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TECHNOLOGY CREATION IN THE BIOTECHNOLOGY SECTORS: THE FRENCH CONNECTION

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ABSTRACT

This paper examines how a government committed to the development of biotechnology sectors succeeded in a country where there was a retard in scientific knowledge, weak links between firms and scientific institutions and sluggish capital markets. Based on in-depth interviews with prominent figures from the biotechnology sectors and secondary data, the paper looks the development of the biotechnology sectors in France, as a response of the firms, the research community, and the financial markets, to the coordination and initiatives of the French Government. We show that despite the shortcomings of the state intervention, research in biotechnology is now thriving in France, a small sector of dedicated biotechnology firms has been created and a few large diversified firms are working on creating major innovations with a global market. We then draw inferences from the French experience on the conditions favourable for the development of biotechnology sectors in any late comer country, and conclude with the policy implications that such conditions entail.

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TECHNOLOGY CREATION IN THE BIOTECHNOLOGY SECTORS: THE FRENCH CONNECTION [1]

1. Introduction

Biotechnology refers to the manipulation or processing of living organisms, for industrial use. Considered as such, it has been in practical use since the dawn of civilization in the making of bread, cheese, yogurt, beer and wine, termed as first generation biotechnology. This evolved later, in the making of vaccines, and further on in the making of antibiotics to a second generation technology, involving systematic screening and selection procedures to exploit micro-organisms. Modern biotechnology or third generation biotechnology, however refers to a set of techniques: genetic engineering (recombinant DNA technology, monoclonal antibody techniques, gene synthesis), cell and tissue cultures, protein synthesis and enzymology stemming from recent developments (since 1975) in the biosciences such as biochemistry, biophysics, molecular biology, microbiology, cellular biology and genetics[2,3]. The third generation is distinct from the earlier ones in that it involves manipulation of the genetic patrimony of an organism.

Modern biotechnology is a generic or transversal technology with multisectorial applications as shown in figure 1[4]. It was propelled by the discovery of two radical techniques:

(i) The recombinant DNA (rDNA) technique, discovered by Stanley Cohen of the University of California at San Francisco and Herbert Boyer of Stanford University in 1973, which allowed a gene sequence to be cut and a foreign sequence to be inserted, to 'reprogramme' the gene to reproduce offspring with characteristics of the foreign sequence.

(ii) The cell fusion or monoclonal antibodies technique discovered by Cesar Milstein and Georges Kohler of the Cambridge Laboratory of Molecular Biology in England in 1975, which permitted fusing certain cells with lymphocytes (white blood cells) to create self replicating cells that produced a particular antibody.

Modern biotechnology represents an innovational break from the previous technology because "For the first time scientists have been released from the slow and uncertain techniques of trying to improve on nature by breeding mutant strains, and instead have at their fingertips techniques which enable them to do this with a surprising degree of certitude"[5]. Instead of finding a product (protein, enzyme, antibody etc.) by trial and error through a prolonged search or selection process, products can be designed. Scientists are important because of the high degree of codified knowledge necessary to design the product. It is of interest to the industrialists because simple micro-organisms can be used as factories to create specific proteins and antibodies in large quantities and at low cost.

The first companies to base themselves entirely on modern biotechnology techniques were American start-ups, such as Cetus (1971), Genentech (1976), Genex (1977), Biogen (1978) etc. also termed as DBFs (or dedicated biotechnology firms). With the push coming from the supply side, the modern biotechnology sectors in various parts of the world then emerged, fuelled by a series of product or process innovations. Initially they were made famous by some radical innovations in the pharmaceutical sector [6] (most of them being commercialized by American companies). But over the last ten years an enormous number of incremental innovations accompanied by much less publicity have also been successfully commercialized. [7]

At present, the U.S.A. is still the acknowledged leader in the technological race in most of the biotechnology sectors (see [3]). However since it became evident that biotechnology as a generic technology is crucial to economic power and national competitiveness, development of the biotechnology sectors has been accorded very high priority by the three groups of developed countries: U.S.A., Europe and Japan. Of course, the patterns of development and degree of government commitment to the development of biotechnology sectors have been very different in the various countries of the developed world.

