Paper to be presented at the DRUID 2011

on

INNOVATION, STRATEGY, and STRUCTURE -
Organizations, Institutions, Systems and Regions
at
Copenhagen Business School, Denmark, June 15-17, 2011

What influences the survival of Canadian biotechnology firms

Catherine Beaudry
École Polytechnique de Montréal
Mathématiques et génie industriel
catherine.beaudry@polymtl.ca

Joël Levasseur

joel.levasseur@polymtl.ca

Abstract

This article aims to determine the factors that influence the survival of biotechnology firms in Canada. Certain attributes, such as collaboration, research and development, intellectual property, product management and financing are examined. Our research finds that firms that collaborate for exploration purposes have better chances of survival than others. Acquisition of knowledge by collaboration seems to be essential to innovation in the biotech industry. Results also suggest that a larger number of patents decreases the probability of survival. Investigation of the product development process shows that clinical research also requires a lot of resources which has the result that firms enter the production and commercialisation stage in a weak position, which may then result in firm exit.

Jelcodes:L00,-

What influences the survival of Canadian biotechnology firms

Abstract

This article aims to determine the factors that influence the survival of biotechnology firms in Canada. Certain attributes, such as collaboration, research and development, intellectual property, product management and financing are examined. Our research finds that firms that collaborate for exploration purposes have better chances of survival than others. Acquisition of knowledge by collaboration seems to be essential to innovation in the biotech industry. Results also suggest that a larger number of patents decreases the probability of survival. Investigation of the product development process shows that clinical research also requires a lot of resources which has the result that firms enter the production and commercialisation stage in a weak position, which may then result in firm exit.

Key words: survival, innovation, collaboration, biotechnology

1. INTRODUCTION

This article aims to determine the factors that influence the survival of biotechnology firms in Canada. Survival of biotechnology has been studied for many years with different samples, for instance dedicated biotech firms (DBF) or the human health firms (HH). The novelty of this article is certainly the data used, collected by Statistics Canada with its Biotechnology Uses and Development (BUD) surveys, which is considered by Statistics Canada as a census of all biotechnology enterprises in Canada, from the small to the large firms and in all the different sectors of biotechnology. Many survival factors have also been studied by a number of scholars.

Some studies focus on **collaboration**. As raised by Powell (1996), when knowledge is both complex and expensive, as it is in biotechnology, and expertise sources are dispersed, innovation is generated in learning networks rather than within firms. Baum (2000) hence shows that firms raise their performances through alliances, in organising an efficient network to acquire knowledge and competencies at lower costs, and in forming partnerships with rival firms to decrease risks.

Other studies focus on **managerial** aspect. Evans (1987) shows that age and size increase probability of survival. Most recent studies suggest that the rate of size variation was more influent than the size by itself on firm survival (Agarwal, 1996; Cefis and Marselis, 2005). The quality of the managerial team also has been related to survival rate by other studies (Foss, 1997; Foss and Knudsen, 1996; Hamel and Prahalad, 1994). Woiceshyn and Hartel (1996) suggest that firms with complete managerial teams, composed with the four fundamental functions that are finance, R&D, production and marketing, have more chance to survive than others.

Other studies concern the impact of **innovation** on survival of firms. Audretsch (1995) shows that firms in an innovative cluster survive longer. Christensen (1998) and Banbury and Mitchell (1995) show that innovative firms, which are measured in number of patents, have a greater probability to survive. For the intellectual property aspect, Thumm (2002) suggests that patents are an incentive to R&D in biotech, serve as an argument for alliances between firms, and are necessary to obtain venture capital. In regard of the product development process, Schoonhoven, Eisenhardt and Lymman (1990) show that developing a portfolio of new products is necessary for biotech firms to allow rapid cash entries and to obtain an extern visibility and to increase survival probability.

About the **financial aspects**, other studies show that a lack of funding increases the probability of exit (Carpenter and Petersen, 2002; Becchetti and Trovato, 2002). Audrescht (2004) concludes that in a market only composed by traditional bank funding, high tech firms will suffer lower performance than those with access to venture capital. Other studies (Cressy, 2000; Hurst and Lusardi, 2004) suggest that the lack of funding is in fact the symptom of a deeper problem that is the lack of innovation or collaboration.

Based on the literature of firm survival, this article aims to determine the factors that influence the survival of biotechnology firms in Canada. The objective is to establish recommendation on the collaboration, the managerial aspects, the intellectual property, the product development process and the financial aspects. We build a survival model, based on the proportional hazard model introduced by Cox (1972), to determine the factors that contribute to the survival of biotechnology firms in Canada. Characteristics such as size, origin, contracts, IP, collaboration, financing, product development stage, tax credits, etc. are examined.

The remainder of the article is organised as follows: the second section presents the theoretical framework for our study, the third section describes the methodology used, the fourth section present

a brief portrait of the evolution of biotechnology in Canada, the fifth section analyses the regression results, and finally the sixth section concludes.

2. THEORETICAL FRAMEWORK

Collaboration

As raised by Powell (1996), when knowledge is both complex and expensive, as it is in biotechnology, and expertise sources are dispersed, innovation is generated in learning networks rather than within firms. Baum (2000) hence shows that firms raise their performances through alliances, in organising an efficient network to acquire knowledge and competencies at lower costs, and in forming partnerships with rival firms to decrease risks. Collaborations are common in biotechnology since they contribute to spread both the costs and risks related to research. Moreover, collaborations allow the establishment of a pool of multidisciplinary knowledge that benefit all collaborators (Woiceshyn and Hartel, 1996).

More recent literature examines alliances as sources of funding. Robinson (2002) draws the similitude with alliances between new small biotechnology firms and large pharmaceutical companies. In addition to the stage investment and convertible shares, regulation is often dealt with by an executive committee. In contrast to venture capitalists that provide funds, however, the large pharmaceutical enterprises sponsor projects through strategic alliances. So in addition to alleviating the asymmetric information problems, alliances may also lessen the problems linked to the multitask nature of biotechnology and to supply a range of tools and competencies. Furthermore, large pharmaceutical companies provide the knowledge necessary to the exploratory phase, the R of R&D, and to direct the product on the market in the exploitation phase, the D of R&D (Rothaermel and Deeds, 2004).

Moreover, collaborating through alliances brings a number of benefits other than funds. Baum *et al.* (2000) show that firms reduce their 'liability of newness', i.e. the risk of new firm exit, by entering into alliances with well established firms. Oliver (2001) also suggests that biotechnology firms with fewer alliances face higher exit rates. Rothaermel and Deeds (2004) further confirm that collaboration for the purpose of 'exploration' is beneficial to both small and large firms as it facilitates knowledge acquisition. This is consistent with Powell (1996) who states that the importance of collaboration is due to the very nature of knowledge in biotechnology. Rothaermel and Deeds suggest that collaboration for the purpose of 'exploitation' is beneficial to large firms because it allows a better alignment between discoveries and the market. Niosi (2003) however warns that small enterprises that collaborate too soon, regardless of the reason for the collaboration, risk harming their performances. In light of these arguments, our collaboration hypothesis is subdivided into three hypotheses distinguishing the type of collaboration:

- H1 (Collaboration): Biotechnology firms that collaborate for exploration purposes (a) or exploitation purposes (b) have a greater propensity to survive.

Innovation and R&D

Certain firms focus their innovation strategy on the elaboration of scientific knowledge closer to research than to development. The OECD (2009) also emphasises the emergence of development in the research activities of certain firms aimed at developing a technological portfolio. Moreover, the emergence of the biopharmaceutical model is mainly due to the desire of large pharmaceutical companies to diminish the risks related to the R&D projects that are increasingly exploratory and thus risky. Rosenberg *et al.* (1994) show that the presence of R&D projects within firms increases their

knowledge absorptive capacity. The factors of innovation therefore have a role to play on firm survival, which brings us to our fourth hypothesis:

- H2 (Research and development): Biotechnology firms that invest the most in R&D have a lesser chance of exiting the market.

A number of studies have devoted their attention to the importance of innovation as a survival factor. For instance, Audretsch (1995) shows that an innovative environment may constitute an entry barrier if new firms are not able to adapt to it. Once firms have past the first critical stages of survival, and have thus adapted to their innovative environment by becoming themselves very innovative, they have a tendency to survive longer and to grow faster. Audretsch justifies this relation from the product differentiation emanating from innovation that constitutes a considerable competitive advantage on the market. Christensen (1998) as well as Banbury and Mitchell (1995) demonstrate that the most innovative firms, measured in terms of number of patents or new products, have a greater survival probability.

