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Performance measurement and evaluation of R&D units in pharmaceutical companies

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Introduction

This thesis will analyse the way pharmaceutical companies evaluate and understand the performance of their Research and Development (R&D) Units.

The decision to make a study on this subject sees its birth in difficulties R&D Units lead to in terms of performance analysis and data interpretation for managers.

Evaluating an R&D Unit in pharmaceutical companies is extremely complex from the moment that the entire process required to develop a drug from its first phases (the molecular targeting) to the last ones (approval of the drug from the competent authority) lasts between fifteen and twenty years, requiring incredibly high amounts of investments without having any reassurance on the success of the project.

The thesis is structured in three chapters.

The first one describes the different performance measurement systems known and that might be adopted from the companies of any industry to make analysis and have a picture of their current situation by adapting these systems to their own necessities. It will then be explained what Key Performance Indicators are, their importance for the companies and the characteristics that these must have to be effective in a managerial analysis and from a generic explanation of the KPIs it will be depicted how they can be adapted and set to a Research and Development Unit of a pharmaceutical industry and the correct way to interpret them.

Following, the second chapter goes more in detail with the pharmaceutical industry and its R&D Units. The objective of the chapter is to understand how the research and development process works and is structured, which are the main risks that a pharmaceutical company deals with when working on a project.

Finally, the second chapter will analyse the way managers can understand (and if this is actually possible) if the process put in place is leading to the desired results or not and the eventual preventive (or corrective) actions that might be undertaken to try reducing the damages the wrong path may generate.

Lastly, the third and final chapter will provide the results obtained by the personal research on the field by the author getting to the final elaboration of data collected through interviews. The information collected will be analysed and

interpreted so to depict which common indicators can provide the most critical information to the companies when evaluating R&D Units performances and how managers practically interpret them during the phases of the process.

Every company will have an individual way of monitoring and will give an individual meaning to the results obtained and the aim of this thesis is to use the data collected from the different companies interviewed to develop and identify a common behaviour related to the most critical and determining indicators.

Chapter 1

Performance measurement systems

1.1 Performance measurement systems

Performance is one of the most used words in a firm. Whatever the industry, age or condition of a company is, its performance is always one of the most important topics, sometimes the most important of all. Literature and years of economic evolution brought experts to create and study an incredible number of systems useful to obtain determined indicators that represent certain results and every result must be always, with no exception, quantifiable. This last consideration represents one of the toughest challenges for managers: it is a crucial step to be able to represent whatever element in a numerical way and make sure that that value is the exact image of the situation the company is in. However, there is one thing that has to be kept constantly under consideration: indicators are numbers. These ones are irrelevant if other elements are not considered; the same numerical value of an indicator can have completely different meanings in companies of different age, industry and so on. The fact that values must be chosen carefully and subsequently interpreted lead to the logical conclusion of how important it is for a firm to have a skilled managerial team, able to interpret the indicators' results and determine a strategy according to these. Kazandjian and Lied (1999) state this by saying: "performance indicators do not measure performance, people do" (p.2).

As said previously, many factors can affect the meaning of a certain indicator and its value and this is why is fundamental to use the performance measurement system that best fits with the information that that precise company is looking for. This is a factor of vital importance from the moment that decisions and strategies taken by managers must follow the data collected, "a performance measurement system is only as good as the outcome it tracks" (Hatry, 2006, p.43). Using a wrong system or not being able to gain the correct indicators, will lead to determining a wrong path that will represent a relevant waste of resources in the future.

We could finally say that by using correctly performance measurement systems, it is possible to identify a path able to bring the company to achieve certain results and it can lead to a greater understanding of how an industry works and in which way the firm reacts to certain conditions.

Imagine adapting indicators and performance measures in Research and Development (R&D) units. The level of investment required is particularly high and the level of uncertainty also. This links logically to what has been said previously about the necessity of using correct performance measurement systems and having a skilled management. In R&D units, performance indicators have to be monitored continuously to allow managers to take decisions to avoid dangerous waste of resources.

