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Cindy Amsellem

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UNIVERSITÉ GRENOBLE ALPES

UFR DE PHARMACIE DE GRENOBLE

Année : 2017

**QUELS SONT LES FACTEURS DETERMINANTS POUR UN DEVELOPPEMENT ECONOMIQUE
PERENNE DES PETITES ENTREPRISES DANS LE SECTEUR DES BIOTECHNOLOGIES ?**

THÈSE

PRÉSENTÉE POUR L'OBTENTION DU TITRE DE DOCTEUR EN PHARMACIE

DIPLÔME D'ÉTAT

Cindy AMSELLEM

[Données à caractère personnel]

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 JR : Jean Roget
 LAPM : Laboratoire Adaptation et Pathogénèse des Microorganismes
 LBFA : Laboratoire Bioénergétique Fondamentale et Appliquée
 LCBM : Laboratoire Chimie et Biologie des Métaux
 LCIB : Laboratoire de Chimie Inorganique et Biologie
 LECA : Laboratoire d'Ecologie Alpine
 LR : Laboratoire des Radio pharmaceutiques

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QUELS SONT LES FACTEURS DETERMINANTS POUR UN DEVELOPPEMENT ECONOMIQUE PERENNE DES PETITES ENTREPRISES DANS LE SECTEUR DES BIOTECHNOLOGIES ?

1. Introduction

12 juillet 1999 : la loi sur l'innovation et la recherche a été créée par Claude Allègre. Cette loi française a permis aux chercheurs et universitaires de créer leur start-up et de breveter leur technologie. Cette loi a considérablement modifié le monde des start-ups et de l'innovation : 388 sociétés ont été créées entre 1999 et 2002. La majorité d'entre elles sont issues de pépinière de recherche financée par l'État [1]. Cette étude porte sur des entreprises spécifiques - créées après 2000 et appartenant au secteur de la santé. Les entreprises étudiées ont toute un esprit novateur. Elles ont également toutes une activité très développée en recherche et développement. Pour atteindre leurs objectifs, avoir un partenaire financier ou académique est indispensable.

L'environnement d'une entreprise de petite taille, innovante en biotechnologie dans le secteur de la santé devient de plus en plus concurrentiel. Nous pouvons observer que même la start-up la plus performante ne peut pas éviter l'acquisition par de plus grandes sociétés ou une offre publique initiale ou encore une licence. En effet, ces start-up innovantes sont destinées à se développer et lorsqu'elles atteignent une certaine taille, elles nécessitent des moyens financiers plus importants pour un développement durable afin d'éviter les opérations d'acquisition des grandes entreprises [2]. En effet, la stratégie de développement à travers les acquisitions potentielles de start-ups est assez récurrente de nos jours. La littérature a souligné que les grandes entreprises ne pouvaient pas se permettre de développer leurs projets internes de recherche et développement en raison de leurs coûts et plus particulièrement du temps nécessaire aux projets de recherche à long terme. Les start-ups sont plus petites et donc souvent plus innovantes et plus réfléchies en termes d'orientation de la recherche. Les petites entreprises de l'industrie pharmaceutique ont de plus en plus de mal à se développer et à devenir un acteur important sur le marché. Elles sont confrontées à de nombreux obstacles tels que : les coûts de développement d'un médicament (le taux d'échec lors des essais étant très élevé), la pression concurrentielle, les exigences réglementaires. Dans cette stratégie gagnant-gagnant, les start-up et les grandes entreprises ont leurs propres intérêts.

De plus, les start-up doivent traiter avec des investisseurs non scientifiques. Ces derniers ne comprennent pas toujours le timing et les risques que les start-ups rencontrent au démarrage. Si les entreprises ont la possibilité de lancer leur produit, elles auront affaire à des politiques de prix. L'entreprise devrait rembourser tous ses coûts de développement afin de générer du profit. En raison de toutes ces difficultés, ce projet étudiera certains facteurs clés pour les petites entreprises de l'industrie pharmaceutique afin de maintenir leurs forces d'innovation et leur performance afin de rester en compétition.

L'objectif de ce travail de recherche est d'identifier les éléments économiques clé à considérer concernant le développement d'une petite entreprise dans le secteur de la santé. Certains éléments ont été identifiés par des auteurs dans la littérature et seront comparés à ceux que nous avons trouvés. Une étude de cas d'un type d'entreprise étudié sera effectuée. Ensuite, des interviews de quelques entrepreneurs, avec leurs propres expériences, leur savoir-faire, leur succès mais aussi leurs échecs, suivra cette étude de cas. Nous recueillerons quelques conseils dans le monde de l'entrepreneuriat.

Résumé de la thèse

L'objectif de ce travail de recherche est d'identifier les éléments économiques clé à considérer concernant le développement d'une petite entreprise dans le secteur de la santé. Certains éléments ont été identifiés par des auteurs dans la littérature et seront comparés à ceux que nous avons trouvés. Pour cela, une étude de cas d'un type d'entreprise étudié sera effectuée. Ensuite, des interviews de quelques entrepreneurs, avec leurs propres expériences, leur savoir-faire, leur succès mais aussi leurs échecs, suivra cette étude de cas. Nous recueillerons quelques conseils dans le monde de l'entrepreneuriat.

Ce travail de recherche démarre par la définition des mots clefs utilisés tout au long du document. Les termes « biotechnologies », « industrie pharmaceutique », « start-ups en biotechnologie » ont été définis selon plusieurs instances. Le cycle d'un médicament dans l'industrie pharmaceutique a également été expliqué. Puis les grandes différences entre start-ups en biotechnologie et grand groupe pharmaceutique ont été élucidées.

Les 3 questions qui animent ce travail sont les suivantes :

- 1. Quels sont les principaux éléments ou facteurs pouvant assurer le développement économique pérenne d'une entreprise de biotechnologie ?**
- 2. Quelles sont les composantes représentant un enjeu important pour les start-up dans l'industrie des biotechnologies ?**
- 3. Ce qui a été observé dans la réalité : les start-ups sont-elles absorbées par les grandes entreprises ?**

Dans un premier temps, nous avons recensé tous les facteurs de développement économique, présent dans la littérature. Nous avons dressé une méthode de classification. Le premier niveau de classification est "**famille** de facteurs ". La classification a deux familles. Les "facteurs endogènes" et "facteurs exogènes". Ce que nous entendons par facteur « endogène », c'est un facteur intrinsèque à l'entreprise en tant qu'entité. Donc, ces facteurs sont directement liés à l'entreprise. Contrairement aux "facteurs exogènes" qui sont des facteurs observés dans l'environnement externe de l'entreprise mais qui ont un impact sur l'entreprise. C'est le premier niveau de classification des facteurs trouvés dans la littérature.

Ensuite, à l'intérieur de chaque famille, les facteurs sont divisés en **catégories**. La catégorisation est un niveau qui apporte plus de précision au sein de la famille des facteurs endogènes et exogènes, et cela aidera à remplacer les facteurs identifiés dans les bonnes catégories. Dans chaque facteur familial, qu'il soit exogène ou endogène, nous pouvons identifier :

- Facteurs humains
- Facteurs opérationnels
- Facteurs sociaux et politiques
- Facteurs financiers

Les facteurs humains sont directement liés à une personne. Ces facteurs concernent la personne qui peut être par exemple un employé ou un entrepreneur. Les facteurs sont des caractéristiques personnelles intrinsèques à un individu. Les facteurs opérationnels sont liés à la façon dont les entreprises « opèrent ». Dans cette catégorie, nous trouverons tous les éléments qui permettent le bon fonctionnement de l'entreprise.

Certaines catégories seront ensuite réparties en "sous-catégories". Par exemple, les facteurs sociaux et politiques appartenant à la famille des facteurs exogènes concernent les facteurs externes de l'entreprise. Enfin, les facteurs financiers concernent la situation financière de l'entreprise. L'ensemble des facteurs exogènes et endogènes trouvés dans la littérature sont présent dans les deux tableaux suivants. On peut voir apparaître leur classement en famille, catégories et sous catégories.

EXOGENOUS FACTORS	
FINANCIAL FACTOR	SOCIAL & POLITICAL FACTOR
NATIONAL POLICY	POLITICAL FACTOR
- Government Funding - Tax Reductions	- Government Support for Start-ups

FACTEURS EXOGENES TROUVES DANS LA LITTERATURE

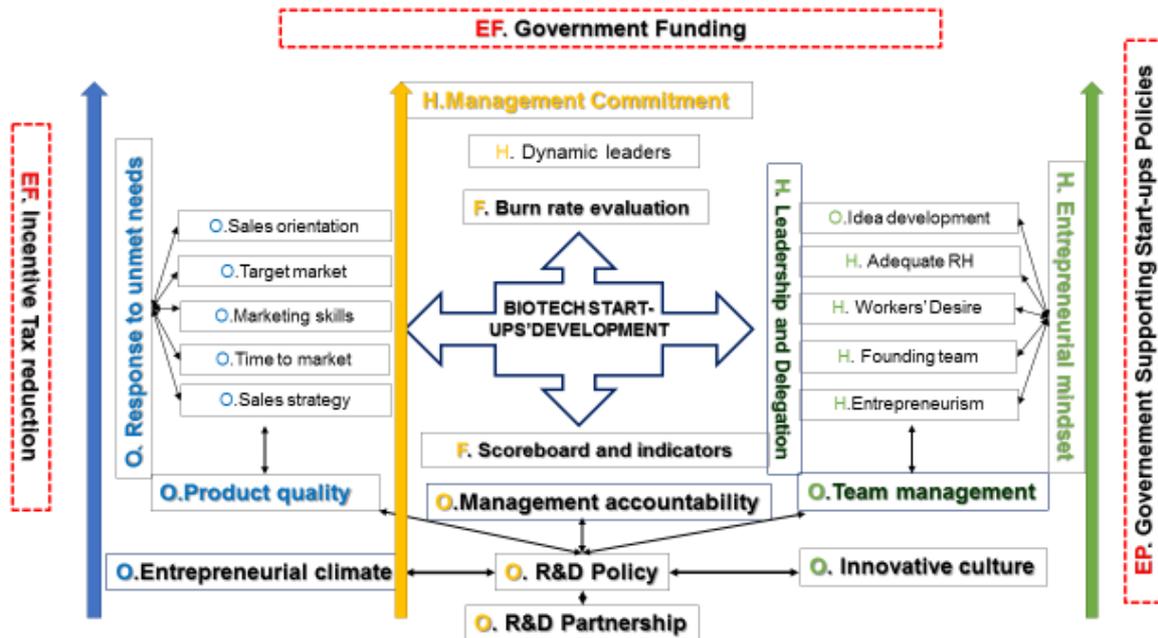
Une fois que les facteurs ont été recensé dans la revue de la littérature, il faut valider s'ils sont effectivement présents dans des cas concrets. Pour cela, nous avons menés une étude de cas dans une société type de celles étudiées dans ce travail de recherche. Nous avons adopté la méthodologie Yin décrite dans le travail de recherche. Tous les facteurs présents ont été recensés sur une période de 6 mois. Afin de compléter les données récoltées, et pour donner plus de robustesse à ce travail, il a été complété d'interview de 8 entrepreneurs dans le secteur des petites entreprises de biotechnologies.

Un guide spécifique a servi à chaque interviewé, où tous les facteurs trouvés dans la revue de la littérature étaient présents. Nous avons simplement à cocher une croix dans la case liée au facteur mentionné par l'entrepreneurs en l'écouter parler. Si un nouveau facteur est mentionné, il sera ajouté dans les notes. Avant d'assister au rendez-vous, nous avons étudié chaque fois la société de la personne interrogée via son site internet et son réseau. De cette manière, nous avons connaissance de toutes les informations.

Les entretiens se sont fait par téléphone ou sur place, selon la disponibilité de la personne interviewée. Concernant la confidentialité des données recueillies, l'anonymat a été garanti.

Endogenous factors						
1. Human Factors		2. Financial Factors		3. Operating factors		
1.1 Entrepreneur skills	1.2 Employee skills	2.1 Financial Skills	3.1 Human resources Management Skills	3.2 Marketing Skills	3.3 Production Management Skills	3.4 R&D Policy
-Senior Management Commitment	-Employee Skills	-Evaluate the burn rate	-Adequate resources of people	-Early Marketing	-A high quality new product process	-Innovative climate and culture
-Senior Management Accountability		-Develop a financial scoreboard and financial indicators	-High Quality team	-Estimate the time to market		-Research and development spending
-Structuring Management Team				-Focus on your goal : to sale		
				-Have a good marketing and sales strategy		
						-IP Transfer via a licensing agreement
						-Value added supply
						-Answer to Unmet Needs

TABLEAU RECAPITULATIF DES FACTEURS ENDOGENES

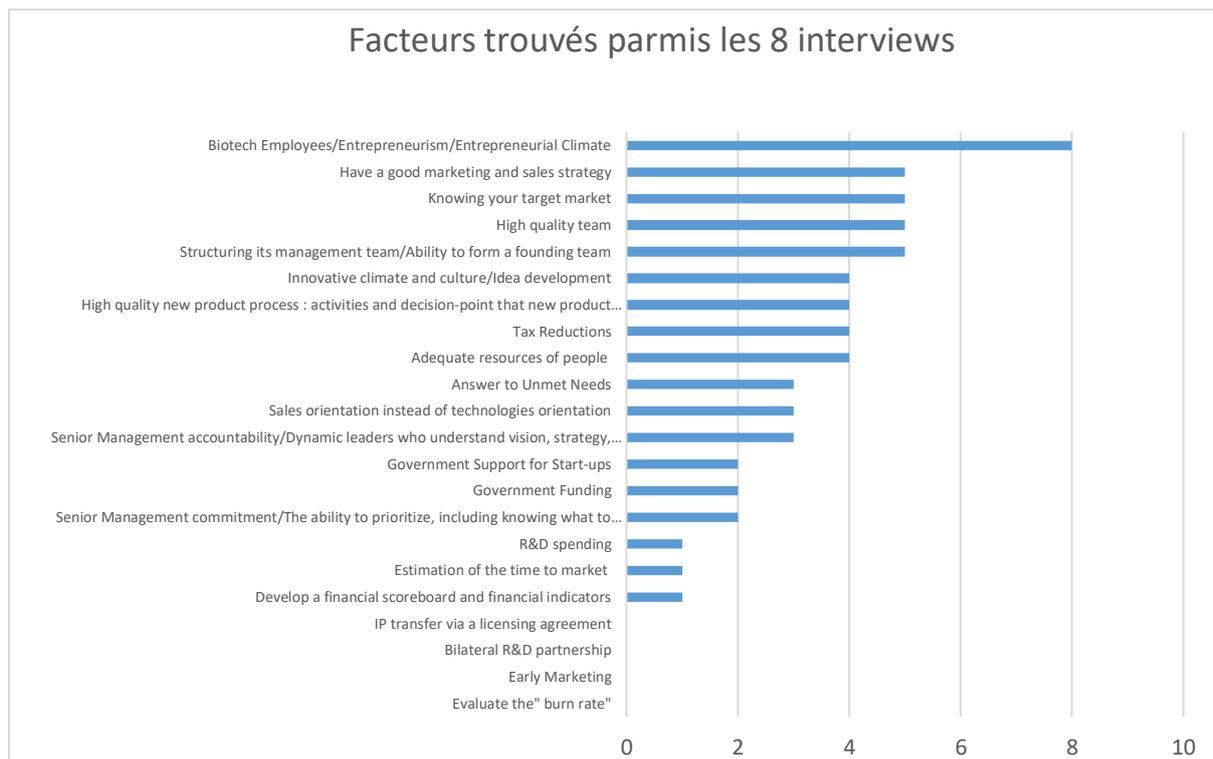


FACTEURS TROUVES DANS L'ETUDE DE CAS DE STAR COMPANY

La figure ci-dessus montre que tous les facteurs définis sont interdépendants. Chacun d'entre eux est intégré dans l'organisation de l'entreprise. Nous ne pouvons parler que du développement pérenne des entreprises à travers la relation indissociable et inséparable qui lie toutes les caractéristiques que nous faisons émerger à travers nos lectures.

Nous pouvons observer trois axes : Axe Produits en bleu, Axe Humain en vert, Axe de Management en jaune. Ils sont tous entourés d'un quatrième axe: Axe financier en rouge.

L'Axe Management couvre à la fois les compétences humaines (H), les compétences financières (F), les compétences opérationnelles (O). En effet, les trois axes convergent tous vers la santé financière de l'entreprise. Cela signifie donc que l'axe financier résulte d'éléments humains, d'éléments opérationnels et d'éléments stratégiques.

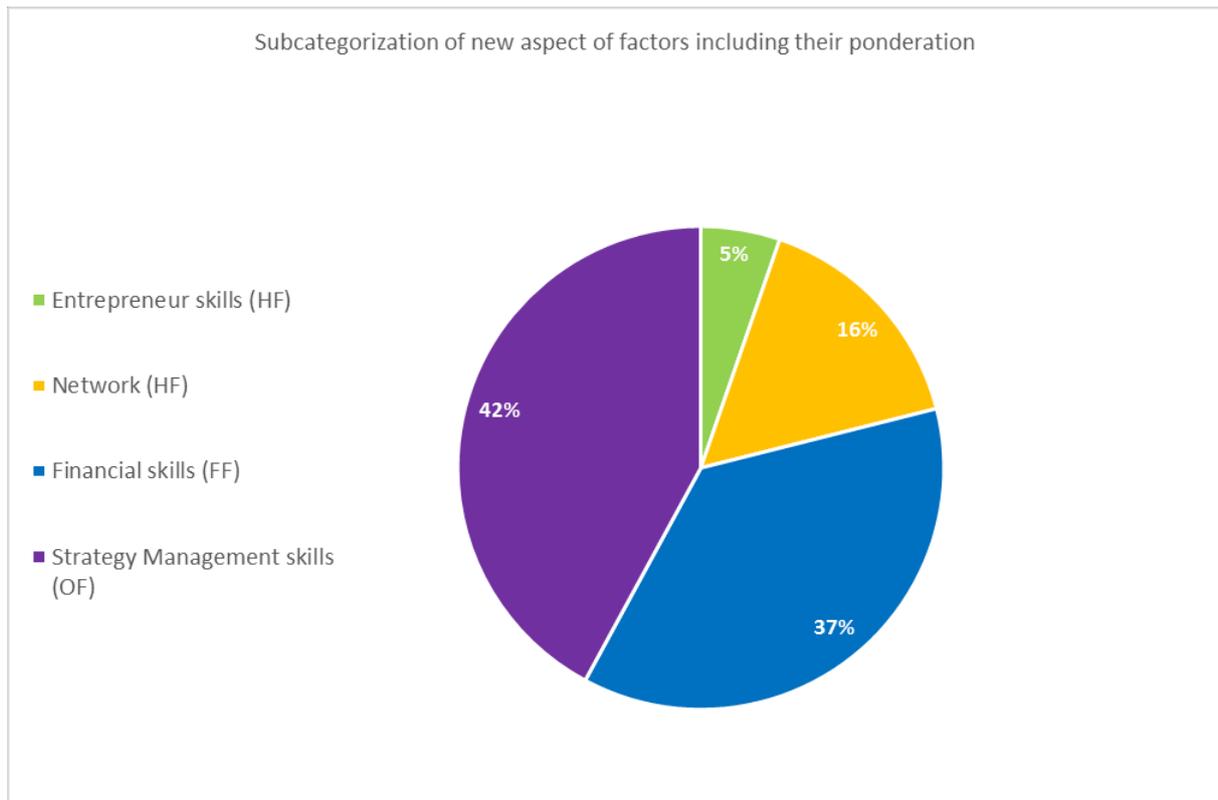


FACTEURS RETROUVES PARMIS LES INTERVIEWS DES ENTREPRENEURS

Vingt-deux facteurs ont déjà été identifiés dans la revue de la littérature (dix-neuf facteurs endogènes et trois facteurs exogènes). Au-delà de ces vingt-deux facteurs, dix-huit ont été trouvés au cours des huit entretiens. Le facteur le plus mentionné était les compétences des employés. Il a été cité par chacun des huit entrepreneurs. Ce facteur est dans la catégorie des facteurs humains. En d'autres termes, ces facteurs sont liés à l'équipe ; sélectionnez la bonne personne avec des compétences complémentaires, et un savoir-faire spécifique et motivée.

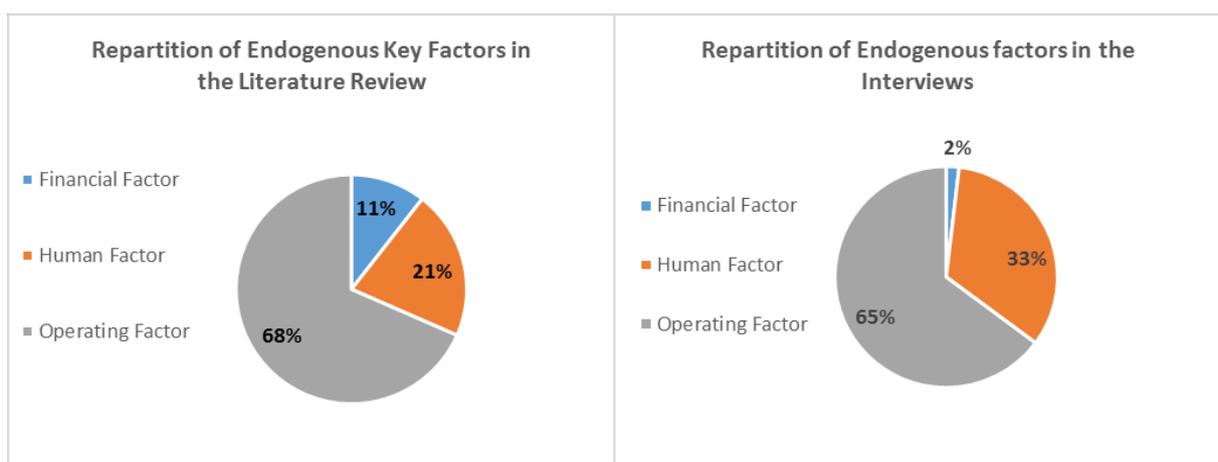
Concernant le deuxième facteur le plus évoqué : ce sont quatre autres facteurs qui arrivent ex aequo avec un score de cinq sur huit :

- Structuration de son équipe (compétences entrepreneuriales)
- Équipe de haute qualité (compétences en gestion des ressources humaines)
- Connaître son marché cible (compétences marketing)
- Avoir une bonne stratégie de marketing et de vente (compétences en marketing)



NOUVEAUX ASPECTS DE FACTEUR DECOUVERTS LORS DES INTERVIEWS

La figure ci-dessus définit la classification de nouveaux aspects de facteurs en utilisant leur sous-catégorisation. Au-delà de ce nouvel aspect des facteurs trouvés, la sous-catégorie la plus représentée avec un score de 42% était celle des compétences de gestion de stratégie et elle appartient à la catégorie des facteurs opérationnels.