A firm's IP protection strategy constitutes an important decision, especially in biotechnology because of its crucial role in the appropriation of innovation. Grabowski (2002) writes that a few hundred millions of dollars are necessary to discover, develop and have a new drug pass all approval stages. Furthermore, DiMasi and Grabowski (2007) show that the acceptation and homologation process of new drug costs on average 559 million US dollars (2005 constant dollars) on top of the 1,241 million US dollars required in investment. It is thus clear that the biotechnology R&D process is extremely costly. In addition to these costs, the firm must face the menace of generic drugs that only require a few million dollars to develop and have approved. It is thus imperative that firms appropriate the benefits from their innovations. For all these reasons, Grabowski (2002) suggests that patent protection is much more important in the biotechnology and pharmaceutical domains than in other sectors. Patents seem to be a priority tool to alleviate the appropriation problem as well as to face the danger from imitators.

- H3 (Intellectual property): Biotechnology firms that possess patents are better equipped to survive.

And because IP is intrinsically linked to the products in this domain, we add the following hypothesis:

- H4 (Products): Biotechnology firms possessing a greater number of products closer to commercialisation have a better chance of survival.

In a highly innovative domain such as biotechnology, it is however important to take in consideration not only the innovation intensity but also the quality of the innovation process. Hall (2001) hence suggests that the regulatory system is the greatest innovation barrier for Canadian firms. The Organisation for Economic Co-operation and Development (OECD, 2009) also recognises the presence of two predominant business models: producers and service providers. First, the producers concentrate their activities on the production of biotechnology products. The typical firms are small and medium enterprises (SMEs) and multinational enterprises (MNEs) with diversified activities, i.e. not concentrated in a sole sector, that have acquired a certain know-how in the production of intellectual property (IP) internally developed or bought through licenses.

Second, the typical firm of the biopharmaceutical model refers to service firms that specialise in using their know-how in support to other firms (OECD, 2009). These firms are often employed via contracts to contribute to the R&D of more important firms, such as other biotechnology firms of the producer type or pharmaceutical enterprises. An important aspect of these firms relates to the fact that more often than not, the fruits of the R&D process, particularly the IP, do not belong to the firm itself but to its clients. Furthermore, services providers must be considered as they operate closer towards

research than development, rendering traditional innovation measures, such as patents and/or products, not representative of the firms' research efforts. The number of contracts in which a firm is involved may better capture this research effort:

- H5 (Contracts): Biotechnology firms that generate more revenues from its contracting activities have a better chance of survival.

Management, human resources and strategies

Human resources that compose an enterprise are an important element of consideration because those people are involved in decisions that will directly impact on survival of the firm. Woiceshyn and Hartel (1996) suggests that biotech firms with complete managing teams, composed of the four principal functions that are finance, R&D, production and marketing, obtain better sales results then those with incomplete teams. That implies, in a strategic optic, that firms would have advantage to diversify the managing team. The quality of the managing team also was considered by Foss (1997) to explain the survival of firms while Woiceshyn (1993) examined specifically the biotech industry. These papers suggest that survival of the firm depends on the quality of the managing team, and most specifically on its capacity to conduct R&D. Bagchi-Sen and Scully (2004) suggest that the difficulty of firms to employ qualified workers was the most important factor that affects the innovative capacity in the Canadian biotech industry. On the same optic, Deeds (2000) shows that the percentage of managers with PhDs has a positive impact on development of new products. Hall and Bagchi-Sen (2002) suggest that the lack of employees in marketing functions is a barrier to innovation for Canadian biotech firms and also conclude that marketing knowledge has a positive impact on firm's performance. To control for size effect, the proportion of employees for each different function is used rather than the number of employees and because of multicolinearity, the proportion of employees dedicated to production is neglect in this study.

- H6 (employees): Firms with a high proportion of R&D employees (a), managers (b), employees dedicated to regulation (c) or employees dedicated to finance and marketing (d) have a better chance of survival

Biotechnology funding and support

The biotechnology 'industry' is characterised by very risky R&D, spread over a long period of time where a number of steps are necessary for the emergence of a new product (Kellogg, 2000). R&D costs are thus high and represent a high entry barrier. This R&D necessitates knowledge sharing which raises a number of interrogations regarding its financing (Revest, 2007), which has a direct effect on the durability of the sector.

A new enterprise evolves through a number of phases (Hall, 1992; Gompers, 1995). The very first investments come from the founders. In the order of a few hundred thousand dollars, these first funds contribute to making the firm attractive to external investors. Of these firms, only a few will survive because of the risky nature of the investment (Prager, 1999). According to Zorgati (2006), within the first year, firms start their external funds search in order to begin their expansion. During the second or third year, a second round or financing is launched by firms that continue to grow and within five or six years, the firm will aim for an initial public offering (IPO). Once that step is reached, firms have access to capital at a better rate and to greater amounts as well (Deeds, 1997). Mergers and acquisitions remain a viable exit strategy for firms with financial difficulties (Danzon, 2004).

Historically, as stated by Murray and Schiff (2004), three sources of external funds have sustained the biotechnology industry: capital markets (public and private stocks, debt), corporate partners and governments. Because of the asymmetric information problem, however, biotechnology funding diverges for the normal funding cycle of more traditional industries. This asymmetry of information

between entrepreneur and investor is detrimental to financing because of agency costs (Jensen and Meckling, 1976, Berger and Udell, 1998). According to Lerner (2003), these information problems are more important in the beginnings of a firm because it possesses little information to convince potential investors. It is thus very difficult for new firms to approach traditional funding institutions because it is limited to the types provided by banking institutions. To the asymmetric information problem one can add the concept of risk linked to the nature of R&D. Senker (1998) considers biotechnology as one of the most risky business of the modern economy. Baeyens (2006) explains this by three reasons: first, biotechnology enterprises have a greater probability of death; second, they necessitate a lot of funds over long periods of time; third, the asymmetric information problem and the risky nature of the industry make the traditional financing tools little applicable during the birth period of a firm.

The literature on biotechnology funding points towards two mechanisms to resolve this problem: venture capital and alliances. Audretsch (2004), among others, demonstrate that small innovative firms are more inclined to be financed by venture capital than by banks. This confirms the work of Gomper and Lerner (2001) that suggest that banks are incapable of adequately financing innovative firms, particularly high technology firms. Audretsch even adds that in a market restricted to traditional bank financing, new innovative high technology firms will suffer from an inferior performance to those benefiting from a venture capital market. He then identify four factors that explain the impact of venture capital: First, venture capitalists own part of the firm which acts as an incitation towards its success and spreads the risk; Second, they have a wide technical expertise that allows them, better than banks, to identify projects with great potential; Third, stage investment limits agency costs[1]; Fourth, they guide the firm through its exit strategy, selling their shares to other investors (acquisition) or through an initial public offering (Gompers, 1995; Cummings and MacIntosh, 2002). Baeyens (2006) arrives to the same conclusions regarding the importance of venture capitalists, he suggests that the selection methods of venture capitalists reduce the risks and uncertainties because of their managerial qualities, knowledge of the market and IP protection strategies.

Without being specific to biotechnology, these studies demonstrate that the lack of capital limits the survival probability of firms (Carpenter and Petersen, 2002; Becchetti and Trovato, 2002). Ndonzuau *et al.* (2002) show that European spin-offs clearly suffer from the lack of venture capital and that this is the most important problem for European biotechnology. These firms remain in their infancy compared with US firms because of the lack of funds available during these early years. Other studies (Cressy, 2000; Hurst and Lusardi, 2004) suggest that the lack of funding is in fact the symptom of a deeper problem that is the lack of innovation or collaboration. Our funding hypotheses are therefore:

- H7 (Funding): Biotechnology firms that have succeeded in raising capital from government sources (a), venture capital (b), or debt (c) have a greater chance of surviving longer.

To these private sources of funding can be added a number of public measures that contribute to solving the problems that can emerge between entrepreneur and investor. Information asymmetries may also lead to the social suboptimum problem (Nelson, 1959), when the entrepreneur, or the investor, does not foresee that he will be able to fully appropriate the innovation, i.e. the innovation will yield less than its investment. Consequently, the resulting investment will be below what would be socially desirable. Even in a rich venture capital market such as the US can the socially suboptimum problem persists. Certain innovations may have a great value in term of social good,

[1] In addition, venture capitalists team up with consultants and accountants whose primary role is to insure growth for the firm (Bergemann and Hege, 1998; Gompers, 1995), and whose secondary role of information sharing reduces the information asymmetry problem.

when they represent a poor pecuniary potential. In these cases, private funding is improbable and government intervention is crucial.

To overcome these problems, Enzing *et al.* (2004) identify three mechanisms through which the government can intervene. First, government assistance may take the form of grants, loans with favourable conditions or the creation of venture capital funds. This kind of direct funding takes place during the first few moments of the firms and aim to provide the necessary support for the elaboration of the business plan that will facilitate access to private markets. Second, government may help enterprises to raise private funds by organising networks and entrepreneur-investors meetings. This type of support may also take the form of tax credits specifically dedicated to investment in biotechnology. The third instrument, so called indirect, takes the form of general tax credits that can apply to all firms that satisfy certain criteria, such as the number of employees dedicated to R&D. The goal of these tax credits is to encourage innovative activities within the firm. Our last hypothesis goes as follows:

- H8 (Fiscal incentives): Biotechnology firms that have benefit from fiscal incentive programs have greater chances of survival.

