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PASTEUR BIOTOP : AN INFECTIOUS BUSINESS DESIRE

by

Pascale Altier
Director, BioTop,
the Pasteur Institute's business start-up incubator

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Report by Élisabeth Bourguinat
Translation by Rachel Marlin

Overview

In December 2000, the Pasteur Institute created Pasteur BioTop, a company incubator, whose purpose is to commercialise the Institute's patents by helping create start-ups. This organisation, which employs very few people, functions very closely with other bodies in the business development and technology transfer department (*DARRI* in French) which carry out scientific co-ordination, provide a service for patents, inventions and technology transfer, and also handle industrial agreements. The Pasteur Institute automatically holds a stake in the capital of each start-up, but it is the revenues from licenses sold to start-ups which motivate the Institute. In total, of the 16 businesses which BioTop helped to develop, two of them were floated successfully on the stock exchange, a third failed to be floated, and only one went into voluntary liquidation. These surprising outcomes are the result of the incubator's very clear objective of commercialisation, as well as the care BioTop takes in choosing and implementing projects.

TALK : Pascale Altier

The Pasteur Institute employs 2,600 people and had a budget of 233.2 million Euros in 2007. 43 % of its financing comes from the activities it generates itself (such as royalties, research contracts, services provided, and expertise) ; 30.3% from patronage and income from its assets ; and 26.7 % from State subsidies. The State subsidies are diminishing every year which is why it is important to commercialise patents in order to create business income.

After an initial professional experience at Bio Critt Île-de-France, I devoted myself to business creation and technology transfer when I started working at Genopole® Entreprises. I have been in charge of BioTop, the Pasteur Institute's business incubator, since 2001. Like Bernard Maître (president of CEA Valorisation and a venture capitalist), I am convinced that 'the creation of a company is probably one of the most elaborate manifestations of great modern-day adventures.' This does not mean in any way that it is a pushover. I share the opinion of Bernard Daugeras' (a scientist, turned venture capitalist) that 'one does not create in bliss, but when one can no longer live with one's contradictions'. For example, when one can no longer tolerate the head of the laboratory or when one has had enough of being criticised by one's mother-in-law for not earning enough money.

The Business Development and Technology Transfer Department (*DARRI*)

Pasteur BioTop's incubator is one part of the Business Development and Technology Transfer Department (*DARRI*) which is part the Pasteur Institute's general management. The *DARRI* has four departments. The Scientific Coordination department is directly in contact with scientists. It 'spreads the word' about industrial applications : it encourages researchers to publish, but particularly to register patents before publishing, it urges them to obtain industrial contracts, and it welcomes PhDs and post-doctoral students. It is often members of this department who identify the researchers who are ready to launch their own start-ups, and advise them to meet me.

The second department is the Office of Patents and Inventions. It verifies invention descriptions and is in charge of registering patents and applying and defending them. The objective of the third department, the Office of Technology Transfer, is to commercialise patents by means of license contracts and R&D. Lastly, the Office of Industrial Agreements has an 'after-sales service' responsibility, and checks that the manufacturers, who have signed contracts with the Pasteur Institute, have fulfilled their side of the deal.

How it all came about

In 1999, Claude Allègre, the French Education minister spread the well-known law on innovation and research which allowed researchers to create their own companies. A year later, he launched an invitation to tender for the creation of certified business incubators. Since the Pasteur Institute is a private foundation, it could not apply for the invitation to tender. However, Philippe Kourilsky, the Institute's director at that time, wanted to promote the Institute by equipping it with an incubator. An international benchmark showed that the most successful method was to set up an incubator on the research campus so that it was in contact with all the scientists, and had access to all the human and technical resources available. These conditions were agreed, and the Pasteur BioTop incubator was launched on the Institute's campus in December 2000. I was recruited two months later.

Three contracts

The Pasteur BioTop incubator is really designed as a tool to commercialise patents. We only welcome companies which promote the Institute's scientific areas of expertise.