REPARTITION DES FACTEURS ENDOGENES DANS LA REVUE DE LA LITTERATURE VERSUS INTERVIEWS

Il y avait deux facteurs financiers endogènes dans la revue de la littérature :

- Évaluer le « taux de combustion des liquidités » et
- Développer un tableau de bord financier et des indicateurs financiers

Selon la figure ci-dessus, ils représentaient 11% de la revue de littérature. Au cours de l'entrevue, seulement un de ces deux facteurs financiers endogènes a été cité et par un seul entrepreneur. Il représente la petite partie de 2%, de ce résultat obtenu après huit interviews.

Ce travail comporte certaines limites, qui sont présentées comme suit :

- Temps : les disponibilités des entrepreneurs étant réduites mais ils sont arrivés à trouver du temps pour les entretiens. Il était nécessaire de faire toute l'interview dans une même période afin de les comparer et de garder la méthodologie en tête.
- Géographie : tous les entrepreneurs interrogés proviennent d'un même département, donc l'échelle des entretiens n'est pas très large mais elle peut donner un aperçu de l'écosystème alpin concernant les petites entreprises du secteur de la biotechnologie.
- Nombre d'interviews : huit entrepreneurs ont été interrogés sur quinze entrepreneurs contactés. Ceci est lié à la disponibilité réduite des entrepreneurs mais plus de 50% de réponses ont été obtenu.
- La partie subjective du travail : concernant le type de facteurs et leur classification, c'est un travail personnel fait avec une opinion personnelle. Un autre chercheur adoptera probablement une classification différente ou utilisera la même chose mais placera un même facteur dans une autre sous-catégorie ou dans une autre catégorie.

Si nous souhaitons aller plus loin, nous devrions peut-être continuer ce travail en interrogeant plus d'entrepreneurs. Cela pourrait confirmer ou infirmer le résultat que nous avons trouvé précédemment. Avoir un échantillon plus vaste serait une bonne solution pour compléter ce travail de recherche.

2. Definition of key words

We will first define the central term of this work of research which is biotechnology. Biotechnologies are defined by the ANSES (National Agency for Public Health Food, the environment and work) as follow: “The application of science and technology to living organisms, as well as its components, products and modeling, to modify living or non-living materials for the production of knowledge, goods and services.” [3] Inside biotechnologies, they are many types classified by colors:

Green Biotechnologies	Yellow Biotechnologies	White Biotechnologies	Red Biotechnologies	Blue Biotechnologies
Food Sector	Environmental Protection	Industrial applications Sector	Health Sector	Products in relation to marine biodiversity

TABLE 1 - CLASSIFICATION OF BIOTECHNOLOGIES

This classification using colors is the European typology. Other countries use classification such as « healthcare biotech, agrifood biotech, industrial biotech » [3]. In our study the term “biotechnologies” and its derivatives refers to red biotechnologies particularly in the pharmaceutical industry.

The **Biotechnology Innovation Organization (BIO)** is the “world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations”. [4] Their members, are either small sized company both large one: “from entrepreneurial companies developing a first product to Fortune 500 multinationals”. All these company have a common point define by BIO, they are involved in “the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products”. [4]

BIO defines biotechnologies as “Modern” who “provides **breakthrough products and technologies to combat debilitating and rare diseases**, reduce our environmental footprint, feed the hungry, use less and cleaner energy, and have safer, cleaner and more efficient industrial manufacturing processes.” [5]

As the term biotechnology wasn't very clear in the healthcare sector, in this study, we will use this second aspect of biotechnologies, as explained by BIO “**breakthrough products and technologies to combat debilitating and rare diseases**” and will focus on healthcare

industry. All the structure that we will study, could product/have a product and/or also a technology, and the final objective is to combat “**debilitating and rare diseases**”.

A **pharmaceutical firm** is a company can be distinct thanks to what it produce: “whose products involve the design, discovery, development and marketing of new agents for the prevention, treatment and cure of disease.”[6] To market a product issued of pharmaceutical industry, it takes very long time, from 15 to 20 years. This correspond to the development of that product. Development can be divided by stage which are mainly preclinical trials (testing the molecule on animals) clinical trials (testing the molecule on human with 3 phases) and then the launch on the market as presented in the Figure 1.

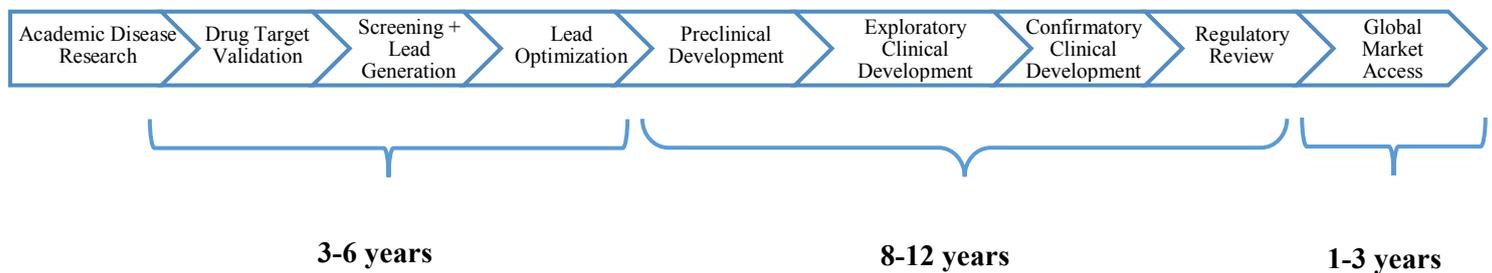


FIGURE 1 - BIOPHARMA R&D PROJECT LIFE CYCLE [10]

Figure 1 [10] presents the life cycle of a drug in the pharmaceutical industry. The process is very long and costly, and the rate of success is very low. It is a challenging environment where a molecule in development can fail at every stage.

A **startup in biotechnology** can be define as a company with current project in development: “vehicle needed to translate technologies out of the academic lab into the market”. These companies face with technical risks and are involved with important decision and little financial resources: “go/no-go decision points with relatively low amounts of capital” [7]. Realizing milestones is a condition for survival. These company are based on publication but it is not all, there is mostly shareholders «millions of investors' dollars » and before creating this start up, lot of work was done in the research laboratory “years of work behind it”. [7] That’s why “assessing” risk is a daily activity for founders who must guaranty a return on investment for the shareholder. Most of the startup in biotechnology see their drug in development.

Table 1 sets the differences between a biotechnology company (“biotech”) versus traditional pharmaceutical firm. It changes from many scales such as capitalization, cash flow (CF), dividend, way of financing the company, globalization (how many site the company

benefits), years from creation, investment risk in the company. It is very high for small companies as they do not generate profit yet, whereas established companies, generally have already some product on the market, and increase revenue.

	EARLY STAGE AND BIOTECH COMPANY	ESTABLISHED PHARMACEUTICALS FIRMS
CAPITALIZATION	Small	Big
CASH FLOW	Burn cash	Strong cash inflow
DIVIDEND	None	Moderate/Strong
FINANCING	Almost all equity	Debt & Equity
GLOBALIZATION	One site	Globally
HISTORY	30 years	100 years
INVESTMENT RISK	Very High	Moderate
MAJOR ALLIANCES	1 to 2	20 to 40
COST CENTERS	R&D	R&D/Manufacturing/Marketing
MAJOR INVESTMENT	80% on R&D	20% on R&D thanks to sales
EMPLOYEE	200	50 000
PIPELINE	Strong	Moderate/Weak
PRODUCT SALES	Low	> 5Billion USD
PROFITABILITY	Rare	> 1Billion USD

TABLE 2 - DIFFERENCE BETWEEN START UP AND BIG COMPANIES IN THE PHARMACEUTICAL INDUSTRY [8]

As our study focuses on small-sized companies, the definition given by European Commission indicates that small sized company, is a firm “with less than 50 employees and a turnover less or equal to 10 million €”. [9] We will focus on biotechnologies businesses, which could own the previous characteristics of Table 2. Cost centers is the department where the businesses spend the resources, so we can see that in biotechnology company, it is mostly in research and development.

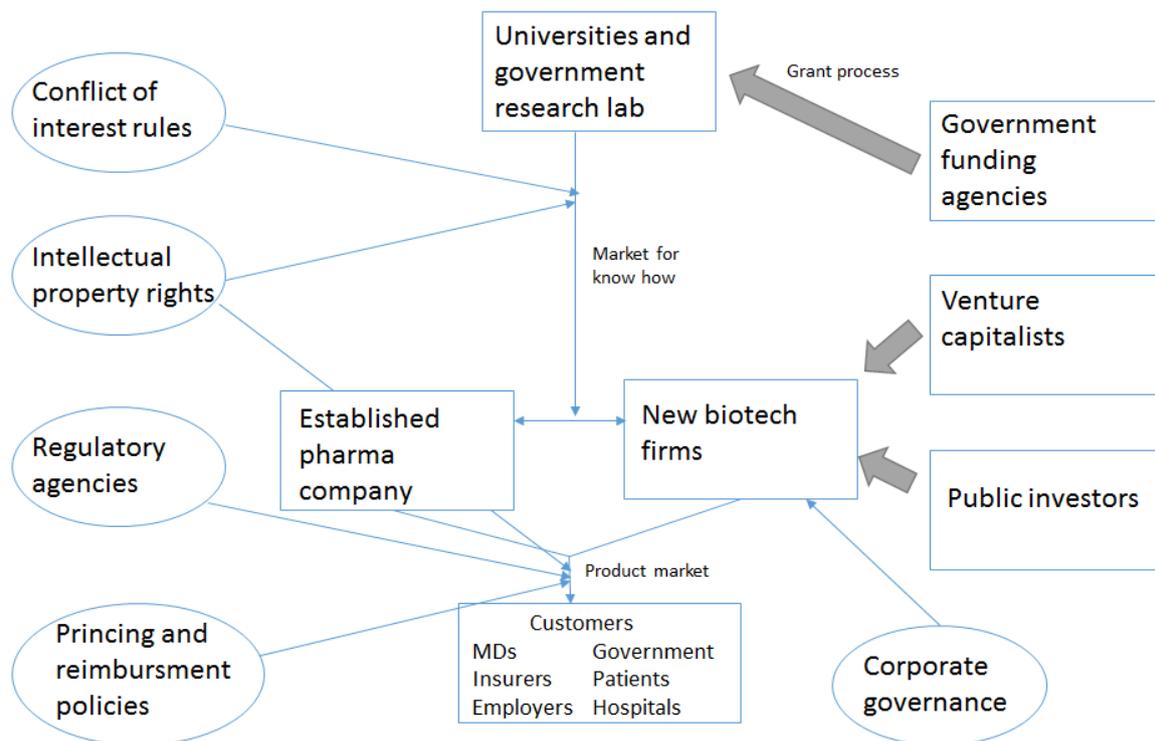


FIGURE 2 - BIOPHARM INDUSTRY ARCHITECTURE [2]

Figure 2 comes from the article « Building a Conducive Environment for Life Science-Based Entrepreneurship and Industry Clusters ». Present the organization of pharmaceutical industry with its problems for biotechnologies firms and also for established pharmaceutical companies. This project will focus on small sized pharmaceutical firms but established pharmaceutical companies will be evoked in part such as partnership for example. Moreover, these huge structure often turn to small companies to buy them or create license with them. “30 to 50 percent of new molecules came from in-licensing versus internal development”. [2]

This project concerns all the small-sized innovative company (SSIC), involved in pharmaceutical industry (less than 50 employees). Our research has the ambition to come up with understanding on following questionings:

1. **What are the key components or factors that can assure a sustainable development for a biotechnology firm?**
2. **What are the components which are really a big stake for start-ups in biotechnology industry?**
3. **What has been observed in reality: are the start-ups absorbed by big incorporations?**

To answer to these questions different functions within a SSIC are concerned such as: accounting, corporate finance, marketing, communication, strategy and external factors having an impact on its business such as regulations. This project includes keys events related to the evolution of the company e.g. investments in new equipment, moving into a bigger place, hire new employees, having new types of partnership.

3.Literature review

Before beginning to read the literature review, we will explain the **methodology used to classify** all the factors that are found in the literature review. The first level of classification is “factors family”. The classification has two families’ factors. The “endogenous factors” and “exogenous factors”. What we mean by “endogenous” factor is that it’s a factor intrinsic to the firm as an entity. So those factors are directly related to the firm. Contrary to “exogenous factors” which are factors which are observed from the firm external environment but that have impact on the firm. This is the first level of classification of factors found in the literature.

Then, inside each family factor, the factors are split into categories. Categorization is a level that brings more precision inside both endogenous and exogenous factors family, and it will help to replace the identified factors in the good categories. In each family factors exogenous or endogenous we can identify:

- Human factors
- Operating factors
- Social & Political factors
- Financial factors

Human factors are directly related to a person. These factors concern the person who can be for example an employee or an entrepreneur. Factors are personal characteristics intrinsic to an individual.

Operating factors are linked to how firms “operate”. Inside this category we will find all the elements that permit the well-functioning of the firm. Some categories will be then dispatched into “sub categories”. For example, Social & Political factors belonging to exogenous factors family concern firm’s external environment factors. Meanwhile, financial factors concern firm financial situation.

The multi-level hierarchical classification aims at presenting a clear presentation of the factors identified. This classification was set this way because, with this methodology, factors can be logically compared between them inside subcategorization. The idea of this classification is to start by the larger notion such as endogenous and exogenous factors families

and to arrive progressively to reduce and personalize the factors classification. With this way to proceed, it helps to understand where the factor comes from (inside or outside the company), and how it can have impact (through subcategorization) before explaining it.

ENDOGENOUS FACTORS							
1.HUMAN FACTORS		2.FINANCIAL FACTORS	3.OPERATING FACTORS				
1.1 Entrepreneur skills	1.2 Employee skills	2.1 Financial Skills	3.1 Human resources Management Skills	3.2 Marketing Skills	3.3 Production Management Skills	3.4 R&D Policy	3.5 Strategy Management skills

TABLE 3 - CLASSIFICATION METHODOLOGY USED IN THIS PROJECT

Table 1 explains what we propose concerning identified factors identification. We will now discuss these different factors and skills presented in the literature review.

Section 1 relates the endogenous factors characterizing Biotechnology firms. Human factors are the first endogenous factors we would like to present. Within the human factors category, we distinguish Entrepreneur skills and Human resources management skills.

3.1. Endogenous factors – Human factors

Let’s focus on the Endogenous factors family in the Human Factors categorization, explained previously.

3.1.1. Entrepreneur skills

The first Sub categorization we will talk about concerns Entrepreneur Skill. This sub categorization concerns all factors attributed to the founder of a company or person involved in the management (as board of directors is not the traditionally observed in the small sized companies). So the next developed factors are all intrinsic to the manager of the company.

Senior Management Commitment

The first factor of this classification is “**Senior Management commitment**” [11]. “Businesses with greater senior management commitment to, and involvement in, new products boasted more profitable total new product efforts.” This factor is related to the way the manager is involved into the project. When the management team is committed and involved in the process of a product development, it is more profitable then. This factor is beneficial for the development of the company in two dimensions: “How profitable the businesses’ total new product efforts are, including: the profitability versus competitors” on the one hand and “impact of new products on both sales and profits of the unit” on the other hand. This factor is seen as

a skill because the manager can feel to be either involved or not in a new project and the consequences in terms of profit and impact could be different. When senior management is involved into a new project, they “committed the necessary resources to achieve firm’s new product goals”. Moreover, senior management is “involved in spending decision”. Spending decisions are driving the business and are involved in cash flows management.

This factor also includes “**The ability to prioritize**” [12]. The founder should have the capacity to choose what to delegate and what to do on his own. Although there are constantly many current projects and decisions to make, the founder had better put in order the tasks that can generate a risk for the company (which should be implemented as fast as possible) and task that are not so important. The most difficult is to know how to identify what can be risky or an opportunity for the company, and what is not a priority for the time. The choice is not possible without commitment from the entrepreneur.

Senior Management Accountability

The second factor is “**Senior Management accountability**” [11] expressed as follows “Help to drive the profitability that the business unit achieved from new products.” This factor is related to profitability in terms of “performance”: “Management accountability captures the degree to which new product performance was measured, and senior management is held accountable for the program results. “This is an entrepreneur skill who is related to the profit attributable to the product, which take part of the development of the firm. Then the factor management accountability is cut into different component to help to understand this notion. These are: “performance objectives”, “bonus scheme”, “performance result” concerning a new product performance (related to the percentage of sales). Then the literature specifies that the performance of a new product, related to “Senior Management accountability” is “not even measured at all for a great many firms”.

Senior Management Accountability factors was completed later [13] through “**Execution**” skills”. The latter is described as” dynamic leaders who understand vision, strategy, risk, and tactics”. These notions take part off the huge class of entrepreneurship world. This is highlighted by the ability for the leader to manage four risks over time “people, technology, market, and financial” risks. It is important that the leader should have a good vision and strategy but the most important here is “execution” and the way an entrepreneur will drive a company facing or not all risks identified. Although there are lots of competitors and lots of challenges for a company, the skills of the leader have a huge impact on the company. Important decisions and the way those will be implemented are directly related to the leader.

Structuring Management team

“**Structuring its management team**” is the third identified factor [14]. It can be defined as follow: “the ability of the management team to organize the integration of new recruits”. It was completed further years after with the “**Ability to form a founding team**” (Harvard Business Review, 2017) [12]. “A founder must be able to assess their own strengths and

weaknesses” and know “how to recruit and motivate complementary founding team members.” It introduces the fact that a good team is essential. To come to this point, the person who will hire them should have the talents to value the skills everyone. It is suggested that if the team “is not fully committed – it will likely kill your company.” Although it is essential to have a team, they ought to be involved in decisions. Decisions should not be only taken by one person, responsibilities and consequences must be shared with all the management team. By this way not one single person will be responsible for consequences and the team spirit will stay.

All these key skills constitute the endogenous factors intrinsic to the firm. There are human factors and more precisely related to the entrepreneur: his ability to drive the company, and the team. We can see that some factors are related to the behavior and posture such as commitment, accountability, whereas others are related to the choice he makes: execution skills, structuring the management team, establishing priorities. These endogenous factors have an impact directly or not on the firm development. The impact can be observed on firm operating activities and therefore indirectly on firm profit. They can help to anticipate risks, e.g. allocation financial, economic and human resources in inefficient activities and/or projects in order to consolidate firm strengths and to overcome weaknesses. For small sized firms, these managerial skills mainly refer to founder and co-founder’s ones.

3.1.2 Employee skills

We will now discuss the Employee Skills. The firm founder is important as she or he has the responsibility in the taking of strategic decisions. But these decisions need to be implemented and the executive task forces are management teams and their workers. Both roles are complementary and have an impact on the development through many factors that we will expose now.

The first identified factors are “Desirable Biotech Employees” [15]. By desirable the author means the many qualities employees own by themselves. "Biotech companies often need special individuals with the right balance of certain traits to allow success". These are the following: Flexible, Resourceful (“whatever it takes to get things done”), Entrepreneurial (finding and making something out of things that others miss), Open-minded, Quick study, Focused, Mentor-derived, Broad grounding in physical and life sciences, “Ownership” (taking special pride in having an impact).

But it is so complicated to get all these characteristics in only one person, and what can matter may be trying to find at least one for each employee. By this way, everyone can bring his own skill into the team. There is not one characteristic better than another one. The competence results in the combination of factors creating a real strength for the individual worker, for the team for the management and for the business in fine.

Another item described, concerning employee skills is “Entrepreneurism” [16]. At first, we can think it’s an entrepreneur skill and a way to see the future for the founder. That’s not the case here, “Entrepreneurism” points to the team, the employee. This factor is described as “people who are generalists, who are able to do many things – people who have the ability to maintain enthusiasm and speed in business development”. It is a general characteristic, similar to “persistent” with “maintain enthusiasm” both “speed in business development”. This quality can either be acquired thanks to experiences in life or that are innate. The notion of motivation appears thanks to “able to do many things”. Even if the employee doesn’t have the prerequisite qualification to manage a task, he can learn by doing and then be able “to do many things”. The idea of dynamic emerges also with “speed in business development”. Persistent motivation, dynamics can be hidden included within the term entrepreneurship.

“Entrepreneurial Climate” [17] completes the previous skill in terms of internal environment. What does “entrepreneurial climate mean? Hiring people with “entrepreneurial characteristics who will support organizational learning (acquisition, analysis, and exploration of new knowledge, information and technologies)”. This element confirms the previous one in terms of motivation, dynamics and persistence attributable to the team. The word “climate” is close to “internal environment” here. The internal environment, is linked to the employee/team. The fact that the team acquires analytical skills or “new knowledge” will have effects on firm development. If each employee brings a new skill by exploring “new knowledge”, the global climate of the firm becomes more dynamic. Then if all the employees develop more competences thanks to this climate, the business is endowed with competences sustaining its development. Thus, this key factor supported in 2001, was still mentioned in 2015. The team, like the founder, plays a fundamental role in the firm development in terms of skills, be they native or acquired.