Innovation, R&D, products development, collaboration and finance was analyzed to determinate their impact on the survival of firms. However, ultimately, all those choices should raise revenues for the firm. Different sources of revenue are associated with different states of advancement of the firm. Woiceshyn and Hartel (1996) classified the advancement of the firm in function of the sources that predominantly composed its revenues. The first group is composed of less advanced firms, those that receive funding and have revenues from contracts with large establish firms. The second group is composed with enterprises that license technologies or products, sell R&D products or receive small revenues from products on the market. The third group refers to firms with predominant revenues from products on the market. With this in mind, it's possible that firms do not have the same probability of survival depending of the sources of their revenues because they refer to different states of advancement.

Niosi (2002) suggests that the internationalization of firms was necessary because of the high costs involved in R&D. A growing market enhances potential sales, which allows the firm to benefit from economies of scale. Even in a large market such as the United States, Qian and Li (2003) show that export revenues augment profitability of firms by increasing revenues from sales, which allow rapidly return on investments and the maximization of profits before innovation become obsolete. Because firms that already have a well established distribution network should have a greater propensity to survive, we propose a third revenue hypothesis:

- H9 (Revenues): Revenues from IP rights (a), sales (b), or exports (c) have a positive effect on firm survival.

Importance of the sector

The sector could also be an important factor of firm survival. Giovannetti and Morrison (2000) show that less than 5% of human health's products will reach the clinical research. Hermans *et al.* (2006) suggest that the time between an invention and their arrival on the market is very different between the different sectors, particularly when human health and others are compared. Developing products in human health is much expensive and regulated which implies higher vulnerability. For these facts, HH's firms may suffer of higher exit rates.
This distinction between the three sectors brings the following hypothesis:

- H10 (Sector): Because of the risky nature of the clinical trials necessary for human health biotechnology, firm survival should be negatively affected by this sector.

3. METHODOLOGY

Data

The data used in this study was collected by Statistics Canada. The responses to the four Biotechnology Uses and Development (BUD) surveys[2] of 1999, 2001, 2003 and 2005 have been linked to one another to build a quasi-longitudinal database. This unique database was then merged with the Business Register to assess the yearly status of the firms that responded to the surveys and hence determine the survival or the death of biotechnology firms in Canada over a ten-year period from 1999 to 2009. This additional information allows the distinction between the firms that did not survive in year *t* from those that did not fill the questionnaire. The four surveys in question have never been used in a longitudinal analysis, let alone in a survival analysis.

In the first half of 2009, Statistics Canada merged the four surveys using the unique firm identifier of the Business Register. The status[3] of each firm for each year between 1999 and 2009 was added to the linked BUD survey results to build a quasi-longitudinal database of firm survival. The resulting database allows survival analysis over a ten-year period, from 1999 to 2009. From this merger, four cohorts were identified, used for descriptive statistics analysis, each corresponding to the firms that answered a specific survey. The four cohorts have been merged in order to construct a panel dataset that allows the elaboration of models covering all the surveys in the same model. To control for the repeated occurrences of a certain number of enterprises[4], in the models data was clustered by enterprise.

Model

The model used for this survival study is the proportional hazard model introduced by Cox (1972). This model is well known in literature studying the survival analysis of firms (Audretsch and Mahmood, 1995; Mata and Portugal, 1994; Suarez and Utterback, 1995; Shane and Foo, 1999; Klepper and Simons, 2000a; Klepper and Simons, 2000b; Klepper and Simons, 2005). The Cox model estimates the probability of the occurrence of an event (death) at a time *t* based on *k* regressors x_k. The following model describes a hazard function of the individual *i* and a *k*-vector of explanatory variables $X_i = (x_{i1}, x_{i2}, ..., x_{ik})$

$$h(t|X_i) = h_0(t)\exp(\beta'_x X_i)$$

$$h(t|x_1, x_2, ..., x_k) = h_0(t)\exp(\beta_1 x_{i1} + \beta_2 x_{i2} + ... + \beta_k x_{ik})$$

where $h_0(t)$ is the common basic hazard function and $\exp(\beta'_x X_i)$ is a parametric hazard function where β' is a *k*-vector of coefficients.

Because surveys were not originally built for longitudinal study by Statistics Canada, enterprises were not necessarily observed in all four surveys, this results in interval truncation of the independent variable. Furthermore, because the information about survival or death comes from the Business

[2] Each BUD survey is carried out in two steps. A first questionnaire is sent to the Canadian enterprises that are potentially capable of using or developing biotechnology, in order to identify the reference population. For economic reasons, sampling generally reaches about a 70% response rate. The methodologists of Statistics Canada then apply non-response weights to the sample by strata (firm size, province and NAICS code). Then a second detailed questionnaire is sent to all firms of the reference population. The same procedure for the non-response correction is applied; the resulting weights are thus a combination of the two non-response weights, from the first and second questionnaire. As such, Statistics Canada considers these surveys as a census of all biotechnology enterprises, hence our sample is representative of the population.

[3] Status can be active, amalgamated (merged or acquired) and integrated, which are all considered as survival, or status can be inactive, bankrupt and dead which are treated as firm exit.

[4] Recurrences are not independent within each firm.

Register and the information about covariates is issued from the four surveys (1999, 2001, 2003 and 2005), this results in an incapacity to elaborate traditional survival models with time dependant covariates. Consequently, variables were treated as non-dependent of time and in a panel. To control for the repetition of enterprises in the panel, a clustering function was used, in addition to dummies variables for the survey years.

The Cox model evaluates the time to event considering a binary variable that specifies if an enterprise has exited or if the temporal interval doesn't observe its death (right censoring). The time to event variable *time_survival* corresponds to the year of exit minus the survey year used, this represents the time of survival after a characteristic is observed. To control for right censoring, a variable *death_cox* was used to differentiate enterprises that failed from those that quit the interval of study. The variable *death_cox* takes the value 1 when the enterprise failed and 0 when the enterprise survived. For all models, the proportionality of hazard functions was tested to verify that the hazard function has the same shape for every enterprise and the global results are shown for each regression.

Independent variables

Earlier in the paper, we have categorised the survival factors into four categories: collaboration, innovation, management and financing. The following paragraphs introduce each of the variables within each category.

The BUD surveys ask the firms to identify the objectives of the **collaboration** agreements. We group these objectives in two categories: agreements related to knowledge (exploration) deal with R&D, regulation, access to knowledge, competences, patents and IP of the partner; agreements related to production and commercialisation (exploitation) aim to gain access to capital, markets and distribution networks, to reduce expenses and for production and manufacturing purposes. We constructed four variables corresponding to the number of collaborations for exploration [*necc*] and its dummy variable [*ecc*] (H1a) and the number of collaborations for exploitation [*necpc*] and its dummy variable [*ecpc*] (H1b).

Since biotechnology is at the heart of the knowledge economy, **innovation** factors will certainly have an effect on firm survival. Acknowledging the importance of science research, it is not surprising to find that almost all biotechnology firms spend non-negligible amounts on R&D [*rd*] (H2)[5]. Furthermore, we examine a variety of indicators of innovation, such as the number of existing and pending patents [*nb*] (H3) as well as the number of products and processes at different stages of development: R&D [*nprodrd*], preclinical research [*nprodpc*], clinical research [*nprodrc*] and in production or on the market [*nprodpm*] (H4). We consider the fact that enterprises contract biotechnology activities out using the total expenditure on contracts [*CCont*][6] and the fact that enterprises buy intellectual property rights using the total expenditure on IP [*CIPR*] (H5).

For the **management** aspects, the surveys measure the proportion of employees dedicated to biotechnology for each function: research [*properd*] (H6a), management [*propemngt*] (H6b), regulation [*propereg*] (H6) and marketing and finance [*propemark*] (H6).

In our last category of explanatory variables, we examine the **funding and support** of biotechnology firms. The survey asks whether firms have tried to raise funds and if the answer is positive, then asks if they have succeeded in raising capital and the amount obtained [*Cap*] (H7). The questionnaire then measures the proportion of this funding that is provided from various sources in the year of the survey

[5] The amounts spent do not differ much from one year to the next within the same survey, we will thus use the data for the survey year rather than for the previous year.

[6] This variable is unfortunately not available in the 1999 survey. For regressions with 1999, a dummy [*dcont*] was used if an enterprise contracts biotechnology activities out.

which we convert into dummy variables[7]: *dsourcekgov* for government funds (H7a), *dsourcekvc* for venture capital (H7b), *dsourcekdet* for borrowed funds (H7c). Additionally, we consider in this category the fiscal incentives, or whether a firm has demanded tax credits to the federal government [*dfiscfed*] (H8).

