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The Conditions of and Requirements for the Formation of Clusters in Biotechnology

In this article, with the help of the value chain model, I explain the functioning of biotech clusters. The "cluster" phrase was originally defined by Porter. In my opinion, the problem with Porter's and other classical definitions of a cluster is that they are static, whereas the main feature of clusters' is actually their dynamic nature. This is the reason why the following should also be included in the definition:
– clusters emerge in a turbulent way: processes cannot be foreseen due to the lack of linearity.
– a cluster, however, is a kind of an arena, because dense and changing vertical input-output relations and connections between horizontal organizations always generate a sort of a need for change.
– clusters cause changes in the innovation policy, as they support the evolution of a policy which is appropriate for cluster formation. That is, they act as catalysts for the formation of better conditions.
Accordingly, Porter's original definition needs modification.
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In biotechnology, as in other innovative, high-tech industries, changes in knowledge level, paradigms, and projects, are very rapid. In regards to biotech project costs, minimizing risk is essential for business organizations. They usually fulfill this requirement through the division of labour.

In this article, with the help of the value chain model (*Porter 1998*), I explain the functioning of biotech clusters. I describe the main tasks completed during biotechnology pharmaceutical manufacturing and division of labour generally applied in the sector. Business organizations were forced to cooperate due to the tendency of transformation within the sector, the extension of tasks, and the increasing costs. One type of this cooperation is called clustering.

The main features of cluster functioning are dynamics, feedback, and a great number of interactions, which cannot be explained by the traditional value chain model. The value chain model was intended to be made more dynamic by illustrating the feedback.

According to Porter, regional clusters are geographic concentrations, based on the innovative relation network of a particular field's competing and cooperating companies,

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associated and supporting branches, financial institutes, providing and cooperating infrastructural (background) institutes (education, research), and entrepreneur alliances (chambers, professional associations). (*Steiner 1998, Lengyel 2001, Porter 1985, Porter 1998, Porter 2000*).

In red biotechnology[1], this means a project-based interconnection of pharmaceutical companies, biotech companies, R+D organizations (universities, research institutes), and other advisory organizations.

In my opinion, the problem with Porter's and other classical definitions of a cluster is that they are static, whereas the main feature of clusters' is actually their dynamic nature. This is the reason why the following should also be included in the definition:

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– clusters cause changes in the innovation policy, as they support the evolution of a policy which is appropriate for cluster formation. That is, they act as catalysts for the formation of better conditions. Accordingly, Porter's original definiton needs modification.

There are several theories describing the motivations for cooperation. I will use the value chain model, which is popular in the pharmaceutical industry, to describe the operation of clusters. The problem with this model is that it is static, meaning feedback dynamisms, so characteristic in biotechnology, are missing. I will try to fill it in, based on my practical experience.

Biotechnology and pharmaceutical companies

Medical biotechnology is used by two main types of companies. They are either large companies drawing on a long history in the given field and developing into more and more innovative biotechnology users, such as large pharmaceutical companies ("big pharma"). Or, modern biotechnological companies emerge, which the previously stated large companies purchase knowledge, projects or services from. Mainly the large companies control the biotechnology industry with regard to revenue. However this does not lead to strict adherence to traditions and the conservation of states of power. This is because, in terms of knowledge and the number of innovative projects, altogether small biotech companies have the comparative advantage.

Many biotech companies were founded in the 70-s and 80-s. First they sought to become completely vertically integrated companies, encompassing everything from R&D to production and sales. They used closed innovation only. Gradually, these companies brought new trends in their innovation strategies. At first the companies lacked two things that kept them from reaching their goals: the lack of funds, and experienced managers. However these two things are essential (in addition to technology) for a company to grow from a spin-off enterprise to a large pharmaceutical company. The classic pharmaceutical companies, being on the top that time, already possessed these resources. Thus some of

[1] *Red biotechnology is applied to medical processes. Some examples are the designing of organisms to produce antibiotics, and the engineering of genetic cures through genetic manipulation.*

them purchased biotech companies while others however were not open to biotechnology in terms of investment and cooperation (*Murray 2002*).

The volume and complexity of biotech and pharmaceutical projects grew in relation to the amount of available information and acquired knowledge in an environment of steadily growing needs for new knowledge. This placed further emphasis on cooperation, the sharing of costs and risks of producing new R&D results. An industry of high risk – high benefit type emerged. This led to problems, but opportunities as well. Concerning the problems it was asked: Who will finance the costs of research? Will investors think that the industry is too risky? Naturally the significance of professional investors and specific tenders increased with this.