3.2. Endogenous factors - Financial Factors

Besides human factors, financial ones are considered indispensable for any kind of firm and particularly small sized companies. The individual sub-categorization found here is Financial Skills. In other terms, it is all the competences, acquired or developed concerning financial action or financial decisions.

3.2.1 Evaluate the burn rate

“**Evaluate the burn rate**” [14]. What does “burn rate” mean? It’s the Ratio which designates the rate of destruction of liquidity, which is often equity. As the literature explains, “It is essential to establish a financing plan including future expenditures”. Furthermore, it is important to know the number of months of availability of cash: the one that the firm holds and the one that the firm needs. The higher the rate of destruction of liquidity is, (by investing monthly in some devices for example) the riskier the business is. This notion can be explained as follows: if a firm needs lot of cash every month to run, it is necessary to evaluate the working capital. Moreover, generating profit is dependent on too many elements and is not automatic.

The literatures advises to establish a cash flow plan and organize its follow-up in order to anticipate the evolution of the burn rate. By this way, the amount of current expenses or loads will be anticipated and projected. It is also important to have in mind, that an investment for a new project will be profitable once it is sold. During its development, the firm needs to anticipate the necessary amount of cash to develop its product.

3.2.2. Develop a financial scoreboard and financial indicators

“**Develop a financial scoreboard and financial indicators**” [14]. Financial scoreboard represents synthetic information that is necessary to the director to evaluate the activity of his company, to anticipate its risks in order to adapt the management accordingly. This managerial tool allows to follow the activity and to anticipate the decrease of cash. Financial scoreboard puts forward the most relevant indicators for Management team, *e.g.* sales revenues and their evolution in time. This element helps the company to position itself periodically and proceed analytical comparative analysis with its competitors in order to be reactive by responding to the market evolution. Financial scoreboard can be considered as the boat compass for Management Team. On the one hand the financial scoreboard plays the role of warning system for the Management Team; and on the other hand existing data can be used as estimates for forecasts.

3.3. Endogenous factors – Operating factors

We will now focus on **Operating Factors**, still intrinsic to the firm (endogenous factors). Operating Factors are the most important source of data presented in this literature review. As Figure 1 sets, 68% of key factors found are operating factors.

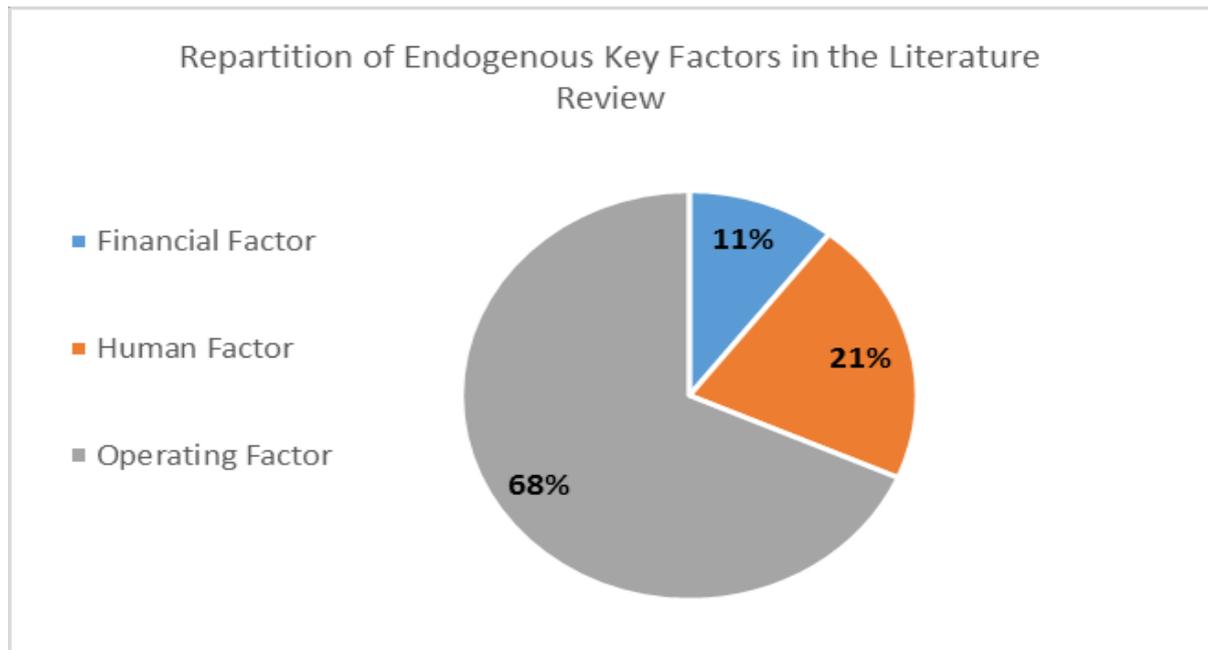


FIGURE 3 - REPARTITION OF ENDOGENOUS FACTORS FOUND IN THE LITERATURE IN THIS WORK OF RESEARCH

These are all the operating factors found in the literature. In this categorization, there are fewer sub categorizations such as:

- Human resources Management Skills
- Marketing Skills
- Production Management Skills
- R&D Policy
- Strategy Management skills

3.3.1 Human Resources Management Skills

The first subcategorization is Human Resources Management Skills. This part is not referring to Human skills, as it was described previously. We will not look at skills of people but how together they play an important role to make the business running itself.

Adequate resources of people

“Adequate resources of people” [11]. This resource is necessary to achieve firm’s objectives. “Even the best game plan in the world comes to nothing if there aren’t players on the field!” Resources in terms of people should be adequate to business’s objectives. Moreover, when a new project is in progress, tasks should be given appropriately. Most of the time, employees work on many projects at the same time. It most often concerns people working in marketing or manufacturing departments. If a new one project is started, and planning are in conformity with all the people involved and their allocation time, the project will be developed in adequate conditions. “Assignments of personnel to specific projects are made realistically, and in full awareness of their other duties and obligations.” “Release time is given for specific

new project”. This is the role of senior management to implement the needed resources in order to achieve the firm’s objectives.

High quality team

“**High quality team**” [11]. Through this factor, the author means that it’s a team who “interacted and communicated well and often, with frequent project update meetings, progress reviews, and problem resolution sessions.” It is finally a team where employees are connected to each other as often as possible. Thanks to that, every employee receive the same information about the current project. Another benefit of this factor is that nobody wastes time to explain the state of affairs again, to the other members of the team. Each employee receives the same information at the same time. Communication is seen as a central notion. “The best teams we witnessed had short but weekly meetings to ensure that the entire team was up to speed.” Additionally, companies with high quality team such as the one described previously, had best performance result in the author’s study.

3.3.2 Marketing Skills

We will now look at Marketing Skills, which are also Operating Factors. “In the market sector, the role of marketing is to create economic value for the company by creating the value perceived by customers” [18]. Both notions “economic value” and “value perceived by customers” constitute/are part of marketing. The goal of “value added” permit to gain “economic value”. It is essential to bring a value to the element that will be sold.

Early Marketing

Practicing “**Early Marketing**” [16] is the first factor of this next part. By “early marketing” the author means “Planning rapid market penetration” and qualify this factor as “essential to any company’s success.” This can be done thanks to “analysis of market positioning and profile of the products”. The goal here is to achieve a quick penetration of the market after studying both position on the market and “profile of the products”. The element which differing is when to do that? It can be done for “every phase of the development” of a product either just once time because “the entire product development process” can be seen as the “initial phase of marketing”. Likewise it is advices to start the relationship with possible partner as soon as possible. The objective is “to get people interested in what you are doing” as quickly as possible. What seems important here is to anticipate and mostly take advance in the marketing process. It is also important to get partner early who can play a role in the marketing phase, for example thanks to grant or financial help.

Estimate the time to market

Another factor found in the literature is “**Estimation of the time to market**” [14]. The “time” mentioned here is the one to “develop a marketable version of its product”. In other words, it is essential to know the time that it takes to conduct the product on the market. The cash that is generated thanks to this product through sales, should have been normally forecasted previously. If a company that forecasts to collect cash in a certain period, and finally it doesn’t, it will take more time to finish the product. Then, sales of the product are moved latter. And “6-month lag in the estimation of turnover has devastating effects for the company”. This is considered “devastating” because during this time, cash is consumed, sales are not yet

effective and financial partners “commitments” are not respected, and finding others funding sources will be difficult. Contrary to that, if the time to go to the market is well estimated, it will be a real success for the company and its shareholder. Every actor will be satisfied, both investor and founder.

Analyzing your target market

“Knowing your target market” [14]. It is precised that “market experience or knowledge of solvent applications greatly increases the chances of success”. How to get market experience? For example, to work with a person with some experience in sales on this target market. This enables the company to gain time (3 to 6 months) during the first month of sales of a product. The consequence is “A tremendous leverage effect in terms of cash” both “acceleration spiral effect for subsequent sales”. An employee with experience on the target market will be able to give a better analysis of this market and will also have a better reactivity. It enables then a better credibility with investors, who will be assured that the company knows to whom it is selling its product. Even if the company includes an employee who has already worked in the targeted market, “the entrepreneur must appropriate his environment”. This can be done through strategic studies both field enquiry. The first one will explore all the product benefits. The second one will consist of meeting the future client of this product or actors with an important position in this product. By this way some “anticipated” feedback can be collected.

Focus on your trading goal

“Sales orientation instead of technologies orientation” [14]. This is defined as follows: “put light on client benefit instead on its technical characteristics”. The innovative interest of a product is not only related to the technological aspect. Moreover, it is not the technical aspect that will trigger sales. There is a risk with technicians and scientists according to the project, found by these authors. The first risk is that, since competitive advantage of the product appears to them sufficient in the strategy of access to the market, there is a risk of under estimation of the strategy of access to the market. Another risk in technology orientation, though technicians and scientists, is a permanent commitment to improvement of the product “without fixing a definitive version” of this one. Then technicians and scientists who conduct the project will hardly challenge the initial competitive advantage. Contrary to that, when the pilot of the project has a commercial or marketing profile, he or she prefers “to cash in and sell products and services adapted to the market in term of both offer and timing”.

Have a good marketing and sales strategy

“Have a good marketing and sales strategy” [14]. It is essential to know who is going to be your client and how to sell the product to those clients to get efficient profit through sales, who takes part in the development of a company. The future price of the product takes part/depends on “how” to sell this product. This work of pricing should be done during the development of a product. To manage that work, the cost price must be set, including all the elements that are necessary to create the product including resources management. The most expensive parts are mostly the research and development phases because they are the longest parts in the biotechnology sector. Then another element about how the product will be sold, is how to penetrate the market and by which marketing strategy? It is not only thanks to **communication** that sales will increase. [14]

3.3.3 Production Management Skills

This part will concern production management skills. It concerns all the decisions or actions implemented to produce the product since its launch and then after.

A high quality new product process

“**A high quality process**” corresponds to “step activities and decision point that new product projects follow from idea to launch and beyond” [11]. Before going to the development phase, there is an “upfront homework, both market and technical assessment”. The study of technological feasibility, concerning a product, also a biotechnology product, is an important part of the process. The development cannot start before studying if it is possible to produce that product. This is the first part of the production process. A quality process also includes “quality of execution”. If during the process, a quality default appears for a batch, the process should not continue and “Go/Kill” decision must be taken. Moreover, the choice to “skipp or combine” some stages when it is necessary to make product revision, is also a production management skill. It is the ability to supervise and take decisions in the process that will be likely to gain some time for the company and then sell the product more quickly. So the speed of taking decisions and the “quality of execution” are both parts of the product process. It will impact the time to drive a product on the market and indirectly profit earnings thanks to the sales.

3.3.4 Research & Development Policy

Innovative climate and culture

“**Innovative climate and culture**” [11] inside a company can be for example: a company that gives to its scientists some “time off to work on projects” or resources to make them work in the best conditions as possible. It’s all the new management decisions, not tested before, that are involved in the research and development phase. Beyond an “innovative climate” the “**idea development**” can be added. [17] “Selecting the right idea can be very effective in the new product development process”. In the screening process, for example, which is the step where molecules with potential are selected, many ideas can be proposed in term of different methods or features to develop it. It could be, by using a new process of manufacturing instead an old one for example. These ideas are essential because the development of a product will be based on those ideas during the development of the molecule. These decisions could play an important role for the company: it may help to launch the product quickly on the market, and develop the company.

Research and development spending

“**R&D spending for product development**” [11] is the total cost of production of a product. “Increased R&D spending is the most obvious lever to pull” the percentage of sales concerning this product. This factor notifies that the more the company will spend for product development, the more sales of this product will occur. R&D spending can increase for example during the synthesis of the molecule, then during the manufacturing of all the drugs when different types of product could be used. It can also be made by making supplementary test

during the development either during preclinical or clinical trials. Finally, the molecule will maybe be more likely to be launched on the market and then to be sold.

R&D spending represents an important part for the valuation of those companies. Moreover, “there is a strong **correlation with their market value**” [19]. In other words, the more the company spends on R&D, the more it will impact positively the value of the company. This factor is attributable to biotech companies with one or more products that are currently in clinical trial. This valuation is “mainly dependent on the stage of progress of its intangible assets (R&D projects)” [19]. This task is even more complicated knowing that although the company put money in the research and development phase, it cannot predict its “technological success”.

3.3.5 Strategy Management Skills

Answer to Unmet Needs

“**Answer to unmet needs**” [16] is for example creating a drug that will solve or cure a disease that was not possible to cure with this existing drug. Choosing that strategy requires a real market analysis and also paying attention to the large pharmaceutical industry that may have an interest in the product. It is even more complicated knowing that to develop a molecule that answers to unmet needs, more resources will be necessary. The result is that bringing something “new” will create more visibility for the company which develops the product. Then many possible issues appear in terms of collaboration with a bigger company or achieving to bring that molecule on the market.

Value added supply

“**Value added supply**” [10] is a partnership between a big company and a small sized company. One company supplies a product or a service to a bigger company in order to add a certain value. This process consists in outsourcing some R&D tasks such as "chemical reference compound synthesis" or outsourcing preclinical and clinical trials in a small sized biotech company (the case fort Contract Research Organization CRO) for example. By this way both of the big and small companies are winning, it is a “win-win relationship”. This generates profit for the small sized company and an added value for the big one.

IP (Intellectual Property) transfer via a licensing agreement

“**IP Transfer via a licensing agreement**” [10]. A small company transfers its IP to a bigger one that can use it for its project. It can be for example a platform to conduct some tests or a platform where to synthesize a molecule. That platform would be developed by a small sized company and the bigger one could contract with it a licensing agreement. By this way the small company obtains fee and royalty payments from the bigger one. It is also a “win-win” strategy that could be implemented by the small sized companies.

The operating factors part is over. Beyond its 5 families, we can see thanks to Figure 4 that Marketing Skills are the most represented in the literature. The part concerning endogenous factors is now over. Table 4 summarizes all the endogenous key factors for a viable development of a small sized company, found in the literature.

ENDOGENOUS FACTORS

1. HUMAN FACTORS		2. FINANCIAL FACTORS	3. OPERATING FACTORS				
1.1 ENTREPRENEUR SKILLS	1.2 EMPLOYEE SKILLS	2.1 FINANCIAL SKILLS	3.1 HUMAN RESOURCES MANAGEMENT SKILLS	3.2 MARKETING SKILLS	3.3 PRODUCTION MANAGEMENT SKILLS	3.4 R&D POLICY	3.5 STRATEGY MANAGEMENT SKILLS
<ul style="list-style-type: none"> -senior management commitment -senior management accountability -structuring management team 	<ul style="list-style-type: none"> -employee skills 	<ul style="list-style-type: none"> -evaluate the burn rate -develop a financial scoreboard and financial indicators 	<ul style="list-style-type: none"> -adequate resources of people -high quality team 	<ul style="list-style-type: none"> -early marketing -estimate the time to market -analyzing your target market -focus on your goal : to sale -have a good marketing and sales strategy 	<ul style="list-style-type: none"> -a high quality new product process 	<ul style="list-style-type: none"> -innovative climate and culture -research and development spending 	<ul style="list-style-type: none"> -answer to unmet needs -value added supply -IP transfer via a licensing agreement

TABLE 4 - SUMMARY OF ALL THE ENDOGENOUS FACTORS

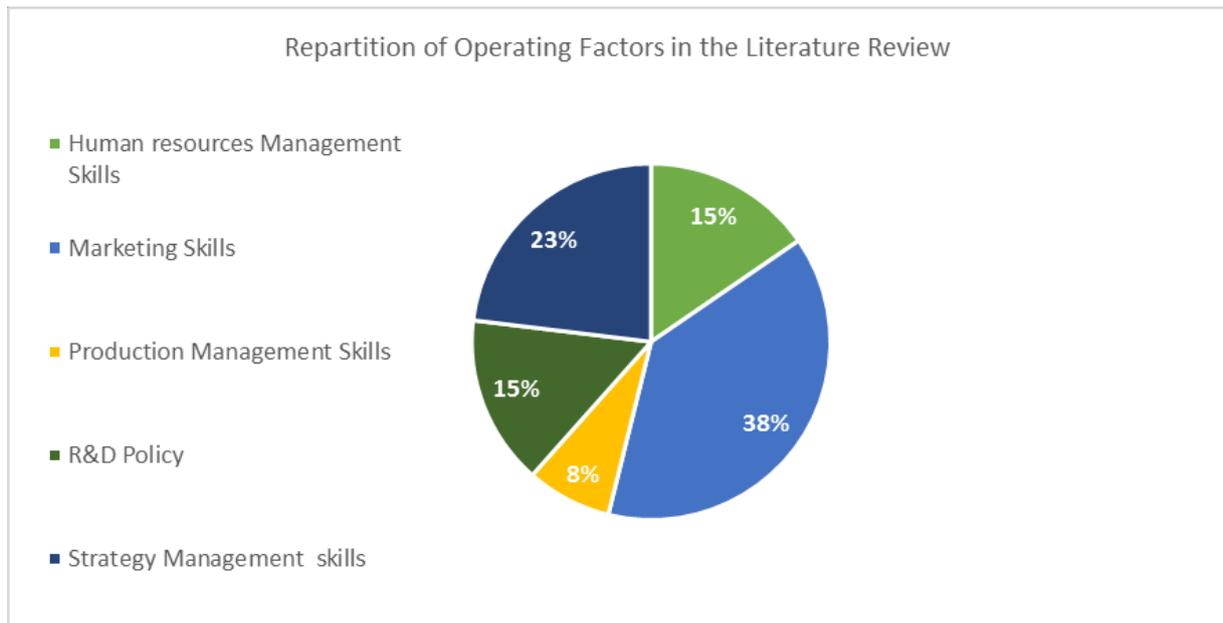


FIGURE 4 - REPARTITION OF OPERATING FACTORS

3.4. Exogenous factors – Financial factors

We will now look at the exogenous factors, those which are extrinsic to the firm but they have an impact on firm sustainable development.

3.4.1 National Policy

Government Funding

The intervention of government in terms of funding helps playing an important role for the company. For example, in the United States, the National Institute of Health (NIH) attribute grants to research groups. [16]. “The fact that research conducted by federal funding could be commercialized was also rated as highly important.” This is almost “early stage sources” of funding. Grants are of great help for a project in its earliest stage, and they encourage innovation.

Tax Reductions

Small sized companies in the biotechnology sector benefit from tax reduction for their R&D expenses. [16]. Although these companies do not generate profit yet, because their product is in development, they benefit from grants depending on their national policy. For example, in Washington, “there is no corporate or personal income tax.” Moreover, capital investments are “exempt from the state sales tax”. The consequence of this element is that small sized companies have more resources and then can employ more people, to run the business.

3.5 Exogenous factors – Social and Political factors

3.5.1 Political factor

Government Support for Start-ups

According to Tom Byers “political and government influences are the primary market drivers” [13]. This is the case for biotechnology industry, where academic institution can provide an incubator environment. [16]. An incubator is nothing else than a place dedicated to hosting small sized companies, in order to help them to grow. These companies are the ones that bring new ideas, new products, connected to research or university environment. This is very helpful in terms of logistical aspect. These structures can also help the company to find investors and partners.

The literature review part is now over, with 22 factors found: 19 endogenous factors and 3 important exogenous factors. The most represented factor beyond endogenous factors was operating factors and more precisely marketing skills. The next part of this work will present the different methodologies used to collect key factors, in order to compare with those who have been found.

4. Research Methodology

4.1 First Methodology of research: Case Study

To explore this project, two methodologies will be used. The first one will be the case study of Star company, a subcontracting small sized biotechnology firm in pharmaceutical industry created in 2005 where we will identify key factors thanks to Robert Yin's case study methodology. The company will be presented later in the next part of this work of research.

The second methodology used, will concern a group of small sized biotechnologies companies in the pharmaceutical industry, where entrepreneurs will be surveyed. This second methodology will be inspired from Madeleine Grawitz with her typology of interviews. Through these two methodologies, we will identify key factors encountered which played a role in the development of a biotechnology company.



FIGURE 5 - THE ITERATIVE PROCESS OF CASE STUDY RESEARCH (YIN, 2009)

Figure 5 shows the different steps we will be confronted with, in doing this case study, concerning Star Company. Before designing the case, we will justify why we choose this methodology. The first phase, concerning the case study is the identification of the research question. In our case this question is the following one: what are the key factors for a sustainable development, in the case of a small sized company in the sector of biotechnology?