Different types of revenues[8] were added to evaluate the impact on survival considering the advancement of the firms; revenues from intellectual property [*revIPR*] (H9a), revenues from contracts [*revCont*] (H9b) and revenues from sales, which we infer from other revenues [*revOth*][9]. Because firms that already have a well established distribution network should have a greater propensity to survive, total export revenues [*revExp*] was added to evaluate whether biotechnology exports can affect survival (H9c).

We also add a number of control variables for the status of the firm: whether it is a public firm [*dpub*], a spin-off [*dspin*], or a subsidiary of an international firm [*dsubsi*]. Finally, the influence of the sector on survival is measured by a dummy variable that take the value 1 if the firm is categorized as human health [*dsectorhh*] by Statistics Canada (H10). We used human health because of the high costs of R&D and the risks related to the regulation process.

4. BIOTECHNOLOGY IN CANADA

For each of the four surveys, Statistics Canada obtained an overall response rate greater than 60%. Our sample is composed of 223 enterprises (62.3% of the population) for the 1999 cohort, 253 enterprises (67.5%) for the 2001 cohort, 375 enterprises (61.8%) for the 2003 cohort and 352 enterprises (66.2%) for the 2005 cohort. To counterbalance the strata that may over or under represent the biotechnology population, non-response weights are used to adjust the results. The distribution of firms in the population[10] (*N*) for 1999, 2001, 2003 and 2005 according to size, sector and province is presented in Table 1.

Table 1 – Distribution of Canadian firms developing biotechnology by size and sector

Size	***1999***	***2001***	***2003***	***2005***
Small	270	267	352	397
Medium	51	62	77	83
Large	37	46	61	52
Sector	***1999***	***2001***	***2003***	***2005***
Human health	150	197	262	310
Agriculture and food product transformation	119	113	137	146
Environment	35	33	38	39
Other	54	32	52	37
Total	**358**	**375**	**490**	**532**

Source: Statistics Canada

The number of small enterprises, which constitutes the vast majority of biotechnology firms in Canada, has grown by 47% between 1999 and 2005. The number of medium size enterprises has

[7] We have tests three versions of the funding variables: the logarithm of the total amount received from each source (Cap x percentage from the source); the toal amount raised (Cap) with the percentage from each source; but the best results were obtained from the total amount raised (Cap) with a dummy variable for each of the three most important sources as listed in the text.
[8] Different sources of revenue aren't available for 1999. For regressions including 1999, total of revenue was used [*lrt_0*].
[9] *revOth* is a proxy for sales revenues, *revOth = rev - revIPR – revCont.*
[10] Unfortunately, we cannot disclose the size of the sample for each stratum.

however increased faster (62.8%), while the number of large firms has grown by 40.5% over the same period. Biotechnology firms dedicated to human health have more than doubled their numbers (106.7%) compared with those involved in agriculture and the transformation of food products (22.7%), as well as environmental biotechnology (almost no growth).

What this table does not reveal however is the number of entering and exiting firms throughout the years. A more elaborate analysis of the number of firms that survived over the years, and particularly of the distribution of the firms that exited the market from each cohort is thus called for.

Distribution of biotechnology firm exit in Canada

Before turning to the factors that affect firm survival, it is interesting to first examine which type of firms exited, in which sector, as well as where and when they ceased their activities. Table 2 presents the proportion of firms that exited for each cohort in the short (2 years later), medium (4 and 6 years later) and long term (8 and 10 years later).

Table 2 – Distribution of firm exit in the short, medium and long term in the population (N) by size and sector for the 1999, 2001, 2003 and 2005 cohorts (weighted data)

	Cohort 1999						*Cohort 2001*					*Cohort 2003*				*Cohort 2005*		
		ST	*MT*		*LT*		*ST*	*MT*		*LT*		*ST*	*MT*			*ST*	*MT*	
		1999-2001	*1999-2003*	*1999-2005*	*1999-2007*	*1999-2009*		*2001-2003*	*2001-2005*	*2001-2007*	*2001-2009*		*2003-2005*	*2003-2007*	*2003-2009*		*2005-2007*	*2005-2009*
Size	***N***	***%***	***%***	***%***	***%***	***%***	***N***	***%***	***%***	***%***	***%***	***N***	***%***	***%***	***%***	***N***	***%***	***%***
Small	259	2.1	6.6	13.3	16.6	28.9	267	1.6	6.0	8.2	23.0	352	5.2	7.0	16.6	397	1.4	5.3
Med.	60	0.0	2.0	3.4	10.2	19.9	62	7.3	7.3	14.9	36.4	77	4.0	12.4	23.0	82	4.0	13.7
Large	38	2.6	7.8	7.8	7.8	20.9	47	9.8	9.8	9.8	18.9	61	4.6	7.4	17.9	52	3.0	14.4
Sector	***N***	***%***	***%***	***%***	***%***	***%***	***N***	***%***	***%***	***%***	***%***	***N***	***%***	***%***	***%***	***N***	***%***	***%***
HH	150	2.6	8.3	11.4	15.4	34.7	197	5.2	9.5	12.5	32.3	262	3.6	7.9	21.6	310	2.9	9.4
Agr	118	1.2	2.1	13.5	19.3	25.5	113	2.9	4.1	8.3	15.9	137	9.9	10.9	16.4	146	0.0	5.8
Env	35	0.0	0.0	0.0	0.0	0.0	33	0.0	0.0	0.0	4.9	38	3.6	3.6	8.0	39	0.0	0.0
Other	54	1.8	11.9	11.9	11.9	23.4	32	0.0	5.0	5.0	29.6	52	0.0	3.2	9.5	37	3.1	7.0

Source: Statistics Canada (data weighted by non response weight)

Notes: N represents population of biotechnology firms for each cohort; % represents proportion of biotech enterprises that did not survive at the end of the period in the short (ST), medium (MT) and long terms (LT).

First of all, the size distribution suggests that even if the majority of firms are small, small firms do not exit as much of the others in proportion, with the exception of the 1999 cohort where small enterprises were particularly affected by the technology bubble of 2000, and the credit crunch that ensued. This contrasts with Geroski (1995) who suggests that small firms have a smaller probability to survive then others. Agarwal (2001) however suggests that technology and life cycle should be taken into consideration to determinate whether size is an influent factor. The author advances that in mature industries or in high technology industries, size should not be an important factor of success. Survival should thus depend on the strategic niche occupied by the firm. Agarwal's conclusions seem to apply in our case. A large proportion of enterprises are in the "biopharma" sector with its small specialized firms. Small biotechnology firms certainly are in a strategic niche for the big pharma because a lot of the intellectual property and of products developed by those companies depend on the research made by the small biotechnology firms (Cooke, 2003).

At the sector level, the number of biotech firms in environment (Env) is extremely stable and only a few firms exit in this sector. The situation is completely different in the human health (HH), despite a 106.7% growth in the number of firms between 1999 and 2005, between 8.3% and 21.6% (cohort of

2003) of enterprises stop their activities in the medium term, and in the long term, 34.7% (cohort of 1999) and 32.3% (cohort of 2001) exited. The future is more than uncertain for firms in human health as close to one firm out of three exits in the long term. Regarding the agriculture and food products transformation sector (Agri), the situation seems to deteriorate for the cohorts of 2003 and 2005 during the post 2007 era; While 2.1% of the firms of the 1999 cohorts and 4.1% of the 2001 cohort exit in the medium term, it grows to 10.9% for the 2003 cohort and to 5.8% for the 2005 cohort. In fact, 2007 and even more so 2009 are the problematic years as they correspond to a period of turmoil in the financial markets. Let us now turn to the factors that may influence firm survival to try to explain some of these results.

5. RESULTS – SURVIVAL FACTORS

Two series of regressions were estimated because not all the variables are available in 1999: one including the cohorts of 1999 and the other excluding this cohort. All those models are run on small enterprises and on SME only, excluding large firms. The Cox model gives exponential coefficients (e^b), but it's possible to transform these coefficients in percentages to reflect the percentage associated with the risk of not surviving an extra year. When the exponential coefficients (e^b) is superior to 1, the difference ($e^b - 1$) yields a percentage that indicates an augmentation of the mortality rate when the independent variable grow by one unit, and hence implies a reduction of the chances to go through to the next period. When the exponential coefficients (e^b) are inferior to 1, the difference ($1 - e^b$) represents an augmentation of the chances to go through the next period[11]. Results are presented in Table 3.