The partnership between the Institute and companies it welcomes is based on three types of contracts. The first is a license contract which allows companies to use our patents.

The second is an agreement with the shareholder. By ceding its patents to a start-up, the Institute takes a considerable risk, when one considers the percentage of failures when companies are created : it would obviously be much less risky to give a license contract to a large, well established pharmaceutical company. In order to compensate for this risk, the Institute holds a financial stake in the company of between 15 and 30 %.

The third contract is the provision of an incubation service which will allow the company to use the premises and have access to all the technical platforms.

How the incubation is established

The pre-incubation phase is by far the longest phase. It covers the period when the person in charge of the project comes to see me for the first time until the creation of the company. During this stage of project development, I ask all the other departments of the *DARRI* to analyse the market, study whether any other of the Institute's patents could strengthen the company's portfolio, maybe even carry out further studies on the possibility of using the patent, the company's strategic positioning, its business plan, and so on. Eventually, the different pieces of the jigsaw fall into place and then I can judge whether the conditions are sufficiently viable for the company to be created or not.

When the project appears to be ready, it is submitted to the Institute's selection and monitoring committee. This is made up of experts at the Institute and other scientists who have all been involved in the creation of companies. Following the presentation, the committee either accepts the project, refuses it (if it does not appear likely to create sufficient value), or asks the project manager to revise it.

Once the project has been endorsed, we start preparing the three contracts which I have mentioned. When this last stage has been completed, the project manager has the right to set up his offices in the Pasteur BioTop building where pre-equipped premises await him, as well as platforms which he will share with three other companies on the same floor.

A supporting role

The researchers who come to see me are not looking for a scientific guarantee, but for someone who can listen to them, and who can supply them with a network and information about areas which are unfamiliar to them. I am what inhabitants from Quebec refer to as a 'marginal secant', in other words, someone who can serve as a link between the entrepreneurs, the venture capitalists, and the lawyers. I must listen to them, but I am also aware that in the beginning they do not know what their needs are. I have to set them on the right track gradually, because they cannot assimilate all the information at once : information diffuses progressively, like tea from a tea bag plunged into boiling water. I deliberately suggest training programmes, in particular HEC's Challenge programme which helps new entrepreneurs learn about the various functions of a company. Even if they are never going to be the financial and administrative director nor in charge of the intellectual property of their future company, they still should know the vocabulary so that they can talk intelligently with people whom they may recruit in the future.

For my part, I have to learn the vocabulary of their area so that I can understand better the kind of company which can be created with the technology they can offer. The most important factor in this approach is to establish trust, which the inhabitants of Quebec call the 'bandwidth of knowledge'. Trust is all the more necessary because when one is a research scientist, becoming an entrepreneur is like committing a crime. Once mutual trust has become established, these future entrepreneurs can come into my office whenever they want and pour out their problems to me, but also share their good news, which is just as important.

A few examples

Since December 2000, we have assisted in the creation of fifteen companies. The sixteenth is currently being launched. I shall present three companies which have very different scenarios.

Cellectis was created in December 1999 by a Pasteur scientist, Dr. André Choulika, who studied the molecular genetics of yeast. He did his post-doc in the United States where he acquired a taste for enterprise. He came to my office of his own accord and explained that he had registered a patent which he thought presented a great opportunity for creating a company. He said he knew exactly what to do because he had thought about it ever since he had registered the patent. Today, having floated Cellectis on the stock exchange, André Choulika is still in charge. He is both an excellent research scientist and a brilliant manager. Both of these characteristics make for quite an exceptional entrepreneur.

BT Pharma was founded in October 2001 by Dr. Benedikt Timmerman who was not a Pasteur scientist, but was interested in one of our patents. He sought a license contract and asked if he could use the incubator. His company develops different types of vaccines against cervical cancer, cancer of the lungs and digestive system, and some infectious diseases. Having received help from business angels, he has just managed to raise funds from venture capitalists.

