Original Article

Fostering technology transfer in industrial biotechnology by academic spin-offs in Europe

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ABSTRACT

Industrial biotechnology is the commercial application of biotechnology using cells or components of cells, like enzymes, for industrial production processes including consumer goods, bioenergy and biomaterials. In the last years this area has gone through a fast technological development resulting in a high number of basic technologies based on research efforts at universities and research institutions. But a technology transfer gap exists between basic research and the commercialisation of the results. This gap can be closed by academic spin-offs which manage the technology transfer from universities and research institutions to industrial companies. After the spin-off process, the technology is further developed within the new venture normally using additional resources from external investors. As soon as the technology reaches a certain grade of maturity, the spin-offs can co-operate with an established company and work for them as a service provider or be acquired. The chosen approach of technology transfer depends on the type of company. Whereas multinational enterprises (MNEs) are very active in making new technologies available both by acquiring spin-offs or engaging them as service providers, small and medium enterprises (SMEs) are focused on partnering with spin-offs, due to limited financial and management resources.

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INTRODUCTION

Biological production technologies are being increasingly applied to produce high value products, such as fine or consumer chemicals, but also bulk chemicals and polymers.[1] The development of these technologies has progressed at an enormous rate and has led to several technological breakthroughs. For example, the genetic engineering of microorganisms has enabled the biotechnological production of new products and, in combination with improvements in process design and reactor technology, it dramatically increases the performance of biotechnological production processes. The applicability of enzymatic catalysis, as another example, was subject to major improvements regarding the reaction environment and process conditions. For instance, the use of non-aqueous solutions increases the substrate spectrum and the application of enzymes from extremophile sources increases the robustness of the processes and the choice of reaction conditions.

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The capability and efficiency of these biotechnological processes often exceeds the existing chemical ones and even enables reactions and production steps that had not been possible with established techniques. In addition, these new processes will comply with modern requirements in eco efficiency including the use of renewable raw materials, mainly agricultural products such as starch and their residues, for industrial purposes. This use of renewable feedstock is widely regarded as the solution to find alternatives for diminishing fossil resources.[2,3] The ecological effect of industrial biotechnology is also due to low operating temperatures of biotechnological processes in contrast to rather energy intensive processes using chemical catalysts and high temperatures required by many chemical reactions.[4] There are numerous examples of successful applications of industrial biotechnology for the generation of innovative and valuable products, including products that cannot be produced using traditional chemical synthesis.

The application of renewable resources will result in economically and environmentally sustainable production processes influencing the economic development of industries, like the chemical industry. This makes industrial biotechnology a key technology for future economic development and offers dynamic growth opportunities for the chemical and related industries.[5,6] Governments in Europe,[7] the United States[8] and other regions recognise the potential of industrial biotechnology and ensure support to remove growth barriers and exploit the application opportunities. This becomes obvious by the many financial incentives given by governmental programmes encouraging investments in this area.[9]

But there are also some barriers to overcome. The chemical industry has optimised chemical synthesis over a long period of time and the production facilities are normally depreciated making the synthesis of existing products using chemical procedures so inexpensive that the development of a biotechnological production process is often not cost efficient.[10] The change of existing chemical processes towards biotechnological processes might require massive new investments so that companies have to manage the high capital requirements to build up new production facilities.[11] Economic advantages due to the implementation of biotechnological processes can only be achieved by lower production costs, since biotechnological products do not achieve higher prices compared to their chemically produced counterparts. A price premium for biotechnological products can be accomplished only in a few segments, such as the food industry.

To achieve this transition from chemical synthesis to biotechnological processes on a cost competitive level compared to chemical synthesis, state-of-the-art technologies have to be employed. Therefore, technological innovation is important for industrial biotechnology which makes the transfer of academic R&D results towards innovative industrial applications a key aspect for the industry.[12] Academic research is typically governmentally funded and conducted in non-profit governmental or semi-governmental institutions (e.g. universities and research institutions, like Max Planck, Helmholtz or Fraunhofer Society). One possibility to commercialise new technologies are entrepreneurial activities by creating new ventures within these institutions.[13-15] These academic spin-offs can bridge the technology transfer gap to use academic R&D results for innovative industrial products and services.[16-18] Due to their lean structure they are more flexible and faster in the commercialisation of new technologies than established companies.[19] The importance of entrepreneurship for universities and research institutions has steadily increased during the last decades.[20] This is accompanied by a change in government policies that encourages universities and research institutions to commercialise their R&D results.[21,22] This means that, besides teaching and research, an additional mission is the support of the economic and social development through the commercialisation of the output of basic research.[20,23,24]

This article investigates the role of technology transfer in industrial biotechnology by creating academic spin-offs. After describing the methodology of the research and describing the role of established companies and spin-offs within the industrial biotechnology sector this article discusses the creation of spin-offs as a method to transfer academic R&D results into industry. The aim is to raise interest for this topic especially within the community of policy makers and traditional companies. Therefore, based on the conclusions in the last chapter concrete recommendations for universities and research institutions, established companies and policy makers are given. It is important to mention that this article has a focus on the situation in Europe and particularly Germany.