In this context, the objective of the paper is to study the development of the biotechnology sectors in France, a late comer to this field. We first propose four conditions as being necessary for the full development of any hi-tech sector that is growing or is greatly influenced by the 'technology push' factor. We very briefly show how they were not met in France with respect to biotechnology and how the government took steps to rectify the situation. We then focus on the present problem, classifying the French firms in the field according to the type of their present technological competence and its possible evolution. We conclude with lessons from the French experience for other late comer countries. We have used secondary sources and we also conducted in-depth interviews with prominent figures from the biotechnology sectors to obtain additional tacit information on the issues concerned.

1.1 Necessary Conditions for realizing the maximum potential of a highly science based industry

By a highly science based industry, we refer to those where the technology embodied in the final product or process is changing rapidly (say between 2 to 6 years) leading to improved quality or lower price in the market thereafter. Such industries include microelectronics, new materials, telecommunications and the biotechnology sectors.

(i) The scientists are up to date in the disciplines constituting the foundation of the particular science based industry. This is evident from the definition.

(ii) There is mobility of resources (information, labor, people and capital) between the research market formed by the creators of knowledge and the product market formed by firms involved in manufacturing. For the most efficient cross fertilization of effort between the creators of scientific knowledge and the creators of products and processes for economic use, it is necessary to forge strong links between the two types of agents. In many countries research is conducted in universities or research institutes that are supported financially by the state. Unless there are strong links between the two, scientists may overly focus on abstract research which yield scientific publications but otherwise have little economic potential. If industrial researchers are not up to date and competent on the latest research, they would

neither be aware of the technical potential of research output nor have the capacity to absorb the scientific results and transform them into usable technology.

(iii) There are incentives for conversion of research output into product or process innovations. Any costly R&D investment whose returns are uncertain, will be undertaken only if the expected profit is of a particular magnitude. Expected profit is determined by a number of technological, firm and market features such as: possibilities for imitation, individual competence, production capacity, market share, market structure, ownership of required and complementary assets, level of entry barriers, market competition and macro factors such as government subventions, government regulations, intellectual property rights, functioning of financial markets etc. The sum result of the interaction between these parameters must be so as to result in a high enough profit to make R&D investment worthwhile.

(iv) There are agents in the economy (the government, the public, the firms or the capital markets) who are willing to bear the cost of risky R&D investment. As indicated earlier, R&D effort for any firm is distinguished from other activities such as manufacturing or marketing, in that it is essentially a search activity on which an efficiency criterion can not be imposed. As a search activity its output is uncertain and therefore an R&D investment involves risk. When the degree of risk is high as in the biotechnology sectors, it may not be possible for an individual firm to bear it. In such cases the sector will not grow unless firms group together to share the risk, or other agents such as venture capitalists, the public, or the government share the risk with the innovating firm.

1.2 France: a late comer in the race

At the end of the seventies, clearly the first two conditions were not satisfied in France with respect to biotechnology. Most of the 'academic' research in France is conducted in its public research institutes. The '*Centre National de la Recherche Scientifique*' (C.N.R.S.), the largest one, conducts research in virtually every discipline. Others are more focussed on specific areas: *'Institut National de la Recherche Agronomique'* (I.N.R.A.), *'Institut National* *de la Santé et de la Recherche Médicale'* (I.N.S.E.R.M.), *'Commissariat à l'Energie Atomique'* (C.E.A.), *'Institut Pasteur'* (which is actually semi-public because it is also part of the Mérieux group). Despite a strong tradition of scientific research and a likewise centuries old tradition of centrally administered and funded educational and research institutions, the French scientific community was years behind those of the United States and England in the knowledge of the latest developments in the sciences that helped create the modern biotechnology sectors. As Sharp [see 5] records, in 1978, apart from Institut Pasteur, "neither the C.N.R.S., nor the I.N.S.E.R.M. laboratories were fully aware of what was happening in the U.S., nor the potential impact genetic engineering was likely to have upon their work. Meanwhile, the laboratories of I.N.R.A. had hardly begun to contemplate the potential impact on agriculture".

Till the beginning of the eighties, the academic community for the most part had little contact with the industrial community and functioned in isolation with its own set of rules. This was basically the result of having a state funded research structure where researchers and professors were public servants, similar to civil service personnel. Their objective was to produce scientific knowledge and they had no incentive to seek the industrial community. Such a lack of interaction over the years also created a barrier of mutual antagonism, lack of communication and divergent interests and preoccupation between the R&D executives of the firms and the academics.

