

The place of biotechnologies in France and in Europe

by

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The concept of a 'bioeconomy', in other words of an economy based on knowledge of living matter and of life technologies, is new in Europe.

Yet life sciences and their applications have formed an essential although often underestimated element of the scientific, industrial and agricultural power of Europe and more specifically of France, and also of the well-being of populations, meeting their food and health requirements and also their environmental concerns.

Another paradox resides in the perception of biotechnologies in France and in Europe, which appears increasingly 'out of step' with respect to the rest of the world. Biotechnologies are sometimes considered as technologies 'breaking with the past' and sometimes as a mere step in a scientific and technological continuum.

Jean-Yves Le Déaut studies the prospects offered by biotechnologies in the first application sectors, their diffusion, the economic stakes and the constraints surrounding their development, and the situation in Europe and in France.

On the basis of the mechanisms implemented in various countries, he identifies the levers for the development of biotechnologies requiring the mobilisation of high amounts of finance and the involvement of all the players, universities, research organisations, industrial groups and small and medium sized companies, which shall mutually strengthen one another.

As part of this report, Jean-Yves Le Déaut, analyses in particular the development of biotechnologies in the pharmaceutical sector, but he also addresses the issue of GMOs in agriculture as a follow-up to his report devoted in 1998 to the use of GMOs in agriculture and food.

Summary

The strategic dimension of life sciences and biotechnologies must be rapidly acknowledged in France which, unlike many States, has not become aware of the national stakes of a development of knowledge and support for innovation in this field. There are a variety of causes for this first delay, but they are mainly political as the State has favoured an excessively defensive approach. It has not managed to introduce the essential statistical instruments that would have allowed it better to adjust its choices, nor has it defined means of action adapted to a 'proliferative' sector. It is precisely by questioning oneself on the capacity of a country like France to 'rise to the biotechnologies challenge' that one can size up its economic dynamism.

Biotechnologies form a 'key technology'. France and Europe are lagging behind.

As it takes time to develop biotechnologies, the delay incurred by France can be overcome, provided however the necessary stimulus is given now.

Biotechnologies, the result of a continuum between research, technology and products, are bound to be used in a very wide variety of sectors, even if presently the application fields are mainly limited to health, agriculture and food. They have given rise to new research instruments, which have today

become routine, and to innovative production processes. While the use of biological matter forms their common point, they cover many techniques and methods and are based on a series of scientific disciplines, some of which are 'applied' and others more fundamental. The same technology can have a multisectoral application: for instance, vegetal biotechnologies could be applied not only in the agricultural and food field, but also in the medical field and in other industrial fields, for the production of textiles, fuels or biodegradable products.

The scientific and technological breakthroughs of recent years allow many benefits to be anticipated, which the report endeavours to identify: creation of substances of medical interest, development of new therapies, detection and diagnosis, improvement of knowledge, diminution of pollution caused by pesticides, increase in yields to meet food needs, improvement in the nutritional quality of products, reduction in the consumption of raw materials and energy, treatment of wastes, and depollution...

Biotechnologies have become widely disseminated. In the pharmaceutical sector, for example, their use in the research and development processes of medicines has become generalised. As for the production of new products, the trend is clearly in their favour. Biopharmaceutical products represent 10% of the sales of the world pharmaceutical

market but if the number of new molecules is taken into account, this share would be comprised between 20 and 30%; in the United States, biotechnology products approved by the FDA (*Food and Drug Administration*) already formed a majority in 2004.

But it is above all in the field of knowledge that biotechnologies have really ‘exploded’, as evidenced by the growth in the number of publications and the number of patents filed.

The positions of Europe and of France have weakened, particularly with respect to the United States, and, in the biotechnologies field, the ‘European paradox’ is quite visible. Europe’s scientific excellence in the field of life sciences and biotechnologies has not materialised as regards innovations. Despite progress made in Europe, the situation of France is worrisome. In the field of pharmaceutical innovation, American domination is overwhelming, as also in the field of agricultural innovation.

Biotechnologies are emerging in a constraining context

The economic stakes of biotechnologies cannot be underestimated, particularly for France.

In a context marked by a process of industrial concentration and sectorisation, **innovation has become an essential factor of survival.** Whereas France still has some assets, it is lagging behind in a worrisome manner in the field of biotechnologies. **The seeds and pharmaceutical sectors are particularly threatened.** For want of a sufficiently strong stimulus promoting innovation in this field in France, biotechnologies will strengthen the domination of a few companies in world markets, whereas they can help resist such domination. The pharmaceutical industry is moreover likely to experience a full-blown crisis. Whereas a growing number of synthetic drugs are falling into the public domain, fewer and fewer new products are reaching the market; successive concentrations and delocalisations are leading to the pure and simple abandonment or to the disappearance, in some countries, of research and development activities. Consequently, if new companies do not develop and if they do not manage to fund their research and development work, the trend cannot reverse.