METHODOLOGY

The initial literature research was carried out in both academic and practitioner oriented journals as well as publications of relevant institutions (e.g. company presentations, annual reports, press clippings). The main key words, which were searched, were technology transfer, spin-offs, spin-outs, start-ups, new ventures, co-operation, joint development, acquisition, mergers & acquisitions (M&A), service provider and technology provider. Main result was a database with relevant institutions (industrial companies, academic spin-offs, universities and research institutions including TTOs and venture capital investors including corporate venture capitalists) as well as technology transfer examples including involved parties, background, relevant activities and results.

To understand technology transfer by academic spin-offs interviews with 12 academic spin-offs, 12 universities and research institutions, 22 companies and 15 venture capital investors (of which 4 were corporate venture capitalists) were conducted. The interview partners were selected from the database by 1) ranking them regarding fit to the research scope and 2) interest in and availability for an interview. All potential interview partners with a good fit were asked for an interview and all those who agreed were interviewed. Each interview partner was interviewed by a single interviewer in one sitting of approximately one hour. A reference set of questions was used as a guideline for the interview, thereby leaving enough room for spontaneous answers, which gave a semi-structured nature to the interviews. The questions were structured around different topical groups containing 1) importance and usage of technology transfer from academia, 2) co-operations with academic spin-offs and 3) technology transfer mechanisms and results regarding co-operations with spin-offs.

Before each interview, the interviewer had gathered in-depth information on the company or institution through various sources (e.g. databases, website, press releases), enabling an efficient conduct of the interviews. The analysis of the interview results was based on a comparative analysis to identify specific aspects referring to grounded theory techniques.[25,26] The results of this analysis were used to describe the role of the different company types including spin-offs and especially their involvement in technology transfer.

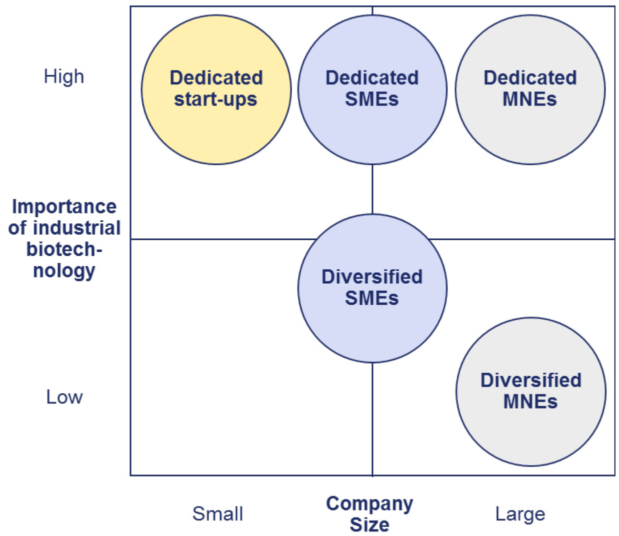

Figure 1: Company types within the field of industrial biotechnology

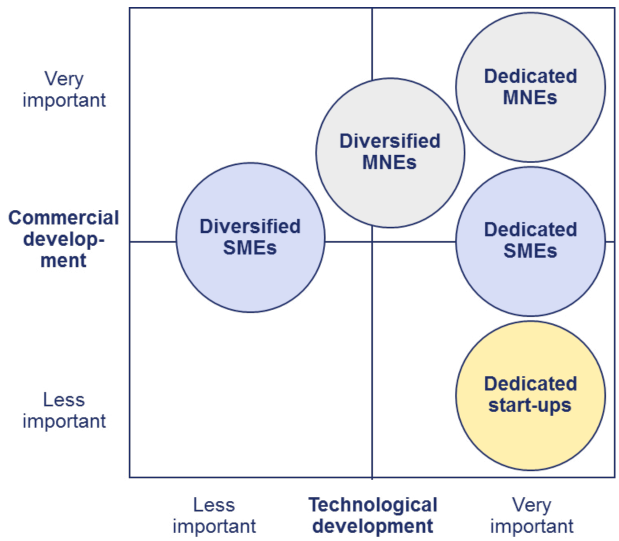

Figure 2: Importance of the different company types for the further development of industrial biotechnology

