The French Evolution of Biotechnology

Will government initiatives in France help establish a biotechnology industry?

Shyama V. Ramani

The conditions that allowed biotech to flourish in the U.S.—in the form of the successful startups like Cetus (1971, Emeryville, CA), Genentech (1976, S. San Francisco, CA), and Biogen (1978, Cambridge, MA)—did not exist in France at the end of the 1970s. Despite a strong tradition of scientific research, the French scientific community was years behind those of the U.S. and the U.K. in its knowledge of the latest developments in the biosciences that helped create the modern biotechnology sector. The French academic community, for the most part, had little contact with the industrial community and functioned in isolation, with its own set of rules that were the result of a state-funded academic research structure. Its objective was to produce scientific knowledge and gain recognition through publications. The only firms that actively 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—and they, too, were unaware of the potential of biotechnology.

Strategy of the State

It was under such circumstances that the French government took the initiative at the end of the 1970s to launch the development of a biotechnology sector. It began a number of programs whose common aim was to stimulate cooperation between public and private research and promote the conversion of fundamental discoveries in the biological sciences into products of economic value. The evolution of this government strategy can be broken into four phases: the initial stage (1979-82), the mobilization program (1982-86), the national program (1986-90), and the BioAvenir program (1992-97).

The initial-stage program of the government concentrated on three areas: bringing the academic community up to date in the biological sciences, establishing links between the academic community and the industrial community, and implementing certain "pilot" programs, of which the biomass alcohol program was accorded priority.

The mobilization program also involved a three-pronged approach. The first was to find the best structure for the creation of new technology by looking at various types of organizational networks—in the form of government-engineered research collaborations between big firms, small firms, research institutions, and university laboratories, etc. The second was to build awareness of the potential of biotechnology by involving firms not directly in the biotechnology sector in research programs. The third was an ambitious restructuring and reorienting of the national research institutes to gear basic research toward projects of commercial value. The objective was both to raise the aptitude of French researchers and to develop competence in the following areas: microbiology, fermentation, enzymology, genetic engineering, improvement of seeds and plants, vaccines, and logistics and supplies of equipment.

A third, toned-down—but more focused—national program was launched in 1986. Instead of instigating collaborations between firms, incentives were provided for precompetitive research and development (R&D) in a narrower set of generic technologies, namely genetic engineering, microbiology, and protein engineering.

According to a report of the National Committee for the Evaluation of Research[2] (CNER, Paris), the funds distributed under the two programs increased the potential of public research, propelled new work in industrial laboratories (especially those of Limagrain, Beghin-Say, Rhône-Poulenc, Elf-Sanofi, Lafarge-Coppée, and Roussel-Uclaf—all headquartered in Paris), and had a positive effect on startups. However, most of the collaborations between the different partners instigated under those programs were not effective, probably because there were too many modifications to the structures of the public bodies responsible for the biotechnology sectors as a consequence of political changes in the government.

A third wave of interest in biotechnology came in the form of the BioAvenir program, instigated by Rhône-Poulenc,[3] a firm with international technological and market leadership in the chemicals and pharmaceutical sectors. BioAvenir represented a major shift in policy in which taking the lead in biotechnology research changed from being a government-initiated effort to being a close cooperative effort between government and the private sector. And the focus was on a single firm—Rhône-Poulenc—instead of being spread out over various

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Shyama V. Ramani is associate professor in the sociology and economics research & development unit, National Institute for Agronomic Research, Grenoble, France (e-mail: ramani@grenoble.inra.fr).[1]

firms. Under BioAvenir—a $290 million program—Rhône-Poulenc was to provide $180 million, while $110 million was to be provided by the government. The program involves fundamental research on biological processes, medical research, and agricultural research. BioAvenir has already resulted in over a 100 academic publications and a similarly large number of public conferences.

Response of the Sector

On the basis of present technological competence and its possible evolution, we can classify firms in the French biotechnology industry into three categories: the food sector; the small league—firms with capital bases of less than $20 million; and the big league—medium to large firms with capital bases of more than $20 million.

The majority of firms in the food sector are competent in traditional biotechnology methods and seek to improve them further through learning by doing and collaborations with national research institutions. With centuries-old processes and products perfected over the years, these firms have little incentive to undertake a large R&D investment that might lead only to marginal improvements and hence they invest very little in R&D (less than 1% of revenue, on average).

Dedicated biotechnology firms (DBFs), as elsewhere, were most often created by researchers from public research laboratories who came to the market

TABLE 1. Activity of large French firms in the biotechnology sector.

