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Country Focus

Biotechnology in France

24.02.2006
The biotech sector in France faces something of a paradox. On the one hand, the French research landscape has been in a state of upheaval for some years. New advancement programs and funding structures have been established and new clusters have formed. On the other hand, there is still a striking shortage of money and the medium−sized sector is barely finding the money to advance the development of their active substances. On a legal level, only research on human embryonic stem cells has so far come under authoritative direction. A genetic engineering law is still pending and is likely to be passed in 2006 whereas the ?Pacte pour la Recherche? (research pact) came into effect in april this year.

Introduction

23.06.2006
The most recent key figures presented in the current industry report by France Biotech, the French biotechnology business association, show a difficult situation in France: in 2005, investment decreased fifty percent in comparison with the previous year, despite a better−stocked company pipeline. Now hopes are resting on the three Biotech enterprises which dared the leap on to the stock exchange floor in 2005: Ipsen, BioAlliance and ExonHit. These moves come some time after the previous stock exchange entry by NicOx in 1999. As regards the areas of which French biotech companies or research institutes are active they are concentrated particularly on the fields of health and nutrition. Supported by millions of euros in funding programs, it?s in these areas that the industry expects its first products.

On the political agenda, 2006 should still provide some surprises. For stem cell research, obligatory guidelines for researchers working with human embryonic stem cells were published February 2006, while a decision for green genetic engineering is still pending. The Ministry of Research presented a first draft in February 2006, but the question of a liability fund for farmers who cultivate genetically changed plants has been a subject of much debate. Likewise debated was the research pact, intended to strengthen French research in the context of international competition, but in april it came into effect. First forerunners for the restructuring and reorientation were the creation of a project−based funding structure**,** the establishment of centers of excellence and the fortification of industrial research in 2005.

Economic situation

23.06.2006
At the end of 2005, the Biotech organization France Biotech published the data from its annual report. The results are hardly euphoric, being largely based on a bad financial situation. The 300 existing French Biotech companies only managed to acquire 50 million euro starting capital in 2005, as opposed to 70 million in 2004. The breakdown of secondary round financing is also surprising: While in the previous year 159 million euro was collected, only 27 million euro was pulled together in 2005. With this, the pipeline of the companies came to a standstill: In all phases, the number of products sank (see table 1). France Biotech sees the reasons for this in a fear of the existing investors to continue to support innovative enterprises. The tax reforms from the French government was received positively: Since 2004 there is the Young Innovation Status with tax and social security contribution relief for companies which are younger than eight years old who invest a certain portion of their budget in research and development. 74 per cent of the Biotech enterprises were given this status, which resulted in an increase of the employee numbers in 2005. The success of this program has also inspired other European countries: In a shared initiative, Biotech trade associations from Norway, Sweden, Finland and Estonia made a demand for similar tax benefits for Biotech enterprises.

As regards the most active areas of the French Biotech industry, the companies are particularly emphasized on health, followed by cosmetics and nutrition, but the emphasis remains on research. Many market watchers also criticize this. In their view, it will be difficult to create a genuine company culture from this scientifically−oriented field. What is more, there is a lack of sufficient risk capital. According to OSEO, the organization funded by the Finance, Economics and Research Ministries, and which supports small and medium−sized enterprises, there are too few financial sources that are investing in biotech companies in France. In 2004, in an analysis of the financial situation, they counted five national funds and seven regional funds, from which however only one − Bioam ? is focused exclusive on biotechnology. Bioam, founded in 2000 and set up to operate for ten years with public funds of 51 million euro, has so far invested in ten biotech companies. In 2004, Pharmavent was established as a VC fund and was set up with, amongst other contributors, 75 million euro assistance from Sanofi Aventis. In 2005, the Fonds de Technologique (FFT), with a budget of 150 million euro, was added to the reserves of the OSEO, from which 50 million euro came from the European Investment bank.

At the beginning of 2006, the biomedical ?incubator? Inserm−Transfert presented its own risk capital fund for the first time, at a value of 4.5 million euro, which will be used in order to support promising scientists with funds of up to 300.000 euro, long before the establishment of a company. "Inserm Transfert initiative" is supported by CDC Entreprises, Ventech and Sofinnova Partners.

Among the most important Biotech companies in France are: Cerep, Flamel technologies, Genfit, Biogemma, ExonHit, IDM, Greentech, Proteus, Idenix, Innate Pharmaand Transgène.