ROLES OF THE DIFFERENT COMPANY TYPES

Companies active in the area of industrial biotechnology range from small and medium enterprises (SMEs) to multinational enterprises (MNEs). Based on the definition of the European Union, SMEs have less than 250 employees and less than 50 million Euros annual turnover. Companies with more employees or higher annual turnover are seen as MNEs, because they normally have operations in more than one country. The differentiation into specific company types based on size, i.e. MNEs versus SMEs, and areas of activity, i.e. dedicated to industrial biotechnology versus diversified over a broader range of areas, is necessary to understand the industrial biotechnology sector, as industrial biotechnology is of different importance for these company types (Figure 1).[27] Additionally, these different company types have very different roles regarding the technological and commercial development of the industrial biotechnology sector (Figure 2).

Dedicated SMEs focusing on industrial biotechnology were founded mainly in the 1990's (BRAIN) or early 2000's (Codexis). After performing intensive R&D during the first years, they are now focused on the development and market introduction of their own products. This requires a stable revenue situation to finance own R&D projects, development and production facilities, as well as enable market access, e.g. by acquisition of appropriate business units. Dedicated SMEs with their technology focus strongly support the technological development of industrial biotechnology. Diversified SMEs (e.g. Döhler, Pentapharm) have a longer tradition and focus on established industrial sectors, like the chemical or food industry. Serving already developed markets with highly specialised products, these companies are introducing step by step biotechnology processes and products into their markets to realise growth opportunities despite restricted technological resources. It is expected that diversified SMEs will introduce industrial biotechnology to a wide range of processes and contribute to the commercial development of this segment.

Dedicated MNEs are dominated by companies, which have been active in the area of natural products for decades (e.g. Purac, Lesaffre). Normally, they use optimised biotechnological processes for traditional markets (e.g. starch, yeasts) over many years. Industrial biotechnology is one cornerstone in their technology portfolio and increasingly they are moving towards new biotechnology based products and processes. Other companies in this segment (e.g. AB Enzymes, Novozymes) are more R&D oriented and have industrial biotechnology as core activity. This group contributes significantly to the technological and commercial development of the industrial biotechnology sector. Diversified MNEs are mainly established companies from the chemical industry (e.g. DSM, DuPont), agro industry (e.g. Archer Daniels Midland, Cargill) or food industry (e.g. Danisco, Nestle). Their strength is the broad and integrated technology portfolio which complements industrial biotechnology processes (e.g. purification technologies). They have the technical resources (e.g. engineering) as well as financial resources to commercialise biotechnological technologies and products globally. As biotechnology is only one of many core technologies these companies have a smaller impact on the development of industrial biotechnology than dedicated MNEs.

TECHNOLOGY TRANSFER THROUGH SPIN-OFFS

Dedicated and diversified MNEs have enough in-house resources to realise most of the technology developments in-house. Additional R&D capacity and cost reduction (reducing fixed costs or people on the payroll) is not relevant for working together with external partners, like spin-offs. But these companies have a high interest in additional, external know-how which is not available in-house or too expensive, if it would be built up internally. Expanding in-house capabilities through external expertise is seen as the most important advantage of using external technologies by way of co-operations with service providers. An important task for established companies is to optimally integrate internal and external knowledge within the innovation process, so as to be able to benefit from synergy effects. This strategy has often been used in the past and almost all industrial biotech companies have such co-operations (e.g. R&D co-operations of BASF, DSM, Henkel and others with BRAIN as an example from the chemical industry or co-operations of Shell with Codexis and Total with Gevo in the area of biofuels).

The situation for SMEs is very different, compared to MNEs, as they are more dependent on technology transfer from academic research to develop new products internally or together with partners, due to limited financial and management resources. They see technology transfer from the academic world as an effective method to capture capacity and expertise without investing much money in in-house resources. The preferred option to access new technologies involves R&D co-operations with universities and R&D institutions but also with specialised spin-offs.