Companies were forced to cooperate due to the high risk associated with biotechnology, the complexity of strategic management rules and the then unusually high amount of needed funds. First of all, the necessary monetary tools are available only at the largest companies. Second, the necessary competencies are often missing with smaller companies. For example, a smaller company, a market leader in R&D, does not have the necessary experience either of the capability needed to clinical testing or production. Cooperation is necessary to fill these gaps. With this sharing of different sorts of risks will be realised. These risks, actually non-calculable uncertainties several times, may be technology, market, regulatory or competition related. The later reflects on the segments of all the other risks, since the rapid development of China, South Korea and India. The only advantages can only be quality and knowledge for the traditional pharma producing countries. But precisely these are areas where China and India are developing rapidly, while maintaining the seemingly natural price advantage. Europe and the USA can only compete with these products if they do not count on price advantage, but on therapeutic advantage. This means producing a newer, better molecule, first of all. However this larger added intellectual value brings larger risks on behalf of technological, market and registration. These tendencies are also catalysts of cooperation.

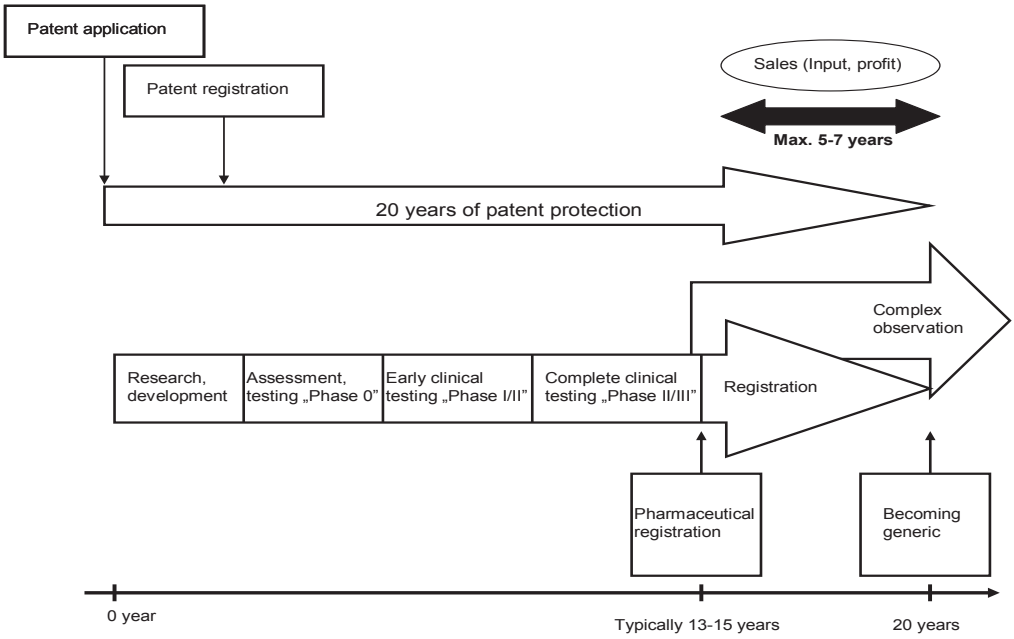
It is precisely these different, yet interrelated risks that make pharmaceutical biotechnology complex. To successfully manage complex processes and instability necessitates cooperation. Instabilities are cross-linked, they can even strengthen or weaken each other. An example of mutual strengthening is the technological uncertainty of producing a new molecule, and the registration and legalization which follow. Registration gives the same molecule an added economical value and can, if it is registered already, decrease market instability, since it can become a market leader, a so called "blockbuster"[2], with multi million dollar yearly turnover.

Thus instabilities constitute a kind of synergic system. Instabilities are difficult to predict individually, their interrelations are even more so.

[2] *A blockbuster drug is a drug generating more than $1 billion of revenue for its owner each year.*

Figure 1:

A typical time-schedule of a new biotech identity (based on (*DeBresson-Hu 1999*) composed by the author)



Necessity of cooperation can be explained from another point of view as well (figure 1). Validity period of a patent is 20 years from the date of application, which, in case of pharmaceuticals can be extended by at most 5 years (SPC[3]). According to Figure 1, the product generally appears on the market 13-15 years after the patent application. With the end of the patent period, one must also count with the appearance of generic and biosimilar products.[4] Thus there is, at most 10, but more often only 5 years to cover the entire costs of R&D and clinical costs and make some revenue. Thus everyone seeks to make the time needed for R&D as short as possible. One method could be some sort of open innovation, which supports cooperation and outsourcing instead of solving everything in-house. There are numerous factors which make a part of the R&D earlier fully integrated in the vertical control target of outsourcing. To shorten the needed time to find a molecule and make it a drug, the steeply growing costs of keeping all the needed expertise within the firm, the decreasing costs of reaching the needed expertise outside, together the transaction costs

[3] SPC means supplementary protection certificates. SPCs were introduced by the SPC Regulation to improve the protection afforded to innovations in the pharmaceutical sector. SPC is designed to compensate for the reduction in effective patent life caused by delays in the regulatory approval process and will give up to five years' additional protection beyond the life of the patent or 15 years from the date of the first marketing authorisation, whichever is less.