Texcell was created in 1987. It is a spin-off from the Pasteur laboratory and provides services for the pharmaceutical industry and biotechnology companies. The transformation of this laboratory in 2002 into a public company enabled it to be more reactive with regards to its clients and opened up new prospects of development.

In total, of the 16 companies in the incubator, there was one voluntary liquidation and two successful flotations on the stock exchange. A third company just failed being floated.

DISCUSSION

A surprising success rate

Question : *Your surprisingly successful results can probably be explained by a draconian selection process. How many projects have you reviewed in total ?*

Pascale Altier : We have looked at about sixty projects and we are indeed very selective. The Pasteur Institute's aim is not to help economic expansion. We are very pleased when we create companies and jobs, but our number one objective is to make money. We avoid taking risks with companies which we think would not be able to develop their technology, as such a delay might suspend the patents which we could only get back after the bankruptcy petition is filed and they would not have many more years left to run.

Creation of jobs

Q. : *How many jobs have these companies created ?*

P. A. : Cellectis, which is located in the Biocitech business park on Aventis' former site at Romainville, has about thirty employees like Hybrigenics, which is situated in the 14th arrondissement in Paris. Texcell is in the Genopole® in Evry and has about fifteen employees. Diatos, which failed to be floated on the stock exchange, had to make a choice between the subsidiary which it had developed in Belgium and what remains of its R&D department in France. It employs about fifteen people. Ariana, which has about ten employees, raised funds this summer and has recently moved near the Institute, in the 15th arrondissement. BT Pharma employs about fifteen people, as does Theraptosis which is in the Biocitech business park. Anaconda employs five people and has set itself up in the Paris Bioparc. Theravectys, like GenomicVision, is still in our incubator : each employs about ten people. Finally,

Cognium System is a very small company with three employees.

Benefits for the Pasteur Institute

Q. : *What was the return on investment for the Pasteur Institute for creating these companies ?*

Alain Guédon (director of the *DARRI*) : *The Institute's stake in each company's capital ranges from 25 to 30 % of the initial capital but since we do not generally participate in the subsequent pools, the stake diminishes with time and may fall to 10 or even 5 %. According to an estimate based on the latest fundraising, our stake has a total value of between 10 and 15 million Euros.*

P. A. : The commercialisation of companies which we support is the 'icing on the cake'. What we expect, above all else, are revenues from licensing contracts but if we can also earn money when they are floated on the stock exchange, it is even better.

Q. : *What is the annual budget of the incubator and what is the annual revenue of the licensing contracts ?*

P. A. : The annual working budget for the incubator is about 100,000 Euros which covers studies and external consultancies which are necessary for the creation of each project, and all the expenses associated with my job (such as business trips, conferences, seminars, training and so on).

A. G. : The vast majority of the companies that we are talking about are less than 7 years old, and therefore are very young for this sector. They have not yet launched any products on the market, and for the most part, it is their service activities which so far have enabled them to survive so we cannot expect very high returns in the near future. Our policy of commercialisation of patents is a more long-term project. Having said that, they have already brought in between 1 and 2 million Euros per year, which is far from negligible by comparison with the Institute's budget. These sums are likely to increase even more in the coming years.

P. A. : If one works with a pharmaceutical company, it takes between 8 and 10 years from the moment of creating the company to the time that it markets a medicine. However, as we often give out exclusive licenses with the right to sub-license, companies can sell this right and reap the revenues without waiting for a market launch.

Pre-incubation

Q. : *I imagine that you have in-house experts who are capable of assessing the technologies presented by your researchers, but how can you be sure that there is a market for the products envisaged ?*

P. A. : The pre-incubation period lasts between 12 and 18 months. Most of the time, when a researcher comes to see me, he still has to validate some scientific findings, or even has some additions to make to his patent. During this time, I meet with the people in charge of the technology transfer department. They know the market, and can give an opinion on the potential of the proposed technology. I also consult external experts.