4.1.1 Why doing a case study?

(Yin, 2009) [20] identified five methodologies of research which are:

- Experiment
- Survey
- Archival Analysis
- History
- Case Study

Method	Form of research question	Requires control of Behavior Events?	Focuses on Contemporary Events?
Experiment	How, why?	yes	yes
Survey	Who, what, where, how many, how much?	no	yes
Archival Analysis	Who, what, where, how many, how much?	no	yes/no
History	How, why?	no	no
Case Study	How, why?	no	yes

TABLE 5 - RELEVANT SITUATIONS FOR DIFFERENT RESEARCH METHODS (YIN, 2009)

Concerning the type of question: “if research questions focus mainly on "what" questions, either of two possibilities arises. First, some types of "what" questions are exploratory, [...] this type of question is a justifiable rationale for conducting an exploratory study, the goal being to develop pertinent hypotheses and propositions for further inquiry.” (Yin, 2009) [20]

As our research question is explanatory, consisting of the “exploration” of key factors inside a company, we choose/have chosen to conduct a case study. The way to find all these key factors is also explanatory because we will investigate during a six month period.

A case study is an empirical inquiry that:

- *“investigates a contemporary phenomenon in depth and within its real-life context, especially when*
- *the boundaries between phenomenon and context are not clearly evident.”*

Case study is chosen among the other (Table 1) for examining “contemporary event”. This is the case for our investigation, as the information is collected at the same time the case study is done and in its “real life context”. The pieces of information that we will collect are all the key points which/that played an important role for the development of our company. « Compared to other methods, the strength of the case study method is its ability to examine, in-depth, a “case” within its “real-life” context. » (Yin, 2009) [20]

We choose to conduct a case study to verify if key factors identified in the literature review of the part III are present in this case study. Then, in the next part we will be able to sum up key factors found through this work of research.

4.1.2 Method of analysis

Then, concerning the design of this case study, once the research question is set, we should implement what its “unit of analysis” (Yin, 2009) [20] are. In our case, these units of analysis are the key factors identified through the period that play an important role in the growth of Star company. The factors found through the case study will be classified with the same methodology as the one used in the literature review part III.

To prepare collecting case study evidence, some important element have to be implemented such as: principal objectives of this case study, issues, procedures used, and guide concerning the case study.

The principal objective of conducting this case study, is to collect all the key factors that are directly or not, linked to the development of the company.

The final issue of this case study is to compare the key factors that have been found through this investigation with what has been found before in the literature review. By this way, we will be able to see if new key factors have been identified for a sustainable development and how it helps in the development, in other words their own characteristics. If new factors are identified, it would be useful for new companies and entrepreneurs but also existing businesses who would like to compare if these key factors are present in those companies.

Concerning the procedure used: all the information will be collected through a 6 months’ period from May to October 2017 through mission conducted through this period. The progress of the case study will become more precise according to what will be found. The rhythm of these findings are period of three weeks each time called “sprint”. This notion will be explained latter. Inside each of these sprints of three weeks, key factors will be identified through mission conducted for the company, and employees will also be interviewed.

Human protection is also a point that we take into account in our work of research: “gaining informed consent from all persons who may be part of your case study, by alerting them to the nature of your case study and formally soliciting their volunteerism in participating in the study” (Yin, 2009)

4.2 Type of data collected for the Case Study

About collecting case study evidence: 6 six sources of evidence are identified (Yin, 2009) [20]

Source of evidence	Strengths	Weaknesses
Documentation	<ul style="list-style-type: none"> ➤ Stable-can be reviewed repeatedly ➤ Unobtrusive-not created as a result of the case study ➤ Exact-contains exact names, references, and details of an event ➤ Broad coverage-long span of time, many events, and ➤ many settings 	<ul style="list-style-type: none"> ➤ Retrievability can be difficult to find ➤ Biased selectivity, if collection is incomplete ➤ Reporting bias-reflects (unknown) bias of author ➤ Access-may be deliberately withheld
Archival Records	[Same as those for documentation] <ul style="list-style-type: none"> ➤ Precise and usually quantitative 	[Same as those for documentation] <ul style="list-style-type: none"> ➤ Accessibility due to privacy reasons
Interview	<ul style="list-style-type: none"> ➤ Targeted-focuses directly on case study topics ➤ Insightful-provides perceived causal inferences and explanations 	<ul style="list-style-type: none"> ➤ Bias due to poorly articulated questions ➤ Response bias ➤ Inaccuracies due to poor recall ➤ Reflexivity-interviewee gives what interviewer wants to hear
Direct Observations	<ul style="list-style-type: none"> ➤ Reality-covers events real time ➤ Contextual-covers of "case" 	<ul style="list-style-type: none"> ➤ Selectivity-broad coverage difficult without a team of observers ➤ Reflexivity-event may proceed differently because it is being observed ➤ Cost-hours needed by human observers
Participant Observation	[Same as above for direct observation] <ul style="list-style-type: none"> ➤ Insightful into interpersonal behavior and motives 	[Same as above for direct observation] <ul style="list-style-type: none"> ➤ Bias due to participant observer's manipulation of events
Physical Artifacts	<ul style="list-style-type: none"> ➤ Insightful into cultural features ➤ Insightful into technical operations 	<ul style="list-style-type: none"> ➤ Selectivity ➤ Availability

TABLE 6 - 6 SIX SOURCES OF EVIDENCE IDENTIFIED (YIN, 2009)

Robert K. Yin gives the “Common Sources of Evidence in Doing Case Studies” that we can use doing our case study with their strength and weaknesses. **(Table 6)** There are mainly Documents (newspaper articles, letters and e-mails, and reports) but also archival records, or Interviews, Direct Observations, Participant-Observations, and Physical Artifacts.

In our Case Study, we will use Document: precisely company report, Interview of each employee, Direct Observation during the internship period of six months, Participant Observation: which are mainly information collected indirectly for example presence at a meeting. We will collect data and work at the same time: «A key demand of the case study method is the investigator’s skill and expertise at pursuing an entire (and sometimes subtle) line of inquiry at the same time as (and not after) data are being collected. » (Yin, 2009) [20]

Concerning interviews, many employees will be independently interviewed about a very same topic. The “triangulation” method will be used: it’s when independent source, different employees indicate the same fact, the same answer to a question. It makes the data obtained stronger because many people have given independently the same answer. Generally, it is better to use “multiple source of evidence” that means for example asking many people instead of only one in a company. For the case of Star company, all the employees will be interviewed.

4.3 Second Methodology of research: Interviews

4.3.1 Research based on interview

We choose to conduct some interview, to see if there are key factors that can complete the ones identified in the case study. We will not be able to inventory all the existing key factors of the case study because time, is one limitation of this work of research.

Some entrepreneur or manager in companies comparable to those we studied (small sized company in the sector of biotechnologies) are going to be interviewed either by phone or through an appointment. They will previously be contacted by email to explain them the subject of this research and their agreement to collaborate to this research.

Concerning the second methodology, we will draw our inspiration from Grawitz’s book (Social Science Methods, 2001) [21]. In this book, six types of interviews present in three categories are mentioned. Their characteristics evolve continuously between the two extreme categories of interview. These two extreme categories are non-directive interviews which consist of the greatest freedom for the interviewer and the respondent and the directive interview which is made of the least freedom for both people.

Two essential factors beyond this classification are degree of freedom which is related to the form of question and level of “depth” which is the quality and diversification of the answers, and information collected.

Non-Directive : greatest freedom	Semi-Directive	Directive : least freedom
Clinical interview : Psychoanalysis and psychotherapy	Interview with free answers	Open-ended interview
In Depth interview	Focused interview	Closed-Topic Interview

TABLE 7 - THE DIFFERENT TYPES OF INTERVIEW ACCORDING TO MADELEINE GRAWITZ (2001)

The field of study is fixed upstream and it concerns the development of the company, that's why we will not use non-directive interview where the field of the study is free. The goal of all these interviews is to identify through a guide previously prepared, key factors that play an important role in the development of the company.

Although a guide of interview will be prepared before the interview. If the interviewee starts to talk about an event concerning his or her company where we can extract important information, we will let him or her talk and cross in our guide, which factor is mentioned. This is semi-directive interview where the thematic has been defined before but the order of the interview can change according to the answers.

Directive interview will also be used and more precisely open-ended interview. A guide will be set before the interview. According to/Depending on what the interviewee is going to answer, the interview could be both semi-directive and directive.

Closed-topic Interview will not be used because this type of interview concerns most of the time statistic interview where the interviewee answer with yes or no and it will not enrich our research work significantly.

4.4 Conducting the Interviews

A specific guide will serve for every interviewee, (Appendices 1) where all the factors found in the literature review are present. We will just have to put a cross in the box related to the factor mentioned. It can be inter-related with others factors, in this case we will cross two different box. If a new factor is mentioned, it will be added in the notes. Before assisting to the appointment, we will study each time the company of the next person interviewed via its website and network. By this way we will arrive with all the basics information on mind.

The interview will be by phone or meeting, depending on the availability of the person interviewed. Concerning confidentiality of the data collected, anonymity will be guaranteed and if the interviewee doesn't want to be recorded, his will will be respected and we will manage the research with notes.

At the end of each interview, the interviewee will be thanked and we will propose him or her to share our work of research.

5. Case study and Interviews

5.1 Case Study of Star biotechnology company

5.1.1 Presentation of the company

As our work of research is entirely anonymous, we decided to name the company studied "Star company". Today, the majority of large pharmaceuticals companies outsource their work. [22] This processing way provides benefit to large pharmaceuticals companies in terms of cost and time savings. Large pharmaceuticals companies can therefore outsource and restrain their internal R&D activities. They prefer outsourcing research and development phases or buy smaller companies which deal with new technologies and innovation. By this way, these big players on the life science market can increase their capital (by saving cost for nonclinical phase infrastructure for example), saved their time, focused in other field, and also increase their pipeline. [23]

Star company is an innovative company created in 2005. Its mission is to support drug developers in discovering new treatments for Central Nervous System disorders. They help their client to move forward in their R&D programs by identifying and qualifying the therapeutic potential of their molecules on Epileptic, Cognitive, Movement or Neurodegenerative disorders.

The company is composed by 15 people which are mainly technician or PhD. Most of all employee have a scientific background completed for 2 of them with a master of management. This company is driven by 2 persons. Star company is made up of 3 units: Research and Innovation, in charge of Star company's innovation and research and development policy, Business Development, for the marketing of international offers and customer relations, and the Laboratory which is responsible for the execution of client projects.

Concerning the location, this company is located, in a "biocluster", near hospital, center of research (Neurosciences) and university. Headquarter of Star company is located in a building that houses many young biotechnologies company. The goal of this building is to help companies to develop themselves by renting them appropriate local until they grow and go to a bigger and own place. Star company is about to move in a bigger place in September 2017, and take its independency. This process will include many element taken for consideration.

The orange frame in the Figure 1 shows where Star company plays a role during the development of a molecule. The first step is the discovery of a new compound by chance, screening or synthesis for example. Then this compound is tested on animal during preclinical studies. The preclinical studies are composed by Pharmacology, Pharmacokinetics, and Toxicology studies. Once its pass the previous steps, it can be tested on humans during clinical studies which includes 3 phases. After that there is the application to launch the drug on the market with different procedures. Once, the drug is on the market, the last phase is the Pharmacovigilance phase, which is the oversight of this molecule, for example if there is a side effect link to its use.

The company is performing mostly pharmacology studies. It tests the efficacy of a compound on the brain of rodent. Composition of preclinical studies are presented in Figure 2.

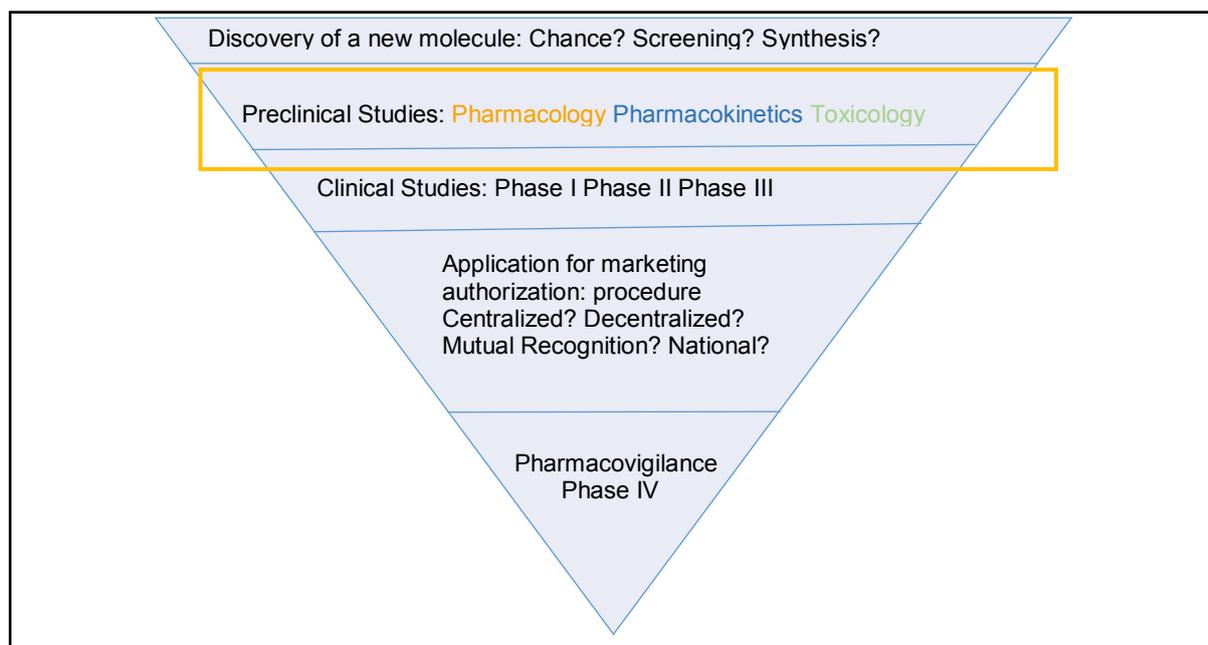


FIGURE 6 - PLACE OF STAR COMPANY IN DEVELOPMENT OF A MOLECULE

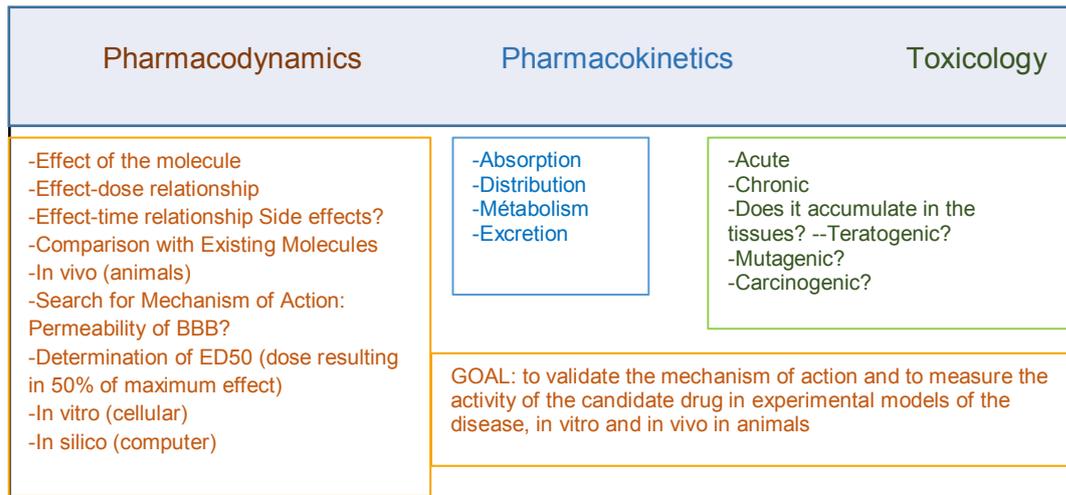


FIGURE 7 - PRECLINICAL STUDIES COMPOSITION

Beyond preclinical studies, we can find both pharmacodynamics, pharmacokinetics and toxicology studies. The figure 7 sets each characteristic of these 3 majors' subdivisions of preclinical studies.

Star company acts mostly in the first columns, pharmacodynamics studies (beyond preclinical studies). Star company tests the efficacy of a compound by doing, for example dose-response curve.

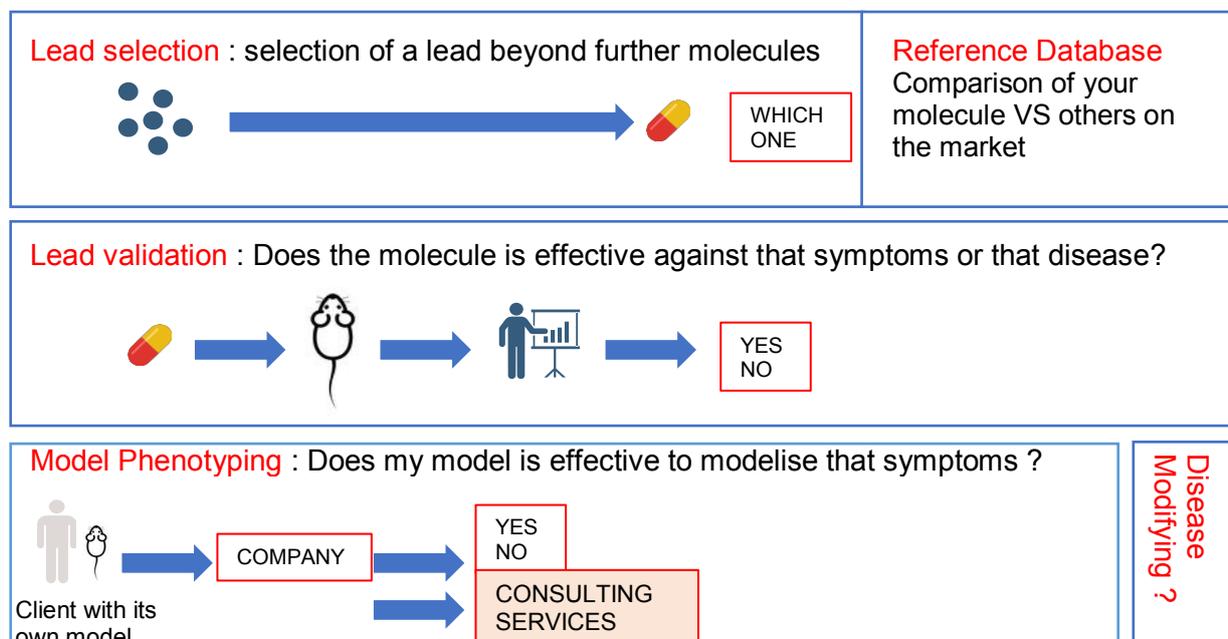


FIGURE 8 - ACTIVITIES PERFORMED BY STAR COMPANY

Figure 8 shows the different activities performed by Star company for its client for each therapeutics area presented previously. Models developed by Star company, are rodent models in which the pathology is induced using molecules: epileptic rodent model, for example is induced willingly by a specific molecule. Then Star company gives an antiepileptic molecule to its “epileptic rodent” and analyze if the rodent stops to be epileptic. If the rodent stop to be epileptic, it can be used by Star company to test the molecule of the client. Then, in this “epileptic rodent”, the molecule developed by a client is going to be tested. The final goal is to test if his molecule is effective on epilepsy (if the client came for this therapeutic area).

The company does **lead selection**: this means to select a molecule beyond a pool. The molecule selected is the one which has the more of success to be effective. Then the company can do **lead validation**: this means to test one molecule already selected beyond a pool, in rodent model owned by Star company, and analyze through electroencephalography, the how this rodent responses. The third activity is **model phenotyping**: in this case, the client bring his own model of rodent, and Star company tests the model with its own platform technology. The goal is to verify if the model of the client works and if he will be able to use his own model on its side, to test molecule. It is a sort of consulting service.

Reference database activity consist of comparing the efficacy of the molecule of the client with other molecules already launched on the market. The final goal is that the new molecule (of the client) tested be more effective than the one already on the market. To manage this service, the new molecule is tested on a rodent model and an electroencephalography is performed. The same process is performed on the same model but with the molecule already on the market. Then the 2 results obtained are compared between them and thanks to this information the client can decide to continue or not the development of his molecule.

Disease Modifying is the term used for a molecule that is able to have an action on the disease entirely. Some molecule have an action on the symptoms only: for example for Parkinson disease, some molecules are able to stop the tremors. These molecule doesn't act on the disease itself. Disease Modifying service, permits to see if the compound of a client act on the disease itself. Star company, as we said previously, performs its services on the neurological field.

Star company, thanks to its development, particularly in the epilepsy market, was able to acquire an image of drug discovery experts for the pathologies of the brain. Its global network is established within pharmaceutical and biotechnology companies.

Star company has partnered with companies of all sizes in Europe, North America and Japan. Its reputation and visibility allows it today to benefit from a growing flow of incoming requests from manufacturers.

5.1.2 External Study

Before exploring the internal part of Star company, we decided to explore first the environment, the external part of the company. By this way it will helps to locate the company between its competitors and also have a better understand of the sector where the company acts. It will gives an overview of the environment of contract research organization, as Star Company is part of this type of structure. A contract research organization, is in charge of the development phase of a molecule. Generally the molecule studied came from a pharmaceutical industry. The work is outsourced.

The external study will consist of a **competitive intelligence research** with an **interpretation** of it and a **positioning study** of Star company between the main competitors. These 3 elements will be helpful to identify endogenous and exogenous factor of Star company thanks to this analysis.

Key word of this part are going to be explained in the current paragraph. A competitor, is considered here as someone who answers at a same problem, at the same question than the company studied. For example, here, a competitor of Star company will be a company which tests the efficacy of molecules on the brain, during preclinical stage. Even if these companies doesn't use the same methodology to answer to a specific question, they are considered as competitor when the finality is the same. Here the finality is to know if a molecule is effective on a neurological disease.

A competitive intelligence research is the analysis of the most competitors as possible, of the company studied. The more competitors are identified, the more it will be easy to position this company on a specific market. The market studied here, is molecules in development for neurological disease. It can be for Parkinson, Alzheimer, Schizophrenia, Essential Tremor or Epilepsy.