Collaboration

Results show that collaboration for exploration (*ecc*) has a positive impact on small firm survival for regressions including 1999. The fact of collaborating increases by 27.52% the chances to survive until the next period. The same result is observable for the regressions excluding 1999, as the number of collaboration agreements for exploration purposes (*necc*) increase by 11.36% chances of survival for small firms and by 5.92% for SMEs. Collaborations for exploitation purposes (*ecpc* or *necpc)* does not have an impact on survival, so it seems that different types of collaboration do not have the same impact. Rothaermel and Deeds (2004) suggest that exploration collaboration is more benefic for small and large firms because it facilitates the acquisition of knowledge, in contrast of collaboration for exploitation purposes that is more beneficial to large firms because it allows the alignment of the latest discoveries with their market perspectives. Powell (1996) shows the importance of collaboration due to the complexity of knowledge. The author also mentions that in a high technology industry, innovation will occur inside knowledge networks more than inside the firm. Firms that collaborate for exploration purposes should be more innovative. This type of collaboration allows the acquisition of knowledge that is necessary for firms to conduct research and innovate. In the biotech industry, which is highly innovative, it seems that collaboration is not only necessary for innovation, but also for survival since innovation is the *leitmotiv of this industry.*

Innovation

R&D expenses (*rd*) do not affect firm survival. This can be surprising for an industry where activities are concentrated towards innovation. However, since almost all the firms have R&D expenditures, this characteristic is not a discriminating factor to distinguish firms that survive from those they do not.

[11] The period in this study is 1 year, which is the best interval that was provided to us from the Business Register.

Table 3 - Results of Cox proportional hazard models

	Including 1999				Excluding 1999			
	Small		SME		Small		SME	
	%	Relative risk	%	Relative risk	%	Relative risk	%	Relative risk
Collaboration								
ecc	27.52	**0.7248***	13.04	0.8696				
		(0.1417)		(0.1446)				
necc					11.36	**0.8864***	5.92	**0.9408***
						(0.0573)		(0.0345)
ecpc	-12.24	1.1224	4.11	0.9589				
		(0.2428)		(0.1796)				
necpc					-0.51	1.0051	1.39	0.9861
						(0.081)		(0.0574)
Innovation								
nb	-0.72	**1.0072*****	-0.13	1.0013	-0.73	**1.0073*****	-0.07	1.0007
		(0.0025)		(0.0014)		(0.0025)		(0.0016)
ln(rd)	-3.43	1.0343	-3.29	1.0329	-3.75	1.0375	-6.49	1.0649
		(0.0788)		(0.0695)		(0.1023)		(0.0923)
ln(nprodrd)	-1.39	1.0139	-0.68	1.0068	5.50	0.9450	3.63	0.9637
		(0.1032)		(0.0846)		(0.0983)		(0.0802)
ln(nprodpc)	10.91	0.8909	5.10	0.949	-4.53	1.0453	-9.12	1.0912
		(0.1328)		(0.0949)		(0.1522)		(0.1373)
ln(nprodrc)	-9.21	1.0921	-10.49	1.1049	-16.48	1.1648	-16.88	1.1688
		(0.1431)		(0.1092)		(0.2066)		(0.1698)
ln(nprodpm)	-22.18	**1.2218*****	-13.89	**1.1389****	-30.89	**1.3089*****	-16.69	**1.1669***
		(0.0934)		(0.0735)		(0.1344)		(0.0979)
dcont	Non respect of prop of the hazard functions		-8.16	1.0816				
				(0.183)				
ln(CCont)					1.84	0.9816	1.3	0.9870
						(0.0388)		(0.032)
ln(CIPR)					-2.11	1.0211	-3.39	1.0339
						(0.051)		(0.044)
Management								
properd	-0.19	1.0019	0.13	0.9987	-0.18	1.0018	0.29	0.9971
		(0.0039)		(0.0033)		(0.0055)		(0.0044)
propemngt	0.53	0.9947	0.49	0.9951	0.02	0.9998	0.12	0.9988
		(0.0067)		(0.0061)		(0.0076)		(0.0066)
propereg	3.03	**0.9697***	2.00	0.98	2.37	0.9763	1.79	0.9821
		(0.0178)		(0.0131)		(0.021)		(0.0156)
propemark	-1.23	1.0123	-1.34	**1.0134****	-1.43	1.0143	-1.07	1.0107
		(0.0086)		(0.006)		(0.0102)		(0.0073)
straKnow					-7.03	1.0703	-7.71	1.0771
						(0.1282)		(0.1133)
straIP					10.84	0.8916	0.15	0.9985
						(0.0947)		(0.0879)
Funding and revenues								
ln(Cap)	0.48	0.9952	-1.62	1.0162	3.20	0.9680	0.21	0.9979
		(0.0302)		(0.0252)		(0.0311)		(0.027)
dsourcekgov	-0.36	1.0036	-1.76	1.0176	-9.00	1.0900	-14.2	1.1420
		(0.245)		(0.2204)		(0.3019)		(0.2919)
dsourcekvc	-40.98	1.4098	-27.34	1.2734	-71.53	**1.7153****	-39.63	1.3963
		(0.3276)		(0.25)		(0.457)		(0.33)
dsourcekdet	28.44	0.7156	28.51	0.7149	-2.11	1.0211	0.24	0.9976
		(0.3174)		(0.2519)		(0.4712)		(0.3581)
ln(rev)	8.37	**0.9163****	5.50	**0.945***				
		(0.034)		(0.0303)				
ln(revCont)					6.15	0.9385	1.53	0.9847
						(0.0468)		(0.0372)
ln(revIPR)					-8.52	1.0852	-3.03	1.0303
						(0.0734)		(0.0664)
ln(revOth)					6.53	0.9347	4.76	0.9524
						(0.0435)		(0.0356)
difiscfed	9.42	0.9058	0.95	0.9905	19.31	0.8069	9.53	0.9047
		(0.2264)		(0.2264)		(0.244)		(0.2339)

	Including 1999				Excluding 1999			
	Small		SME		Small		SME	
	%	Relative risk	%	Relative risk	%	Relative risk	%	Relative risk
ln(revExp)	0.35	0.9965	-0.84	1.0084	3.30	0.9670	-0.14	1.0014
		(0.0448)		(0.0371)		(0.0534)		(0.0422)
dsectorhh	-56.03	**1.5603****	-72.03	**1.7203*****	-69.37	**1.6937****	-65.69	**1.6569****
		(0.3209)		(0.3115)		(0.433)		(0.3494)
dsubsi					-91.17	**1.9117***	-36.62	1.3662
						(0.716)		(0.4402)
dpub					-25.94	1.2594	-24.98	1.2498
						(0.3895)		(0.3319)
dspin	10.73	0.8927	13.19	0.8681	-17.97	1.1797	-0.77	1.0077
		(0.1892)		(0.1668)		(0.3016)		(0.2248)
Observations		836		1005		673		811
# of entreprises		526		609		447		528
Log likelihood		-855.78		-1165.17		-557.43		-796.80
Test prop.-hazards assumption		0.9563		0.7797		0.1961		0.5992

Notes: Standard errors in parentheses (robust and adjusted for clustering of enterprises). *** p < 1%, ** p < 5%, * p < 10%. All regressions contain control variables for survey year.

In the case of intellectual property, results really clearly show (significant at 1%) that the number of patents (*nb*) is not helping small firms. One more patent decreases by 0.72% to 0.73% the chances to survive until the next year. Filing for a patent is a large expense for an enterprise and it seems that this activity contributes to rendering the firms more vulnerable. Patenting however represents a necessary strategy for firms to prevent imitators. Grabowski (2002) suggests that protection by patent is lot more important in the pharmaceutical and biotech industries because of the costs and the delay involved in the development of products. Furthermore, Thumm (2002) suggests that patents are an incentive to R&D in biotech and serve as an exchange value for collaborations between enterprises or for access to venture capital. Firms can aim to obtain a portfolio of patents for negotiation purposes, which leads to patenting discovery without real guaranties of return on investments.

The number of products at the R&D stage (*nprodrd*), preclinical research stage (*nprodpc*) and clinical research stage (*nprodrc*) do not have an impact on firm survival.

A priori, it should be possible to think that enterprises that go through clinical research to ensure their survival, however the analysis of the number of products in production or on the market (*nprodpm*) shows another reality since its impact is negative on firm survival. For the regressions including 1999, small firms have 22.18% less chance to survive until the next period and for the SME, this risk decreases to 13.89%. For the regressions excluding 1999, the risk of not surviving until the next period increases to 30.89% for the small firms and to 16.69% for SMEs. It seems that firms, particularly small firms, have difficulties to appropriate the fruits of their labour linked to the product development process. Since the prior development stages require very large investments and clinical research is also extremely onerous, it seems that firms with approved products are less able to commercialize possibly due to a lack of resources. An alternative hypothesis could be that enterprises reaching the commercialization stage are at the end of their 'useful' life and stop investing in R&D to generate the next generation of products.