Some days ago, two Pasteur researchers gave me a company project to look at. My colleagues confirmed that the screening methods they were perfecting were very interesting. I sent an article that these researchers had written to an external expert. He agreed that this technology will certainly be used in the future but he does not think it is enough to create a company. I now have to report back to these two researchers and suggest to them that they provide additional services, or a mixed model which incorporates both a screening platform and the development of their own molecule. We will work together for 12 to 18 months to develop a business model and try to devise the sort of company which could be created.

A. G. : Initially the business plan is only two or three pages long, and is entirely scientific. Pages are added gradually so that it becomes a document which will enable one to judge whether it is possible to launch a process of business incubation or not. The pre-incubation period also helps one to realise whether the project manager is capable of creating a company and running it.

The candidates

Q. : *How do you identify the potential entrepreneurs ? Do you expect them to come to see you, or do you seek them out in the corridors and the cafeteria ?*

P. A. : Most of the time, it is the scientific coordination department which gives out information about the incubator. Its head, Daniel Larzul, encourages researchers to come to talk to me. Some come and see me spontaneously to present their project, but this is unusual. Sometimes former Pasteur scientists, who themselves have created a company, encourage their colleagues to do the same. It is obvious that not everyone on the campus knows that the incubator exists, and some do not even want to hear about it, because they are very interested in fundamental research and think that moving into applied research would too much of a deviation.

A. G. : The transition from the laboratory to the business world is seen by many as moving out of line and therefore there are many barriers which have to be removed.

Q. : *Does the creation of a company always come from an individual's initiative, or do you ever decide that a specific patent justifies the creation of a company ?*

A. G. : The creation of a company always combines two aspects. It is out of the question for us to decide to create a company, and then look for someone to take on the project. However, we can benefit from certain opportunities. Recently, an excellent research scientist had reached retirement age, but had no wish to leave the Institute. We suggested that he create a company based on the research that he had carried out. Since he was a doctor, he was very keen to develop a medicine. We spent days and nights helping him draw up a business plan. Today, he has made it his own, and we are currently in the phase of looking for a licence agreement.

Researchers and managers

Q. : *In your model, it seems that it is always the researcher who becomes the company manager. Elsewhere, the researcher continues with his research and other people take on a more operational role.*

P. A. : Both scenarios are possible. André Choulika clearly had both qualities. Other people prefer to rely on someone else as a manager. The founder of Genomic Vision wanted to stay in his lab, and so we had to find him a partner. During the first pool, the venture capitalist said 'You are the key person. If you do not take part in the company, we won't sign the cheque.' He spent a few sleepless nights before making the decision. Today he is delighted. The second meeting took place last summer.

No sale of patents

Q. : *How do you decide between taking out a contract or the choice to selling the patent ?*

P. A. : We never sell our patents. They constitute a sort of guarantee for the companies and their investors. If necessary, we will not hesitate to file law suits for patent infringement, or spending millions of dollars on the other side of the Atlantic to defend our patents, which a new company might not be able to do if it is up against an important pharmaceutical company.

Assessing patents

Q. : *What do you think of the methods used to assess patents ?*

A. G. : We are currently equipping ourselves with a 'proof of concept' fund which will enable us to invest large amounts of money (between 500,000 and 1.5 million Euros) in the initial part of the project. We are being helped by a venture capitalist. Each of us has agreed to contribute 50 %. Bankers are always trying to develop models which do not only try to look to the future, but attempt to predict it. Even though I began my career in finance, I do not believe in these models at all. I only believe in matching up an offer with a demand, which admittedly, may be subject to a great number of hazards. However, the risk is not the same if the product is aimed at a market of about one billion dollars or just sixty million. Apart from these very generalised considerations, I do not believe in models at all.