Similarly, the firms which conducted research were large ones with in-house laboratories. They had no need to establish a culture of working together with the public research institutes beyond entering into punctual research contracts. Thus, most of the products of research that entered the market came from the in-house industrial laboratories and rarely from a public lab-industrial lab collaboration. Furthermore, at the end of the seventies most of the industrial houses also were not aware of the potential of biotechnology [8,9]. The retard of French firms vis-à-vis the American firms was also reflected in the number of patents granted to the two sets of firms concerned.[10,11]

It was under such circumstances that the French government took the initiative at the end of the seventies to launch the development of the biotechnology sectors. In America, the engines of growth of the biotechnology sectors had been the start up DBFs and the venture capitalists who helped create them. In Germany they were the large established firms with existing infrastructure for manufacturing and marketing units which had the means to undertake R&D research as part of in-house development of innovations. In Japan it was the government and in England it was the academic community. France represented a hybrid system exhibiting features of all the above countries but with the driving force coming from the government and with government coordination at the heart of the system.

2. Strategy and role of the state

To tackle the situation the French Government initiated a number of programs whose common aim was to stimulate public research and promote conversion of fundamental discoveries in the biological sciences into products of economic value through facilitating the interface between public research and industrial research. The evolution of government strategy can be categorized into four phases: (i) initial stage; (ii) 'Mobilization Program' (1982-1986); (iii) 'National Program' (1986-1990); (iv) 'BioAvenir Program' (1992-1997). As will be shown, the governmental policy evolved through the various programs from taking the leading role, from scanning all the technological and organizational possibilities for the creation and diffusion of new technology, to taking the back seat, to focussing on a few sectors, and on a few big firms.

2.1 Initial stage

In 1978, after a trip to South America, where he became interested by the Brazilian sugar to alcohol programme, President Giscard d'Estaing initiated a broad based inquiry into the recent developments in the biological sciences and their implications for society. This resulted in the report '*Sciences de la vie et Société'* by Gros, Jacob and Royer in 1979. The report stressed the tremendous potential of biotechnology for all sectors of economic activity including the three sectors: agriculture, agro-foods and energy, that were of importance to

France. It indicated that a substantial investment in R&D and interdisciplinary research effort were needed to exploit the scope of biotechnology.

The government's immediate response to this report was to concentrate on three areas: (i) bringing the academic community up to date in the biological sciences; (ii) establishing links between the academic community and the industrial community; (iii) implementing certain 'pilot' programmes of which the biomass alcohol programme was accorded priority as the Prime Minister was particularly keen on it.

Universities were asked to double the number of students in the biological sciences. Technology transfer centers in research institutes were created to provide consultancy services to businessmen. Soft loan packages were created to help scientific entrepreneurs obtain professional help and funds to convert ideas into products. As Philippe Renault, director of the biotechnology division at the *'Institut Français du Pétrole'* explained, "at the end of the seventies, the government launched '*Plan Carburol'* a grand program for the valorisation of vegetal biomass. This resulted in the '*Soustons Experiment'* whose objective was to build a factory to convert cellulose (plant) wastes into a carburant. That way the farmlands which are forced to be untilled under the Common Agricultural Policy of Europe could be valorized. However the cost of production turned out to be far higher than that of petrol and therefore of no commercial value and ultimately the project was abandoned".

2.2 Mobilization Program (1982-1986) and National Program (1986-1990)

A more concerted effort was made in 1982 in the form of the Mobilization Programme '*Essor des Biotechnologies'* under the aegis of the Ministry for Research and Technology. The target for France was to produce 10% of the world's biologically based production by 1990. The program involved a three pronged approach: (i) scanning various types of organizational networks in the form of government engineered research collaborations between big firms, small firms, research institutions and university laboratories etc. to find the best mode for the creation of new technology; (ii) creation of awareness of the potential of biotechnology by involving firms not directly in the biotechnology sectors in research programs; (iii) ambitious restructuring and reorienting of the national research institutes to gear basic research towards projects of commercial value. The objective was to develop competence in the following areas: microbiology, fermentation, enzymology, genetic engineering, improvement of seeds and plants, vaccines, logistics and supplies of equipment, and formation of researchers.