Several studies have underscored the economic potential of biotechnologies. However, these studies have apparently not convinced all European governments, despite the commercial success of some products, particularly biopharmaceuticals, and the rapid development of American biotechnology companies some of which can now

compete with the big pharmas, and also despite the successes of several European biotechnology companies which have managed to develop in a nevertheless difficult context.

In Europe, the assessment of the ‘economic risk’ related to biotechnologies has formed a brake on their development. Large European industrial groups remain most prudent when it comes to taking risks regarding innovation, especially biotechnological innovation. In the pharmaceutical field, for example, many biotechnology companies came into being through the spin-off policies of large groups, which were in fact abandonment policies applied by these groups. The funding of biotechnologies through other channels, especially risk capital, has proved insufficient. This is due to the dispersion of European stock markets, unable to compete with the volumes drained by the NASDAQ. Another cause is the specific characteristics of biotechnologies based on particularly long and costly development processes.

The regulatory framework of biotechnologies imposes severe constraints on research and development activities. The report takes a first inventory of the various rules defined at the European and national levels in this field. The European Union can be credited with having tried to define a strategy taking these regulations into account and promoting biotechnologies. But the positions adopted by the States, even within Europe, remain divergent. The conditions of use of embryonic stem cells, of the patentability of biotechnological inventions, and of the creation and management of biological resources centres are the subject of approaches that are still highly different. The same applies to the regulations on the production, marketing and dissemination of some biotechnology products, a field where two ‘models’—the American and the European—are in direct opposition. As regards the assessment of the risks and benefits—a major issue for the development of biotechnologies—the situation also remains marked by a very strong contrast. While, for medical biotechnologies, harmonisation is more advanced than in the field of agricultural biotechnologies, new debates are appearing on the horizon, such as those on **the assessment of biogenerics**, and the application conditions of common principles may also vary from one State to another, which leads to poor European compromises.

The greater or lesser flexibility of these rules is not a matter of indifference to either investors or producers. A new competition, based on regulations, now takes place between States. And the costs of procedures, and of their complexity which requires support from specialised services,

form barriers to small companies or commercialisation structures trying to enter the market. The complexity of the rules promotes concentration.

Agricultural GMOs illustrate the crisis of biotechnologies in France and in Europe.

The debate has got bogged down and has given way to a full-blown ideological battle. The report paints a sort of comparative picture of the potential benefits and possible risks of GMOs. The potential benefits allow breakthroughs to be envisaged in the fields of environmental protection, improvement of the health and nutritional quality of food, and also control of production costs in the countries of the South. This cannot but encourage us to promote research and support innovation. Nor can the possible risks convince us to turn away from this new technology, provided it is regulated.

GMO crops have become widespread. They today cover more than 70 million hectares and 'MONSANTO technologies' are very largely dominant. In this context, areas under GMO cultivation in Europe are almost non-existent. The risks of economic domination by countries owing the patents are real. However, the most effective means of opposing this economic appropriation is not to block the use of this new technique but, on the contrary, to use it to the best of our interests, by pursuing research on genetically modified plants, particularly open-field experiments. Failing that, Europe will lose even its expertise capability.

At the same time, the decision-making process has seized up. The scientific assessments are not responsible for this. The main difficulty today resides in the fact that it is impossible to reach a political consensus between States whose economic interests diverge.

Identification of the main levers for the development of biotechnologies in France and in Europe leads to focusing on funding and commercialisation.

The crucial issue of funding

The most pronounced delay with respect to the United States concerns the funding of biotechnologies and the gap has tended to grow wider. But that does not mean the delay cannot be overcome.

The limits fixed in France and in Europe on public action, when the latter extricates itself from the strict field of regulations, probably forms a major brake on the development of biotechnologies.

Yet State intervention is necessary. The first fields of application of biotechnologies are those where the State is traditionally involved and a comparison with the United States on this point cannot justify abstention of the State—quite the contrary. The research effort made in biotechnologies is based moreover on an interweaving of the public and private spheres; **the important matter is that sufficient resources should be globally set aside to reach the expected progress. Visibility of a public policy helps attract and retain private capitals.** The status of public aid to private research remains ambiguous. In Europe, the ceiling rules, aimed above all at regulating competition in the European Union, are likely to weaken companies located in its territory and reduce its attractiveness. Lastly, in the biotechnologies field, the European States have initiated a very wide variety of policies taking account of their specific national characteristics.