It is characteristic for all spin-offs to start with a technology that is immature and requires further development. The proof-of-concept is normally done at laboratory scale. Before larger investments in production, marketing and sales it is necessary to reach the technical proof-of-concept. The need for further development of the technology is directly linked to additional financial requirements and other resources to facilitate the R&D work. Due to restricted resources in their first years, academic spin-offs focus mainly on a service oriented business approach offering their particular know-how to support other companies. The intellectual property (IP) from these co-operations normally belongs to the customer resulting in a limited growth as well as value creation potential. But the business risk is also limited as there are only low capital requirements to realise this business model. The spin-offs avoid the time and cost consuming development of own products, while their customers are able to transfer the spin-offs' technologies into new products.

Nevertheless, the development of own IP and products is necessary for the further growth of new ventures. It can be observed that, over time, the service oriented spin-offs are taking on a more IP/product oriented business approach. This is possible as it is accepted that a significant part of the developed IP within research co-operations belongs to the technology provider. For example, companies like Autodisplay Biotech, C-Lecta and Evocatal are developing biocatalysts for established companies within R&D co-operations whereby a special biocatalyst including all related IP belongs to the customer and new IP regarding further developments of the technology belongs to the spin-off. As a result, with growing maturity, spin-offs are increasingly able to develop and commercialise own technologies and products.

After building up an attractive technology or product portfolio with correlating IP protection or, if the technological and market proof-of-concept is shown, technology transfer through the acquisition of these spin-offs by MNEs or SMEs is an option. The first step of an acquisition is often an R&D co-operation which gives the established company the opportunity to assess the technology of the spin-off and the fit into the own technology portfolio. In the case of an acquisition, the spin-offs are normally more or less integrated into the buying company so that the complete know-how and IP is fully available for the new owner. There have been numerous examples during the past years, like the acquisition of IEP by Cambrex or the purchase of X-Zyme by Johnson Matthew.

CONCLUSIONS AND RECOMMENDATIONS

It could be shown that academic spin-offs can close the technology transfer gap between academic research and industrial application in the area of industrial biotechnology. Spin-offs make state-of-the-art technological expertise from academic research available for established companies which can use these to leverage their product development and global sales capabilities. Technology transfer from academia to industry creates a win-win situation for all participants leading to a faster dissemination of academic knowledge into practice and resulting in an economic advantage.

The views regarding technology transfer and especially the expected increases in performance of own R&D are similar when comparing the different company types, but the chosen approach of technology transfer depends on the type of company. Whereas MNEs are very active in making new technologies available both by acquiring spin-offs or engaging them as service providers, SMEs are more focused on partnering with spin-offs, due to limited financial and management resources. An important insight is that none of the company types performs all technology developments internally. Working together with external partners, like spin-offs, strengthens internal competencies by combining internal and external know-how. A task for established companies is to optimally integrate internal and external knowledge within the innovation process, to be able to benefit from the positive effects each activity has on the other. The advantage for the established companies is that they can focus more on their core competencies and especially on their markets as external technological competence can be brought into the company.

But creating spin-offs is not yet systematically used for technology transfer from universities and research institutions into the industry. Despite some elements of "entrepreneurial thinking" within the new Horizon 2020 program and some national initiatives within governmental funding programs (e.g. GoBio in Germany) there is still no general awareness about the value of entrepreneurial thinking. Companies should use the advantages of new ventures like more target-oriented R&D work or faster time-to-market to improve the innovation capabilities within their companies. R&D managers in established companies should be more open to actively use new ventures for technology transfer and understand that entrepreneurial behaviour can support technology transfer to improve innovation processes.

Spin-off activities can also be fostered by so called founding angels. With Autodisplay Biotech and Butalco there are success examples in Germany.[28] Founding angels found together with scientists high-tech start-up companies to successfully commercialise the results from academic research. They complement the scientific team members coming mainly from universities and research institutions with business expertise.[29,30] Besides initial funding in the pre-seed phase, founding angels are operationally very much engaged bringing in their expertise from other successful start-up projects. Because of their very early and much more operationally engagement they have more the role of a founder and entrepreneur and less that of an investor. Universities and research institutions should be more open to work together with founding angels because they can support academic institutions in the identification and realisation of interesting start-up opportunities.

As high quality research at universities and research institutions in Europe has not been sufficiently translated into commercial applications, policy makers should more foster this technology transfer mechanism. Policy makers should further support the creation of new ventures for technology transfer through providing incentives for business oriented and experienced people like founding angels or business angels to join new ventures and to successfully help realise technology transfer. These incentives could be tax incentives for the new ventures (e.g. preferred depreciation models for R&D expenses), entrepreneurs and investors (e.g. reduced tax rates on exit profits).

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