Table 1: Key datas of the french biotech sector

	2004	2005
number of companies	300	300
sum of investions in million euros	268	165
of which Venture Capital	242	93
at the stock exchange	26	72
product pipeline	69	86
Products in phase I	30	41
Products in phase II	32	38
Products in phase III	7	7

Source: France Biotech (Date: 12/2005)

Table 1: Biggest financing rounds 2004 in pharma and biotech

company	sum of investitions in million euros
Novexel	40
Neuro 3D	31,5
NicOx	26
CareX	25
Faust Pharmaceuticals	16
Innate Pharma	15
Novagali Pharma	14,2
IDM	13,2
Clinigenetics	13

TxCell	10,5
Novagli	9,2
ExonHit	8,3
Mutabilis	8
Bionexis	6,5
Opi	6,4
Intragen	5,6

Source: France Biotech (Date: 12/2005); OSEO (Date: 2005)

Table 3: Biggest financing rounds 2005 in pharma und biotech

company	sum of investion in million euros
Ipsen	323 (IPO)
Transgène	34,9
BioAlliance Pharma	6,3 (4. Finanzierungsrunde)+30 (IPO)
Cerenis Therapeutics	25
Fovea Pharmaceuticals	20,5
ExonHit	7,3 (davon 3,8 durch IPO)
Nautilus	7,25
BMD	5
DAS	5
Endotis Pharma	4
Cytheris	3,5

Source: France Biotech (Date: 12/2005)

Research landscape and funding strategy

23.06.2006
As regards the field of biotechnology, the French scientific research landscape is mainly concentrated on the areas of health (cancer, neurology, virology) and nutrition (Functional Food) and to some extent agriculture. Public research institutes such as the Centre Nationale de la Recherche Scientifique (CNRS), Institut nationale de la santé et de la recherche nationale (INSERM), the Institut Pasteur or the Institut nationale de la recherche agronomique (INRA) dominate the research landscape, and most biotech enterprises have developed from these institutes. An example of this is ?Pasteur biotope?, a incubator from the Institut Pasteur, which has been promoting the founding of biotech companies and supplying financial support since 2000. A similar strategy is pursued by INSERM with the *Incubator* Inserm−Transfert. Marine biotechnology is conducted under the supervision of the Institut francais de Recherche pour l'exploitation de la mer (IFREMER), but makes up only a comparatively small portion of French biotech research. Above all, Paris, Lyon and South France are the most active areas.

Research funding in flux: Emphasis on cancer

The research funding for the bio and life sciences has been in change for some years. Thus, for example, in 2003 a sizeable cancer research program was established with the aim of converting scientific results into clinical products. Research establishments and hospitals from seven regions were brought together under the

framework of this so−called ?Cancéropôles?. On a national level, the program was coordinated with the launch of the newly−founded Institut Nationale du Cancer (INCa), also responsible for a range of national and international research projects and public campaigns regarding cancer−related illnesses and preventive medical examinations. The budget of the INCa amounted to 70.2 million euro in 2005, which will rise to an annual figure of approximately 100 million euro on a long−term basis. The funds come from both the Ministry of Research and the Ministry of Health.

Table 1: Funding ofCancéropôles through INCa

Year	Budget of INCa for Cancéropôles in million euros
2003	16,5
2004	17,68
2005	28

Source: INCa (from Date: 2/2006)

In addition to cancer research, the funding is also targeting the fields of neurology and virology. In 2004, a program to promote the fight against rare diseases was announced.

Reorientation of the funding politics: More competition

2004 saw a further innovation in French research funding with the establishment of the Agence Nationale de la Recherche (ANR), which plays a similar role to the project management organizations (Projektträger) in Germany and will coordinate the promotion of projects from the French Ministry of Research. Behind the founding of this agency is a reorientation of the research funding strategy in France. Before, research groups in public bodies could expect to receive a certain amount of funds each year by means of near−automatic procedures. With the establishment of the ANR, this system has now been supplemented by a competition−like application procedure, whereby the individual projects − as in Germany − must apply for funds and a jury decides on the allocation. The budget of the ANR was 350 million euro in 2005 (for 35 selected projects), 650 million euro has been put aside for 2006, set to rise to 1.5 billion euro by 2010 (see table 2). Nevertheless, in comparison with the entire budget of the Ministry of Research, which stands at approximately 20 billion euro in 2006, the portion granted to the ANR is still relatively small. As before, the largest portion of the research funds is targeted at the financing of institutes and research establishments. In all, the research funds for the life sciences amounts to approximately 1.8 billion euro.