1.1.1 The balanced scorecard

The balanced scorecard is a performance measurement system created by Robert Kaplan and David Norton and it is probably the most common and known system. The aim of the balanced scorecard is to divide the performance measurement into four different perspectives: financial, customer, internal business process and learning and growth. Each of these perspectives are linked with each other and are all related to a common vision and strategy that is the one of the firm. In fact, what the balance scorecard does is to drive and translate vision and strategy through the perspectives into performance measures (Kaplan & Norton, 1996).

Each perspective has to answer to certain questions that make it possible to analyse in the correct way the performance we want to obtain:

- Financial: To succeed financially, how should we appear to our shareholders?
- Customer: To achieve our vision, how should we appear to our customers?
- Internal business processes: To satisfy our shareholders and customers, what business processes must we excel at?
- Learning and growth: To achieve our vision, how will we sustain our ability to change and improve?

This system is extremely considered and used by companies all around the world as it has demonstrated to be able to lead to positive results through a clear scheme and

make managers develop the best strategy to follow, according to the four main dimensions and an exhaustive analysis of them.

It is possible to imagine how the balanced scorecard is a system that can be used in different situations also in the same firm. According to different units and their necessities, the managers, to provide the results their unit is asking for, will adapt the balanced scorecard.

What would this matrix look like if a firm decides to adapt it to its R&D unit?

As we know, it is particularly difficult to define with certainty a straight strategy and the processes to achieve the final goal in such an unpredictable unit. We could understand that the path we are following is leading us in the wrong direction when it is too late to change. Naturally, no management should proceed straight on once it understands something is not going in the predicted way. However, sometimes it can happen that who decides might fall into the trap of being afraid of the costs of changing path or into an excess of self-confidence that might make them convince themselves that their decision is correct although values say the opposite and will bring in any case to positive results. From this, it is possible to understand how difficult it is to create correctly a balanced scorecard for R&D units.

Kerssens-Van Drongelen and Andrew Cook have developed and adapted a basic balanced scorecard to R&D processes.