[4] A generic drug (generic drugs, short: generics) is a drug which is produced and distributed without patent protection. The generic drug may still have a patent on the formulation but not on the active ingredient.
Biosimilars or follow-on biologics are terms used to describe officially approved new versions of innovator biopharmaceutical products, following patent expiry.

arguments and the abundance of expertise outside are all for giving advantage to trust R&D tasks to outsiders who are already experts in the given field. This method definitely saves time and possibly costs as well and systematically open access to better solutions than those available in a "closed innovation" method.

Naturally, in this case, different interests collide. The interest of the originator company as they are called in the pharma industry is to hold on its monopole status as long as possible. This is exactly opposite to the interests of the generic companies, who would like to appear on the market as soon as possible. Consumers are located between the two parties, thus favouring an intermediate approach. They profit from the appearance of generic pharmaceuticals in two ways. Their appearance leads to a decrease in prices, while at the same time, the original companies have to develop new pharmaceuticals, which will be protected from the generic companies for a while. A too short patent period is not good for the consumers, as in this case it will not be profitable for originator companies to produce new pharmaceuticals, or the testing period will not be long, thorough enough, leading to potential hazards.

The structure of biotechnology clusters

Interest groups were formed between geographically proximate business and other organizations through comprehensive, shared projects. The associations can be formal, or informal. There can be distant or close bonds. In knowledge-based branches, research organizations such as universities, research institutions, and spin-off companies can also become part of these networks. Due to global competition, successful company models were born, relying on the spatial concentration, in other words, the local grouping (clustering), of advantages. The central concept of the interaction is that the creation of a powerful local branch becomes preferable (especially in technological sectors) in which (*Presidis 1999*):

- the output (added value) is increasing,
- the number of employees is rising,
- the chances for the survival of the enterprise are better, thus it can stand its ground against global competition,
- it improves the competitiveness of the region (salaries, work output, employment),
- the number of people in the given field exceeds the critical mass, thus providing economical strength.

The company sphere is trying to react upon environments with rapidly changing dynamics with developing radical innovations, while they are aware of the fact that they have to make high stakes decisions on a very unstable knowledge base. Usually, there is a complex, multidimensional, nonlinearly interacting instability around the radical innovation, the solution of which often requires cross-linked steps. In terms of management, it is important to emphasize that, unlike small innovations, the managing ability of radical innovations involves the navigating ability which is necessary when unpredictable events unexpectedly happen. As for innovations, we should apply the approach of evolutionary economy. We make models considering variations, selective media, niche, and active adaptations.

In our globalizing world, due to the more and more frequently formed „close interactions" (they are „close" because of the strength of interaction), the medium is often turbulent; it is characterised by the occurrence of an unsteady state in both small or large areas.

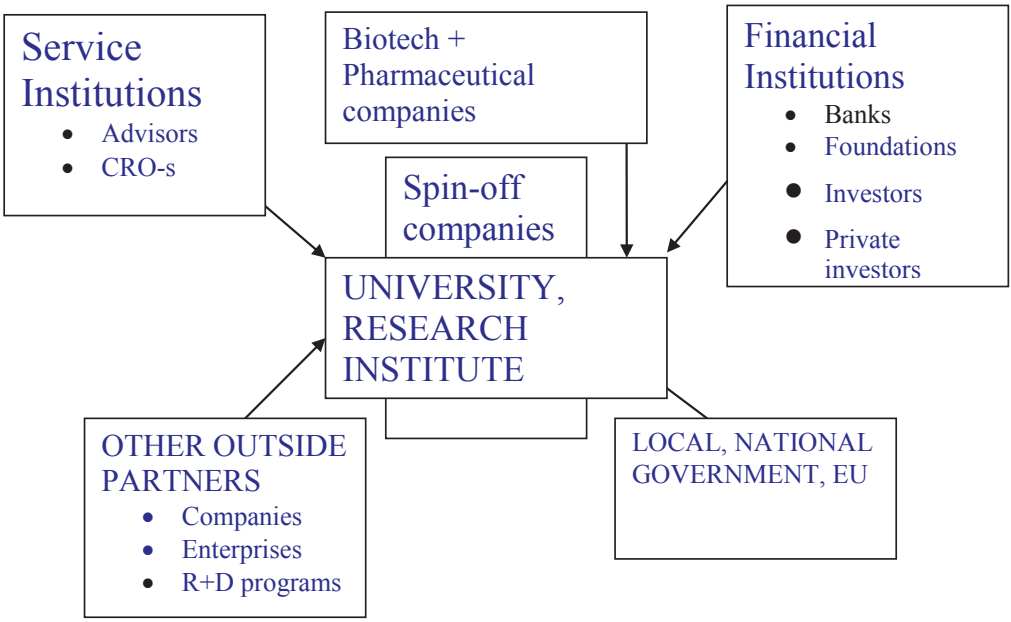
During this process the previously latent needs of consumers develop into needs which determine production technology/product in the system of interactions, which are realized in coevolution. Of course, trends also emerge. They, nevertheless, are generally shorter and more conditional than in earlier historical eras. (*Hronszky - Várkonyi 2006*)