Table 2: Financial endowment of ANR

Year	Budget of ANR in million euros
2005	350
2006	650
2007	910
2010	1.500

Source: French ministry, Financial Plan 2006 (date: 2/2006)

Besides energy research, ANR funding is clearly oriented towards the bio and life sciences: 16 out of 24 advancement programs were set up in this area. Two of these have been created for the benefit of biotechnologists in general (RIB and EMPB). Furthermore, alongside the European−level Era−Net programs (Eurotransbio, Pathogenomics, Plant Genomics) there is an emphasis towards GMO−research, nutrition, neurociences, nano−technology, rare diseases, biophysics and biochemistry, and microbiology, as well as

system biology. In principle, the ANR has set itself the goal of supporting both basic research and application−orientated projects in public/private partnership. Projects that work within the framework of the ?Pôle de compétitivité?, receive additional financial support. Alongside the topic−specific funding programs, there are also general initiatives for the promotion of young scientists and the promotion of foreign guest researchers in France.

Industrial funding politics

Since 2005, the French government has also been looking to strengthen the promotion of industrial research. With this in mind, the Agence de l'Innovation Industrielle (AII) was created, which, together with existing programs and mechanisms (see chart), should push forward innovation in the private economy. It is aided by a budget of one billion euro. Alongside, the organization OSEO ensures for the support of small and medium−sized enterprises (SMEs). This is financed equally by the Economics, Research and Finance ministries, and is intended to make financial aid available for SMEs. In 2004, 21 million euro was allotted to pharma biotech companies.

Chart 1: French Innovation policy

Source: Agence de l'Innovation Industrielle (2/2006)

New laws projected: Pacte pour la Recherche

The establishment of the ANR and the AII are the forerunners of a new "Pacte pour la search" − a legal project, which, together with changes in the law, is intent on broad reorganization. To this end, in 2006 and 2007, approximately 4 per cent of additional financial funds will be put aside each year. Leading up to 2010, the budget is set to increase to 24 billion euro. In 2004 it amounted to 18.8 billion euro. Alongside the further development of the ANR and the AII, the establishment of an Agence d?évaluation de la Recherche is planned, which is to take over the evaluation of public funding measures. Moreover, it is intended to promote new forms of co−operation between public research establishments, with the ultimate aim of creating internationally visible large research centers (pôles de recherche et d'enseignement superrieur − PRES). Besides this, the founding of new companies by scientists is to be eased, requiring the dismantling of existing bureaucracy and the targeted promotion of young scientists. Apart from this the government is implementing the possibility of giving financial support to the building of a dozen thematic clusters (résaux thématiques de recherche avancées ? RTRA). (konntest du noch nicht wissen ? hab ich grad noch einfügt!)

With the aim of a strategic adjustment of the politics of innovation, a consulting committee made up of high−ranking scientists (Haut Conceil de la science et technologie) has been created, which will give direct advise to the President of the Republic. The bill has come into effect in april although many scientists criticize the draft, as it does not plan an actual increase in research expenditure, if inflation is taken into account. What is more, they see a threat to their jobs in the progressive project financing and an increase in limited positions.

Centers of Excellence Competition ?Pôles de compétitivité?

23.06.2006
In 2004, in a development much like the BioRegions competition in Germany, the French government initiated the Centers of Excellence competition ?Pôles de compétitivité?. In February 2005, research establishments and companies were asked to integrate themselves into *thematic* clusters and to submit their suggestions for a ?pôle de compétitivité?. Unlike Germany, the Centers of Excellence included all fields of research and was not limited exclusively to biotechnology. Around 30 applications were expected but a total

of 105 applications were ultimately received, with 26 biotechnologically related clusters. From these suggestions, the Interior Ministry Committee for Land Planning and Development (CIADT − comité interministériel pour l'aménagement et le développement du territoire) eventually selected 67 which, since July 2005, can carry the title of ?pôle de compétitivité?. The geographical distribution is as follows:

Research projects that form under the umbrella of such Centers of Excellence can count on an additional financial support. The Agence Nationale de la Rechereche (ANR), for example, has put aside a total of 205 million euro − 40 per cent of their budget − for such purposes. Additionally, every ministry will be assigning at least 25 to 30 % of its funding budget to companies or mechanisms taking part in Center of Excellence projects. Moreover, tax exemptions and as well as a minimization of social security contributions have been granted to the participating companies.