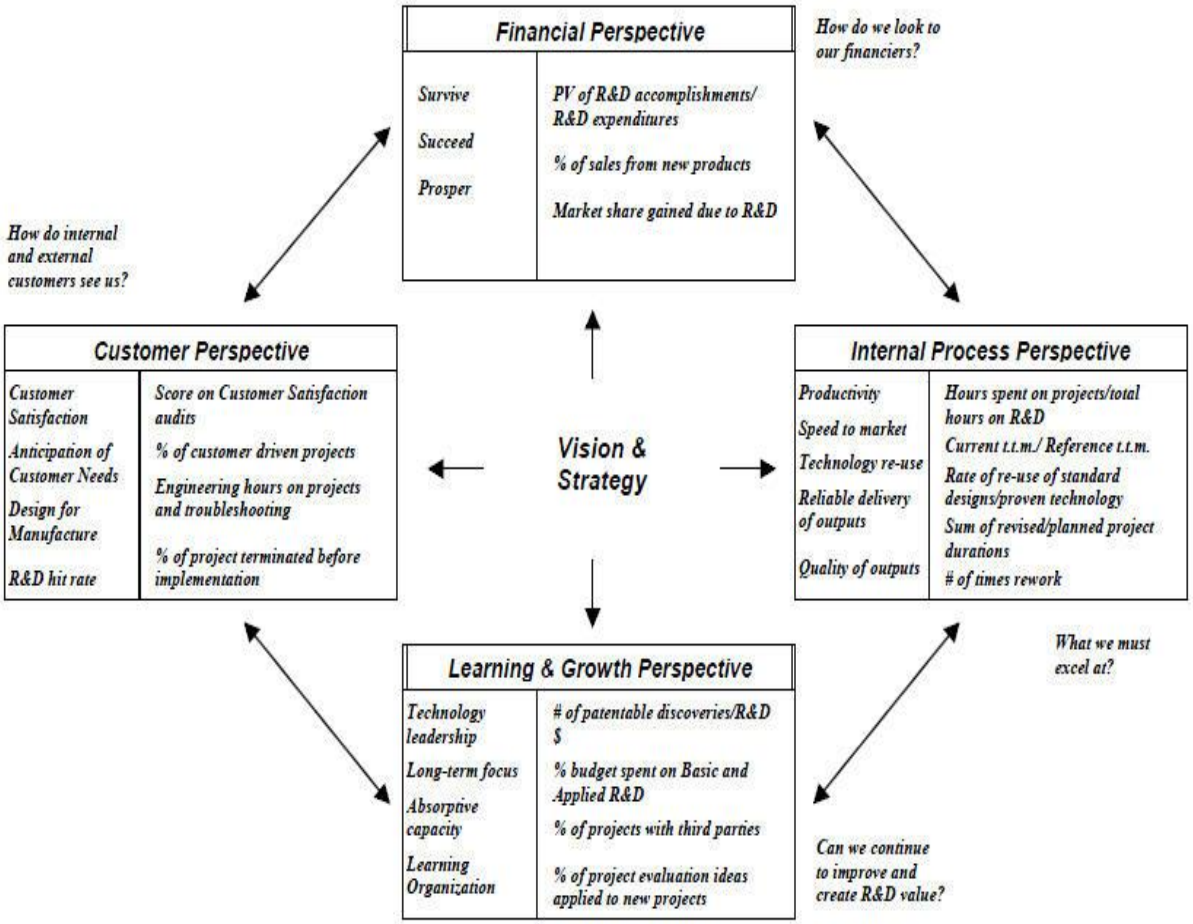

Figure 1: Balanced Scorecard example for an R&D department.
Source: Kerssens-Van Drongelen and Cook, (1997).

It is possible, however, to identify some elements that result lacking with this performance measurement system such as the level of competition of the industry. When the management of a firm has to determine a strategy to follow, that as we can see influences the entire matrix, it is of vital importance to know how competitors move and act. Having a benchmark is necessary and being able to identify the correct one fundamental and with the balanced scorecard this theme is not treated properly. However, it is evident that if we contextualize this problem in R&D units, where the level of uncertainty is high, certain processes are pre-set and according to different industries, companies that compete with each other tend to follow the same steps when investing in the R&D.

Finally, another critical element of the balanced scorecard is that this system requires a clear strategy and a strong coordination and cooperation between managers. These must be able to understand results, to give the correct meaning to feedbacks and have the capacity to change path if results are not correct, but as

mentioned previously, all these things tend to be particularly complex when dealing with research and development units. Changing the road the company has invested in, being able to identify the meaning hidden behind a feedback may result extremely expensive and complex. Let's take as example a pharmaceutical company investing in R&D for the development of a new product. During the processes, this will be created, tested *in vitro*, then on several animals, then on human guinea pigs, analysing its effects on a particular virus that generates a certain disease and so on. The risks that the unit will have to face are not measureable and predictable in any way through the balanced scorecard. The feedback that researchers may have received from one product in the past might be completely different if set in new scenarios: for example, a medicine may be able to defeat the disease on an animal, but not in human bodies for countless reasons.

However, the balanced scorecard is a great instrument to measure performance, but it is not the only one as it is possible to imagine.

1.1.2 The Performance Prism

The performance prism is a performance measurement tool elaborated by Andy Neely and Chris Adams, which consists in the interrelated analysis of five different facets that must be able to answer certain questions:

- Stakeholder satisfaction: who are the stakeholders and what do they want?
- Stakeholder contribution: what do we want and need from our stakeholders?
- Strategies: what strategies do we need to put in place to satisfy the wants and needs of our stakeholders while satisfying our own requirements too?
- Processes: what processes do we need to put in place to enable us to execute our strategies?
- Capabilities: what capabilities do we need to put in place to allow us to operate our processes?

As we can see from Figure 2, the performance prism takes into consideration two aspects for the stakeholders: their satisfaction, as also the balanced scorecard does, and their contribution, which in the performance measurement tool analysed previously is missing. In fact, differently from the balanced scorecard, with the

performance prism Neely and Adams understood that the environment in which a firm finds itself is big and complex, with many actors affecting its decisions and so it is not enough to consider only customers and shareholders as the stakeholders but also regulators, employees and suppliers. The two authors of the performance tool also realized that it had to be measured how these stakeholders could contribute in achieving the goal of the company.