Public subventions were provided to labs of C.N.R.S., I.N.S.E.R.M., I.N.R.A. and Institut Pasteur and also to several firms under the B.C.R.D. [*Budgets Civils de R&D*] Public budget of R&D, the F.R.T., Funds for Research and Technology and A.N.V.A.R., the National agency for the valorization of research. Reengineering the research institutes as Sharp (see[7]) documents meant that, "... innovation oriented to industrial needs was given the highest priority. Programs of applied research were introduced, new advisory committees with industrial representation were set up, institutes were advised to undertake industrial contract work, and a major decentralization created a series of regional technology transfer centres (C.R.I.T.T.)".

A second toned down but more focused 'National Programme' was launched in 1986 after a change in the political party in power. Instead of instigating collaborations between firms, incentives were provided for pre-competitive R&D in a narrower set of generic technologies namely genetic engineering, microbiology and protein engineering. A number of smaller programs were also started as 'Aliment 2000' [Food 2000], 'Protéine 2000' and a few public bodies such as the national bioindustry organization (Organibio) started collaborative research programs between industrial corporations involving biotechnology. France was also actively involved in a number European collaborative research programmes such as BEP, BAP, BRIDGE, FLAIR, ECLAIR and EUREKA.

During this period, the government funds going to the national research institutions followed an inverted U-shape curve, rising from 1982 to 1985 and decreasing steadily thereafter. However the proportion going to applied research in the public research organisms increased and a variety of incentives were provided to researchers to improve their contact with the industrial community (see table 1).

According to the report of the National Committee for the Evaluation of Research[12] (C.N.E.R.) most of the collaborations between the different partners instigated under those programs were never effective, probably because there were too many modifications in the structures of the public bodies responsible for the biotechnology sectors as a consequence of political changes. The collaborations could have also failed because of an insufficient examination of incentives for the firms concerned[13] . Under the system of subventions put in place, there was no means of monitoring or control which gave rise to problems of non-implementation of promises made. However C.N.E.R. concedes that the funds distributed under the two programs increased the potential of the public research, propelled new work in the industrial laboratories (especially those of Limagrain, Beghin-Say, Rhône-Poulenc, Elf-Sanofi, Lafarge-Coppée and Roussel-Uclaf) and had a positive effect on the start ups.

2.3 BioAvenir (1992-1997)

A third wave of response came under the form of the program 'BioAvenir', instigated by Rhône-Poulenc (privatized since 1993), a firm with an international technological and market leadership in the chemicals and pharmaceutical sectors. It represented a major shift in policy whereby: (i) the lead in biotechnology research passed from the hands of the government to being a close cooperative effort between the private sector and the government (i.e. the Ministry of Industry and the Ministry of Research); (ii) and the focus was on a single firm, namely Rhône-Poulenc instead of being spread out over various firms.

Under BioAvenir, a $290[14] million program, Rhône-Poulenc provides $180 million, while $110 million is given by the government (75 in the form of subventions from F.R.T. and 35 in the form of loans). It constitutes the largest subvention that has ever been given by the F.R.T. to a single company in the bioindustry. It mobilizes 500 researchers, engineers and technicians in programs involving fundamental research on biological processes, medical research and agricultural research. The program has already resulted in over a hundred academic publications and a similarly large number of public conferences. But the economic consequences for national competitiveness, of this shift in policy, whereby a single large firm is allowed to have even (quasi) propriety control over the products of a vast program of fundamental research, is not yet clear.

3. Response of the public research institutes and the private firms to the government initiatives

3.1 Response of the public research institutes

Firstly in a number of universities, the course work and research in the sciences supporting biotechnology have been brought to the state of the art level. The universities most actively involved in biotechnology are: '*Université de Technologie de Compiègne*' (UTC), Bordeaux University, Toulouse University (Paul Sabatier), and Strasbourg University (Louis Pasteur).

Interaction between the research community and the industrial community has increased greatly. The C.N.E.R. report indicates that 6% of the industry-university scholarships given between 1981-1991 have been on doctoral work related to biotechnology. Professor Thomas notes that, "since the mid 1980s there has been a tremendous improvement in relations between universities and private firms especially in terms of common research programs and financing of doctoral theses". The number of industrial contracts of C.N.R.S. has increased from 120 in 1982 to 3700 in 1992 and 7% of the scientific publications carry a signature of a public lab researcher and an industrial scientist[15] . Universities begin to regard transfer of technology from university laboratory to industry as an important objective and seek high level scientific collaborations with the best international companies. But according to most of the people we interviewed, there is still a lot of scope for improving the interaction between the research community and the industrial community.

