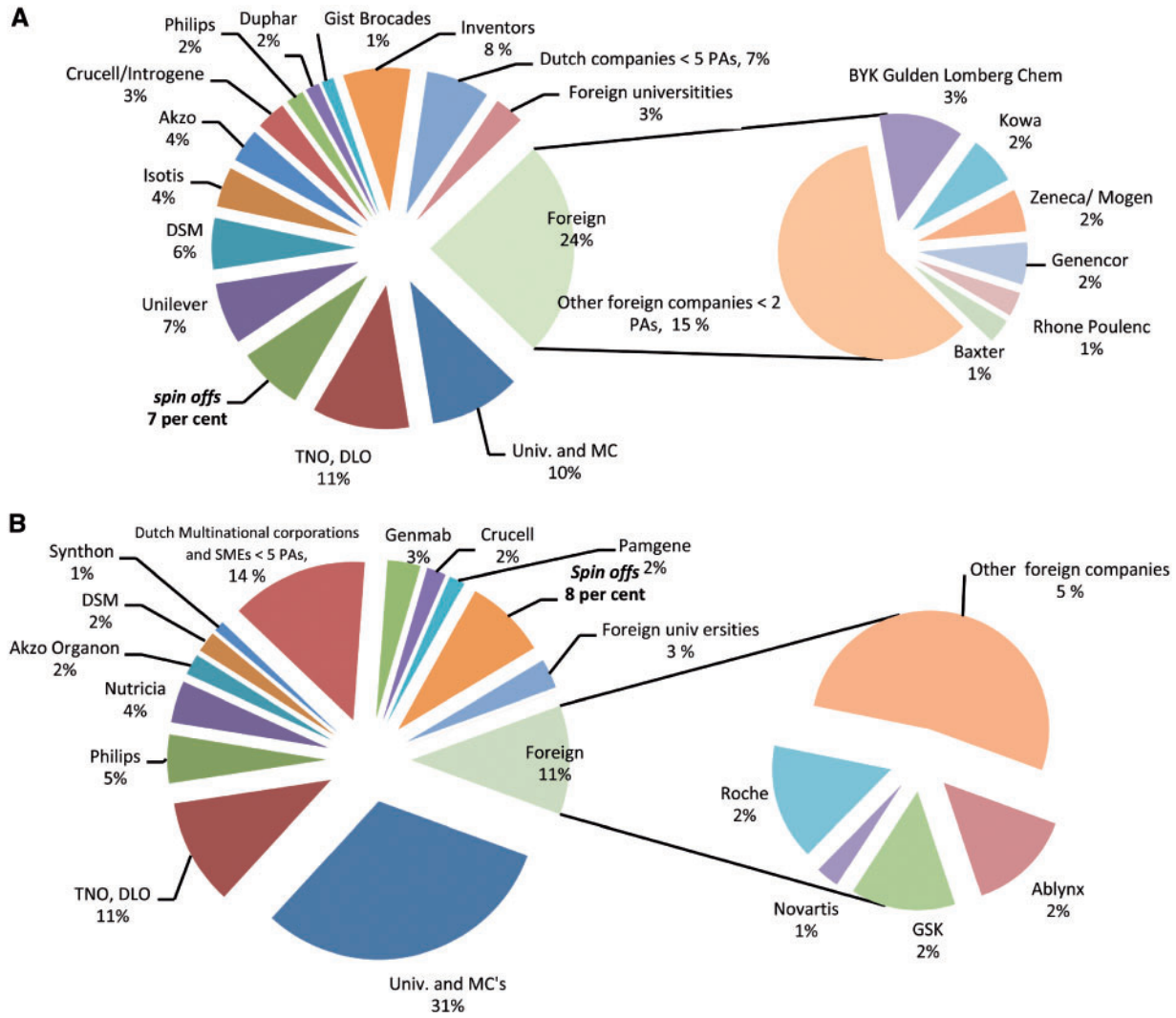

Figure 6. (A) Most important applicants of academic biotechnology patent applications from 1990 to 1999, before the BioPartner programme (percentage) ($N = 449$). (B) Most important applicants of academic biotechnology patent applications from 2000 to 2009, since the BioPartner programme (percentage) ($N = 565$) (PA = patent application).

one interviewee of the, in total, eighteen interviewed university spin-off companies responded positively to a question we noted this response with a score of 6 per cent.