Nowadays "organisations are more demanding in what they expect from their own stakeholders…. the most development in the Performance Prism is the focus on identifying the needs of a wider range of stakeholders, as well as identifying what the organisation wants from its stakeholders in return" (The Performance Prism, 2015, para. 4, 8).

The realisation of this framework has been studied to make it possible for the companies to have a flexible tool that could be easily adaptable to new conditions according to the kind of economic environment that is developing in recent years.

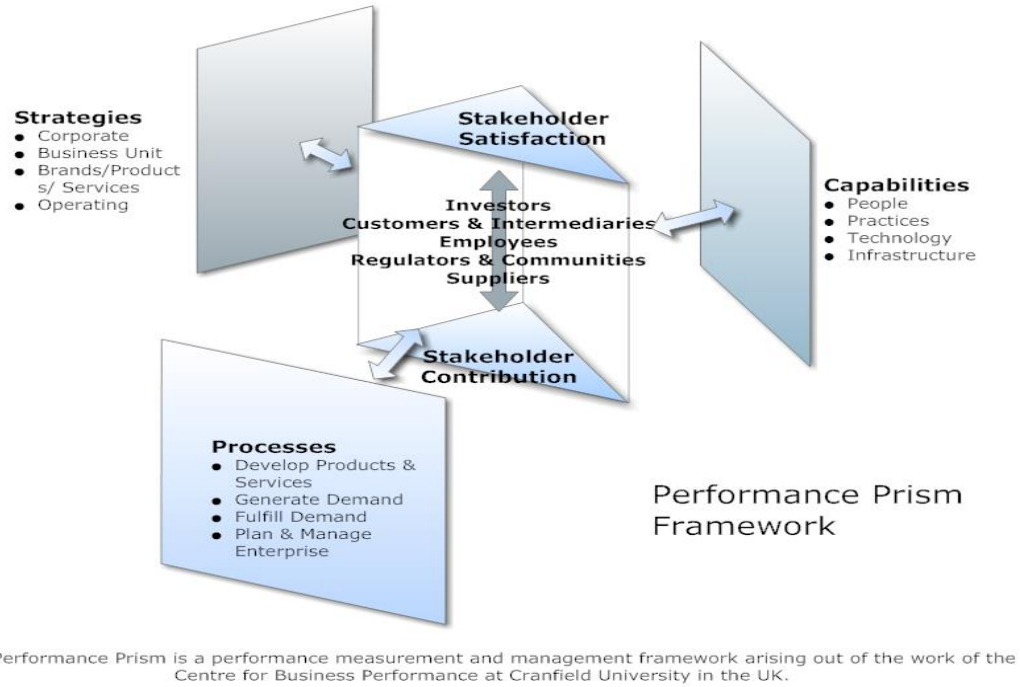

Figure 2: The Performance Prism
Source: www.smartdraw.com

For this reason, Neely and Adams (2001) state that "the Performance Prism is a second generation measurement framework designed to assist performance measurement selection – the vital process of picking the right measures" (p.6) and

that through different practical cases “it has proved itself to be malleable to the various needs of a wide variety of different organisations and measures development conditions” (p.11).

This demonstrates how such framework takes in high consideration the groups of stakeholders that are increasingly becoming more influential nowadays and allows us clearly to say that it follows “a stakeholder-centric view of performance measurement” (Neely, 2007, p. 151).

Finally, it is possible to state the aim of Neely and Adams, when developing the performance prism, to combine the strengths of different performance measurement frameworks in one single system.

1.1.3 The EFQM Excellence model

The European Foundation for Quality Management (EFQM) is a non-profit foundation formed in 1989 by fourteen presidents of multinational European companies (including Umberto Agnelli CEO of Fiat Auto SpA, Carlo De Benedetti CEO of Ing. C. Olivetti & C. SpA or Carl Horst Hahn CEO of Volkswagen AG) and developed a self-assessment model. This excellence model was founded with the aim “to stimulate and assist organizations throughout Europe to participate to improvement activities, leading ultimately to excellence in customer and employee satisfaction, and to result in changes to society and business” (Klazinga, 2000, as cited in Legido-Quigley, McKee, Nolte & Glinos, 2009, p. 34).