The companies realized, that by relying on local background, or local business partners, they could survive in a very competitive global environment. Furthermore, they can not only just survive, they are capable of becoming more adaptable and of increasing their income as well (*Swann - Preveze 1996*). In general, the profitability of companies operating in clusters increases by 2-4 %, and the survival rate of small and mid size companies is much higher than for individually operating enterprises. (*Domonkos 2007*)

Basically, there are two possible methods for cooperation. One gives stability and the other innovation. The two types of cooperation require different institutional structures, since the cooperation is for a different purpose. In different branches of industry, associations, which in this case are clusters, form for different reasons. In biotechnology, they are formed primarily to aid innovation, whereas in the furniture industry they are formed to stabilize the current state.

Figure 2.:

The structure of a typical biotech cluster composed by the author[5]



As we can see in figure 2, the core of the biotechnological cluster is formed by research institutions and universities. Biotechnological enterprises from different areas are grouped around this core, since their most important input is knowledge, or new information. Spin-off companies are important members of the group. By using the knowledge generated

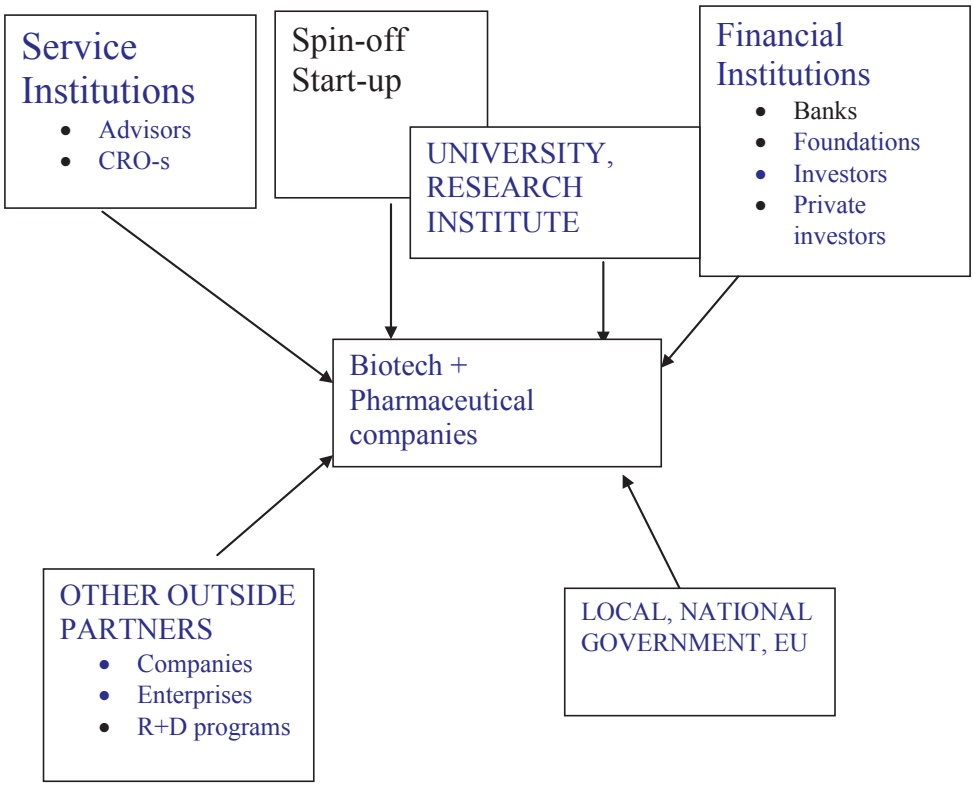
[5] *CRO means Contract Research Organization*

at universities, new spin-off companies are formed, and start-up companies are founded. Some of them generate new investments, as a result bridging the gap between academic and industrial sectors. Thus, the key to the dynamism of the cluster is the spin-off and innovation oriented start-up companies. However, the cluster is necessary for their successful operation, because, due to their small size and lack of funds, without their input knowledge from universities, industrial relations, and the funding from investors, they cannot complete the innovation. Cooperation between different sectors and support from service (trade) oriented companies, financial institutions, government authorities and foreign partners (other clusters) is necessary for the successful operation of a cluster.