Where SMEs use academic biotechnology patents to demonstrate their innovative capacity and develop products, the large companies apply them both for market development and protection. Many spin-offs use a patent, or a patent license (after the academic patent application has been granted), to show their innovative capacity and to acquire extra funding. On the other hand, university TTOs use biotechnology patents to demonstrate the innovative capacity and to license them to third parties. The responses from research funding organisations, university TTOs, spin-offs and companies for question 8 confirm the general outlook that BioPartner has stimulated the filing of patent applications. Although two categories of respondents did not answer the questions 9 and 10, we observe that according to research funding organisations, university TTOs and spin-offs the patent awareness amongst scientists has increased, while 50 per cent of the TTOs and almost 80 per cent of the spin-offs acknowledged that they noticed that over the years universities have become more business minded using biotechnology patents.

From data in Fig. 3B in Section 4.1, we know that twenty-four of the ninety spin-offs which started between 2000 and 2004, received financial support from BioPartner when filing (forty-seven academic) biotechnology patent applications. Based on both our quantitative (see Figs 4, 5, and 7) and qualitative data (see Table 3), we will accept hypothesis 2, which stated that BioPartner will contribute to an increased 'patent awareness' amongst scientists and a sustainable 'business culture using biotechnology patents' at universities.

Finally, Fig. 8 shows the increase in the annual numbers of academic patent applications and academic biotechnology patent applications in all disciplines (see also Fig. 4) that were filed in the time period between the 1990 and 2009. A statistical analysis shows that the numbers of both kinds of patent applications had increased significantly and that the numbers of annual academic patent applications in all disciplines had increased more than the numbers of annual academic biotechnology patent applications. The data in this figure also show that the contribution of the number of academic biotechnology patent applications to the number of academic patent applications is substantial at 28 per cent annually and varies between 15 and 44 per cent per year. Considering that the R^2 for

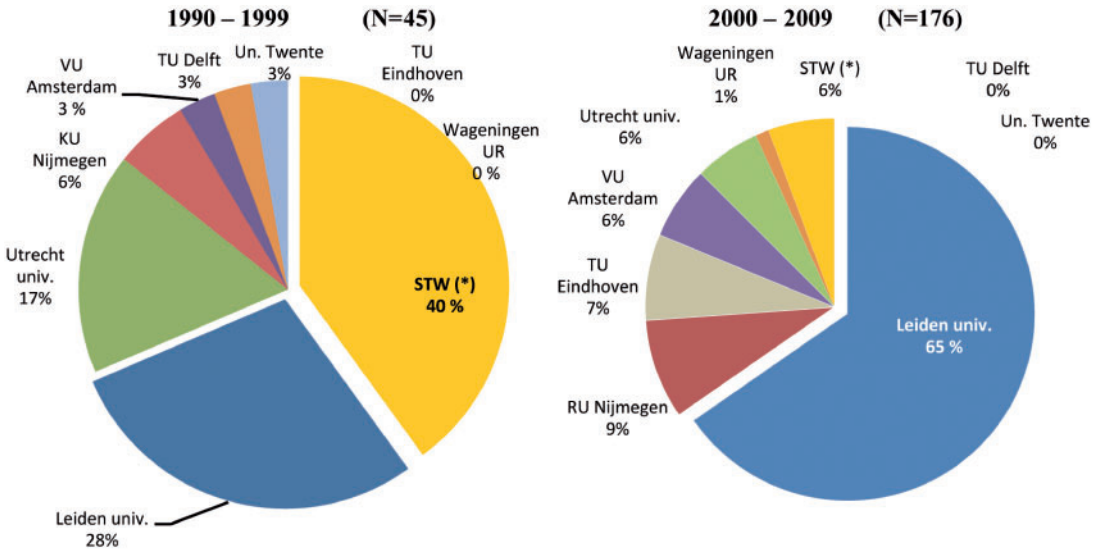

Figure 7. Biotechnology patent applications (%) filed by Dutch universities and STW [Technology Foundation STW (Dutch research funding organisation)] before (1990–9) ($N = 45$) and since the start of the BioPartner programme (2000–9) ($N = 176$).

Table 3. Relative importance of the use of academic biotechnology patents, categorised per type of organisation (percentage of interviewees with positive responses).