During the years, an increasing number of companies from different country in Europe started adopting the EFQM Excellence model as performance tool. The relevance of the framework has its basis on the fundamental concepts that together bring to what it can be considered an excellent organization and they are listed below:

- Adding value for customers: it is of crucial importance to focus on customers. They provide the biggest feedback, they make a company successful or not. It is vital to understand their needs and satisfy them.
- Creating a sustainable future: bringing a positive impact not only to the company’s performance, but also to the entire economic environment and to the actors that are part of the same community.

- Developing organizational capabilities: being able to satisfy stakeholders increasing the efficiency of the processes, possible only with a common growth of the organizational capabilities.
- Harnessing creativity and innovation: being able to innovate and improve ourselves is a way to reach excellence.
- Leading with vision, inspiration and integrity: it is important to understand what the company has to achieve and make things happen to reach that result within ethical borders.
- Managing with agility: fundamental is to have a managerial group able to understand before the competitors the opportunities and threats and act in the most effective way.
- Succeeding through the talent of people: having a strong organizational culture, able to involve employees and managers and to make the organizational goals become the workers goals is the best way to exploit at the maximum level the talent of people.
- Sustaining outstanding results: obtaining good results able to satisfy stakeholders is positive. Obtaining outstanding results is excellent.

These eight concepts necessary to reach excellence are based on the observation of different companies in Europe, understanding their strengths and the reasons that made such companies obtain an incredible success.

Starting from the concept of excellence and from these eight elements, it has been possible to structure the final EFQM model (Figure 3) based on five criteria considered key “enablers” of excellence, consisting in how the organization works, and four criteria of “results” that cover what the organization is able to achieve.

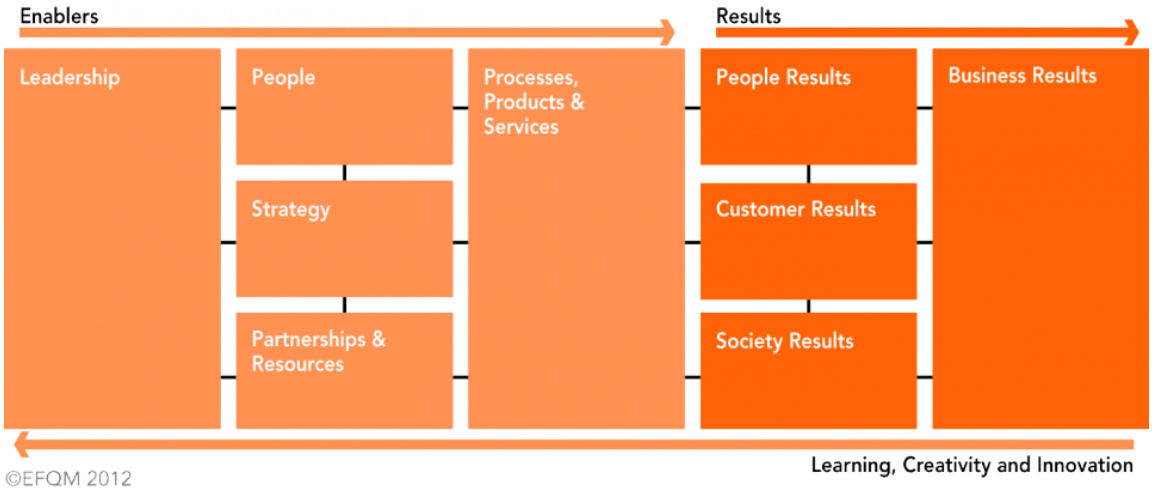

Figure 3: The EFQM model
Source: www.efqm.org

As it is possible to see from Figure 3, the five enablers for excellence are leadership, people, strategy, partnership and resources and processes, products and services that "provide ways to assess what has been done in the organization" (Hakes, 2007, p. 16). While the four results criteria are people results, customer results, society results and business results and "provide ways to assess what has been achieved" (Hakes, 2007, p. 16).