The first step is to look at companies which can test the efficacy for molecule at their preclinical stage for those specific disease. The methodology used to search information are multiple: network, internal information, brochure, article on internet for example are source of information that are used.

Once competitors are identified, criteria's of identification are set. Near than 20 factors are used to classify competitors. name, years of creation, type of company (focused or multiple service), electroencephalography practices (yes/no), model of rodent used by the company, size of the company in term of employee, therapeutic area, technology used, partnership, establish client, accreditation (quality aspect), congress participation, location of headquarter or subsidiaries, competitive advantage highlighted by the company, slogan and financial data. When the more competitors as possible are identified, an interpretation of this analysis would

be useful to position the company. As the company decided to manage a competitive intelligence study, which is an external study, it will be profitable internally.

The figure 9 sets the apparition of some key competitive advantage “word”. We will use the most representative ones to position Star company beyond its competitors.

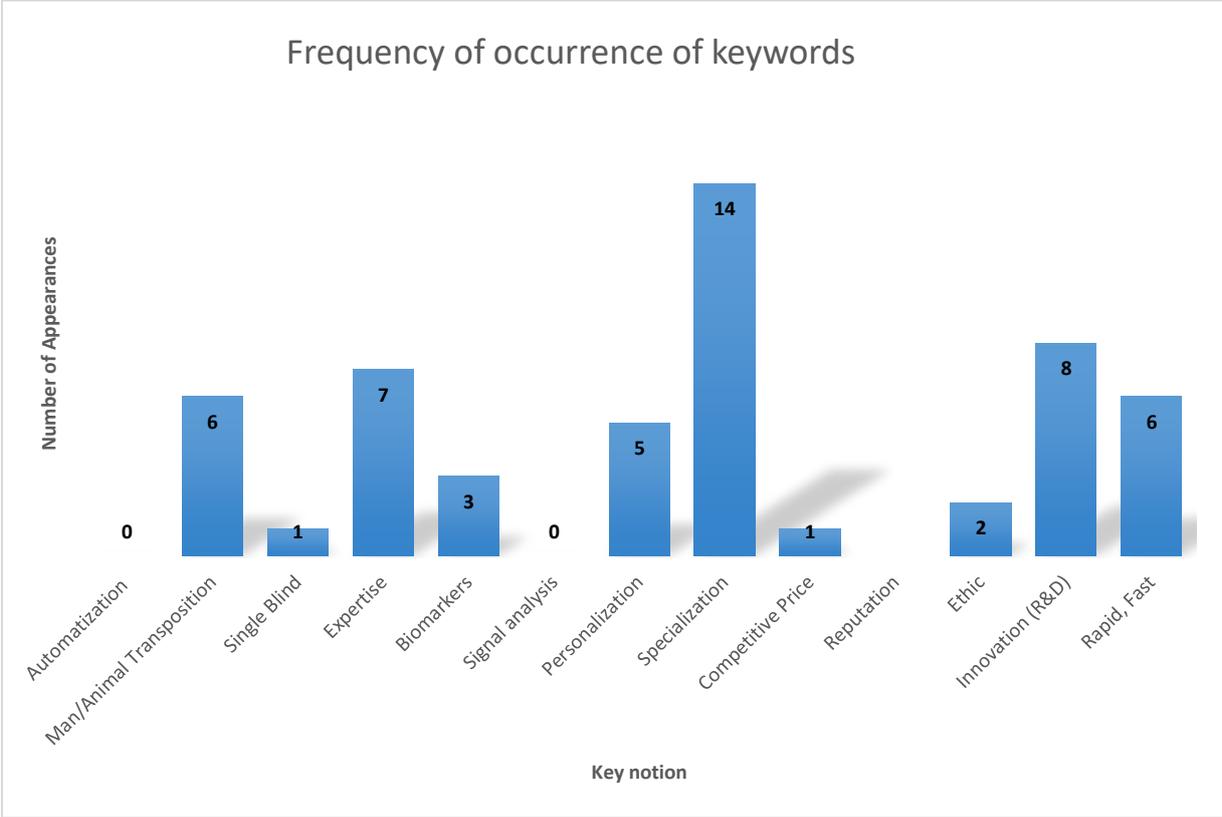


FIGURE 9 - FREQUENCY OF OCCURRENCE OF COMPETITIVE ADVANTAGES NOTION

The competitive intelligence study shows the frequency of occurrence of key notion for all competitors identified. Sources of data were found thanks to their website. More than 20 companies (Star company is not included) were identified through the figure 9.

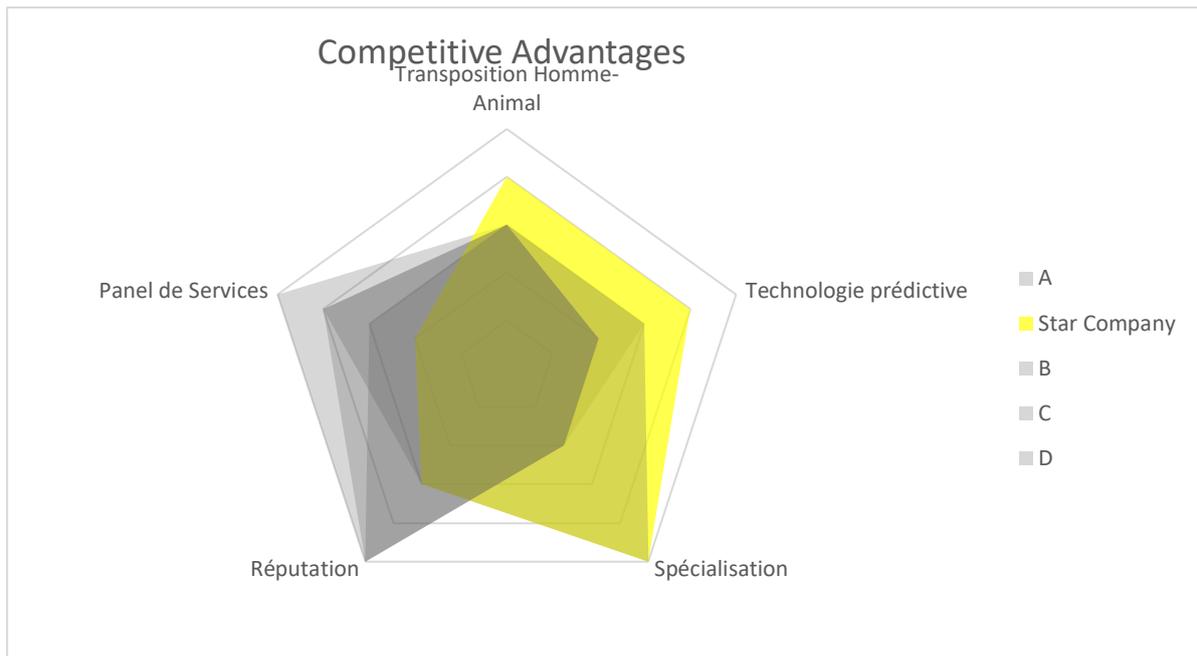


FIGURE 10 - INTERPRETATION OF COMPETITIVE INTELLIGENCE STUDY: POSITIONING

Figure 10 shows the interpretation of the competitive intelligence study: on the right side, the main 4 competitors of Star company are presented. At each extremity of the figure, one competitive advantage, identified previously is represented. This study takes the main competitive advantage of the study, (the ones that appears the most during the research and which are in common with Star Company). These four competitors are those that are the closest to what is done by Star company. The yellow area represent Star company. If the yellow area goes to the extremity of the figure its means that the company has the highest score for this competitive advantage. From the center to the extremity, the scale scores from 1/5 to 5/5. When the yellow area does not go at the end of the figure, it means that the company has to improve itself for that factor. The figure shows that Star company dominates in 3 areas compared to its competitors which are better in the 2 others areas.

Among an environment of contract research organization, follows a position for Star company, issued of this research. This work requires **marketing skills** beyond the team, and it allows to **target market**. For example, Star company is specialized in neurological disease, so it will concentrate its effort of communication in this specific market compared to its competitor which has a large panel of services in different therapeutic area, that will not target a single market. Star company, thanks to its **marketing skills**, can adopt a **sales strategy**. It is the only company that has a predictive technology, so it will plays on its competitive advantages to sell.

Another external aspect of Star company is the fact that it receives the research tax credit. It's a **tax reduction**, in France, based on R&D expenditures. This **tax reduction** is a financial help for research and development company "support for business research and development (R & D) activities, with no sector or size restriction".[13] This research tax credit is equivalent to 30% for research expenditure "up to € 100 million" and "5% beyond". Concerning small sized companies, "For the tax credit applicable to innovation expenditure by SMEs, the rate is 20%, on expenditure capped at € 400 000 per year". [24]

Then, **tax reduction** is related to **R&D Policy**: if this tax reduction didn't exist, maybe the company would not spend as much money in R&D. It is one department where most of the money is spent, to improve future services for clients. Thanks to R&D, Star company develop full packaged solutions (or products) and become a leader on the market of epilepsy. Another factor appears, related to R&D policy is the **product quality**. Thanks to **tax reduction, R&D policy** allows an important expenditure in this department to create or improve solution for client and that makes the product/service quality. These 3 factors are inter-related and complementary.

Concerning the logistic part, Star company is currently located in a site that hosts several companies and propose office, corporate and scientific services. Although Star company is about to change location and take its independency, this business incubator helped it to start and increase turnover thanks to its saving concerning loads. This business incubator is owned by university. It is **government supporting for startup policy**. This saving allows more expenditures in R&D or in employment for the company. Thus, this key factor of **government supporting for startup** is also related to **R&D policy** and expenditures. All of these factors play in favor of the development of the business, and it cannot impact alone. It is when factors are in combination that it impacts the development. Moreover, the business incubator includes an entrepreneur network where advice, idea, or an opinion can be shared. Then, entrepreneurs are not by their own and can share their difficulties between them, and solve problem thanks to idea from another firm.

5.1.3 Internal Study

After an external study of Star company and its environment, we will explore in more details the internal side. This part will begin with a **SWOT** that will present strengths weaknesses, opportunities and threats of Star company. **Strengths** identified during this investigation are the followings:

- **Automation during the process**

Since employee have to generate a huge amount of data, they decided to create an Excel matrix that generates data automatically with only one click. By this way there is no “human” intervention during generation of data. The consequence of that, is less human errors due to lack of attention. Effectively, during a study lot of data are generated and if employee should enter all of them by their own, human errors would certainly happen and distorting data. This automation was generated through an employee. **Employee skills** play here, an important part in productivity since everything is automated and reduces human error.

- **Human protocol**

Human protocols are used on their rodent model. Star company, as we see in the external study, tests molecule on the brain of rodent model. To manage that they realize an “human protocol” on these rodent. It means that they apply on their rodent model, the protocol used on human during clinical trials, to test the molecule. This is a part of their **competitive advantage**, they are expert in “transposition” from animal to human. Process like this provides a greater reliability. Moreover, the person (technician) who tests the efficacy of a molecule on the brain of a rodent, doesn’t know what this molecule is. This type of condition is called “simple blind” test. The fact that the technician doesn’t know the molecule tested, add a degree concerning reliability. If the technician known the molecule and its effect, he could be attempted to modify the results. By this way, there is no human bias.

- **Expert in neuroscience**

Star Company has chosen to be specialized and expert in neurology and to concentrate its know-how around neurology. This choice paid off as today Star Company, with its focused expertise, is the world leader in epilepsy, in efficacy testing.

- **The way to communicate**

Another strength found during this investigation is **communication skills** inside the company. Star founders and employee consider the way to communicate as an important part of sales. They decided to implement some special sessions called “TILT” sessions with the following goal: adapt the way to communicate to target more client. For example, to sell a service to a scientist client with a scientific personality, we will use a different communication than for a business client, who use business vocabulary, for a same service.

Before using this personalized language, all the team should be convinced that this new methodology will be useful, and it is the role of “TILT” sessions, to show everybody, that depending on their background, people has different way of perception of a same presentation.

Then, Star founder evoked also the **time to market** as a very important factor. The time here is not seen as the time it takes to sell but the fact that the product will be “up to date” corresponding with the trend of its current time. Then the CEO of the company present us the following notion of technology adoption life cycle.

Geoffrey Moore which is an author, speaker, and advisor has been consultant for several start-ups. [25] Figure 1, issued from Geoffrey Moore’s book presents different group of people and the way they adopt an innovative product, depending on the group they take part of.

The **Innovators** are people who pursue all the new technologies, they are more focused on the fact that the technology is new than the option it can have. They are not so many people but it’s the first one who will buy the product. The **Early Adopters** are less attached to the technological aspect, they will buy the product not because it is well established on a market, but because it is connected to their hobbies. They buy it because they believe in it, thanks to their intuition.

The **Early Majority**, which is one of the bigger group, will buy the product after having some returns from the previous buyer. They need reference before investing in a new product but they have the ability to handle with a technological product contrary to the **Late Majority**. This group comprises about “one-third of the total buying population”, so it can be a very profitable for a company. To make them buy a product, they need to be confident with it, they need some standards. That’s why they often buy from large well-established companies.

Finally, the **Laggards**, are people who doesn’t want to deal with new technologies for personal or economic reasons.

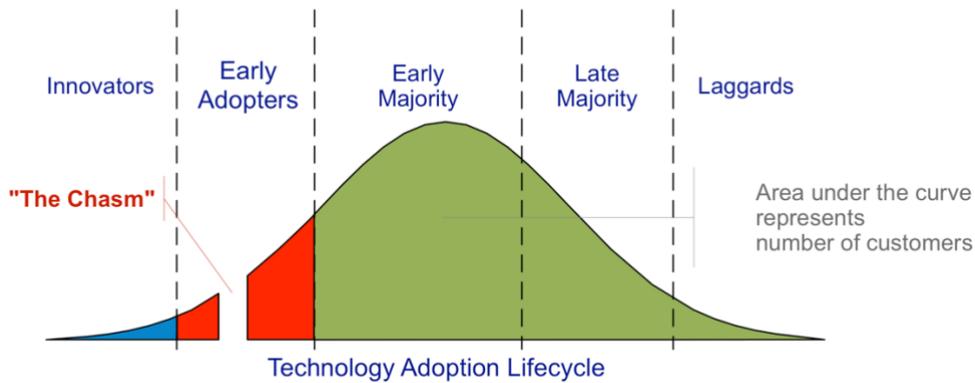


FIGURE 11 - THE REVISED TECHNOLOGY ADOPTION LIFE CYCLE [26]

We can see some holes in the figure 11 [26] between all the categories of people. The challenge for a company is to sell its product to each kind of people and trying to reduce the more possible holes. Difficulties are that each categories of buyers will not buy at the same time and not for the same criteria. The second hole can be a risk of failure for a company. A company can believe that its business is currently growing a lot thanks to early adopters' buyers. This company will may raise some fund to develop itself instead of analyzing its change of customer's type. We realize then how review his primary strategy is important in this example, to convince the others customer type.

- **Agile Management,**

Methodology concerning work is agile management. The work is shared between the team and there are some objectives with deliverables and a rhythm adopted. The goal is to produce all the deliverable at the end of the period, with the implication of all the team. It requires also to monitor the progress of work.

Weaknesses identified during this investigation are the followings:

- **Some of their services are not fully industrialized yet.**

This is because some service and therapeutic area where added recently, so some of their services are still tested and not completely industrialized as some could already be. Innovation is one of their value, so they have a strong research and development unit where there is all the time application in development.

- **Language used is very technical,**

due to the activity performed and the complexity of this therapeutic area. It is necessary to adapt the vocabulary depending on who the interlocutor is. He can be either technical or business focused so it is imperative to adapt the language used.

- **The quantity of work is not so predictable**

It is difficult to predict the demand concerning contracts, and it is also difficult to refuse a contract from a client, since the company is not a major player in the world of contract research organization. The goal is to accept all the contract and to manage facilities in order to be able to realize them all.

The opportunities identified during this investigation are the followings:

- The neurodegenerative sector will be confronted to the **papy boom phenomenon**:

The number of aging individuals will increase, so we can imagine, neurodegenerative disease will increase too. This can be translated to an increasing need and perhaps an increasing market.

- **A competitive environment**

There was no major discovery, since 20 years: no major treatment has been discovered, which encourages the pharmaceutical industry to search and test always new molecules. It is like a “race” of which company is going to find the right treatment. Moreover, thanks to epidemiologic data, we know that the number of people with Alzheimer’s disease will drastically increase in the next years, the need to find a treatment will be important.

Finally, **Threats** identified are the following:

- **Competitors**, who answer at the same question/same problem

Huge contract research organization, which answer at the same question, “is the molecule effective on brain disease?” are a threats for Star company, even if they do not use the same method, they finally bring the answer. Mostly if they are able to answer at a same service for a lower price.

- **Mergers and acquisition**

The example of a huge contract research organization which acquires a small company specialized in neurology will be a threat for Star Company.

- **Turnover**

Since the expertise and the know-how is one of the bigger competitive advantage owned by the company, departure of employee with expertise and know-how is a real threat for the company.

Concerning the business model, it follows the next steps:

1. Meeting with the client: the project manager of pharmaceutical companies of all sizes, mostly in Europe, North America and Japan. The client is in charge of the development of a molecule against Parkinson's disease, Alzheimer's disease, Epilepsy or Schizophrenia. The latter wants to know which molecule to choose from a "pool" to continue its development. The goal is to maximize its success rate for the market. Thanks to its technology, which includes scientific experts, their know-how, predictive biomarkers, an encéphalogram, algorithms, Star will predict the efficacy of a molecule and select it today.
2. Star's team models the study of the client according to the therapeutic area concerned.
3. The customer signs the contract and pays 50% of the total amount to the signature.
4. Star sends the experience report to the client who pays 50% of the remaining amount.

The average basket per customer is 50k € for a contract, the latter can add additional options and thus increase the total price. A contract takes on average between 3 and 6 weeks from the start of the study to get the first data and 11 to 15 weeks on average to get the final report.

5.2 Interview: biotechnology small sized company in life sciences

5.2.1 Entrepreneur & company A

Company A was founded in 2003 by two brothers; it is a very small company. The company provides Cell Biology Services to client, mostly bigger contract research organization which work for some pharmaceuticals industries. One brings its scientific knowledge and the other one brings its business knowledge. Although there is intern or interim employee, the company counts 2 employees because it is its business model. Accountability, communication, or some other tasks are outsourced. The company does not have investor, but “**love money**” which is money or capital given by family or friends. “**Love money**” can be added in factors of development, it is a financial factors related to the close network of the entrepreneurs, because that contributed to the development of the company. **Network** is also a **human factor** because here, the close network of the entrepreneur **brings him some skills** of communication, marketing, negotiation with client. New skill can be learnt through family, friend, and network of entrepreneurs with expert in their field.

Then, the entrepreneurs A, told us that before doing marketing, it is important to know what are the **key factors of success** of our company (both in Research and development, production and marketing) and what are the competitive advantage. For the company A for example, one of its **competitive advantage** is its huge expertise in its field, and its reactivity. Thanks to the fact that it is a very small company, there are frequents exchanges with the client, which is a benefit of being a very small company. Moreover, their type of client are most of the time pressed, mostly contract research organization, so they appreciate frequent exchange and reactivity. Once these factors are identified, we can then work on marketing. Then, when competitors improve their factors of success, it is necessary **to be aligned to them**. For example, company A, which didn't do communication before, felt the need to practice it, and then create some tools to communicate (a video presenting the company for example).

Each year, these 2 employees improves their strategy and communication, and turnover increases a little every year. The business model is based on “services”, that allows entrance of cash soon, with a scale of weeks or months to get paid, contrary to business model of a company which create a molecule where there is a need of a lot of cash during many years before getting a return on investment.

Further element concerning the increase of the turnover where given: first, it is important to **analyze the economic conditions**, to know when to hire (interim employee in this case), or not. This take part of entrepreneur's skills, more precisely: **dynamic leader who understand vision, strategy, risk and tactics**. Then, marketing skills play an important role in terms of “**knowing your target market**”: entrepreneur analyzes and assesses the activity of their important client, look at their news, their online network, and their current stock market, how their activity evolve.

The company benefits also of the **research tax credit**, it is necessary as the entrepreneur A explained, today more and more company benefit from it, and it has a consequence for the client. This research tax prompts the client to subcontract, because it is deducted from its tax. The research tax credit is therefore an unavoidable factor for small sized

innovative company. It is not a competitive advantage since every comparable company hold it, it is rather a necessity.

5.2.2 Entrepreneur & company B

Company B was created in 2008, and count today near than 20 employees. This company is specialized in the development of physiologically-relevant cellular models and assays. The company has developed its own model of skin and human muscles destined to pharmaceutical/dermatological company, in order to test drug on it.

The company worked first only for academics clients, but the business model wasn't viable. The average shopping basket was 500 € and prospection costs were bigger than manufacturing costs.

They decided to industrialize the process and to change the **business model**, so adopting a new strategy. This take part of the **operational factors**. In 2015, they implement this new economic model and they become a CRO (Contract Research Organization) which tests drug from their client on their model. Principal client were pharmaceutical industries and the average shopping basket goes up to 20 000€: the turnover increased. **Changing the business model** able a new activity, new client and new logistic. The company reduced a lot the number of employees once the activity was industrialized. It was a way to grow for this company, that used **strategy management skills** according to our classification.

Moreover, the **addition of this new activity** of testing drug was also a strategy to create value for the company and also for its shareholders. This is another factor which belong of **financial skill** of the entrepreneur.

Today, the company adds a third activity which consist of creating its own drug against muscular disease. This is first an **idea development**, because they decided to start the development of their own drug. Also they are trying to **answer to an unmet need**, since the target disease does not have efficient treatment on the market today. Moreover, is it a niche market, because it is very specialized. Those notions take part of Research and development Policy of the company according to our classification. Then it permits to **value much more the company**. To finance this new project, the company will maybe look for a **co-development of that molecule with a pharmaceutical industry**, which is a type of strategy management skills. To achieve goals, they implement a projection in 5 years. Concerning quality management, the company decided to spend money and energy for an audit process.