The focus of the Biotech Centers of Excellence: Nutrition and Health

Of the 67 selected projects, the CIADT have selected six as particularly worthy of support as they have a global visibility. Of these six, two are biotechnologically relevant: Lyonbiopole (virology − Rhône Alpes region) and MédiTech Santé (infection biology, cancer − Ile de France region). Nine other Centers of Excellence were classified as ?projects with world−wide appeal?, with three being biotechnologically relevant: Innovation thérapeutique (Noninvasive surgery, molecular biology − Alsace BioValley region), Europol'Agro (use of agricultural products for non−agricultural processes − Champagne Ardenne, Picardie regions) and Végétal spécialisé (Functional Food − Pays de la Loire). Of the remaining projects, there are approximately 15 further Centers of Excellence with biotechnological backgrounds. The majority is occupied with the connection between nutrition and health for a wide variety of Functional Foods−approaches.

High Tech Founder Competition

23.06.2006
In 1999 the Ministry of Research held the ?Concours national d'aide à la création d'entreprises de technologies innovantes? competition. Within the framework of this program, so far 700 enterprises have received help in starting up, of which 87 per cent are still in business. In 2005, 178 new enterprises were supported. The financial assistance is given as start−up financing and can reach up to 450,000 euro, with the annual budget of the competition designated at 30 million euro. Biotechnology represents only one of the subject areas which can apply for this support, representing 24 % of the selected enterprises in 2005, which makes it the largest individual field, after computer science (see table 1). Just over half of the founded companies were begun by scientists working in public research establishments (table 2).

Table 1: Research areas of the competition winners 2005

Research area	percentage of competition winners
Informatics	27 %
Biotechnology and Pharma	24 %
Elektronics und Telecommunication	19 %
Chemistry und Materials	14,5 %
System Engineering	9 %
Mechanics and Metal Processing	6,5 %

Source: Palmarès 2005, 7. High Tech Founder Competition (Ministry of Research)

Table 2: Research institutes of the competition winners 2005

Research inistute	Number of winning projects
Universitiy	33
CNRS	21
other public research institutes	9
CEA	7
INRA	3
Institut Curie	3
Institut Pasteur	1
CNES	1

Source: Palmarès 2005, 7. High Tech Founder Competition (Ministry of Research)

Legal Basis

23.06.2006
Not only the politics of funding but also the legal basis regarding biotechnological research has changed in the past few years. In 2003, in keeping with this trend, the French government initiated a new law for donations, which facilitates the promotion of scientific projects by private backers and reduces bureaucratic obstacles. Among other developments, a new kind of science−promoting foundation was set up (Fondation de Recherche), which allows up to 60 per cent of donated funds to be written off against tax. Furthermore, a budget of 150 million euro has been made available (in the context of the Fonds des priorités de recherche) in order to promote the establishment of such foundations: For every million euros privately donated, the state will add another million euros. In this way, since the new budget became applicable, a total of ten foundations have been set up, five of which are dedicated to the field of health. A further three foundations support cancer research, and are still in the establishment phase. The Ministry rates this small wave of new foundations as a success, there being only four scientifically oriented foundations before the initiative, and when compared with Germany, the USA or England, the previous state of affairs in France was poor.

New genetic engineering law being debated

Furthermore, there is a new genetic engineering law beeing debates which intends to implement the European guidelines 98/81/CE and 2001/18/CE regarding the use of genetically modified organisms (GMOs). The Secretary of Research Francois Goulard put forward an initial draft of the new law to the government cabinet in February. For the first time, the draft would see the oversight of GMO use by a competent authority and the construction of a national register for the production of genetically altered plants forwards (see www.ogm.gouv.fr). The government sees this a first step towards legally sound regulation. Under the new laws, it is intended to couple the authorization of the use of GMOs to a previous public discussion that has taken place on the website, in order be seen to be as transparent as possible over the increasing use of GMOs.