Managerial aspects

For the regressions including 1999, an augmentation of 1% of the proportion of employees dedicated to the regulation (*propereg*) increases the chances of small enterprises to survive until the next period by 3.03%. This can be explained by the importance given to regulation for the continuation of a firm's activities, particularly for enterprises in human health. Since important funds are required to develop a product, it is primordial for this product to successfully pass the regulatory phase. The

recruitment of specialists dedicated to this function seems to be an important asset for the firm. Results including 1999 show that for SMEs the proportion of employees dedicated to marketing and financial functions decrease by 1.34% the probability to survive until the next period. Could it be that firms overinvest in these functions to the detriment of ensuring that the products reach a more mature phase?

Financial aspects

Regressions including 1999 suggest that firms with more revenues are more susceptible to survive, increasing the chances by 8.37% for small firms and by 5.50% for SMEs. It wasn't possible to identify a source of revenue that helps firms to survive. In the regressions excluding 1999, small firms that received funding from venture capital (*dsourcekvc*) have a 71.53% chance to survive until the other period.

***

A number of control variables, one of which relates to our first hypothesis were added to the model. Among all the control variables referring to the type of firm, only the fact that a firm is a subsidiary of a non-Canadian firm (*dsubsi*) has an impact on survival. For the small enterprises excluding 1999 (this variable wasn't measured in the 1999 survey) the impact is negative, reducing by 91.17% the chances to survive. This result confirms other studies (Silverman and Baum, 2002; Baum and Silverman, 2004) that suggest that being a subsidiary increase the probability of death.

Finally, the control variable that measured whether the firm was in the human health sector (*dsectorhh*) shows really clearly for all of the regressions that firms in the human health sector have more chances to exit. Small firms and SMEs in the human health sector for regressions including 1999 have an increased risk of exit respectively of 56.03% and 72.03%, and respectively of 69.37% and 65.69% for the regressions excluding 1999. This result led us to investigate the survival factors of firms in the human health sector. Table 4 presents the regressions that were estimated on human health firms.

Results including 1999 and excluding 1999 suggest that for small enterprises collaboration aimed at the acquisition of knowledge (exploration) does not have an impact in contrast with the results on the entire sample of firms. This is due to the fact that in the human health sector, most firms collaborate to have access to knowledge and IP in order to develop new products. It is therefore not a discriminating factor for this firm development stage. Results excluding 1999 however show that for SMEs the number of collaboration agreements dedicated towards the acquisition of knowledge (*necc*) increases the probability to survive by 6.56%. It seems that medium firms that continue to acquire knowledge have an advantage in the human health sector.

Results are no different for the human health sector regarding the number of patents (*nb*) yielding a negative impact for small enterprises of 0.77% for the regression including 1999 and of 0.69% excluding 1999. In contrast, the negative impact of the number of products in production or on the market (*nprodpm*) is less present. While the impact is negative for the entire industry, in the case of human health biotech, the effect is only observable for small enterprises in the regression excluding 1999 with an impact of -37.88%.

Table 4 – Results of the Cox proportional hazard models for human health firms

	Including 1999				Excluding 1999			
	Small	**SME**	**Small**	**SME**	**Small**	**SME**	**Small**	**SME**
	%	**Relative risk**	**%**	**Relative risk**	**%**	**Relative risk**	**%**	**Relative risk**
Collaboration								
ecc	16.20	0.838	3.10	0.969				
		(0.2087)		(0.1973)				
necc					8.60	0.914	6.56	**0.9344***
						(0.0638)		(0.0363)
ecpc	-3.89	1.0389	7.54	0.9246				
		(0.2902)		(0.2155)				
necpc					1.29	0.9871	0.22	0.9978
						(0.0955)		(0.0785)
Innovation								
nb	-0.77	**1.0077*****	-0.11	1.0011	-0.69	**1.0069****	-0.01	1.0001
		(0.0027)		(0.0015)		(0.0028)		(0.0018)
ln(rd)					-11.53	1.1153	-20.93	**1.2093***
						(0.1359)		(0.1245)
ln(nprodrd)	5.84	0.9416	2.80	0.972	13.17	0.8683	6.07	0.9393
		(0.1134)		(0.1007)		(0.1152)		(0.1016)
ln(nprodpc)	6.55	0.9345	5.94	0.9406	-2.50	1.025	-0.09	1.0009
		(0.1727)		(0.1502)		(0.1912)		(0.1652)
ln(nprodrc)	Non respect of prop of the hazard functions		-24.98	1.2498	-38.45	1.3845	-29.42	1.2942
				(0.1993)		(0.4601)		(0.3171)
ln(nprodpm)	-22.67	1.2267	-7.41	1.0741	-37.88	**1.3788****	-18.09	1.1809
		(0.157)		(0.1199)		(0.2123)		(0.1782)
dcont	Non respect of prop of the hazard functions		-5.29	1.0529				
				(0.2078)				
ln(CCont)					2.14	0.9786	1.32	0.9868
						(0.0461)		(0.0368)
ln(CIPR)					4.26	0.9574	-0.25	1.0025
						(0.0591)		(0.0563)
Management								
properd	-0.71	1.0071	-0.40	1.004	-1.32	**1.0132***	-0.63	1.0063
		(0.0052)		(0.0046)		(0.0077)		(0.0061)
propeman	0.26	0.9974	0.24	0.9976	-0.34	1.0034	-0.11	1.0011
		(0.0092)		(0.0079)		(0.012)		(0.0094)
propereg	1.96	0.9804	1.30	0.987	2.22	0.9778	1.82	0.9818
		(0.0194)		(0.0142)		(0.0265)		(0.0192)
propemark	-2.16	**1.0216****	-1.91	**1.0191***	-3.39	**1.0339***	-2.28	**1.0228****
		(0.0095)		(0.0069)		(0.013)		(0.0095)
stratKnow					-6.78	1.0678	-3.90	1.039
						(0.1754)		(0.1346)
stratIP					12.59	0.8741	0.78	0.9922
						(0.1229)		(0.1115)
Funding and revenues								
ln(Cap)	0.10	0.999	-2.16	1.0216	0.67	0.9933	-1.37	1.0137
		(0.0376)		(0.0297)		(0.0391)		(0.0301)
dsourcekgov	-35.84	1.3584	-32.65	1.3265	-82.05	**1.8205****	-78.14	**1.7814****
		(0.3464)		(0.3217)		(0.5553)		(0.5117)
dsourcekvc	-21.16	1.2116	-15.60	1.156	-77.18	1.7718	-43.93	1.4393
		(0.3314)		(0.2657)		(0.5921)		(0.4159)
dsourcekdet	15.08	0.8492	8.23	0.9177	-20.63	1.2063	-15.03	1.1503
		(0.5259)		(0.4024)		(0.6586)		(0.464)
ln(rev)	7.77	**0.9223***	3.57	0.9643				
		(0.0424)		(0.0365)				
ln(revCont)					5.35	0.9465	2.07	0.9793
						(0.0592)		(0.0415)
ln(revIPR)					-9.96	1.0996	-2.65	1.0265
						(0.0846)		(0.0745)
ln(revOth)					5.59	0.9441	3.77	0.9623
						(0.0528)		(0.0406)
ln(revExp)	3.10	0.969	3.25	0.9675	-0.46	1.0046	-0.53	1.0053
		(0.0577)		(0.0465)		(0.0734)		(0.0622)
difiscfed	-5.24	1.0524	-17.35	1.1735	9.12	0.9088	10.08	0.8992

	Including 1999				Excluding 1999			
	Small	**SME**	**Small**	**SME**	**Small**	**SME**	**Small**	**SME**
	%	**Relative risk**	**%**	**Relative risk**	**%**	**Relative risk**	**%**	**Relative risk**
		(0.3239)		(0.3442)		(0.3151)		(0.2729)
dsubsi					-52.18	1.5218	-12.15	1.1215
						(0.7107)		(0.4479)
dpub					-24.56	1.2456	-22.46	1.2246
						(0.4618)		(0.4009)
dspin	23.86	0.7614	23.89	0.7611	-4.65	1.0465	8.82	0.9118
		(0.1852)		(0.1721)		(0.3081)		(0.233)
Observations		384		466		384		466
# of entreprises		267		313		267		313
Log likelihood		-341.31		-497.27		-341.31		-497.27
Test prop.-hazards assumption		0.1822		0.8368		0.1822		0.8368

Notes: Standard errors in parentheses (robust and adjusted for clustering of enterprises). *** p < 1%, ** p < 5%, * p < 10%. All regressions contain control variables for the survey year.