If we look at the same group based on economic power and the flow of funds (Figure 3.), then the cluster is centered around its industrial partners, which are the pharmaceutical and biotech companies. They form the core of the cluster, meaning they lead the cluster, and since the product will enter the market under their names, they have market goals, ideas, and they sense market needs and possibilities. They bear a significant part of the financial and knowledge related resources necessary for operation as well. The academic sectors in the given industry are grouped around them, providing the knowledge, which is not present in the core of the cluster.

Figure 3.:

The structure of a typical biotech cluster group based on economic power and the flow of funds (created by the author)



The proper functioning of clusters requires that the operation of the different organizations be in tune with the structure of the group. It is important that new members become involved in the organization, and that existing organizations provide new members with space and functionality. This is also in their best interest. New solutions and organizations must be compatible with existing ones, but not the same. They must contribute something new.

There can be several different solutions: formal associations may form through mergers, purchases or joint companies. These do not threaten clusters, because in the USA for example, formal and informal associations can work side by side.

In practice, clusters grew out of different backgrounds, for different reasons. There are different methods for their development and support. A certain percentage of clusters, especially in developed countries arose spontaneously through self-organization. There is no formal relationship between companies competing with each other. So, the representatives of a locally strong, yet innovative industry form a voluntary cooperation, to share the costs and risks of research and development. This cooperation is much more difficult to formalize than artificially generated clusters. So in many cases it is difficult to determine which companies belong to a cluster, since this can change from project to project. However, cluster development policies, the improvement of an industrial branch and tenders aimed at cluster formation, all catalyze the process of cluster formation. In the case of these artificially produced clusters, it is important that they become self sufficient, meaning that the initial support should only function as an incentive to speed up the start-up process.

Operation of biotechnological clusters through (biotechnological) value chain

According to Porter, a *regional cluster* is some sort of geographic concentration, based on the innovative cooperation of competitive companies, supporting industries, financial institutions, service and cooperative infrastructure (background) institutions (education, research), and business associations (chambers, professional unions) (*Porter 1985, Porter 1998*). In my opinion, the problem with Porter's definition and other classic cluster-definitions is that they are static, whereas, the most important characteristics of clusters, is their dynamic nature. Thus it is best to include the following in the definition:

- The formation of a cluster is a turbulent process: the processes are unforeseeable, the absence of linearity excludes perspective.
- At the same time, the cluster is a sort of battlefield, since the frequent changes in vertical input-output and the relationships between horizontal organizations generate a need for change.

Clusters cause the change of innovation policies, generating policies suitable for cluster construction, thus functioning as catalyst in creating a more suitable environment for their own formation.

Accordingly, the preferred definition of clusters is: the dynamically changing vertical and horizontal cooperation of geographically proximate organizations, involving an enterprise support infrastructure, with shared developmental vision for business growth of the clusterized organizations, based on competition and cooperation in a specific market field.

Besides the value chain method, cluster functioning has been described by several other theories as well. European Union experts differentiate four schools when defining the idea of clusters (*Lengyel 2001*):

- Italian school: the school's central category is composed of industrial districts, which are formed due to the geographical concentration of small and medium-sized enterprises with similar activities. The concept can be traced back to Marshall, where externalities, trust, and social capital, all play an essential role.
- Californian school: emphasis is placed on networks of production relations formed due to vertical disintegration. The main purpose of network functioning is lowering the costs.
- Scandinavian school: in the concept of cluster, only locally applicable knowledge, especially non codified, hidden knowledge and the subsequently formed innovations play essential roles.
- Regional cluster: All the previously mentioned three schools described the cluster as a locally bound process which is rooted in the social systems of a particular region. The main emphasis was placed on locally-specific elements. Porter, however, did not examine regional economy and clusters, but the competitive benefits at the company level and their resources. In his case, clusters are based on the cooperation and flow of information between companies and institutes. Several models were worked out for clusters, a general feature of which is that the competing key companies of a particular field are in the centre, they form the „core" of the cluster with their networks, importers and branch institutes. Due to the vast global market, these companies are able to grow dynamically and expand their production rapidly. The key companies (core companies) are independent companies. Often there is no formal cooperation between them (e.g. between German car factories), but they firmly compete with each other. Key companies rely on their business partners, associated industries and supporting (non business) institutes (Lengyel 2003). A cluster is only effective if the background institutes are geographically concentrated around the „core". Porter's value chain concept appeared in the mid 1980's theoretical background. It is based on the recognition that the success of a company is primarily determined by the effectiveness in which it can mobilize its resources in the interest of increasing the value of its services, products and added value. The value chain model handles the enterprise based on the three following criteria (Friedman 2004):
- What interlinked activities result in marketing of the product
- How do these activities contribute to the added value of the end product
- How much of the company's resources do these activities require.