Through all these changing process in the company, **the climate and culture** move from a technology to a product. We can talk of “sales orientation instead of technology orientation” today. The most important advice evoked by entrepreneur's B is first to industrialize a technology, then transform it to a product, and thereafter looking for his market.

Entrepreneurs B, also told us the 3 sources of funding for a start up in biotechnology: first the turnover (in case of business to business company), then the tax research credit given by the government and then public funding through agencies for example.

5.2.3 Entrepreneur & company C

Company C was created in 2005 and counts 6 employees. The company is currently developing an online platform which helps for the prescription of medication in rheumatology when patient do not respond to their treatment. This technology is still in development and is about to be sold soon. The technology performs in combination with a blood test (dosage of protein) on the patient, and then, thanks to this blood test, an algorithm analyzes the data and select an appropriate treatment for the patient. The choice is personalized for the patient. The finality of this technology is beneficial for the patient who gets an appropriate treatment and also for the health system of the country, which won't pay for an unappropriated treatment. Then the system of healthcare would be able to save money through this technology.

We identified here, that behind this technology, there is a strategy skills to make the **healthcare system saving money**. Moreover, **sales are oriented** first through the “need” of patient instead of being oriented only through technology.

Then, the fact to “personalize” treatment of a patient who suffer from that specific area therapeutic, needed Strategy management skills: **Answer to Unmet Need**, because today, there isn't a technology which attribute a personalized drug for the patient in rheumatology. There is also R&D Policy which is involved: **New Idea development**. Indeed, inventing a technology which tells what to prescribe for a patient thanks to its blood testing in the specific therapeutic area of company C is both R&D and strategy combined, if we refer to factors identified in the literature review.

Then, concerning source of financing, the company does not have investors. How the company gets cash to develop its technology? To “survive” the entrepreneur C explained us that company C creates **collaboration with pharmaceutical industry**, and it generates cash. Also they participate to some **contest** and won one (winner prize), which is also a source of cash. It is their main source of financing. This takes part in our classification of **financial skill** both **strategy management skills**. Concerning National Policy, the company benefits also of the **research tax credit**.

Another major aspect, evoked by entrepreneur C, is the **team**. Having **key opinion leader in the board or a credible person** is a major factor. It plays an important role for the company. Company C which technology takes part of a specific therapeutic area count in its scientific board, some Head of department of one hospital: this fact make the contact with industrial actors much more credible. Then it makes it easier to open doors, thanks to the renown of these people. Also these people know the market very well, because they prescribe molecules of this therapeutic area. Moreover, if these people go in a pharmaceutical industry to convince them about the technology, they will be much more credible than a employee. This take part of the **human resources management skills**, more precisely **high quality team**, and this factor

helps to convince client and finally to **generate cash**. High quality team is here both human resources management skill and financial skills.

Then, thanks to the cash generated previously, hiring a team with **complementary skills** is also necessary to develop the technology. This takes part of employee skills. The factor identified here is the ability to **structure its management team**, and bring the fact that each employee can bring his expertise.

5.2.4 Entrepreneur & company D

Company D was founded in 2004 by scientists specialized in microbiology and physiology. The aim of the company is to sustainably produce molecules from renewable raw materials using biotechnology, for pharmaceutical industry. To manage that, they modify the chromosome of a microorganism to make it produce high-value molecules. This can be qualify as a high quality new product process, according to our classification. This is a production management skill, because it need a real expertise. This is the first factor identify which is an operating factor. To arrive performing this activity, it need desirable biotechnology employee and this is the case. It is based on the employee that they decided to create the company. The company was created because of employee skills, officially in 2014.

Most of the employee have a scientific background, so they decided to hire a person with finance skills who helps a lot the founders, which had mainly scientific expertise. This new employee with finance skills, bring his expertise and it has helped to manage the financial health of the company. This shows, how important are human resources management skills, more precisely adequate resources of people.

Concerning fundraising, the company started with love money: when friend or family accept to put money in the company to help to develop it. It is imperative to establish conditions since the beginning because if they want to take back their investment it could be a financial problem for the company. That was the case here; when the company started to gain value, the investor of love money decided to take it back. That's what happen and the company has to proceed to another fundraising round to counterbalance the effect. Following this story we identified fundraising skills as an important factors concerning the development and more precisely establishment of conditions since the beginning.

The next event concerning company D, is that they realized their business model of service was not profitable, partly linked to the decision cycle concerning their client, which was too long. This is **marketing skills**: evaluate their business model and deciding to change it. Also they demonstrated management **commitment and accountability** by acknowledge the end of the “glory hour” of their sector. This take part of **entrepreneur skills** and open-mindedness. They decided to move into a new sector, so changing activity and changing client.

Research and Development Policy is about to change, and this can support the notion of innovative climate and culture.

Marketing skills are involved in changing business model because, for example here, it needs to know the new target market and also estimation of the time to market. Although they decided to change their activity, entrepreneur D told that they need to validate their new process and that will take time and money. Even if the company beneficiaries of **Tax Research credit**, they made a fundraising planification: **financial skills**. For example, their first fundraising concerning this new project will serve to automatize everything.

Another aspect concerning their new business model and also their new sector is **national policies**. They studied all the requirements concerning their new sector, to be sure that they will be able to manage it. For example a list of the list of authorized compounds in cosmetics. This list can change in a country from another and they are trying to anticipate that risk.

5.2.5 Entrepreneur & company E

Company E was created in 2006 and takes part of medical technologies industry in the sector of oncology and more precisely prostate cancer. One of the two founders is engineer with a medical imaging thesis and the other one has a background who brings him marketing skills and innovative market skills. We can see that in this **entrepreneurial climate**, background and skills are complementary with both business and science knowledge.

The technology consists of a software which provides help for surgeon, more exactly imaging tools. A 3D map of the prostate is obtained, and thank to this map the urologist gets a comprehensive and multiparametric approach, which brings much confidence concerning diagnostic. This technology enables patient monitoring, and helps concerning time to implement the treatment: through imaging it is possible to see the stage of the disease. It permits also to conduct a localized biopsy. This is a **high quality new product**, since this technology is unique and not copied. To implement it, it necessitated **production management skills**.

Moreover, the ability to detect and qualify prostate cancer, centralized in a single device, can be qualified as an “**answer to unmet need**”. According to our classification, strategy management skills are involved in this company.

Concerning financial part, the company beneficiaries of **Tax Research credit**, **government grant**, and was the winner of the Global Innovation Competition. This provides financial help. In 2012, one **investor** also put 1 million in the company. Founders decided to **invest that money in** hiring some employees, accelerate sales and production, accelerate R&D

project. Through this point, the company sold its product worldwide, with a consequence increase of the turnover. The important point highlighted here, is the fact to **spend intelligently the funds you get**. This is a **financial skills factor of development** of the company.

Today, this company contains 40 employees and has its headquarter in France and subsidiary in Boston. It has 150 clients worldwide and sold its product in 25 countries. We can say the company **knows its target market**. Beyond the team, each department are represented: R&D, Marketing and sales, Purchase, Quality, Finance, Administration. This success is attributable, for an important part, to the **team**. “Constitute a competent team, motivated and comely with a spirit start-up” said entrepreneur E. According to our classification: **Structuring its management team, high quality team, adequate resources of people and Desirable biotech employee** are all involved here. All these factors are either entrepreneur and employee skills combined to operating factor: human resources management skills. The company was able to hire all of the employee thanks to funds gets previously. Those factors (financial skills: spend intelligently and entrepreneur skills: Structuring its management team) are linked together.

Another phenomenon happened: hospitals tried to get the device for free and proposed in return to write a publication of it. But founders did not yield and instead of that, the company sold it to hospitals.

Concerning intellectual property, the company uses a **patent**, to valorize this advanced technology and also the company.

5.2.6 Entrepreneur & company F

In 2009, founders have participated and won a business start-up **contest**, then the “virtual” start-up joined an incubator to help this company to begin. Concerning national policies, **Government support for startup** played a role for this start up creation during 18 months. Then, founder created the file to participate to the second phase of this contest in 2010 and won again. Once the company gets public grant thanks to contest, bank are willing to lend money.

In 2011, company F was created as a “spin off” of the university which owned the patent of the technology. The know-how of this company is production of membrane proteins. Entrepreneur F told that the company work in 6 different segments and is not specialized in one. Dynamic and market beyond these 6 segment are not equals, and the company would like to **position** itself in 1 or 2 segment, and that’s take part of **strategy management skills**. About the vision, the company has a **technology orientation** more than a product orientation.

Concerning key point for the company, **investors** arrived in 2013 and put money in the company, that's able bank also to lend money. The growth was not as it supposed to be, for the company because first time was underestimated and then there were not enough client contract.

To manage this, the company used an external consultant in communication and marketing, and used network. Also employee go to **congress to communicate**. Then, there are important competitors in that sectors, and some of their client practice this work in interne. Moreover the company was not able to lower prices compare to its competitors. Concerning **structuring management team**: today, the company counts 2 technicians, one engineer and a scientific director. There is also a commercial employee who manage prospection, marketing and congress.

Entrepreneur F, mention also an exogenous factors: the **location** of the company. If the company could have a subsidiary in United States, it would help it a lot to grow, since the majority of their market is over there.

5.2.7 Entrepreneur & company G

The company was created in 2009 based on a patent detained by university and center of research. One of the two founders come from this center of research. The goal of the company is to develop imaging system for surgery. The first factor of development evoked by entrepreneur G is intellectual property, patent of a company and its license negotiated with the university. A strategic point mentioned then, is to develop its own intellectual property thanks to patent around the principal technology. It is like to **“build a forest” around the central patent**. By this way, it enables competitor to block the company. This first factors belongs to the huge family of operating factors more precisely **strategy management skills**. Then, when they created a product thanks to the patented technology, they patented the product, even the design. This contributes to the valorization of the company.

Entrepreneur G, mentioned then the importance of the **team**, from the founder to all the employee with all of their complementary skills. Turnover is difficult for start-up, due to the diversity of skills. Today the company counts more than 20 employees with **all kind of department**: development, industrialization, production, quality and regulatory, scientific aspect, pre-marketing, sales, administration of sales, strategy, administration, finance and human resources. Employees can be both **internal and consultant employee**. Some of them, expert in their field, work once a week for example. From these data, we can see that the entrepreneur G knows how to **structuring its management team**, with desirable biotech employee and it is an important entrepreneur skill, thanks to that company G has **adequate resources of people**.

About the financing part, the company decided to do **successive fundraising** with local and national business angel. These fundraising steps happened **after each new valorization steps of the company**. One example of a valorization step for company G was when one of their product gets the CE marking. Then the company gained value and proceed to a fundraising process. This is a financial skill, to **organize its fundraising**.

The technology is an imaging system; the goal is to “try to see more than what the surgeon can see in the reality”. Hospitals are their client and surgeon the user. Today the 100 technologies are sold in more than 16 countries, and enables more than 10 000 surgical procedures. Concerning the choice of country, entrepreneur G **targeted** first US market since this market is based on technology and innovation. Then Europe was target, because the headquarters of the company are in France. The other market was touched thanks to opportunities with **Key Opinion Leader meeting** (in Singapore for example). The **network** is also a factor of valorization and development, and more precisely KOL. Effectively, these KOL test the technology, then write an article about this technology if they are satisfied, and finally talk of it during congress. After that they are followed by other professional and sales go on. This is an exogenous social and political factor, which plays an important role concerning sales of the technology.

5.2.8 Entrepreneur & company H

The company H was created between 2008 and 2009, in the sector of orthopedic surgery. The technology consists of touch screen tablet and proprietary camera. Thanks to this technology, the surgeon can have a “guidance” during the operation. The camera linked, can be integrated into the sterile field. This technology allows a real virtual control during the surgery.

Before creating this company, the founders have created a previous company in the same sector, with the same goal concerning the previous technology: helping for surgery. Thanks to their previous experience, they already knew the market, regulatory and the environment. Moreover, they keep all of their employee, and so the know-how of this previous company, to introduce it in the new one. They started the company H with: know-how from the employee, very well-known of the market and competitor, and distribution channels. In fact, **previous experience**, played a role in terms of learning for the next ones. Thanks to this previous experience they already have **adequate resources of people** (hardware, quality, regulatory, and production team) and it required entrepreneur’s skills, like **commitment** to convince all of them.

They obtain the FDA approbation and CE marking in only 2 years because they knew how to manage this phase. **Previous experience** plays also a role in the **knowledge of regulations**. There are today 3 founders with an American surgeon beyond them. This was a strategic way to get in touch easily with their market: the American market and their client: **Key Opinion Leader**. This strategic choice able them to **know better their target market** and

to get in touch with it. A **good marketing and sales strategy** follows from all of this (KOL and previous experiences). But the strategy of the company was not to sell directly to hospitals, but to **work with an industrial player** on the American market in the same sector.

They have passed a deal: the industrial player **finances the development** of company H products, and in exchange this industrial player is the only one that sell them to client. In other words, company H sold its product to the industrial player, which sold it to clients, which were nothing else than hospital and KOL. Company H did business to business with this industrial player. In term of strategy, company H benefited of the notoriety and sales forces of its industrial partner.

The final deal was: if this industrial partner was satisfied of the current collaboration, it would acquire company H, in order to add value to its business. That's what happened, this industrial partner bought all the company H with all its employee, in 2015. This was a real success for this company H. This success is attributable for an important part, to **entrepreneur skills previously acquired** during the first business they have created. Since the beginning they had the **vision and goal** (to sell the company), they **took risk** with the collaboration and they used **tactics** (get a patent for their technology). All of these notion are **entrepreneur skills**.

6.Findings

6.1 Case study findings

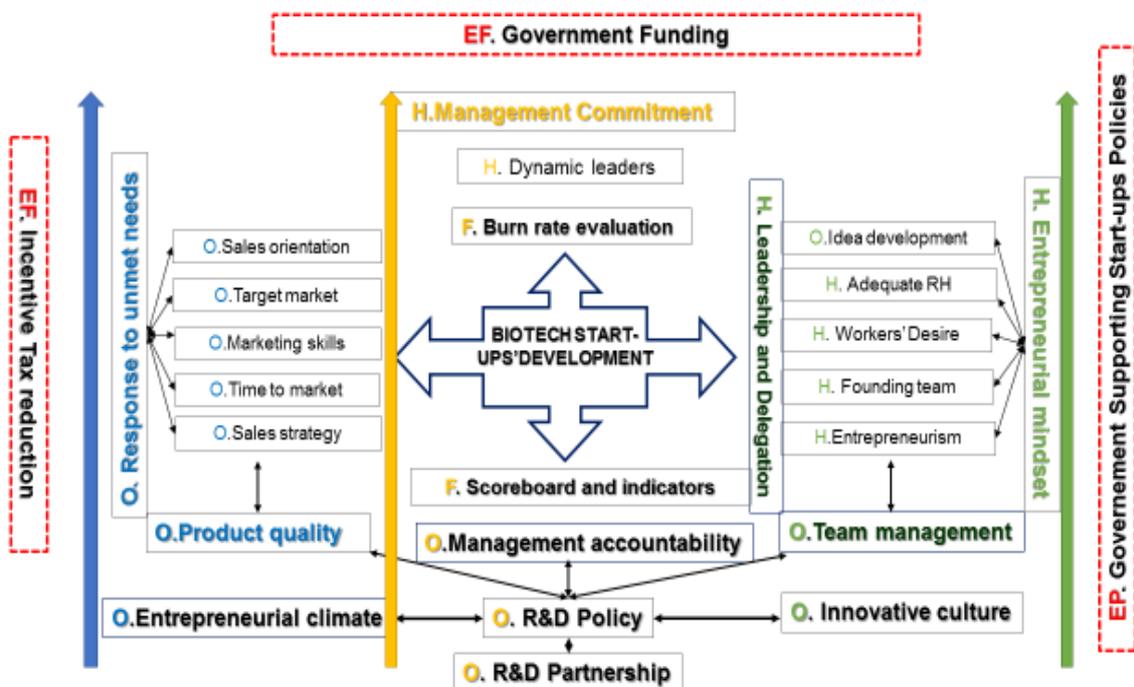


FIGURE 12 - FACTORS FOUND DURING STAR CASE STUDY

The figure 12 shows that all the characteristics defined are interrelated. Each of them is embedded in the firm organization. We can only discuss firms' sustainable development through the indissociably and inseparable relationship that links all the characteristics that we make emerge through our readings.

But we can observe three Axes: Products Axe in blue, Human Axe in green, Management Axe in yellow. They are all surrounded by a fourth axe: Financial Axe in red. The axe Management covers both Human skills (H), Financial skills (F), Operational skills (O). Indeed, the three Axes all converge towards Firm Financial Health. So that means Financial Axe results from Human elements, Operational elements and Strategic elements. Products Axe (in blue) integrates operational elements aiming to sustain the Financial Axe by responding to the new unmet demand.

There is multiple way to read the previous figure since all the factors are related. We decided to read it through the different axes. If we start with the product blue axe: establishing a competitive intelligence research and a positioning study (presented in the part case study) makes emerge many factors. First, the competitive intelligence research is a work which consist of identifying the more competitors as possible. Then, the positioning study will permit to situate Star Company beyond its competitors. In this case, the **positioning study**, has demonstrated that:

- Star company was the only one to have a predictive technology, this correspond to the operational factors **response to unmet needs**.
- Star company was specialized in neurological disease, compared to its competitors which are diversify in multiple service. Knowing these element, able the company to **target a specific market, so to have a specific sales strategy**.
- "TILT" session, are session where all the team talk about the **communication strategy**, presented in the internal part of the case study. **Sales** are now **oriented** through the **product** instead of the technology. This factors was also evoked during the interviews. It showed how important it is, to target every client, and different personalities as we already see through the revised technology adoption life cycle (figure 11, internal study). It also gives an idea concerning the time to market a new application developed by the company. Clients are different group of people, and they will adopt the technology at different time thanks to different criteria.

All of this factors take part of operating factors and more precisely, marketing skills. The implementation of all this factors, conduct to a product quality and so an entrepreneurial climate. We will see that all axes are related to the others.

We will now describe the yellow Management axe. The first important notion is **Management Commitment** which is a human factors and more precisely an entrepreneur skill. Management commitment is link to **dynamic leaders**. For example, founders of Star company go to a minimum of four congress a years and this number is going to grow. Moreover, these founders have a vision of the future: they are able to describe the ambition of the company and

give a photography of the company in five years. They also organize some teambuilding day and 2 days of “convention” a years to do a summary of the previous months, in term of strategy, finance, turnover, objectives, with all department included.

Then, we have the **Burn rate evaluation**: it is the evaluation of months of availability of cash. One founder manages all the financial part of the company including the amount of cash necessary to run every month. This is done thanks an Excel A4 format page, where all the financial information figure. Beyond this document we can found forecasting for the next five years of: the turnover, incomes and expenses, operating profit, net income, cash flow statement and finally cash. **This scoreboard and indicators** are a real help to anticipate changes and need in cash, and in resources both human and equipment. It is also a way to show to the investors that the situation is entirely controlled and forecast. It is a way to reassure them, it can be related to **management accountability**. Concerning **R&D Policy** and **R&D partnership**, Star company has internal both external project, financed by public institution. Concerning external project, it is collaboration project with institution and company. The goal is to share scientific expertise to create new application. Internal project are financed by public institution and the goal of this grant is to help Star company to develop a new application.

Concerning the green axe, it is all the human part of the factors. The general idea is an **entrepreneurial mindset** in Star company. For example, the **team management** used is agile management with a rhythm of three weeks called sprint. At the beginning of a sprint, the objective are set and ranked in order of priority on a board. These objectives are divided into deliverables, and each deliverable is written on a post-it. Once the deliverable is produced, the post-it is moved on the bottom of the board. This type of management in a small sized company can also be considered as an **innovative culture**, since this rhythm can be a source of motivation for employee and no one take the responsibility in case of failure.

All the solution developed in the R&D department came from the research and innovation team, where everyone have a scientific Ph.D and a strong expertise in neurosciences. When it is developed entirely, these solutions are commercialized by the business development unit. This unit is composed by employee with international background. Finally, after selling solution to client, the Laboratory unit, composed by technician and also Ph.D, realize experiences. The company can run itself because of an **adequate resource of people and workers desire**. This is also thanks to founders skills, who had the ability to create a founding team and to hire the adequate and motivate person.

Finally, the red financial axe, which is surrounded, permits the global operation of the company. **Incentive tax reduction**, is the amount given by the government defined during the case study. It contributes to the financial help and it is also a benefit for the company. Then, **government funding** plays an important role concerning subvention and collaboration project. Near than 4 internal projects of Star company were financed by public institution. Government funding allowed to develop and then commercialize some application developed by Star

company. Another element which has helped Star Company is the biocluster/incubator building which hosted the company before its moving in September 2017. In this type of building, expenses are reduced and there is a different type of similar company where employees can bring knowledge to the others. This takes part of **Government supporting for start-ups policies**.

To summarize this case study, all the factors found during the case study, which take part of the different axes are inter-related to each other. It is the dynamic of all of them, that enables the development of Star company. One factor can enable the implementation of another for example **R&D policies** and the amount of money and time decided previously, enables finally to get a **Product quality**, also get thanks to marketing skills of the employee and thanks to **team management** and **workers' desire**. There isn't a list of necessary factors, but a cohesion of all the present factors.