In term of human resources, results excluding 1999 for the small enterprises show that the proportion of employees dedicated to R&D slightly decreases the probability of survival by 1.32%. It seems that small enterprises that do not diversify the team in concentrating principally human resources in R&D have less chances of survival. This supports the arguments of Woiceshyn and Hartel (1996), who suggest that biotech firms with complete managing teams obtain better results then those with incomplete teams. In contrast, the proportion of employees dedicated to marketing and finance (*propemark*) has a negative impact for all the regressions in the human health sector. Results including 1999 for small firms and SMEs show respectively a 2.16% and 1.91% reduction in the chances of survival and for the regressions excluding 1999, a reduction of 3.39% and 2.28% respectively. Hence attributing a too important proportion of the employees to the marketing and finance functions disadvantages firms.

It is not surprising that the revenues (*rev*) also yield a positive effect in the human health sector, but a less important one, with 7.77% more chances to survive for small enterprises for the regression including 1999. The different types of revenue neither have an impact in the regressions excluding 1999. For the sources of funding, only the direct funding from government (*dsourcekgov*) exacerbates the risks of exit, in the regressions excluding 1999 for the small firms and SME by 82.05% and 78.14% respectively. Venture capital (*dsourcekvc*) and federal fiscal incentives do not have a significant impact on survival.

6. DISCUSSION AND CONCLUSION

At the beginning of this article, we proposed to identify the factors that influence the survival of Canadian biotechnology firms. Among the survival factors, we have identified four categories: collaboration, innovation, management aspects and financial aspects. In what follows we will take each of these categories in turn.

The study shows the importance of **collaboration** for firm survival. The hypothesis 1a is supported by the study, however, no strong conclusion can be made about the hypothesis 1b.

It seems that collaboration for exploration is necessary for survival, which suggests that exchange of knowledge play an important role in the dynamic of innovation. Survival of innovative smalls and SME of high technology depend of innovation networks and collaboration networks support by an appropriate national innovation system in supports to their activities. However, all types of

collaboration don't have the same impact on collaboration. Results show that collaboration for exploitation does not have an impact on survival.

About the **innovation** measured, no strong conclusion can be made about the possible impact of R&D expenses and the hypothesis 2 cannot be confirmed or disproved.

In a high technology industry such as biotechnology is it possible that R&D expenses are not a factor of differentiation between firms. It was impossible to use the intensity of the R&D because many firms in the biotech industry have no revenues, it is impossible to compute a proportion to see how the intensity of the R&D effort impacts on firm survival. If the number of patents is used as an indicator of the innovativeness of the firm, it seems that the number of patents decreases probability of firm survival. The hypothesis 3 is not supported.

There are some questions that exist about the relevance of the patent race to the detriment, maybe, of other activities in the enterprise, if those do not have the necessary resources. This seems to be across Canada and it is highlight the importance of tools to ensure that activities related to IP protection are not done to the detriment of the firm and compromising its survival. The results do not support the hypothesis 4 either, as showed the number of products in commercialization or on the market decrease the survival probability.

Vulnerability at the clinical research phase impacts on enterprises that arrived to the stage of production or of market launch. It seems that enterprises with a larger number of products in production or on the market survive less. After the clinical step, a crucial period exists, the product launch. The firm has to ensure the commercialization after investing many resources to go through the clinical steps.

Furthermore, no strong conclusion can be made about the impact of contracts for the biotech firms. Revenues from their contracting activities do not seem to have an impact on firm survival, so it is impossible to confirm or reject hypothesis 5.

About the **managerial aspect,** the study of the different type of human resources allows only to reject the hypothesis 6d.

It seems that a larger proportion of employees dedicated to financial and marketing aspects decrease the probability of firm survival, however, the other types of employees (R&D, management, regulation, production) have no impact on firm survival. A larger proportion of employees dedicated to financial and marketing aspects represent fewer employees in the other types.

Funding and its different sources do not show a particular impact on survival and neither do fiscal incentives. It seems that financial aspects are not a determinant of firm survival and as suggested in literature, the lack of funding can be related to deeper problems such as a lack of collaboration or innovation (Cressy, 2000; Hurst and Lusardi, 2004). However, the venture capital has a negative impact for the small enterprises excluding 1999, but no strong conclusion can be made about it. Hypotheses 7a, 7b and 7c about the different types of funding can be confirmed. It seems to be the same reality for the fiscal incentives, hypothesis 8, since it is impossible to confirm this hypothesis. As the first goal of fiscal incentives is to encourage innovation and not survival, it should be interesting to investigate the real impact of fiscal incentives on the product development process.

The analysis of the revenues suggests that firms with revenues are more likely to survive. But when the revenues from IP rights, contracts, sales and exportations are separated for the analysis excluding 1999, no strong conclusion can be made. The revenues have certainly an impact but it is impossible to determinate which type is more important. Hypothesis 9 is supported by the studies but no strong conclusion can be made about the 9a, 9b and 9c.

Finally, several interrogations were identified concerning the human health sector. Different studies were conducted only on the HH sector because of the high heterogeneity of the biotech industry.

Hypothesis 1 is supported, for all the models the HH sector has a negative impact on firm survival. As suggested by Hermans *et al.* (2006), the time between an invention and its arrival on the market is longer in the HH sector. Developing products in human health is much expensive and regulated, which implies higher vulnerability that conducts to a higher exit rate.

Evolving in the biotech industry implies an environment where the firm has to deal with a large part of uncertainty. Elaboration of products needs collaboration and partners to be able to mix in-house knowledge with external knowledge. Products are also submitted to a complex process of homologation during the different clinical steps, which constitutes uncontrollable factors for the enterprise. This implies that even if the firm takes or has taken the best decision, the firm is always at risk of exiting until the product is on the market and commercialized, and then, ensuring revenues. The future of an enterprise depends in a large way on the product under development, of its quality and also of the capacity of the firm to conduct the product trough the different stages of development. A limitation of this research is the fact that we had no possibility to judge of the quality of the innovation or of the product under development. It should be interesting in the future to investigate in more details the process of product development to better understand how firms organized their innovation process. Also, it should be interesting to see how collaboration networks have an impact on the creation of intellectual property and how the enterprise organized itself to transform this intellectual property in products that will traverse all the different step of regulation and will be commercialized with success.

7. REFERENCES

Agarwal, R. (1996). Technological activity and survival of firms. *Economics Letters*, 52(1), 101-108.

Audretsch, D. B. (1995). Innovation, growth and survival. *International Journal of Industrial Organization*, 13(4), 441-457.

Audretsch, D. and Lehmann, E. (2004). Financing high-tech growth: the role of banks and venture capitalists. *Schmalenbach Business Review*, 56(4), 340-357.

Baeyens K., Vanacker T. and Manigart S. (2006). Venture capitalists' selection process: the case of biotechnology proposals. *International Journal of Technology Management*, 34(1/2), 28-46.

Banbury, C., and Mitchell, W. (1995). The effect of introducing important incremental innovations on market share and business survival. *Strategic Management Journal*, 16, 161-182.

Basu, Paroma. (2003). Biotech firms jump on SARS bandwagon. *Nature Biotechnology*, 21, 720

Baum, J., Calabrese, T. and Silverman, B. (2000). Don't go it alone: alliance network composition and startups' performance in Canadian biotechnology. *Strategic Management Journal*, 21, 267-294

Baum, J., and Silverman, B. (2004). Picking winners or building them? Alliance, intellectual, and human capital as selection criteria in venture financing and performance of biotechnology startups. *Journal of Business Venturing*, 19(3), 411-436.

Becchetti, L., and Trovato, G. (2002). The determinants of growth for small and medium sized firms. The role of the availability of external finance. *Small Business Economics*, 19(4), 291-306.

Berger, A., Udell, G., and Building, F. (1998). The economics of small business finance: The roles of private equity and debt markets in the financial growth cycle. *Journal of Banking and Finance*, 22(6), 613-673(61).

Bergemann, D. and Hege, U. (1998). Venture capital financing, moral hazard, and learning. *Journal of Banking and Finance*, 22(6-8), 703-735.

BIOTECanada, *Ce qu'est la biotech*, consulté le 10 mars 2010, Source du document: http://www.biotech.ca/fr/what-biotech-is/benefits.aspx

Carpenter, R., and Petersen, B. (2002). Is the growth of small firms constrained by internal finance? *Review of Economics and Statistics*, 84(2), 298-309.

Cefis, E. (2003), Is there persistence in innovative activities? *International Journal of Industrial Organization*, 21(4), 489-515.

Cefis, E., and Marsili, O. (2005). A matter of life and death: innovation and firm survival. *Industrial and Corporate Change*, 14(6), 1167.

Christensen, C., Suarez, F., and Utterback, J. (1998). Strategies for survival in fast-changing industries. *Management Science*, 44(12) 207–221.

Cohen, W. M., Nelson, R. R. and Walsh, J. P. (2002) Links and Impacts: The Influence of Public Research on Industrial R&D, *Management Science*, 48(1), 1-23.

Cooke, P. (2003). Biotechnology clusters, "Big Pharma" and the knowledge-driven economy, *International Journal of Technology Management*, 25(1-2), 65-80.