In this framework, R&D stands obviously in the enablers section, more precisely in the processes, products and services from the moment that, as clarified previously, being able to innovate and increase the effectiveness and efficiency of a company is a fundamental step to reach excellence and to be sustainable in the long term. However, we know how R&D is a particular division, that requires high investments giving low levels of certainty in terms of results, but it is still an important section to invest in, since it can bring, in the medium-long term positive results with a contemporary reduction of resources required.

1.1.4 The tableau de bord

The tableau de bord is a system of performance measurement developed in France in the early '900 and it can be considered the system that set up the basis for the creation of the worldwide known balanced scorecard (analysed previously). Many companies that introduced a tableau de bord in their management system where then facilitated when passing to the balanced scorecard.

But what is the tableau de bord and how does it work?

It is “a reporting device, making it possible to control the realization of previously fixed objectives, as well as a tool for diagnosis, reaction and hierarchical dialogue” (Ardoin, Michel and Schmidt, 1986, as cited in Raynus, 2012, p. 226).

To generate a tableau de bord and establish the key performance indicators (KPIs) the management of a firm has to define clearly a strategy and a plan to follow, so to be able to understand exactly what is the result that must be achieved. The indicators can be both monetary or not, but what is important is that they must be quantifiable also if representing quality and not quantity measures; its aim is not only to provide financial results but also efficiency ones. For this reason, the management has to establish only the critical elements that best represent the situation by setting a minimum level of result that can be controlled in the clearest way possible.

This makes us understand how the tableau de bord is not a pre-set matrix or framework, but is a system that is developed and studied according to the necessities of each firm. It must be easy to read and interpret so to give an immediate feedback to managers that can take decisions whether to proceed if everything is going well or change something to solve eventual problems.

Here below (Figure 4), it is possible to see an example of a tableau de bord, that as said, has not a prefixed format and it tends usually to be particularly similar to a dashboard so to have immediately a high interpretability and impact on who is studying it.