A very small structure

Q. : *Could you tell us more about the incubator's' black box' How many people work there, what are their qualifications, how do they divide up the tasks ? I get the feeling that it is all a bit mysterious…*

P. A. : It may seem to be a bit mysterious because I work alone with my assistant, but I constantly rely on the other departments of the *DARRI* and the Institute. I also resort to external experts including lawyers (regarding the legal status of future companies), business angels (for finding the initial funds), and so on. I am a sort of conductor who can call upon different instruments in the orchestra according to what is necessary.

A. G. : The approach is subtle, attempting to provide the client with the means to make his own choice. The aim is not to replace the project leader, but to put forward conditions which would be most appropriate for his company.

Q. : *Do you receive public subsidies, for example, from the region or the State ?*

P. A. : As a private foundation, we cannot receive subsidies intended for public incubators. However, I have occasionally benefited from the financial support of the *DRIRE* (*Direction régionale de l'industrie, de la recherche et de l'environnement* : French governmental body for industry, research and the environment) to set up a group training programme for incubated companies.

Mutualisation and synergies

Q. : *If a symphony orchestra plays in front of a single spectator at each concert, the economic model is not very profitable. Do you manage to share a certain number of services or create some degree of mutual help programme between the incubated companies ?*

P. A. : Each entrepreneur has his own project, its problems, his ego, and it is not easy to share services with anyone else. Once they are in the incubator, they have to use shared equipment : this is an initial form of mutualisation, in other words using the same material and sharing the costs. Additionally, once a month I organise information meetings with external experts. Each company has the opportunity to talk about its difficulties and these exchanges of experiences are very valuable. When there are practical questions such as 'How do I insure my premises so that I can launch clinical tests ?' or 'What collective labour agreement should I choose ?', I often advise them to talk to former Pasteur scientists who, like them, left the laboratory and created their own companies. It is easier to trust someone who has had the same experience as oneself. The former Pasteur scientists play the game and in general are delighted to help. We are now thinking about formalising this process of mutual support by creating a club of ex-Pasteur scientists who have become entrepreneurs, and asking them to become tutors to the newest entrepreneurs.

Q. : *Are there marketing or business synergies between the different companies ?*

P. A. : I tried to create some, but I failed completely. Since new companies are short of funds, I thought it would be very useful to share the business development or the management of human resources, but I was met with a categorical 'no'. The reason given was lack of confidentiality, even though these companies work in very different sectors. I thought it was perfectly possible that the same business developer could sell the services of a meganuclease for one company, while looking for prospects for the central nervous system for another, but I was wrong. People did not want to share their knowledge and products with anyone else. Therefore I abandoned the idea.

Cutting the apron strings

Q. : *How do you manage the moment when you effectively cut the apron strings ?*

P. A. : Very badly ! I am an 'abusive mother' and I do not handle separation very well. Seriously, though, in principle, we can only open our doors to companies for two years. If it were any longer, we would have to have a commercial lease. After 23 months though, it is obvious whether a biotechnology company is mature enough to stand on its own two feet. When it is possible, we let them stay a little longer. When the company has left the incubator, it does not mean that our relationship comes to an end, since the companies still hold our licenses, and we hold part of their capital. The managers generally come to see me whenever they feel the need, and if they do not, I take the initiative and ask them if they need my help.

Links with the original laboratory

Q. : *What is the relationship between the creator of the company and his original laboratory ?*

P. A. : Generally speaking, the ties remain very strong. When we sell a license contract, we try to sell it with a R&D contract because it is always very beneficial for the company who owns the license to profit from the follow-up and the improvements brought by the original laboratory. Recently, a company was created by a researcher who was also the director of his laboratory. He negotiated a contract with the management which allowed him to work 80 % of his time for his laboratory and 20 % for his company. This helps the Pasteur Institute because it makes for a smoother transition. At the end of the incubation period, he will have to make a choice : either to leave Pasteur definitively, or to go back to his research in the knowledge that his company is on the right tracks.