The private funding of biotechnologies is coming up against certain limits

First, major industrial groups are not necessarily encouraged to increase their research effort in this field. In the agrifood sector, only risks are taken into account. In the pharmacy field, the present highly competitive context drives companies to reduce their costs and make their investments pay as soon as possible. The increase in R&D costs and the fall in productivity in the sector, with the arrival of generics, the drying up of drug pipelines and the pressure exercised on prices, are promoting a splitting up of production, commercialisation, and research and development activities. The trend is for the delocalisation of research centres towards the United States and of production and clinical test centres towards Asia. Referring to the evolution of relations between biotechnology companies and major groups, the prospects remain uncertain. New strategies are apparently being set in place in the research field but, while some feel that biotechnology companies will be doing more and more applied research commissioned by major companies, others consider that no pharmaceutical company can survive by exploiting only the results of its internal research.

Second, the private funding of biotechnology companies remains a problem. The American model has evolved, with the existence now of large integrated biotechnology companies and the lagging behind of funding mechanisms based on risk capital and the stock market. Creations appear to be stabilising and many companies have disappeared. For its part, Europe is suffering in particular from the shortcomings of its stock market which remains dispersed.

Public aids are therefore necessary but form only one element of the sectoral policies that can exist in the application fields of biotechnologies. Global innovation policies are essential but do the general mechanisms set in place suffice to take account of the characteristics of biotechnologies? Consequently, are the eligibility criteria for aids adapted and are the file examination procedures suitable?

The public sector must promote the creation of companies and fund the proof of the concept which makes a molecule a drug candidate. The funding of the start up of companies and support for the development of biotechnology products must find rapid solutions as a matter of priority.

However the place of public research remains decisive. Biotechnologies indeed depend on academic research and, through public research, States define strategic orientations. The comparison with the United States in the field of life sciences is enlightening in this respect and the science and technology indicators established by the European Commission are highly revealing of the weakness of the strategic policies implemented in European countries. The difficulties encountered in Europe to develop biotechnologies are therefore the result of this, at least partly. The European Union has on this point attempted to create a dynamic process without really managing to achieve this goal and the nationally funded research effort has been insufficient.

Lastly, Europe is not effectively playing its role as a catalyser, does not coordinate enough, and does not sufficiently support the application of biotechnologies in the fields of the environment, biomaterials or safety.

The problem of relations between the public and private sectors

The rapid development of biotechnologies in France and in Europe depends to a large extent on the capacity to commercialise the results of public research.

While the grouping of research, industrial, and financial activities creates propitious 'synergies' and ensures better 'visibility' at international level, it remains difficult to draw final conclusions from the various experimentations in this field.

By promoting the creation of companies to commercialise the results of public research, the Act of 1999 on innovation has formed a major step forward. However the difficulties encountered by biotechnology companies show that this legislation has been insufficient and must be prolonged by analysis on the desirable maturity of a project allowing the creation of a company to be envisaged.

In any case, the resources devoted to commercialisation have been insufficient and it is necessary to identify potential partners in fields where the French 'industrial fabric' is not very diversified, which militates in favour of the definition of more open partnership strategies, particularly with respect to France's European partners.

The conditions for the commercialisation of patents do not appear to be optimal either, and various States have started to analyse this matter so as to promote cooperation.

The various instruments and mechanisms set in place by the Act of 1999 have been widely used to commercialise research undertaken in the field of life sciences but a long-term strategy engaging all the players has been lacking.

It is also essential to enhance the researcher's job. The current fate of doctorands and post-doctorands is not worthy of a developed country. While geographical and professional mobility must be promoted, it must be balanced and controlled and not 'undergone' by researchers. However, in the field of life sciences, a full-blown scientific employment crisis is being witnessed, which must be resolved.

Fifteen major recommendations are defined, comprising 63 proposals.

- 1- **Combat immobilism and fight against obscurantism.**
 - 2- **Define and display at national level a scientific and industrial strategy promoting life sciences and biotechnologies.**
 - 3- **Enhance the scientific, economic and socio-political assets of France.**
 - 4- **Finally care about the real impact of the regulations decreed at national level.**
 - 5- **Promote training in biotechnologies by upgrading life science jobs and through increased pluridisciplinarity.**
 - 6- **Increase public research means in the field of life sciences.**
 - 7- **Care about the management of intellectual property rights resulting from work funded by public funds.**
 - 8- **Propose adapted training sessions to researchers wishing to acquire entrepreneurial skills.**
 - 9- **Give more support to the creation and development of our biotechnology companies.**
 - 10- **Create an environment favourable to maintenance in the national territory and to the establishment of the research and production centres of industrial groups.**
 - 11- **Give a new impulse to clinical tests in France.**
 - 12- **Act in the European framework to consolidate and strengthen the French position.**
 - 13- **Start major programmes in the field of biotechnologies.**
 - 14- **Better organise the system of assessment of benefits and risks in the vegetal biology field.**
 - 15- **Ensure, at parliamentary level, follow-up to the governmental policy in the life sciences and biotechnologies sector.**
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