Liability fund concept disputed

In the draft it is also planned to introduce new measures for the labeling, market−implementation and use of GMOs. Apart from classifying GMO products according to European standards − starting from a GMO proportion of 0,9 % − the licensing of GMO products will also be limited to a maximum of ten years, and accompanying monitoring has also been suggested. On top of this, a liability fund has been set up to operate for the first five years. The bill states that farmers who cultivate genetically modified plants must pay a maximum of 100 euros per hectare as tax into the funds. Not unexpectedly, ‚farmers? representatives are fiercely disputing this point.

Advice on evaluating biotech safety

Aside from these measures, the bill also plans the creation of a Biotech Council (Conseil de biotechnologies). This will bring together the current advisory committees ?Commission du génie génétiques? (CGG), the ?Commission d?étude de la dissémination des produits issus du génie biomoléculaire (CGB) and the ?Comité de biovigilance? under one roof as a single entity. Alongside from the evaluating the safety−aspects of GMO−use on health and the environment, the advisory body also has the task of estimating the economic and social consequences of each employment of a GMO product.

To date, a deeply felt and passionate debate has been defining the scenery in France, which has held back most farmers from cultivating GM crops. As far back as 1997, the farmers? trade union Conféderation Paysanne (CP) began their fight against the first planting and harvesting of GM oilseed rape on land owned by the Monsanto company. What?s more, France belonged to those European countries that took part in the GMO moratorium, which lasted until 2004, and import prohibitions still exist against certain GVO products. In the autumn of 2005, seven court judgments helped to turn public opinion against the self−named ?field−liberators?. However, the judgments were lenient: The ?field−liberators? were awarded the right to protect the environment from likely uncontrolled cross−pollination.

Meanwhile, seed manufacturers and scientists are striving for an implementation of the European Union guidelines. In the summer of 2005, and in a first of its kind, seed manufacturers voluntarily published figures relating to the exact number of hectares of commercially certified GM corn they were cultivating, which should force the creation of a legal basis. Like Germany, at the beginning of 2006 the French also received a reminder from Brussels that the EU guidelines have yet to be adopted into French law. The French farmer's association, FNSEA, will therefore welcome the current bill. Until now the law was adopted by the Senat and debated in a first plenary session at the parliament where it has now beeing relegated to a special committee for further discussions.

Stem cell research on condition

In 2004 the French government adopted a law relating to bio ethics that would have forbidden working with human embryonic stem cells (heS cells). Nevertheless, some researchers were permitted to work with stem cells if they submitted to specific conditions. A total of 40 authorizations were given in 2004 and 2005. In February 2006 the government adopted obligatory guidelines, which regulates research using hES cells. The basic terms are as follows: ?*Research on embryos and embryonic stem cells may be authorised if such research is likely to facilitate major progress in treatment and could not be carried out by an alternative approach of comparable efficacy, in the current state of scientific knowledge."*

Further regulations relate to the origins of the cells. For instance, French researchers are permitted to revert to surplus heS cells if they were manufactured for an artificial fertilization in vitro in France and if the respective ?parents? agree. Furthermore, importing heS cells that are manufactured under the same conditions as demanded in France is permitted. The official regulation of stem cell projects is being taken over by the Agence de la Biomédicine. After a period of five years, stem cell research will be assessed afresh, and any completed approved research will be evaluated and new legislation possibly initiated.

Context

Companies: 300

Main emphasis: Health, Nutrition

Companies association: France Biotech www.france−biotech.org

Project based funding authority: Agence Nationale de la Recherche (ANR) ww.gip−anr.fr

Institutionel funding authority: Ministère délégué à l'Enseignement et à la Recherche www.recherche.gouv.fr

Special funding programmes: Cancer research ("Cancéropôles"); High Tech companies (Founder competition); Centers of Excellence ("Pôles de compétitivité")

Most important clusters: "Lyonbiopole" (Virology: Lyon), "MédiTechSanté" (Infektions−forschung, Krebs: Ile de France); Europol'Agro (Agrobiotechnology: Picardie); Innovations Thérapeutiques (Molecular biology: Alsace); Végétal specialisé (Nutrition: Pays de la Loire)

Legal basis:

"Genetic engineering law" (in discussion, planed for 2006); "Pacte pour la Recherche", (adopted 2006) Bioethics−Law (adopted 2004, Guidelines for stem cell research published 2006)

Downloads

OSEO analyse of the biotech sector in France (in french)

Download PDF (884.5 KB)