3.2 Response of the firms

On the basis of their present technological competence and its possible evolution, we can classify the firms in the French biotechnology sectors into three categories: (i) the food sector; (ii) the small league: small firms with capital base less than $20 million; (iii) the big league: medium to large firms with more than $20 million capital base.

3.2.1 The 'no' league or the food sector

The majority of the firms in the food sector are competent in first generation biotechnology methods. They seek to improve their competence through learning by doing and outsourcing contracts with the national research organisms. There is little emphasis on developing new technology though some of the most dominant firms such Bel and Bongrain (dairying), Pain Jacquet (bread), Moët-Hennessy (champagne), Ricard (Aperitif) etc. have invested some funds in the biotechnological processes[16]. Such a state of affairs seems related to the fact that the food industry is a mature one with low entry barriers, stringent regulation, where competition is determined by standard marketing parameters such as price and advertising. With centuries old processes and products perfected over the years firms have little incentive to undertake large R&D investment that might lead to marginal improvements (i.e. the third necessary condition listed in section 1.1 is not satisfied). Thus on average the food industry devotes less than 1% of its revenue to R&D. It has been remarked,[17] that even large companies like B.S.N. which is an international leader in the food industry, "did not lose a word on R&D activity in its three last annual reports (1988-1990)".

3.2.2 DBFs in the small league

French DBFs were often created by researchers from public research laboratories who came to the market armed with a novel idea and research experience in a narrow field accumulated in their previous employment. Our examination[18] revealed the fragility of this population. On the one hand, it is made up of micro structures with a turn-over or a capital base of less than 2 million dollars, employing less than 10 persons; while on the other hand, there are small structures with a capital base extending to 20 million dollars, employing up to 50 persons. However the number of DBFs in France is steadily growing. There were about 11 firms in the biotechnology sectors till 1980; 29 more were created between 1981-1985; again the number of births doubled to 32 between 1985-1990. According to Professor Thomas, a founder of the '*Université de Technologie de Compiègne'*, and a former director of the '*Programme Biotechnologies'* at the Ministry of Research and Technology there are about 100 French DBFs operating today[19] . They are active in: tests and diagnostics (16%), pharmaceuticals (13%), agro and food (20%), environment (3%), bio-materials (5%), bio-informatics (10%), biological products for laboratories and firms (16%) and material for laboratories and firms (13%)[20]. Most of them show positive revenues, if not positive profits (see [20]). Some of the more publicized ones with international market shares in certain niches are Transgene (now sold out to Rhône-Poulenc), Sorbio (bioconversions), Genset (DNA manufacturer) and Imedex (biomaterials).

The choice of the majority of the DBFs is to exploit their technological competence in third generation biotechnology and commercialize one or a few products with a short R&D period through in-house development. They also support themselves by undertaking research contracts and conducting research workshops. Diagnostics are thus popular items as they are based on a single technology of monoclonal antibodies and involve a very short gestation period (2-3 years) between the laboratory discovery and market commercialization. As Jacques Latrille the founder of Sorebio, a French DBF that is number 2 in the world in the fabrication of monoclonal antibodies, explained, "the research must last at most 3 years before yielding a commercializable product and it must come from the needs of the market". Barring few exceptions, French DBFs do not have a policy of reinvestment of resources in any medium or long term research projects. In other words any diversification of their technological competence must come from short term projects.

The reason for their behavior is simple: access to capital. According to Philippe Renault: "Given that the cost of a research team is around 1 million dollars per year and an average research project is for 5 or 6 years, it is clear that the small firms with a capital base of less than 5 million dollars cannot engage themselves in research projects that are fundamental in scope".

Avenues for borrowing capital are also limited. The DBFs in U.S. raised money initially by licensing first generation products, market segments and equity financing (little or no debt financing). But there is little incidence of French DBFs selling off product rights to established French firms. They either have a principal-agent relationship where an established French firm gives a pre-competitive research contract to a French DBF or are brought together in some government engineered research collaboration. According to Jacque Latrille, "there are really two sources of finance: A.N.V.A.R., and local or international banks; rarely money raised from the public or venture capital". But even the banks prefer to invest abroad rather than in France (see[5]): "Paribas, [*one of the best known French banks catering almost exclusively to firms*] for example may have invested $2.72 million in Transgene [*the first and best known French DBF now purchased by Mérieux*], but it has put $14.5 million into the U.S. company Centacor; Sofinova, one of the first French investment groups, has put some $5.27 million into U.S. biotechnology compared to $.9 million in France".