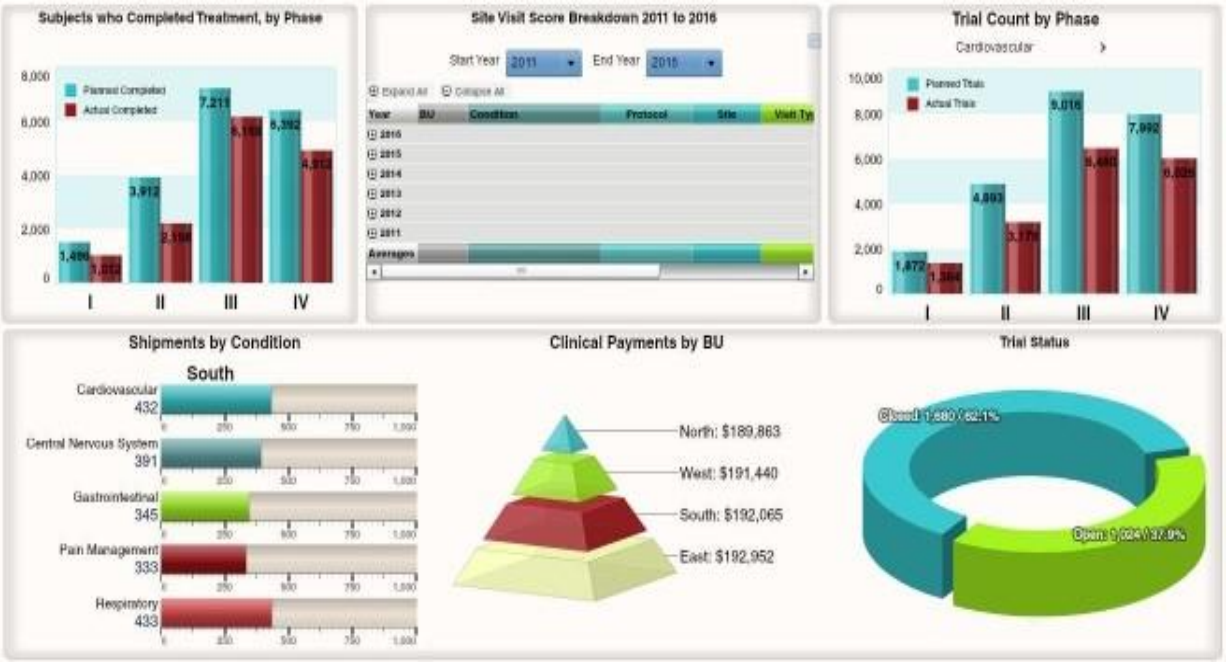

Figure 4: The tableau de bord example for clinical trials in a pharmaceutical company
Source: www.idashboards.com

The example above is obviously just an indication to understand what a tableau de bord could look like in a firm. Every company adapts the system as best it fits with its objectives and perspectives. A small pharmaceutical company that invests in R&D might have ten outstanding projects for the development of a medical product while for a big one the number will be presumably higher. The smallest company, for this reason, will control with more key performance indicators the stages of each project and probably, according to the results it is obtaining, it would decide in a more critical way how to continue if things are going wrong. A big company instead will act differently according to the level of how dangerous might be an indicator that is not reaching the pre-set minimum level.

A deeper analysis of what key performance indicators are and how they are established well be carried out later.

1.2 Other performance measurement systems

The balanced scorecard, the performance prism, the EFQM model performance and the tableau de bord that have been analysed above are the performance measurement systems most known and used by companies all over the world.

However, firms can decide to adopt other systems that are not predefined. What does this mean? This means that every company can autonomously establish which are the main elements that have to be considered to analyse and measure its performance. The process is similar to what happens with the tableau de bord, but the main difference is that no dashboard is used in this cases. The reason is that the indicators to monitor are few, not more than three or four per unit in sometimes, though it is not necessary to develop a dashboard but it is enough just to interpret the numerical value they represent.

This allows us to understand who the main actors to use own formats are: we are talking about small or medium enterprises that do not require the stress to analyse continuously dozens of indicators.

A small pharmaceutical company for example with limited budget and limited network of stakeholders will take into consideration a number of indicators per unit that will allow it to control the mail activities that will inevitably be less than the activities that a big company will have to monitor. The main focus for these small companies will be to waste as less than possible and obtain a result that permits them to continue living in the market. Obviously, also an important and dominant firm will control these elements, but it will also have the economic capabilities to invest in more projects simultaneously and eventually stop one of them if it is not going in the predicted way without to many problems. This means that one monitors indicators for survival reasons, while another one, over that for survival, monitors indicators to increase profits, to carry out more ambitious and risky projects that in case of success could lead perhaps to a bigger share of market and finally, monitors indicators that lead to a higher satisfaction of the many stakeholders it must deal with.

1.3 What are Key Performance Indicators (KPI)

The Key Performance Indicators (KPI) are those indicators that are quantifiable and through which a firm measures its performance and analyses the quality of its strategy. This means that KPIs are different according to the industry in which a firm is set, but not only. They can change by companies that compete in the same sector of market according to their dimensions, their view of strategy or their internal culture.

Every single firm sets by its own the Key Performance Indicators that best fit with its objectives.

A company can also decide not to adopt KPIs and manage to be, however, productive and gain positive feedbacks from its operations and the results it reaches, but it is nearly possible to state with certainty, that in this way, it would still not exploit in the best way all its potential.

What is clear is that a firm will set its own KPIs before starting that particular activity. They are considered as the main drivers that will lead a company to success, efficacy and efficiency. It will allow the firm to understand were something is going wrong and were the performance is going well, were the firm can still improve and were the best condition has been reached.

There are, however, some features that must be common for every company and any industry when setting particular KPIs.