Firm	Product	Biotech Generation	Stage of Commercialization
Rhône Poulenc	• Agro chemicals, animal nutrients	Third	Research
	• Role of cholesterol in atherosclerosis	Third	Research
	• Role of amino acids in degenerative diseases	Third	Research
	• Gene therapy	Third	Research
	• Topoisomerase2—enzyme for tumor inhibition	Third	Clinical trials
	• Taxotere—anticancer drug	Second	Development
	• Herbicide-resistant tobacco	Third	Market approval granted
Merieux & Institut Pasteur	• Raboral—recombinant animal antirabies vaccine	Third	Commercialized
	• Vaccine for herpes and AIDS	Third	Research
Elf Sanofi	• Human growth hormone	Third	Commercialized
Roussel Uclaf	• Vitamin B12	Second	Commercialized
	• Corticosteroids	Second	Commercialized
	• Interferon	Third	Research abandoned
	• Interleukine	Third	Research abandoned
	• Development of bioprocesses to reduce costs	Third	Research
Servier	• No biotechnology, strong in pharmaceutical sector		Investigating incorporation of biotech through market acquisitions or alliances.
Synthélabo	• No product		Equity participation in Texas Bio. Scanning French and American DBFs for buyouts. Contracts with public research organizations.
Fabre	• Ribomunil—increases respiratory immunity	Second	Commercialized
	• Products to combat bacterial diseases & cancer	Third	Clinical trials
Limagrain	• Seeds resistant to insects and herbicides	Third	Waiting for market approval
	• Maize seeds with modified characteristics		
Eurolysine	• Amino acids for animal feeds: lysine, threonine, and tryptophan	Second	Commercialized

armed with novel ideas. On the small side, this market segment, is made up of companies with a turnover or capital base of less than $2 million, employing less than 10 people; and on the larger side, it is made up of companies with capital bases extending to $20 million, employing up to 50 people. The number of DBFs in France is steadily growing. There were about 11 firms in the French biotechnology sector until 1980; 29 more were created between 1981-85; and another 32 were created between 1985-90. According to Daniel Thomas, a former director of the biotechnology program at the ministry of research and technology (Paris), there are about 100 French DBFs operating today. They are active in tests and diagnostics (16%), pharmaceuticals (13%), agronomics and food (20%), environment (3%), biomaterials (5%), bioinformatics (10%), biological products for laboratories and firms (16%), and material for laboratories and firms (13%). Most of them show positive revenues, if not positive profits.

Most DBFs choose to exploit their technological competence in third-generation biotechnology and commercialize one or a few products with a short R&D period. They also undertake research contracts and conduct research workshops to support themselves. 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) from the time of discovery to market commercialization. With few exceptions, French DBFs do not reinvest resources in any medium- or long-term research projects.

The reason for this is simple: Lack of financial capital. Given that the cost of a research team is around $1 million per year, and an average research project lasts 5-6 years, it's clear that the small firms with capital bases of less than $5 million cannot engage in research projects that are fundamental in scope.

Avenues for borrowing capital are also limited. DBFs in the U.S. raised money initially by licensing out first-generation products, market segments, and equity financing (little or no debt financing). But few French DBFs have sold off product rights to established French firms. They either have a principal-agent relationship, in which an established French firm gives a precompetitive research contract to a French DBF, or they are brought together in some government-engineered research collaboration. Even French banks prefer to invest abroad rather than in France: It has been documented that many of the top investment banks have lent more to American DBFs than to French ones.[4]

The big league firms include Rhône-Poulenc, Roussel-Uclaf [Hoechst, (Frankfurt, Germany)], Elf-Sanofi, Fabre (Paris), Synthélabo (Paris) [L'Oréal, (Paris)], Limagrain, and Servier (Paris) (see Table 1). They are working on medium- to long-term projects with large market potential and, given that they have been actively engaged in biotechnology for only about twelve years, more products are in the pipelien than in the marketplace.

These 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 that promise high monopoly possibilities, they prefer to go it alone and are willing to undertake heavy investment. In other sectors perceived to be of strategic interest they enter into a variety of strategic alliances and acquisitions.

Since maintaining inhouse research capacities in a number of fields is very costly, and the degree of spillover may be high (as researchers leave for other firms or form their own), to keep up to date with the latest scientific developments and survey them for possible commercial potential, the large firms undertake R&D codevelopment with research institutions. For example, under the BioAvenir program, Rhône-Poulenc has collaborations with all of the major French research institutes. Moreover, most of the big companies also have established R&D labs in the U.S.—staffed mainly by American scientists—or fund nonprofit U.S. research organizations. They also enter into R&D joint ventures, mostly with other large well-established and diversified firms. Such ventures are motivated by such incentives as cost sharing, risk sharing, group learning, and strengthening the commercialization strategy through economies of scale, scope, logistics, and procurement.

Large European firms, including French ones (like Rhône-Poulenc), have competed with their American counterparts in taking over U.S. DBFs that have developed new technologies to the point of marketing them. There have not been many takeovers of French DBFs because there are so few of them and because their market potential is so low.

Conclusion

Despite the substantial progress made in increasing French scientific and technological competence, many problems remain to be solved. Perhaps most tellingly, there is still not much incentive for a competent French scientist to form a company: In the French scientific community, entrepreneurship is ranked below scientific prowess; there is great uncertainty and difficulty associated with finding finance and organizational help to create a startup; and French banks and large French companies continue to interact more with the American companies than with the local French ones. Continued government involvement is called for because unless the tide is turned, this situation will be detrimental, in the long run, to national competitiveness.

References

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