Organisations' questions	Research funding organisation	University TTO	University spin-off company	SME	Multinational or large companies
1. Did you use the patent to develop a new (niche) market?	N.A.	N.A.	6 %	20 %	25 %
2. Idem 1, to develop a product or process?	N.A.	N.A.	11 %	40 %	25 %
3. Idem 1, to protect your market?	N.A.	N.A.	N.A.	20 %	50 %
4. Idem 1, for a (sub-)license to a third party?	N.A.	50 %	17 %	20 %	25 %
5. Idem 1, to demonstrate the innovative capacity of your organisation?	N.A.	67 %	67 %	80 %	50 %
6. Idem 1, for extra funding e.g. investors?	N.A.	N.A.	50 %	40 %	No answer
7. Idem, for cooperation with other parties?	N.A.	17 %	22 %	20 %	25 %
8. Did Biopartner stimulate the filing of patent applications?	100 %	100 %	72 %	20 %	50 %
9. Did BioPartner enduce 'patent awareness' amongst scientists?	100 %	67 %	83 %	No answer	No answer
10. Did BioPartner contribute to a 'business culture using patents' at universities?	No answer	50 %	78 %	No answer	25 %
Number of interviews per type of organisation	2	6	18	5	4

$N = 35$.
N.A. = not appropriate.

annual academic biotechnology patent applications is smaller than the R^2 for annual academic patent applications in all disciplines, we see no reason to include corrections for the measured effects of the BioPartner programme in the previous sections with regards to academic patenting. Given the multitude of possible relationships between policies, research funding, collaborative research with the industry, scientists' patent awareness and other factors with academic patent applications, such corrections would have been necessary if the patenting results in Fig. 8 would have shown that the increase in numbers of academic biotechnology patent applications (and the R^2 of this increase) would have been much larger than the increase in numbers of all academic patent applications in all scientific disciplines.

Looking at the data in Fig. 6A and B about the number of university spin-offs that appropriated academic biotechnology patent applications, we observed an overall growth of some (8 per cent of 565)/(7 per cent of 449) = 144 per cent between 1990 and 2009. However, due to lack of available data on spin-off companies in other sectors, we cannot examine whether the appropriation of academic biotechnology patents by university spin-offs in the biotechnology sector remained at a comparable level with all academic patent applications by spin-offs in all sectors. Therefore, we cannot prove hypothesis 3 stating that the numbers of Dutch academic patent applications filed since 2000 have to be corrected as they can be correlated with other policy factors than the BioPartner programme.

5. Limitations

Our research is not without limitations. We have focussed on the filings and appropriation routes of academic biotechnology patent applications in order to demonstrate the effects of the BioPartner programme, as a policy instrument to enhance the commercialisation of scientific research in the life sciences by companies in the Netherlands. The quantitative part of this research was carried out

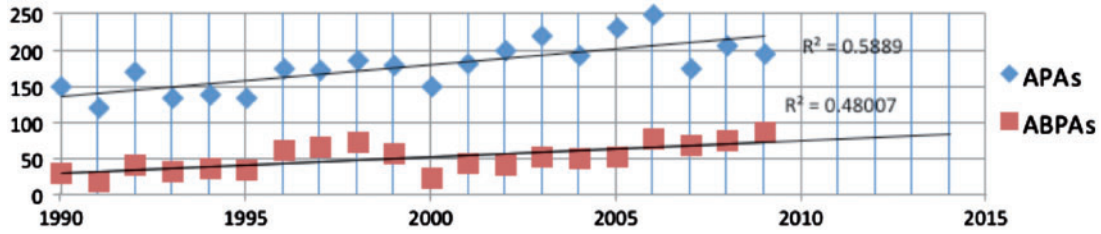

Figure 8. Numbers of annual academic patent applications (APAs) and academic biotechnology patent applications (ABPAs) in the Netherlands. APAs and ABPAs significant at P = 0.05.

between 2012 and 2017 and comprises the data from the universities of Delft, Eindhoven, Twente, Wageningen, Groningen, Leiden, Nijmegen, Utrecht and the Free University (= VU) University Amsterdam only, including four faculties of medicine or university medical centres in the Netherlands (Sections 4.1 and 4.2, and KNAW 2014). Based upon interview data with fifteen IP managers at companies, research funding organisations, university TTOs and with twenty life science entrepreneurs in spin-offs between 2013 and 2016 we have been able to validate our findings (Section 4.3).