The value chain model breaks down the enterprise, based on its strategically important activities, so that we can better understand the process of how expenses are formed and discover the possible differences present. The value chain method has already been used to describe cluster functioning in general cases, not specifically in biotechnology and in the pharmaceutical industry. The value chain method, however, is often used in the pharmaceutical industry, but it defines the R+D phases and the sequence of tasks to complete instead of the motivation for cooperation.

The value chain model can be easily applied for biotech cluster functioning because:

- it is commonly used in the pharmaceutical industry
- it can be easily interpreted
- it can be easily completed, modified and made dynamic

Cooperating organizations must reach activities respective to the holistic[6] model of the innovation in all necessary areas, not one by one, but together. Thus organization within the cluster must produce some novelty at each appropriate step of the value chain. This is not difficult since each organization is capable of most efficiently undertaking the task best suited to its capacities and goals. Thus there is no need for organizations to take the often repetitive steps of learning a new skill, as new organizations will step in to fill the gaps (in well a functioning economy, in a well functioning cluster). As we can see, in the tables in the middle of the figure, the method for acquiring new information is divided in two: within the company and through the use of an outside source.

By applying the value chain model, we can show and explain how the organizations are built on each other. The value chain model is derived from the linear model of innovation, thus there is no feedback in the model. In practice we see strong feedback, as even the sales at the end of the chain have a strong influence on the basic research. For example, on market gaps, or the perspectives found by companies in charge of end marketing and sales feedback to basic research by determining the general directions of projects. In the model, basic research is an especially important linearly sequential process which does not take place in practice. Even though only projects that reach the market are included in the model, it is still not complete, as it does not allow for selection. However, the value chain model is good for describing the cooperation between the organizations, since different tasks can be completed by different organizations, as seen in the value chain in figures 4. and 5. A further weakness in the model is that, due to the lack of feedback, it regards the marketed product as final. Thus, it cannot change, since it is no longer in contact with the product development unit, thus assuming the prolonged balance of supply and demand, with only quantitative changes in demand. Regardless of these deficiencies, the value chain model is suitable for displaying cooperation between organizations, and it creates opportunities for further improvement and eliminating deficiencies.

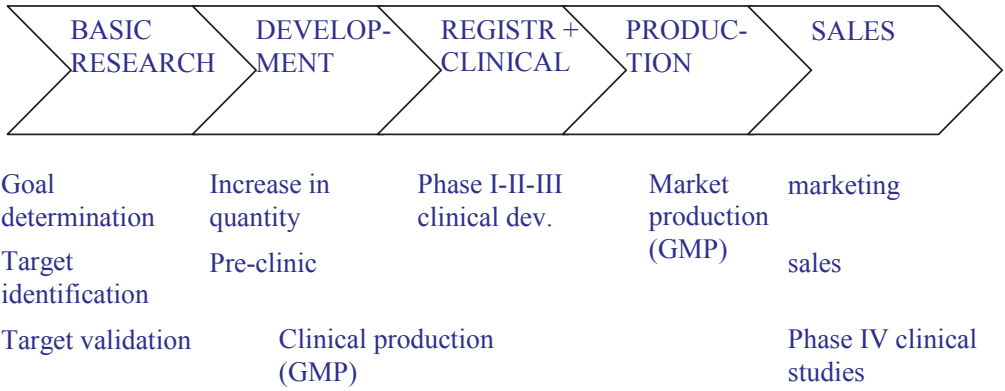
According to the value chain, the sequential technical and economic steps lead to new products. The value of projects, based on this value, is continuously increasing (according to greater added value). The end value can be calculated easily from the last step, as the product of market sales, price, and quantity. If we know the expenses incurred during previous steps, we can also easily calculate the profit from this value.

The value chain applies to the pharmaceutical industry relatively well, since a marketed pharmaceutical product cannot be changed without consequences. If there is a significant change in the product, there are consequences in registration, possibly clinical research, which require significant time and resources. In many cases changing the product is not profitable, even if it could be produced less expensively in better quality. Naturally there is feedback here as well, but in most cases the new innovation will only be used in the next generation of the product.

[6] *The Holistic model shows clearly that innovation can occur throughout a company's operations, triggered in some cases by new knowledge, but in other cases by an opportunity to fulfill a market need.*

Figure 4.:

The pharma value chain (the author)