6.2 Interview findings according to the literature review

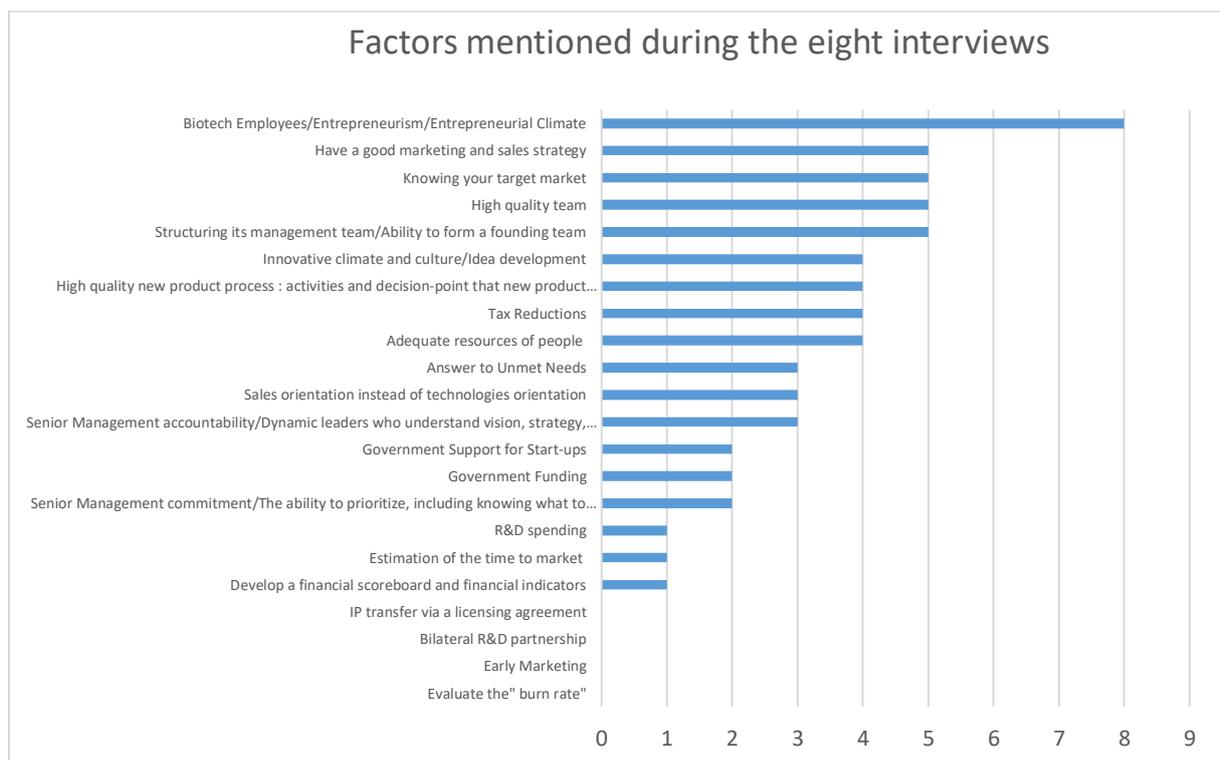


FIGURE 13 - RESULT OF FACTORS FOUND DURING INTERVIEWS

Twenty-two factors were previously identified in the literature review, (nineteen endogenous and three exogenous factors). Beyond these twenty-two factors, eighteen were found during the eight interviews. The factor that most often appeared, was **employee's skills (desirable biotech employee, entrepreneurship)**. It was cited by all of the eight entrepreneurs. This factor is in the categorization human factors. In other terms this factor is related to the team; select the good person with complementary skills, with a specific know how and

motivated. The notion of complementary team, explains the factor “desirable biotech employee”. The fact of having a team, where all skills are present, seems to be important concerning the development of a company, to the majority of entrepreneur’s interviewed.

Concerning second most evoked factor: it is four other factors which arrives ex aequo with a score of five out of eight:

- Structuring its management team (Entrepreneur skills)
- High quality team (Human resources Management Skills)
- Knowing your target market (Marketing Skills)
- Have a good marketing and sales strategy (Marketing Skills)

Concerning “Structuring its management team”, this is a skills relative to the entrepreneurs, and the ability to choose which people to work with. For example, company C works with a key opinion leaser in the founding team, and this element played an important role concerning the sales of their technology. For the entrepreneur of company E, this factor was more to structure precisely department inside the company: create different department with specific employee like quality, finance, marketing in a company of forty employee.

High quality team, is close to desirable biotech employee. The difference is that, here, it is seen has a human resource management skill, more precisely the skills of the recruiter. Concerning desirable biotech employee, it is the skills relative to employee. Most of the time it is founder who hire people but it can be employee sometime. Here the factors high quality team, is for example having a quality team with a specific expertise.

Marketing skills were also well represented with “Knowing your target market” and “Have a good marketing and sales strategy”. “Knowing your target market” can be explained as “who are your client?” This was underlined by entrepreneur interviewed, effectively it is important to know, whom we are going to sell, and having some data. How many clients in France, Europe, Worldwide, and also how many clients already targeted, who already bought the product sold. Company E for example targets urologists. The company knows that its technology is sold in twenty-five countries and have one hundred fifty clients. Company A analyzes the activity of its client (if they have a new molecule on the market, or if they go to congress) to see their evolution and predict their need. It is a way of knowing its target market.

In a second way, “Knowing your target market” will help to adapt better our strategy: “Have a good marketing and sales strategy”. This factor was evoked five times differently. For the company F, their marketing strategy is to take an extern consultant, who will manage all the work concerning marketing and communication. Because the company counts only two employee (it is their business model) they decided to contact a consultant to run that part.

Having Key Opinion Leader in the board concerning company C can also be a sales strategy because their mind and opinion influence the environment. Moreover, key opinion leader have follower who act like them. If a physician client see that a key opinion leader (physician also) is convinced about a technology, he will certainly adopt it. We can note that four factors found in the literature review were not evoked during the interview.

The results are going to be presented and the ponderation of factors explicated. The total numbers of factors mentioned through all the interview is sixty-two. If we look the score obtained for all the categories, (Figure 14) **operating** factors are the most represented with thirty five apparitions out of sixty two total factors mentioned (56%). Human factors represented a portion of 29% beyond all the category of factors and finally Financial and social/political factors were the smallest portion with respectively 11% and 3% of factors.

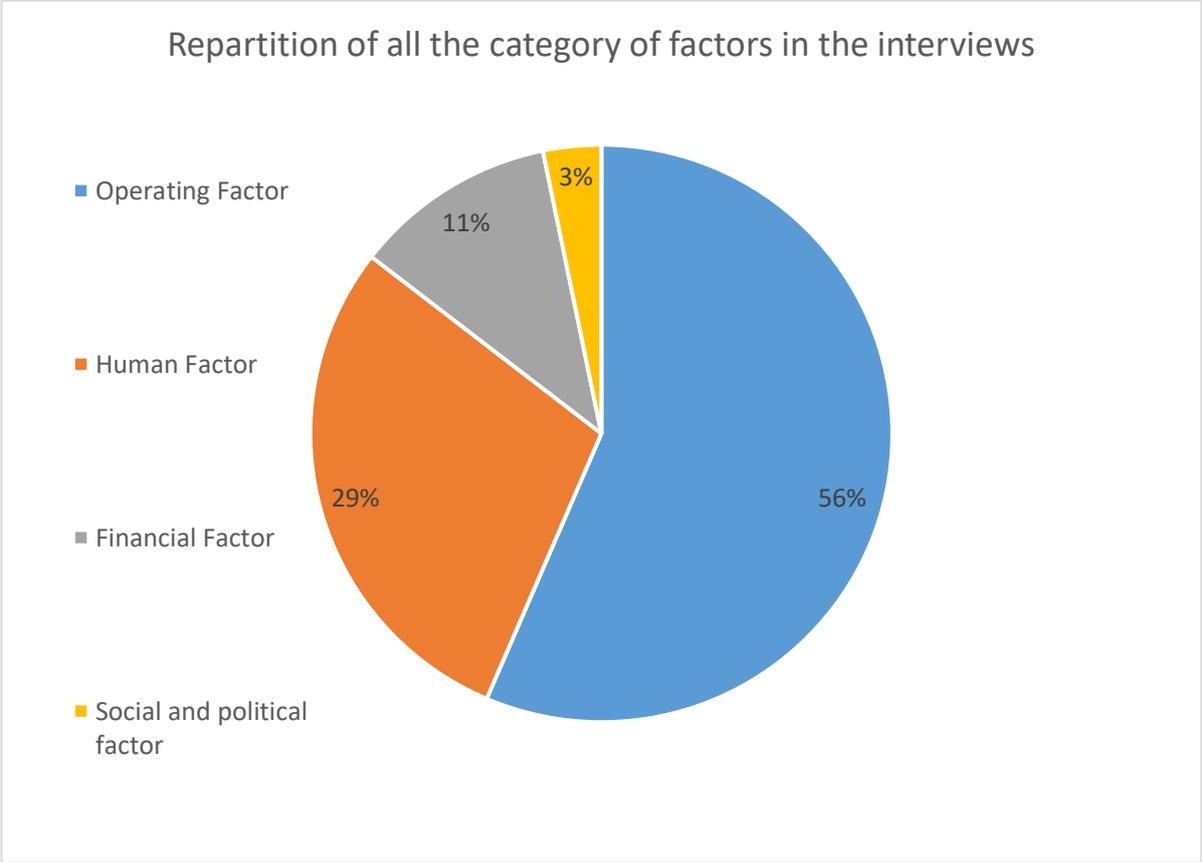


FIGURE 14 - CATEGORIES FOUND DURING THE INTERVIEWS

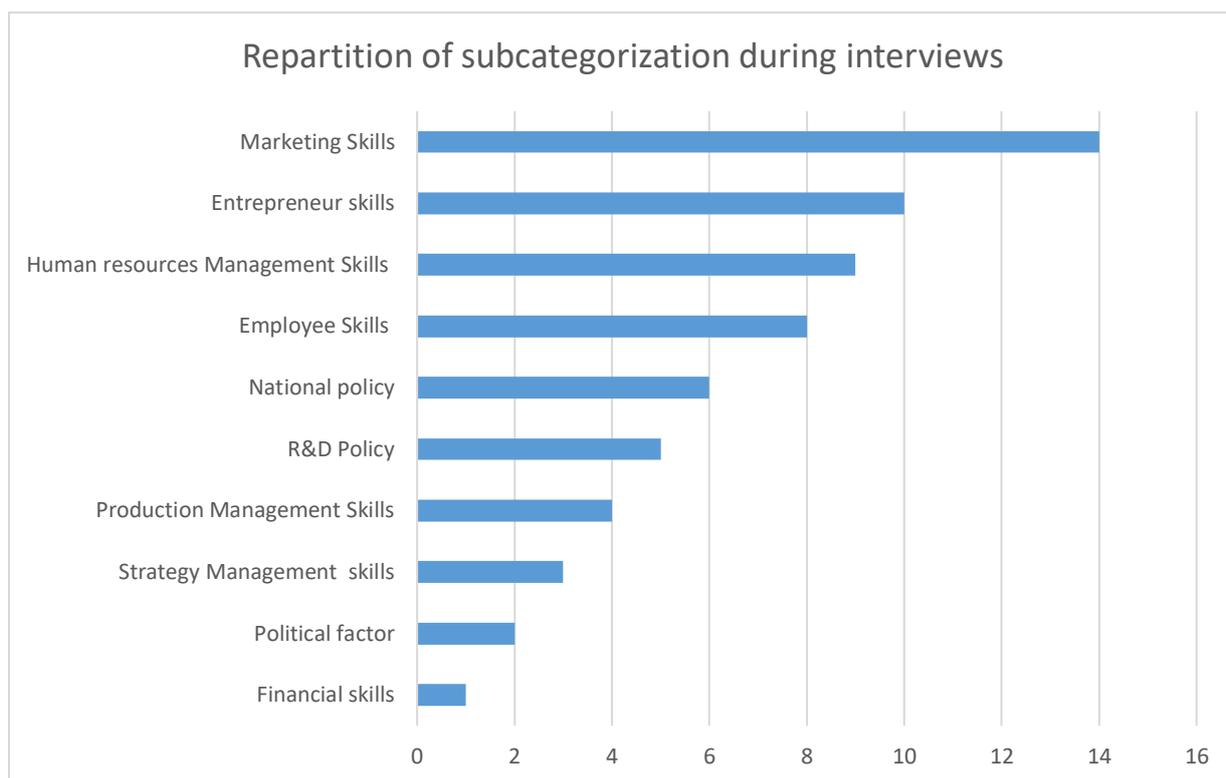


FIGURE 15 - REPARTITION OF FACTORS FOUND ACCORDING TO THEIR SUBCATEGORIZATION

We can look in more details subcategorization the most represented during the interview (figure 15). It is **marketing skills**, the subcategorization the more quoted by entrepreneurs with fourteen apparitions out of sixty-two factors mentioned for the total eight interviews. Even if all the factors were not mentioned (four factors were not mentioned during the interview and were present in the literature review), all the subcategorization were evoked by the entrepreneurs. This means that minimum 1 factors of the subcategorization was evoked by an entrepreneur. The second subcategorization which appears the most is **entrepreneur skills**.

We will discuss in another part, of new factors found during this work of research that were not present in the literature review and we will classify them with the most representable subcategorization through these new factors found. We will also talk about final result and limitation of this work of research concerning factors for a sustainable development.

7. Discussion

7.1 Comparison with the literature review

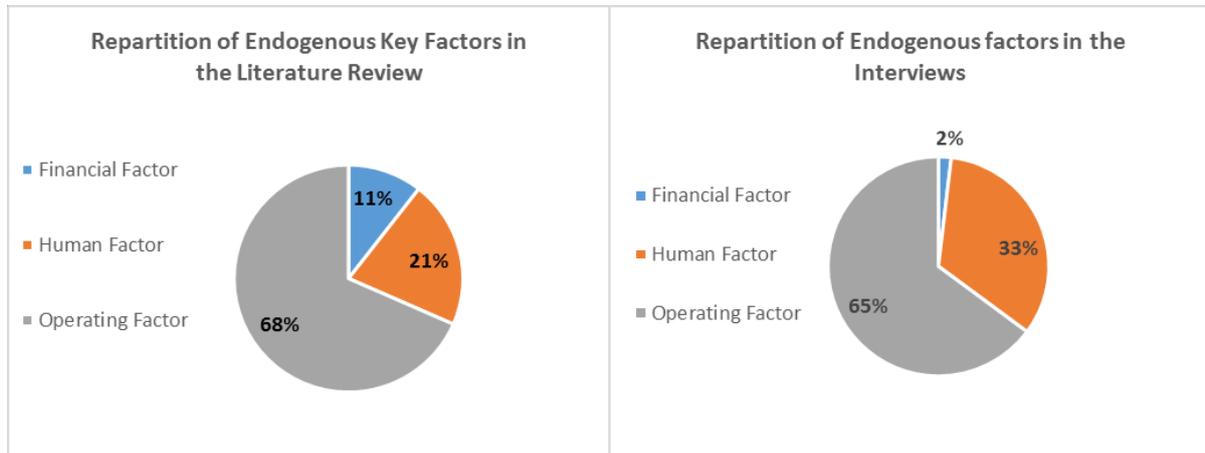


FIGURE 16 - REPARTITION OF ENDOGENOUS FACTORS IN THE LITERATURE REVIEW VERSUS INTERVIEWS

There were two **Endogenous Financial factors** in the literature review:

- Evaluate the "burn rate" and
- Develop a financial scoreboard and financial indicators

According to the figure 16, it represented 11% of the literature review. During the interview only one of these two endogenous financial factors was cited and by only one entrepreneurs. It represents the small part of 2%, of this result obtained after eight interview.

Factors Family	Category	Subcategorization	Factors	Score
Endogenous Factors	Financial Factor	Financial skills	Evaluate the "burn rate"	0/8
Endogenous Factors	Financial Factor	Financial skills	Develop a financial scoreboard and financial indicators	1/8
Exogenous Factors	Financial Factor	National Policy	Government Funding	2/8
Exogenous Factors	Financial Factor	National Policy	Tax Reductions	4/8

TABLE 8 - RESULT OF FINANCIAL FACTORS AFTER THE INTERVIEW

If we include Exogenous factor, there is four Financial factors and this category obtain a score of seven. It means that entrepreneurs did not mentioned all the financial factors previously identify in the literature review. For example, nobody mentioned the factor “Evaluate de burn rate” and only one out of eight mentioned “Develop a financial scoreboard and financial indicators”. Financial factors are composed by two subcategorizations:

- Financial Skills (endogenous factors)
- National policy (exogenous factors)

The Financial factor the most mentioned by entrepreneurs (four out of eight person) was National Policy and more precisely **Tax Reduction**.

Factors Family	Category	Subcategorization	Factors	Score
Endogenous Factors	Human Factor	Entrepreneur skills	Senior Management commitment/The ability to prioritize, including knowing what to delegate and what to do yourself.	2/8
Endogenous Factors	Human Factor	Entrepreneur skills	Senior Management accountability/Dynamic leaders who understand vision, strategy, risk, and tactics	3/8
Endogenous Factors	Human Factor	Entrepreneur skills	Structuring its management team/Ability to form a founding team	5/8
Endogenous Factors	Human Factor	Employee Skills	Desirable Biotech Employees/Entrepreneurism/Entrepreneurial Climate	8/8

TABLE 9 - RESULT OF HUMAN FACTORS AFTER THE INTERVIEW

Concerning **Human factors** which play a role in the development of a company, it represented 21% of the endogenous factors in the literature review according to the figure 16 and it was mentioned eighteen time during the interviews according to the Table 9. This category of factors seems important to the entrepreneur’s point of view, because it counts for 33% beyond the Endogenous key factors for a sustainable development. Human factors is composed by two subcategories:

- Entrepreneur skills and
- Employee skills

If we look at the repartition of endogenous factors in the interview, we see that results converge with what we found previously in the literature review concerning **Operating factors** (figure 1). Without ponderation it was 68% in the literature review and with ponderation it represent 65% in the interview. Finally, the importance of Operating factors concerning the

sustainable development of a company in the literature review was also found in the interview. It confirms the importance of this category of factors which contains the following subcategorizations:

- Human resources Management Skills
- Marketing Skills
- Production Management Skills
- R&D Policy
- Strategy Management skills

We will look in more detail beyond this previous subcategorization of operating factors, if there is a difference between what the literature review present and what has been found through interview. (Figure 17)

Factors Family	Category	Subcategorization	Factors	Score
Endogenous Factors	Operating Factor	Human resources Management Skills	Adequate resources of people	4/8
Endogenous Factors	Operating Factor	Human resources Management Skills	High quality team	5/8
Endogenous Factors	Operating Factor	Marketing Skills	Early Marketing	0/8
Endogenous Factors	Operating Factor	Marketing Skills	Estimation of the time to market	1/8
Endogenous Factors	Operating Factor	Marketing Skills	Sales orientation instead of technologies orientation	3/8
Endogenous Factors	Operating Factor	Marketing Skills	Knowing your target market	5/8
Endogenous Factors	Operating Factor	Marketing Skills	Have a good marketing and sales strategy	5/8
Endogenous Factors	Operating Factor	Production Management Skills	High quality new product process : activities and decision-point that new product projects follow from idea to launch and beyond	4/8
Endogenous Factors	Operating Factor	R&D Policy	R&D spending	1/8
Endogenous Factors	Operating Factor	R&D Policy	Innovative climate and culture/Idea development	4/8
Endogenous Factors	Operating Factor	Strategy Management skills	Value added supply (Bilateral R&D partnership)	0/8
Endogenous Factors	Operating Factor	Strategy Management skills	IP transfer via a licensing agreement	0/8
Endogenous Factors	Operating Factor	Strategy Management skills	Answer to Unmet Needs	3/8

TABLE 10 - RESULT OF OPERATING FACTORS AFTER THE INTERVIEW

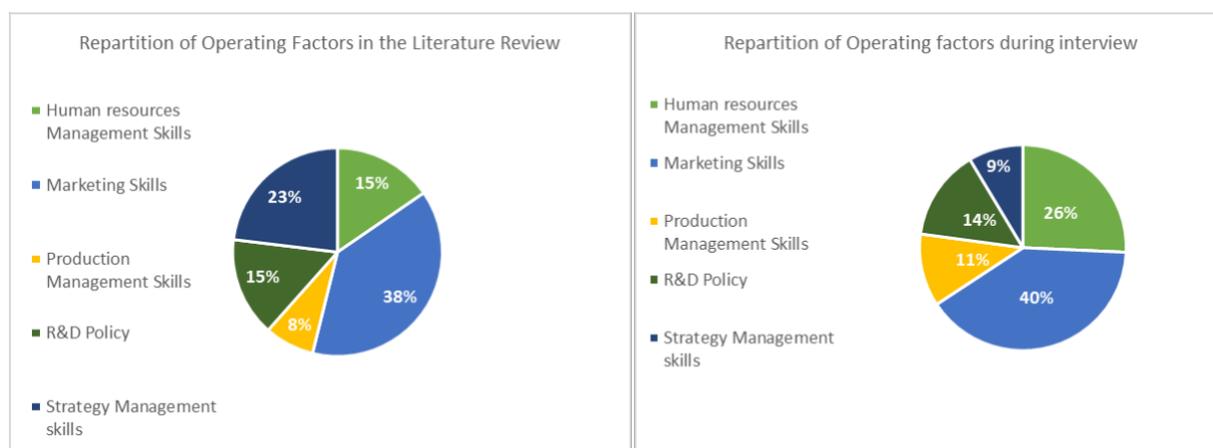


FIGURE 17 - REPARTITION OF OPERATING FACTORS IN THE LITERATURE REVIEW VERSUS INTERVIEWS

The two factors included in the subcategorization: **Human resources management skills**, are:

- Adequate resources of people and
- High quality team

These two factors represent 15% of the operating key factors found in the literature review. During the interview these two factors were cited respectively four and five time out of eight interviews. (Table 10)

Secondly, the subcategorization the most represented beyond operating factors was **Marketing skills**, and it is also what has been found in the literature review. Five operating factors in the literature review were marketing skills (38%). Fourteen operating factors found during the interview were marketing skills (40%). This result highlight the importance of marketing skills concerning the sustainable development of a small sized company in the sector of biotechnology. In other word, it is important not to forget this aspect in a small sized company, and more precisely:

- Estimation of the time to market
- Sales orientation instead of technologies orientation
- Knowing your target market
- Have a good marketing and sales strategy

We can also explain this result, for the interview part as follow: most of entrepreneurs interviewed came from public research center, and have a Ph.D in science and no skills in

marketing. They create a technology and sell with a “technology orientation”. Some of them changed their vision and adopted a “product orientation” for sales instead of a “technology orientation” and participate to training or hired a responsible of marketing. After an important change in the percentage of sales, they realize how marketing, strategy, communication and sales could be important for a product.