In the late seventies[21] and early eighties approximately 300 DBFs were formed in the U.S.A.. To date only 10 have succeeded in becoming highly profitable full scale companies. It took these companies on average 10 to 12 years and $500 million each to get from startup to profitability. The bottom line is that French DBFs can not imagine such luxuries. No sophisticated strategies can cloud the logic of the jungle which forces them to pursue profit maximization in the short run. Thus the French DBFs are forced to concentrate not on making radical innovations but to survive in a hyper competitive market.

3.2.3 The big league

The big league includes firms such as Rhône-Poulenc, Roussel-Uclaf (Hoechst), Elf-Sanofi, Fabre, Synthélabo (L'Oréal), Limagrain and Servier. Their main achievements are captured in table 2. They are working on medium to long term projects with large market potential and given that they have been actively engaged only for about twelve years, products are more in the pipeline than in the market.

The large firms have the financial and organizational means to adopt a medium term to long term horizon permitting a long recuperation period. Like international conglomerates elsewhere, the large firms not only exploit their present technological competence but are also actively engaged in increasing or enlarging their technological competence. In areas which promise high monopoly rents they prefer to go it alone and are willing to undertake heavy investment with long recuperation periods. In other sectors perceived to be of strategic interest they enter into a variety of strategic acquisitions and alliances (see table 3). As Alain Laroche a director of communications at Sanofi BioIndustries explained, "the big firm's research strategy is transversal i.e. engaging in programs which could be applicable to various domains. For instance Sanofi BioIndustries was created on the broad concept of health, a transversal concept covering pharmaceuticals, cosmetics and agro-foods".

The big firms want to keep up to date with the latest scientific developments and survey them for possible commercial potential. Since maintaining in-house research capacities in a number of fields is very costly and the degree of spillover may be high (as researchers publish, leave for other firms or form their own firms), it is more profitable for the large firms to undertake R&D co-development with research institutions. For example, under the program BioAvenir, Rhône-Poulenc has collaborations with all major research institutes. Moreover most of the big companies also have established R&D labs in the U.S., mainly staffed by U.S. scientists or fund non-profit American research organizations. They control the functioning of the institutions and get access to U.S. R&D know-how by attending conferences, seminars. They strengthen their American networks, using U.S. personnel to get contracts with American universities and American DBFs etc. Thus the research institute provides a complementary input, saves money on keeping abreast of scientific knowledge and may create synergy and learning as researchers from the firm and institute interact.

They also enter into R&D joint ventures mostly with other large well established, diversified, internationally leading firms. The reasons for alliances between large powerful firms have been well documented[22,23]. They are motivated by incentives for cost sharing, risk sharing, group learning and strengthening the commercialization strategy through economies of scale, scope, logistics, procurement, a tighter appropriation of new results, better diffusion or creation of entry barriers through closing the market.

By definition take overs are a form of technology acquisition and not technology creation. It is must just be noted here that large European firms have rivaled with their American counterparts in taking over American DBFs which had developed some new technology to the point where it became marketable. There have not been many takeovers of French DBFs because there are few DBFs and the market potential of most of them is not interesting enough for the large French companies to take them over[24] . Thus, though there is a big difference between American DBFs and French DBFs, there is little difference between the large American firms and the large French firms.

These findings of section 3.2 are summarized in table 4.

4. Conclusions: Lessons for other late comer countries

Despite the substantial progress made in terms of creation of scientific and technological competence in France, the initial bottlenecks that weighed down the development of the biotechnology sectors are still those that need to be worked upon. Indeed, from the French experience and the four necessary conditions outlined in section one, we can propose these problems as those that should also be taken into consideration for the national technology policy of other late comer European countries and the big players of the third world like India, China and Brazil as well, where conditions very similar to those in France at the end of the seventies still prevail.

(i) Bring research up to date and strengthen transfer of scientific knowledge into technology i.e. increase cooperation between public research institutes and firms.

As has been widely documented, the French policy makers felt that development of the biotechnology sectors went hand in hand with a scientific community empowered with the state of the art knowledge. But even now, the scientific publications in the biotechnology fields, of European researchers all put together, trail behind their American counterparts[25] . It has been pointed out that the leadership of the Americans in the scientific disciplines is one of the keys to their leadership in the product market.