Cressy, R. (2000). Credit rationing or entrepreneurial risk aversion? An alternative explanation for the Evans and Jovanovic finding. *Economics Letters*, 66(2), 235-240.

Cumming, D., and MacIntosh, J. (2004c). Canadian Labor-Sponsored Venture Capital Corporations: Bane or Boon? in A. Ginsberg and I. Hasan, eds., *New Venture Investment: Choices and Consequences* (Elsevier Science Academic Press), pages 169-200.

Danzon, P., Epstein, A. and Nicholson, S. (2004). Mergers and acquisitions in the pharmaceutical and biotech industries. *NBER working paper*.

Deeds, D., Decarolis, D. and Coombs, J. (1997). The impact of firm specific capabilities on the amount of capital raised in an initial public offering: Evidence from the biotechnology industry. *Journal of Business Venturing*, 12(1), 31-46.

Desmarteau, R. and Saives, A-L. (2004). *Les TPE de biotechnologies sont-elles contre-nature? Découvrir l'identité au Québec (Canada) en explorant leur modèle d'Affaires*. Actes du 7ième Colloque International francophone en Entrepreneuriat et PME, Montpellier, 27-29 Octobre.

Saives, A.-L., Desmarteau, R.H. *et al*. (2008). *Décoder l'hybride de la « coopération créatrice » : le cas des PME de Biotechnologie au Québec (Canada)*. Communication lors du 9e congrès *CIFEPME,* Louvain la Neuve, 29-31 Octobre.

Desmarteau, R. and Saives, A-L. (2006). Les très petites entreprises de biotechnologies sont-elles contre-nature? Découvrir leur identité au Québec (Canada) en explorant leur modèle d'affaires. *Revue Internationale PME,* 19(1), 35-68.

DiMasi, JD. and Grabowski, HG. *The cost of biopharmaceutical R&D: Is biotech different?* Manag Dec Econ (in press)

Evans, D. (1987). The relationship between firm growth, size, and age: estimates for 100 manufacturing industries. *The Journal of Industrial Economics*, 35(4), 567-581.

Enzing, C., Van der Giessen, A. and Kern, S. (2004). Commercialisation of biotechnology: do dedicated public policies matter? *Science and Public Policy*, 31(5), 371-383.

Fisken, J. and Rutherford, J. (2002). Business models and investments trends in the biotechnology industrie in Europe. *Journal of Commercial Biotechnology*, 8 (3), 191-199.

Fontana, R., and Nesta, L. (2009). Product Innovation and Survival in a High-Tech Industry. *Review of Industrial Organisation*, 34, 287-306.

Foss, N. (1997). The resource-based perspective: an assessment and diagnosis of problems. *Scandinavian Journal of Management*, 14(3), 133-149.

George, G., Zahra, S. and Wood, D. (2002). The effects of business–university alliances on innovative output and financial performance: a study of publicly traded biotechnology companies. *Journal of Business Venturing*, 17(6), 577-609.

Geroski, P. A. (1995). What do we know about entry? *International Journal of Industrial Organization*, 13(4), 421-440.

Gittleman M. and Kogut B. (2003). Does good science lead to valuable knowledge? Biotechnology firms and the evolutionary logic of citation patterns. *Management Science*, 49(4), 366-382

Gompers, P. (1995). Optimal investment, monitoring, and the staging of venture capital. *The Journal of Finance*, 50(5), 1461-1489.

Gompers, P., Lerner, J. (2001). The venture capital revolution. *The Journal of Economic Perspectives*, 15(2), 145-168.

Grabowski, H. (2002). Patents and New Product Development in the Pharmaceutical and Biotechnology Industrie, in Duca, J., *Science and Cents: The Economics of Biotechnology* (Federal Reserve Bank of Dallas), pages 87-104.

Griliches, Z. (1998), *R&D and Productivity*. The Econometric Evidence. The University of Chicago Press: Chicago.

Hall, A. and Bagchi-Sen S. (2002) A study of R&D, innovation, and business performance in the Canadian biotechnology industry. *Technovation*, 22, 231-244.

Hall, B. (1992). *Investment and research and development at the firm level: does the source of financing matter?* . NBER working paper, 4096.

Hurst, E., and Lusardi, A. (2004). Liquidity constraints, household wealth, and entrepreneurship. *Journal of Political Economy*, 112(2), 319-347.

Jensen, M. and Meckling, W. (1976). Theory of the firm: Managerial behavior, agency costs and ownership structure. *Journal of Financial Economics*, 3(4), 305-360.

Julien, P-A. (2002). *Les PME à forte croissance. L'exemple de 17 gazelles dans 8 régions du Québec*. Collection PME and Entreprenariat, Presse de l'université du Québec.

Kellogg, D. and Charnes, J. (2000). Real-options valuation for a biotechnology company. *Financial Analysts Journal*, 56(3), 76-84.

Lerner, J., Shane, H. and Tsai, A. (2003). Do equity financing cycles matter? Evidence from biotechnology alliances. *Journal of Financial Economics*, 67(3), 411-446.

Malerba, Franco and Orsenigo, Luigi, (2002). Innovation and market structure in the dynamics of the pharmaceutical industry and biotechnology: towards a history-friendly model, *Industrial and Corporate Change*, 11(4), 667-703.

McMillan, G S., Narin, F. and Deeds, D L. (2000). An analysis of the critical role of public science in innovation : the case of biotechnology. *Research Policy*, 29, 1-8.

Murray and L. Schiff (2004). Biotechnology Financing Dilemmas and the Role of Special Purpose Entities. *Nature Biotechnology*, 22(3), 271-277.

Nelson, R. (1959). The simple economics of basic scientific research. *The Journal of Political Economy*, 67 , 297-306.

Ndonzuau, F., Pirnay, F. and Surlemont, B. (2002). A stage model of academic spin-off creation. *Technovation*, 22(5), 281-289.

Niosi, J. (2003). Alliances are not enough explaining rapid growth in biotechnology firms. *Research Policy*, 32, 737-750.

OCDE (2005). *A framework for biotechnology statistics*, OECD, Paris.

OCDE (2009). *Session II - Structure of the Industry and Business Models.* Outlook for Industrial Biotechnology, Vienne, 13-15 Janvier 2010.

Oliver, A L., (2001). Strategic Alliances and the Learning Life-cycle of Biotechnology Firms. *Organization Studies*, 22(3), 467-489.

Oliver, A L. (2004). Biotechnology entrepreneurial scientists and their collaborations. *Research Policy*, 33, 583-597

Powell, W., Koput, K., and Smith-Doerr, L. (1996). Interorganizational collaboration and the locus of innovation: Networks of learning in biotechnology. *Administrative science quarterly*, 41(1), 116-145.

Prager, J. (1999). Financing Small Business: Venture Capitalists Buy Stakes in Public Biotech Firms, New-York: Eastern Edition. *Wall Street Journal*.

Revest, V. and Le Guehennec, C. (2007). *Capital risque, intervention publique et marché: le cas des biotechnologies françaises*. Working Papers.

Robinson, D. and Stuart, T. (2007). Financial contracting in biotech strategic alliances. *The Journal of Law and Economics*, 50(3), 559-596.

Rosenberg, N. and Nelson, R. (1994). American Universities and Technical Advance in Industry, *Research Policy.* 23(3), 323-348.

Rothaermel, Frank, T. (2000). Technological Discontinuities and the Nature of Competition . *Technology Analysis and Strategic Management*, 12(2), 149-160.

Rothaermel, F. and Deeds, D. (2004). Exploration and exploitation alliances in biotechnology: A system of new product development. *Strategic Management Journal*, 25(3), 201-221.

Senker, J. (1998). *Biotechnology and competitive advantage: Europe's firms and the US challenge*. Science and Technology Policy Research, University of Sussex.

Vanacker, T., Manigart, S. and Meuleman, M. (2009). *Early Differences and Persistence in the Entrepreneurial Finance Process: Evidence from High-and Low-Growth Biotechnology Startups*. Working Papers of Faculty of Economics and Business Administration, Ghent University, Belgium 08/522, Ghent University, Faculty of Economics and Business Administration.

Woiceshyn, J. (1993). Management—Key to new product development in biotechnology. *Long Range Planning*, 26(3), 67-76.

Woiceshyn, J. and Hartel, D., 1996. Strategies and performance of Canadian biotechnology firms: an empirical investigation. *Technovation*, 16, 231–243.

Zorgati, S. (2006). *Determinants of venture capital supply in the Canadian biotechnology sector: Financing issues, performance and evaluation*. Ph.D. dissertation, Université du Québec à Montréal (Canada), Canada.

Zucker L G., Darby M R., Armstrong J S. (2002) Commercializing knowledge : University science, knowledge capture, and firm performance in biotechnology. *Management Science*, 48(1), 138-153.