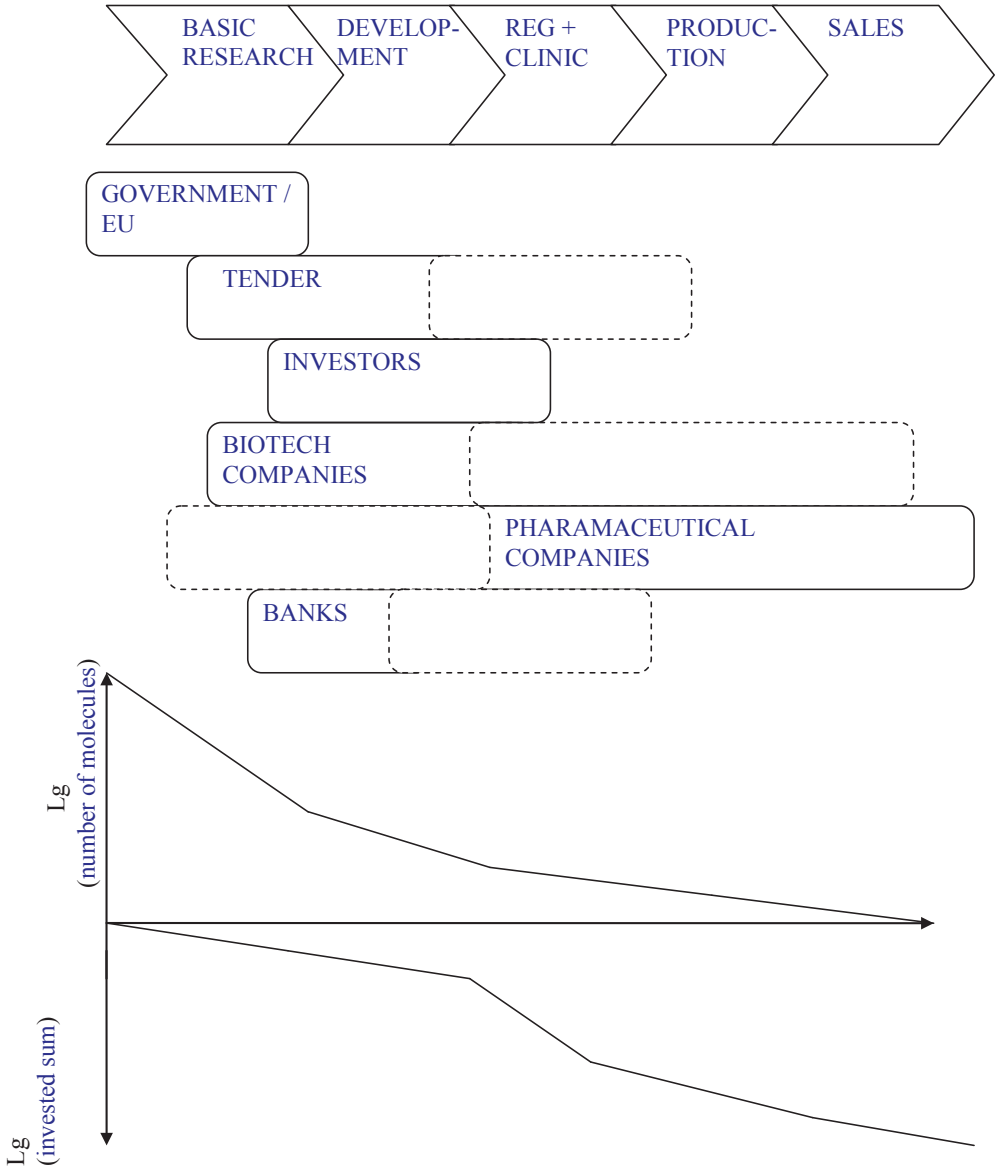


a. Defining specific goals, therapeutic areas, or molecules with specific effects, possibly the definition of specific molecules in basic research. Overview is necessary during project operation. Furthermore, research topics are verified and new phases are planned.
b. By using the basic research results obtained during the development phase, problems involving increasing quantity are undertaken. Some production processes start to appear in this phase, related to pre-clinical testing, as well as for Phase I, Phase II and Phase III tests. Clinical tests also take place during this phase.
c. Registration and accreditation take place, according to the test result of the previous phase.
d. Market production takes place during the production phase.
e. During the last step, in addition to sales, Phase IV, testing is completed, which is essentially product monitoring.

Costs and risks are divided automatically by cooperation and division of labor. Since, for pharmaceutical companies, it is most effective to find the most knowledgeable, most experienced "knowledge importers" in a given field, it will not be viable to develop the in-house knowledge base completely, thus reducing time and cost requirements. Successful projects and industrially applicable results are selected, forming the basis of cooperation. Thus projects cost less altogether, since fewer resources are needed for determining which research result will be viable at an industrial level. Since this way there is no need for producing the research result in-house, smaller companies, or academic institutions, cannot contribute significantly to project funds. Most often projects are sold after verification of "proof of concept," but up until then, the cooperation costs significantly less.