Most firms, large or small, cannot afford to maintain a large research staff who are up to date in a number of fields and allow them to conduct fundamental research which may not yield any tangible result. Here alliances with public research institutes for co-development would allow firms to keep in touch with the latest scientific development and scan for possible market application. Usually the public labs are even less interested in the small firms than in the large ones, since the small firms do not have much money to give to the labs. But there are instances, as the company Sorebio of Jacque Latrille proves, when linking between financial companies, a public research lab and a small firm might prove successful and beneficial to all parties concerned.

Unless there are strong relations between the industries and research institutes, a bi-polar structure will dominate, whereby industrialists conduct R&D purely in terms of immediate market application, and public research is mainly oriented towards publications. Under this structure technological progress will be slow and economic returns to public investment in research will be low, constituting an inefficient allocation of national resources. The strong relations that persists between American universities and firms is often (repeated in most of the references given dealing with America) cited as being another important ingredient for their success. As Laurent Dartiguenave of Ernst & Young (Paris branch), asserted strongly to us, "There is no logical procedure or regular procedure to develop an innovation. It is the fruit of a succession of diverse errors, of tentative speculations left and right, either in the basic science or in the method used or in the experimental results ... but such speculations need a network of alliances or at least a network of communications!"

Furthermore if alliances between local firms and research institutes are not developed the firms might seek them abroad. For instance, it has been warned (see [25]) that unless the French and European governments instigate more local collaborations, the tendency of large

French firms to seek R&D alliances with American institutes will be detrimental to their national competitiveness in the long run.

(ii) *Encourage capital markets and large firms to support a growing sector of DBFs*

Till now, most of the technological breakthroughs in the biotechnology sectors have not emerged from big firms but from DBFs (mainly American)[26]. This in itself should provide a justification for supporting the survival and growth of DBFs. It is true that in France the fate of radical innovations seem to be in the hands of the large French firms rather than the French DBFs. But even though the American pattern is unlikely to manifest itself, the creation of DBFs in France as elsewhere has to be encouraged because they constitute an important source for tapping scientific competence. Given that the development of a product may involve trying out a number of ways, it may be less costly for a large firm to contract out research or engage in strategic alliances with DBFs than to try to develop in-house research competence in a variety of fields. According to the French biotechnology companies interviewed by the associates of Ernst and Young[27] access to capital is the number one problem faced by the DBFs, ranked above market competition, market structure, resources or organization. If sluggish capital markets are responsible for a small number of DBFs then either the government or the large firms themselves may have to step in to fill the void to ensure the existence of a healthy number of DBFs with a wide variety of scientific competences.

(iii) Improve incentives for scientists to create DBFs

Coming to the scientist entrepreneur, most DBFs in America were created by scientists with high competence in their fields who were helped to form firms by creative financing and venture capital. An equally competent French scientist would have less incentive to form a company given that in the French scientific community entrepreneurship is ranked below scientific prowess, and there is great uncertainty and difficulty associated with finding finance and organizational help to create a start up[28]. This could also account for the small number of DBFs in the European countries which distinguish them from the American market.

(iv) Harmonize regulations over neighbouring regions to increase the size of the market and lower costs of marketing.

In order to be sold at the European level, any product has to undergo an evaluation of security, quality, efficiency and fabrication procedure via the Commission. This is difficult for because of the heavy bureaucracy involved and the presence of lobbies opposed to biotechnology[29,30]. An analysis of security is implemented by successive evaluations of risk. There have been instances where countries against transgenic products like Denmark and Germany, have stalled procedures by demanding successive evaluations of risk, or by slowing down the process of granting authorization to disseminate or put on the market. Then if permission is granted at a European level, the firm has to invest in getting market approval from the regulatory bodies of the different nation states of Europe. Though large European and American firms suffer similarly from the heavy regulatory procedures in Europe, the ones to be hit hard are the small European firms. For reasons of geographical proximity, culture, associations etc. it is easier for small European firms to begin by selling in Europe. But often they are forced to sell only within their country or a few other European countries because of the regulatory costs involved each time. This greatly limits the size of their market. Then if market size is crucial to their survival they are forced to sell either in the United States which presents a single market of large size or turn to the Far East where the markets are growing and regulation is soft or go bankrupt. Thus harmonizing regulations over Europe will allow small firms to face a regional market of a critical size that could be crucial to their survival and growth.

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