For the methodology in this research two assumptions are critical: (a) On the basis of interviews with professors and TTO managers, we estimate that in more than 95 per cent of all academic patent applications the names of (assistant/associate) professors are included as one of the inventors, and (b) the number of (assistant/associate) professors in the scientific disciplines where patentable research results might be expected (i.e. engineering, natural sciences, medicine) remained at a stable level of some 15,000 full time equivalents between 1990 and 2009 (ChiangMera 2015). Whether or not the records regarding tenured scientists per university were complete depend on the accuracy of the human resource databases of the universities and medical centres included in the study. Based upon cross checks with patent officers at the university TTOs we expect that we have identified more than 95 per cent of the academic patent applications.

6. Conclusions and discussion

Our research shows that:

a. Between the years 1995 and 2000 the number of biotechnology patent applications of Dutch organisations has increased and has been at a more or less stable level since then, and
b. the BioPartner policy instrument contributed to the appropriation of academic biotechnology patent applications by companies at a level of approximately 20per cent of all Dutch biotechnology patent applications during the 5 years that the programme was operational, and
c. 'scientists' patent awareness' and 'business culture using biotechnology patents' at universities increased which both can be positively associated with the BioPartner programme.

Patenting has increased sharply over the last decades as industries shifted more and more from manufacturing towards knowledge-based high-tech production. In the biotechnology sector, this growth has been even more pronounced as can be witnessed at the major patent granting offices in the USA and Europe (Pugatch et al. 2012). According to international data about the numbers of the Dutch biotechnology patent applications filed at the European Patent Organisation, the Netherlands has a fifth position globally (Lawrence 2007). In our research we observed a spectacular increase of biotechnology patent applications before the start of the BioPartner programme, which is in line with global biotechnology patenting rates (Barone 2005). We have been able to provide empirical evidence about the filings, appropriation, transfer and use of academic biotechnology patent applications in the Netherlands over time and the contributions of the BioPartner programme in this matter.

The observed growth in numbers of academic biotechnology patent applications in the Netherlands between 1990 and 2009 is in line with the growth observed at universities in Europe (Lissoni 2013; OECD 2012), but the percentage of university-owned biotechnology patents in the Netherlands is higher than at universities elsewhere in Europe (Lissoni 2012). The 14 per cent appropriation of academic biotechnology patent applications by foreign companies and universities is within the common ranges of appropriation and attrition by multinational corporations (Arora et al. 2015). This percentage also shows that the contribution of Dutch academic biotechnology patents to the globally operating biopharmaceutical sector is not insignificant (Restaino and Tackeuchi 2006). However, the 47 per cent of co-applications of academic biotechnology patent applications filed by Dutch companies in this research turns out to be considerably higher when compared to data from earlier research (Giuri et al. 2007).

The biotechnology ecosystem in the Netherlands is small and is concentrated in three bio clusters. In this particularly competitive sector industry, funded academic patented inventions are more likely to boost innovations (Wright et al. 2014). The policy instrument BioPartner enabled some 90 Dutch spin-off companies to appropriate 337 biotechnology patent applications based upon scientific research.[7] By the year 2006, some 120 companies and technology institutes in three regional clusters (Leiden Bioscience Park, Utrecht and Amsterdam Science Park) were operational in the Dutch biotechnology sector. By the year In 2014, some 590 dedicated biotechnology companies and institutes were operational in six clusters in the Netherlands (Leiden Bioscience Park, Utrecht Science Park, Amsterdam Science Park, Health Valley, Rotterdam Science Tower, and Groningen Business Generator) and provide jobs for some 34,000 full time equivalents (Van der Giessen et al. 2014). During interviews with university managers and IP managers in the industry, we found evidence that deans of university faculties and life scientists have become more aware of the importance of research commercialisation and patents (KNAW 2014). More recently, research commercialisation and entrepreneurship have also become more important and appealing to academic scientists as a means to enhance their careers (Van Dongen et al. 2017b).