Projects which have been rejected

Q. : *You mentioned that about sixty projects had been reviewed and only fifteen had been accepted. Is it not difficult for project managers to deal with this failure ? What is it like for them when they go back to their laboratories ?*

P. A. : We tell the project managers of our decision very quickly because when one creates a company, time is of the essence. This is also the case when the decision is negative. This may be because the scientific coordination department gave a lukewarm verdict, or because the analysis of intellectual property, or the possibility that the patent highlighted difficulties, or because we did not find the team very convincing. Each time, we explain very clearly why we reject the project. If the project manager still wants to try his luck, I suggest other incubators, and explain to him why we do not support this project. Sometimes, it is because of internal strategy. In any case, we have very little space available : if other incubators are able to welcome projects from the Pasteur Institute, then we are delighted for them.

Relationships with the other investors

Q. : *Are you ever in conflict with other investors, for example, when you draw up the shareholding agreement or in pool discussions ?*

P. A. : The shareholding agreement is generally drawn up by the Pasteur Institute legal department. Often investors negotiate certain clauses which they do not understand. One such clause, for example, states that every new arrival should ask our authorisation beforehand. In the past, a laboratory to whom we refused to give a license had tried to get it back by taking a stake in the capital. We no longer want to be faced with a similar situation. When we explain this to them, the venture capitalists generally understand this very well. As far as we are concerned, we can compromise on a certain number of points because it is in our interest to do so, as is the case for the company, so that the transaction takes place. Up to now, we have never been faced with talks which have broken down.

Q. : *In any case, you are majority shareholders ?*

P. A. : No, we are minority shareholders from the very beginning. We think it is very important that the project manager has the majority because this makes him extremely motivated.

Institutional multi-membership

Q. : *A certain number of laboratories at the Pasteur Institute are 'mixed' units. Can researchers from INSERM (the French National Institute for Health and Medical Research) or the CNRS (French National Centre for Scientific Research) take part in these 'mixed' units ?*

P. A. : Only one of the projects which I supported was the brainchild of a CNRS researcher and a member of a Pasteur unit. Because he qualified for the Allègre Law (which allowed researchers to create start-ups and register patents), he could still be paid his salary during the creation of his company, whereas his associate, a true Pasteurian, had to take a leave of absence and give up his salary, which caused some tension. At the end of the day, the CNRS researcher became the company manager and the Pasteurian scientist simply took a stake in the capital and remained in his laboratory. If in the future, there were other 'mixed' projects, we would undoubtedly try to find a solution to handle these problems.

Q. : *Where does the concept of intellectual property stand in this sort of set-up ?*

P. A. : We are lucky to have an excellent reputation in terms of commercialisation and in the case of double trusteeship, we are generally in charge of defending the patents. We are mandated to commercialise patents for INSERM, the CNRS, and Paris 6 and Paris 5 universities. When we create a company on the basis of a patent depending on a double trusteeship, the procedure takes place in the context of these mandates.

What is the secret ?

Q. : *Your results are remarkable, especially if you compare them to other incubators which sometimes have much larger working budgets and do not make as much profit in such a short space of time. In your opinion, why are the results from other incubators so disappointing ?*

P. A. : My answer to this question is purely personal. Pasteur BioTop is forced to create value which means that we have to be extremely selective and vigilant. Some incubators, which are sometimes substantially financed by public authorities, have to produce activity reports which, paradoxically, encourage them to promote quantity rather than quality, for example, in terms of the number of companies which have been created. However, the longevity of these companies is not always guaranteed. This is not the case at Pasteur BioTop where we are accountable to no-one, but we have an obligation to produce results.

Presentation of the speaker :

Pascale Altier : began her professional career in charge of marketing at INOTEB, a start-up specialising in bone substitutes. She then worked for ten years at Biocritt, specialising in technology transfer applied to the biomedical sector. Afterwards, she joined the Genopole® in Évry when it started. She has been in charge of the Paster BioTop incubator since February 2001.

Translation by Rachel Marlin (rjmarlin@gmail.com)