Concerning **strategy management skills**, there were three factors identified in the literature review, which was translated in 23% of key factors for a sustainable development. Beyond these three factors, only one was cited by three entrepreneurs: **Answer to Unmet Needs**. That’s why **strategy management skills** gets a score of 9%.

7.2 New Imaging Aspect of Factor

Factors Family	Category	Subcategorization	New Aspect of Factors	Score
Endogenous Factors	Human Factor	Entrepreneur skills	Use a previous expertise	1/8
Endogenous Factors	Financial Factor	Financial skills	Raise Love money to start	1/8
Endogenous Factors	Financial Factor	Financial skills	Adding value to a project in development	1/8
Endogenous Factors	Financial Factor	Financial skills	Fix condition for investors since the beginning	1/8
Endogenous Factors	Financial Factor	Financial skills	Studying the strategy to be able to contract loan	1/8
Endogenous Factors	Operating Factor	Strategy Management skills	Align strategy to competitors	1/8
Endogenous Factors	Operating Factor	Strategy Management skills	Changing the business model (activity/client/logistic)	1/8
Endogenous Factors	Operating Factor	Strategy Management skills	Create a benefit for both patient and healthcare system	1/8
Endogenous Factors	Operating Factor	Strategy Management skills	Collaboration with pharmaceutical industry instead of investors	1/8
Endogenous Factors	Operating Factor	Strategy Management skills	Market Patent study research	1/8
Endogenous Factors	Operating Factor	Strategy Management skills	Patent a technology and all that is around	1/8
Exogenous Factors	Operating Factor	Strategy Management skills	Knowing perfectly the regulations about the product	2/8
Endogenous Factors	Financial Factor	Financial skills	Organize its fundraising	3/8
Exogenous Factors	Human Factor	Network	Advice/skills/KOL	3/8

TABLE 11 - NEW ASPECT OF FACTORS FOUND AND THEIR SCORE

Fourteen news aspect of factors have been mentioned by entrepreneurs through the interviews. These factor are connected to the previous ones that we found in the literature review. These factors are not new: it is the accentuation of their aspect, which is highlighted here. In other word it is a nuance of some known factors which will be presented.

Most of the factors was mentioned only one time except the last three factors (Table 11). The first factor evoked by three entrepreneurs was a financial factor, more precisely Financial skills: **Organize its fundraising**.

The way to proceed to fundraising is already explained in the literature review. In other word how to wright a business plan and how to pitch in front of investor. The cursor on this factor was the fact to plan precisely when to do fundraising.

If we remind the case for the company G, entrepreneur planned to raid funds after an important step for the company. When the company obtaining a CE mark for its product it gained value. According to entrepreneur G it was the appropriate time to raise fund. Entrepreneur E planned the amount to raise and what to do precisely at what time. He also planned to accelerate sales and production, and to accelerate R&D project with the funds raised. The fact of “planning” how to spend funds before raising it, will able to save time, focus on the real need and anticipate the growth. For the entrepreneur D, the planning was organized as follow: their next fundraising will serve to automatize everything.

The second factor evoked by three entrepreneurs was about getting advice or help from the network. For example, the entrepreneur A gets some advice from its family concerning its company. Entrepreneur G lend its technology to Key Opinion Leader to test it. If they were satisfied they could write an article on it and that played a role on sales. For the entrepreneur H which count on its board a surgeon. It also played an important role on sales.

The third factor mentioned by two entrepreneurs concerns regulations: knowing perfectly the regulations concerning the service/the area of the company. The example of the company H, where entrepreneurs have a previous expertise in their actual field. Consequently, they already knew all the step to have a certification. The consequence is a huge amount of time saved, and a product faster on the market.

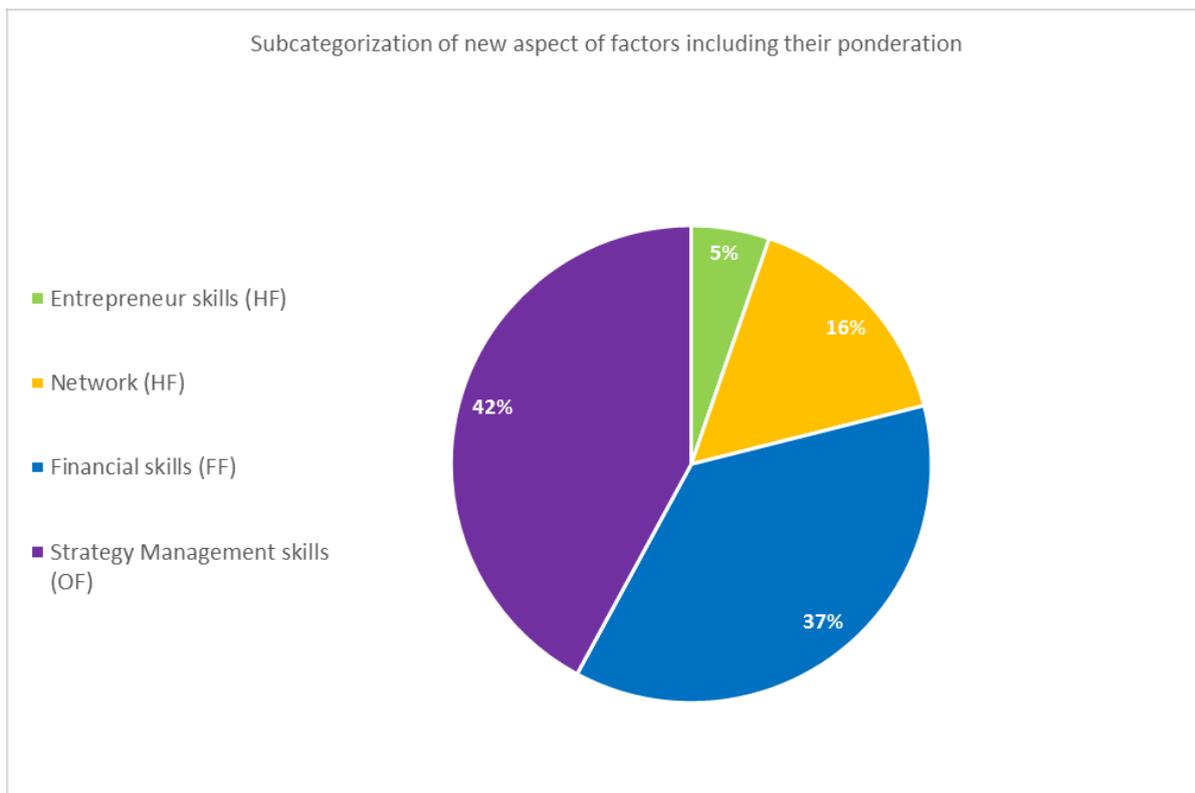


FIGURE 18 - SUBCATEGORIZATION OF NEW ASPECT OF FACTORS

Figure 18 sets the classification with more precision concerning factors. It classifies factors with a subcategorization classification (which precise also the category). Beyond these new aspect of factors found, the subcategory the most represented with a score of 42% was strategy management skills and it take part of operating factors. Beyond fourteen new aspect of factors the total score was nineteen (sum of the point of each factors mentioned by entrepreneurs). Seven factors were strategy management skills factors which obtain the total score of 8. These factors are presented in the Table 11. Five factors were attributable to financial skills and obtained the score of seven out of nineteen so 37%. One new aspect of factors found was attributable to the network and got the score of three out of nineteen or 16% and the last one attributable to entrepreneur skills with a score of one out of nineteen or 5%.

The first ascertainment is that strategy management skills factors are more accentuated than the others subcategorization by entrepreneurs. These factors are mentioned and commented through multiple aspect and news aspects are presented here. (Figure 19)

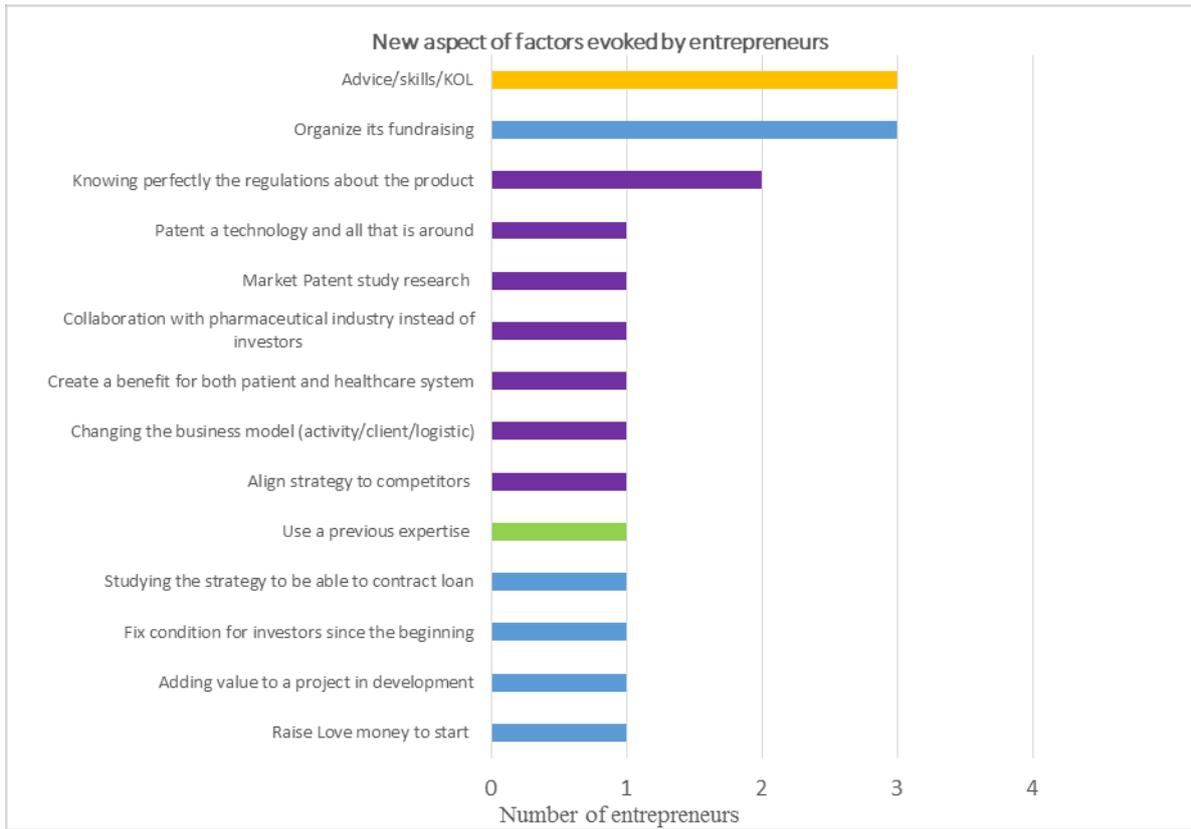


FIGURE 19 - NEW ASPECT OF FACTORS FOUND CLASSIFY BY CATEGORY

Figure 19 dresses all the new aspects of factors found and their score (how many entrepreneur evoked it). Their colors refer to their subcategorization (Figure 18). The subcategorization the most representative is strategy management skills followed by financial skills.

THÈSE SOUTENUE PAR : Cindy AMSELLEM

TITRE :

QUELS SONT LES FACTEURS DETERMINANTS POUR UN DEVELOPPEMENT ECONOMIQUE PERENNE DES PETITES ENTREPRISES DANS LE SECTEUR DES BIOTECHNOLOGIES ?

CONCLUSION :

L'étude de cas de la société Star nous a montré que tous les facteurs qui contribuent à un développement durable dans une petite entreprise agissent en synergie. Il y avait quatre axes : Axe Produits, Axe Humain, Axe de Gestion et Axe Financier. Chaque axe contient les catégories suivantes : humain, opérationnel et financier. Chaque catégorie illustre certains facteurs. La synergie de facteurs, par exemple l'orientation commerciale, les compétences marketing, et connaître son marché cible, permet l'apparition d'un autre facteur : un produit de qualité. Cet autre facteur, produit de qualité, est également influencé par la politique de recherche et développement, elle-même influencée par la culture d'innovation de l'entreprise et ainsi de suite pour les autres facteurs. Cette étude de cas souligne quels facteurs ont joué un rôle pour un développement économique pérenne des petites entreprises de biotechnologies, et comment ils jouent un rôle: en étant mis en œuvre de manière synergique.

En d'autres termes, l'application de facteurs, permet l'apparition d'autre.

Concernant les entretiens, ce travail a précisé quelle sous-catégorie, catégorie et facteurs sont les plus importants pour le développement économique pérenne d'une entreprise. Les facteurs les plus cités par les entrepreneurs étaient les compétences des employés. Effectivement, chacun des huit entrepreneurs indique l'importance de l'esprit, de la motivation, des compétences et des complémentarités de leur équipe. Concernant la catégorie la plus citée lors de l'interview, il s'agissait de facteurs opérationnels. Bien que cette catégorie soit celle qui contient le plus de facteurs, ces facteurs jouent un rôle important dans le développement économique d'une entreprise. La sous-catégorie ayant obtenu le meilleur score était celle des compétences marketing. L'estimation du temps de mise sur le marché, l'orientation commerciale plutôt que technologique, la connaissance de son marché cible ou encore une bonne stratégie marketing et commerciale sont autant de facteurs inclus dans les compétences marketing.

Une autre contribution de ce travail a été la découverte d'un nouvel aspect des facteurs préexistants. Certains facteurs bien connus dans la littérature ont été mentionnés sous un aspect différent par les entrepreneurs. Parmi ces nouveaux aspects, les compétences réseau et financières obtiennent le meilleur score. Pour la partie Réseau, il s'agissait plutôt d'obtenir des conseils ou d'acquérir des compétences auprès de son réseau. Il y avait également la notion d'être en contact avec un leader d'opinion ou en compter un dans le conseil d'administration de son entreprise. Concernant les compétences financières, les facteurs préexistants bien connus étaient : la façon d'effectuer des levées de fonds, et comment écrire un business plan et également comment le présenter devant des investisseurs.

Dans ce nouvel aspect des facteurs, nous avons soulevé l'importance « d'organiser sa collecte de fonds » et de planifier précisément quelle somme il fallait lever où investir et à quel moment.

Ce travail contenait certaines limites, qui sont présentées comme suit:

- Temps : les disponibilités des entrepreneurs étant réduites mais ils sont arrivés à trouver du temps pour les entretiens. Il était nécessaire de faire toute l'interview dans une même période afin de les comparer et de garder la méthodologie en tête.
- Géographie : tous les entrepreneurs interrogés proviennent d'un même département, donc l'échelle des entretiens n'est pas très large mais elle peut donner un aperçu de l'écosystème alpin concernant les petites entreprises du secteur de la biotechnologie.
- Nombre d'interviews : huit entrepreneurs ont été interrogés sur quinze entrepreneurs contactés. Ceci est lié à la disponibilité réduite des entrepreneurs mais plus de 50% de réponses ont été obtenu.
- La partie subjective du travail : concernant le type de facteurs et leur classification, c'est un travail personnel fait avec une opinion personnelle. Un autre chercheur adoptera probablement une classification différente ou utilisera la même chose mais placera un même facteur dans une autre sous-catégorie ou dans une autre catégorie.

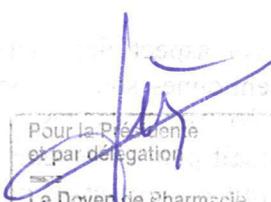
Si nous voulons aller plus loin, nous devrions peut-être continuer ce travail en interrogeant plus d'entrepreneurs. Cela pourrait confirmer ou infirmer le résultat que nous avons trouvé précédemment. Avoir un échantillon plus vaste serait une bonne solution pour compléter ce travail de recherche.

VU ET PERMIS D'IMPRIMER

Grenoble, le : 6/11/2017 -

LE DOYEN

Pr. Michel SÈVE



Pour la Présidence
et par délégation
Le Doyen de Pharmacie
Pr. Michel SÈVE

LE PRÉSIDENT DE LA THÈSE

Jean BRETON



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Appendices

Appendices 1 : Specific guide used for every interviewee

FACTORS FAMILY	CATEGORY	SUBCATEGORIZATION	FACTORS	STATE
Endogenous Factors	Financial Factor	Financial skills	Evaluate the "burn rate"	
Endogenous Factors	Financial Factor	Financial skills	Develop a financial scoreboard and financial indicators	
Endogenous Factors	Human Factor	Employee Skills	Desirable Biotech Employees	
Endogenous Factors	Human Factor	Employee Skills	Entrepreneurism	
Endogenous Factors	Human Factor	Employee Skills	Entrepreneurial Climate	
Endogenous Factors	Human Factor	Entrepreneur skills	Senior Management commitment	
Endogenous Factors	Human Factor	Entrepreneur skills	Senior Management accountability	
Endogenous Factors	Human Factor	Entrepreneur skills	Dynamic leaders who understand vision, strategy, risk, and tactics	
Endogenous Factors	Human Factor	Entrepreneur skills	Structuring its management team	
Endogenous Factors	Human Factor	Entrepreneur skills	Ability to form a founding team	
Endogenous Factors	Human Factor	Entrepreneur skills	The ability to prioritize, including knowing what to delegate and what to do yourself.	
Endogenous Factors	Human Factor	Entrepreneur skills	An entrepreneurial mindset	
Endogenous Factors	Operating Factor	Human resources Management Skills	Adequate resources of people	
Endogenous Factors	Operating Factor	Human resources Management Skills	High quality team	
Endogenous Factors	Operating Factor	Marketing Skills	Early Marketing	
Endogenous Factors	Operating Factor	Marketing Skills	Estimation of the time to market	
Endogenous Factors	Operating Factor	Marketing Skills	Knowing your target market	

Endogenous Factors	Operating Factor	Marketing Skills	Sales orientation instead of technologies orientation	
Endogenous Factors	Operating Factor	Marketing Skills	Have a good marketing and sales strategy	
Endogenous Factors	Operating Factor	Production Management Skills	High quality new product process : activities and decision-point that new product projects follow from idea to launch and beyond	
Endogenous Factors	Operating Factor	R&D Policy	Idea development	
Endogenous Factors	Operating Factor	R&D Policy	Innovative climate and culture	
Endogenous Factors	Operating Factor	R&D Policy	R&D spending	
Endogenous Factors	Operating Factor	R&D Policy	R&D spending for product development	
Endogenous Factors	Operating Factor	Strategy Management skills	Answer to Unmet Needs	
Endogenous Factors	Operating Factor	Strategy Management skills	Bilateral R&D partnership	
Exogenous Factors	Financial Factor	National Policy	Government Funding	
Exogenous Factors	Financial Factor	National Policy	Tax Reductions	
Exogenous Factors	Social and political factor	Political factor	Government Support for Start-ups	



Serment de Galien



« Je jure en présence des Maîtres de la Faculté, des Conseillers de l'Ordre des Pharmaciens et de mes condisciples :

D'honorer ceux qui m'ont instruit(e) dans les préceptes de mon art et de leur témoigner ma reconnaissance en restant fidèle à leur enseignement.

D'exercer, dans l'intérêt de la santé publique, ma profession avec conscience et de respecter non seulement la législation en vigueur, mais aussi les règles de l'honneur, de la probité et du désintéressement.

De ne jamais oublier ma responsabilité et mes devoirs envers le malade et sa dignité humaine ; en aucun cas, je ne consentirai à utiliser mes connaissances et mon état pour corrompre les mœurs et favoriser des actes criminels.

Que les hommes m'accordent leur estime si je suis fidèle à mes promesses. Que je sois couvert(e) d'opprobre et méprisé(e) de mes confrères si j'y manque ».

QUELS SONT LES FACTEURS DETERMINANTS POUR UN DEVELOPPEMENT ECONOMIQUE PERENNE DES PETITES ENTREPRISES DANS LE SECTEUR DES BIOTECHNOLOGIES ?

Résumé :

L'objectif de ce travail de recherche est d'identifier les éléments économiques clés à considérer concernant le développement d'une petite entreprise dans le secteur de la santé. Certains éléments ont été identifiés par des auteurs dans la littérature et seront comparés à ceux que nous avons trouvés. Pour cela, une étude de cas d'un type d'entreprise étudié sera effectuée. Ensuite, des interviews de quelques entrepreneurs, avec leurs propres expériences, leur savoir-faire, leur succès mais aussi leurs échecs, suivra cette étude de cas. Nous recueillerons quelques conseils dans le monde de l'entrepreneuriat. Ce travail de recherche démarre par la définition des mots clés utilisés tout au long du document. Les termes « biotechnologies », « industrie pharmaceutique », « start-ups en biotechnologie » ont été définis selon plusieurs instances. Le cycle d'un médicament dans l'industrie pharmaceutique a également été expliqué. Puis les grandes différences entre start-ups en biotechnologie et grand groupe pharmaceutique ont été élucidées. Les 3 questions qui animent ce travail sont les suivantes :

Quels sont les principaux éléments ou facteurs pouvant assurer le développement économique pérenne d'une entreprise de biotechnologie ?

Quelles sont les composantes représentant un enjeu important pour les start-up dans l'industrie des biotechnologies ?

Ce qui a été observé dans la réalité : les start-ups sont-elles absorbées par les grandes entreprises ?

Mots Clés : Biotechnologies, entretiens, économie, développement, facteurs

Filière : Industrie