Figure 5:

Pharma value chain with organizations (the author)



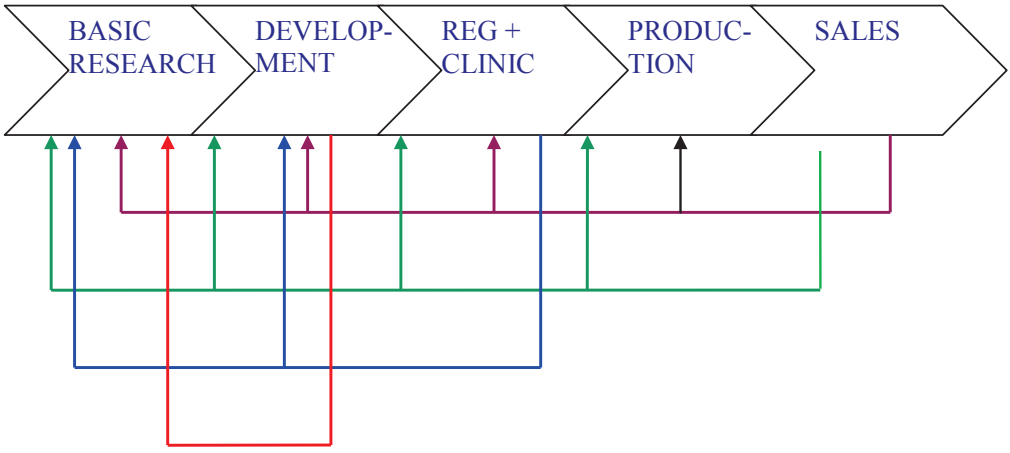
The value chain and (the absence of) a looped dynamism

As I have stated earlier, the value chain model was derived from the linear model of innovation. Thus there is no feedback in the model, which therefore does not reflect reality well. In practice, we see strong feedback, since even sales at the end of the value chain can have strong influence on basic research.

Taking all these deficiencies into account, figures 4. and 5. can be completed by the addition of the feedback, thus displaying the division of labor and the progression of projects accurately (figure 6.).

Figure 6.:

Pharma value chain with feedbacks (the author)



All the feedback displayed on the figure is based on personal experience.

By adding these modifications, it is possible to describe the operation of clusters using the value chain model. It contains the dynamism of clusters and the interaction of different organizations and activities.

Summary

As we have seen in biotechnology, just as in other rapidly evolving branches of industry, changes are very fast; the increase of knowledge is very steep. Since this industry is a very high-risk ("high risk – high benefit") industry, and since R+D phases may require several hundred million dollars, the participants seek to minimize and share the risks through cooperation.

There are several theories that describe the motivations for cooperation. I used the value chain model, which is popular in the pharmaceutical industry, to describe the operation of clusters. The problem with this model is that it is static. The feedback, so characteristic in biotechnology, is missing. I completed this value chain approach, based mostly on my practical experience.

References

Buzás Norbert – Lengyel Imre (2002): *Ipari parkok fejlődési lehetőségei: regionális gazdaságfejlesztés, innovációs folyamatok és klaszterek*, JATEPress, Szeged, 2002,

DeBresson, C. – Hu, X. (1999): *Indentifying Clusters Innovative Activity: A New Approach and a Toolbox. In Boosting Innovation.* The Cluster Approach. OECD,Paris, 1999, 27-59. o.

Domonkos Dávid (2007): *A radikális innovációk hatása a szervezetek közti együttműködések szükségességére a biotechnológiai iparban*. Műszaki Kémiai Napok, 2007, Veszprém

Friedman Y. (2004): *Building Biotechnology thinkBiotech*,. Boston, 2004, 119-144.

Hronszky Imre – Várkonyi László (2006) : *Radikális innovációk menedzselése* Harvard Business Manager 2006.10. szám, 74-95

Lengyel Imre (2001): *Iparági és regionális klaszterek: tipizálásuk, térbeliségük és fejlesztésük főbb kérdései.* Vezetéstudomány, 2001, 11. 19-43. o.

Lengyel Imre (2003): *Knowledge Transfer, Small and Medium-Sized Enterprises and Regional Development in Hungary*. JATEPress, Szeged, 2003,

Murray F. (2002): *Innovation as co-evolution of scientific and technological networks: exploring tissue engineering*, Research Policy 31 (2002) 1389–1403

Presidis A. (1999): *Biotechnology perspectives in Europe*, Drug Discovery Today, Volume 4, Issue 7, 301-303

Steiner M. (1998): *Clusters and Regional Specialisation*. Geography Technology and Networks, Pion Limited, London, 1998.

Swann P. – Preveze M. (1996): *A comparison of the dynamics of industrial clustering in computing and biotechnology*. Research Policy 25 1139-1157

Porter M. E. (1998): *Clusters and the New Economics of Competition*. Harvard Business Review, 6, 77-90. o.

Porter M. E. (2000): *Locations, Clusters, and Company Strategy*. In Clark G. L.- Feldman, M. P.-Gertler, M. S. (eds.): *The Oxford Handbook of Economic Geography*. Oxford University Press, 2000, Oxford, 253-274. o.