The identification of academic patent applications and the quantification of their applicants can pose several problems. When scientific research is financed fully or partly by private companies or research funding organisations, it remains possible for other parties than

universities to negotiate the filing of patent applications and their appropriation (Geuna and Rossi 2011). Patent applications based upon academic inventions by scientists at universities may be filed by third parties and will then represent a blind spot. Given the time period of our research e.g. the KEINS database, with 1.5 million patent applications filed at the between 1978 and 2003 and administrated by the European Patents Inventor database at the Bocconi university in Italy (Lissoni et al. 2008), can provide only partially for a possibility to match these EP applications with Dutch academic biotechnology patent applications and inventors. However, we did not have access to one national database with up-to-date and accurate information about tenured academic staff. And, in line with their internal policy, some universities (e.g. University of Technology Delft), technology institutes (e.g. TNO), SMEs or spin-offs may decide to apply for national e.g. NL patent applications only, without continuations into EP patent applications.

Nowadays, eighteen Codes of Practices for TTOs are available as recommendations for policy makers and research funding agencies in order to facilitate optimal research commercialisation (Arundel 2013). But in 2000, only little information was available to design university patent policies by policy makers at the national and regional levels or at the level of the individual universities (Bekkers et al. 2006). The regular exchange of experiences in matters of IP rights, business development, spin-off creation, and licensing, between personnel of Dutch TTOs and established university TTOs in other European countries started in the year 2005. Discussions within expert committees with TTO personnel (e.g. ASTP, PROTON) also contributed to a professionalisation of TTO governance and structure (Smailes, pers. comm., 2013).

Future research into the effects of policies on the actual use and exploitation of academic patents in various economic sectors require may include a wide variety of areas. The payment of annual patent renewal taxes (e.g. Dechezleprêtre et al. 2017), licensing (OECD 2013), and patent citations by third parties (e.g. Hall et al. 2007; Van Dongen et al. 2017a) can be used as important indicators to determine their use, exploitation and value.

Considering the impact of the BioPartner programme, we conclude that the patenting part of this policy instrument has contributed to the sector as a whole but only on limited scale with regard to the development of university spin-offs. Our data suggest that the 'business culture using biotechnology patents' at universities in the Netherlands has improved since the start of the programme.

Notes

1. PATSTAT, see http://www.epo.org/searching-for-patents/business/patstat
2. EPO (2011). Definitions of patent classifications, see http://www.epo.org/searching
3. KNAW, see https://dans.knaw.nl
4. Innotact (2005), see http://www.BioPartner.nl (pages 65–67)
5. Innotact (2005), see http://www.BioPartner.nl
6. Top Consortia Knowledge and Innovation (2016), see https://www.topsectoren.nl
7. Innotact (2005), see http://www.BioPartner.nl
8. Patent classes used at the European Patent Organisation, see http://www.epo.org/searching accessed in 2015 and 2016.

Acknowledgements

The authors are grateful to interviewees who provided data, for the cooperation with Jos Winnink and Robert Tijssen at the Center for Science and Technology Studies (CWTS) at Leiden University in the Netherlands and for comments that we received from undisclosed reviewers.

Conflict of interest. All authors declare no conflict of interest as to their possible involvement with the work at university TTOs or personnel working at such offices.

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Appendix

International and cooperative patent classes for biotechnology patent applications[8]

White(= *industrial*) *biotechnology*;

C02F3/34 biological treatment of water, waste water, sewage or sludge, C12M, C12N, C12P, and C12Q (resp. apparatus for enzymology or microbiology, compositions of micro- organisms or enzymes, fermentation or enzyme- using processes, measuring processes involving enzymes or microorganisms)

Red (= *medical*) *biotechnology*;

A61K38, A61K39, and A61K48 (resp. medical preparations containing peptides, antigens or antibodies, or genetic material to be inserted into cells of the living body), C07G11, C07G13 and C07G15 (resp. antibiotics, vitamins, hormones), C07K4 and C07K14, C07K16, C07K17 and C07K19 (resp. peptides having less and having more than 20 amino acids, immune globines, carrier bound or immobilised peptides, hybrid peptides), G01N33/53, -/68, -/74, -/76, -/78, - /88 and -/92 (analysing materials involving resp. immunoassays, proteins, hormones, human chorionic gonadotropin, prostaglandins and lipids).

Green (= *agro food*) *biotechnology*;

A01H1 and A01H4 (resp. processes for modifying genotypes and plant reproduction by tissue culture techniques) [Mismatch]