They must be:

- Quantifiable: a number or a percentage must represent the result that the indicator is providing me. The company must set a predetermined value for the process or the activity that must be monitored and the final result must be represented by a number, so to quantify the efficiency and effectivity, making it possible for the manager of that particular function to know where his intervention is required.
- Practical: they must integrate well with the business processes of the firm. Each company has its own processes and way of working and the KPIs must be set according to these elements. They must fit as best as they can with the firm's working model and its variety of functions.
- Real: this means that the values represented by the KPIs must be true and correct. The managers or whoever controls KPIs, would fall into a dangerous mistake by thinking that a little adjustment of the results might lead the company in a good perspective. The growth of a company bases its success on the real improvement of less positive aspects.
- Relevant: the selected indicators must be the most relevant ones. They must be those indicators that best represent the condition of the firm and that give a representation of what is the healthiness of the core business. As we all know, a company is divided into divisions, each of which has its own

> functions to be performed. The selected KPIs must be for each function and must be set in a restricted number generally varying from three to ten. It will not be useful for the manager of the division to set a higher number of KPIs from the moment that not all elements are considered vital or that some of those are simply a reflection of other operations.

So, what results necessary for the set of the KPIs in a firm is that management has well identified the short, medium and long term objectives, clearly defined the business processes and their requirements and finally, have a clear vision of how to monitor them and manage the results.

Each company, according to its necessities, defines the period of control of the indicators and its values. Usually, for multinational firms, an analysis of results is made monthly in site and quarterly with the parent.

When management controls the Key Performance Indicator's results, that for example, in a structured firm can sum up to 180,200 KPIs, it is logic to think that managers will not control the entire indicators, one at a time, but only the ones that represent negative values and solutions. In this case the management will start talking about the so called "CAPA" (Corrective Action, Preventive Action).

For the less critical values, the CAPA, that is the official requirement for intervention, will give a deadline of usually sixty, ninety days.

Concerning, instead, the most critical values for the KPIs, the deadline for intervention and solution will be maximum in fifteen, thirty days.

It is possible to conclude how important Key Performance Indicators are for companies. They are arbitrary and a firm can decide also not to adopt them if it does not consider them fundamental, but it will for sure incur in many risks in terms of waste of resources, identification of critical elements of the processes and functions of intervention.

Finally, as stated by Laura Lake (2015) in an article online:

> Key performance indicators are important to a business because they help it focus on common goals and ensure those goals stay aligned within the organization. This focus will help a business to stay on task and work on meaningful projects that will assist in reaching objectives faster. (para. 4)

Chapter 2

R&D units in the pharmaceutical companies

2.1 R&D in pharmaceutical companies

When we talk about pharmaceutical industry, we are talking about that industry that involves different phases such as the research, the production of medical products in different solutions (i.e. syrup, tablet, spray, for injection, etc.) and finally its commercialization. Every company, obviously, has as principal goal that one to increase its profit as much as possible to survive and gain the highest share of the market possible.

The pharmaceutical industry can see its birth in early 800, when for the first time, companies started to study active ingredients and their behaviour under particular conditions. Before that time, pharmaceutical products were not medicines, as we know them today, but simple extracts of natural products that had therapeutic properties. The step that brought finally to the research and study of the active ingredients was due to the collaboration of pharmaceutical companies with the chemical sector. The development of the entire pharmaceutical industry all around the world lived an incredible increase during the period going from World War I to World War II. The tremendous growth of the poorness rate and the consequent diseases that the historical facts generated, represented the necessity of finding possible medicines able to cure the always higher number of diseases that were affecting population during those years. Although Europe, and in particular Germany, always represented the heart of pharmaceutical development, during the period mentioned above, United States became the pharmaceutical's evolution fulcrum and the house of research. It is easy to imagine the reason of this shift overseas, represented by the different richness and conditions in which USA and Europe lived during the years of World War I and World War II.

Nowadays, R&D in the pharmaceutical field sees every year a growth investments passing from (expressed in US dollars) 108 billion in 2006 to 142 billion in 2014 and predicting an increment reaching an investment equal to 160 billion in

2020 (Statista, 2016). This incredible growth reflects what happened in history during the last century and it is notable do show its effects on life in the figure below (Figure 5) which depicts the percentage of surviving by age and its improvement over the years.

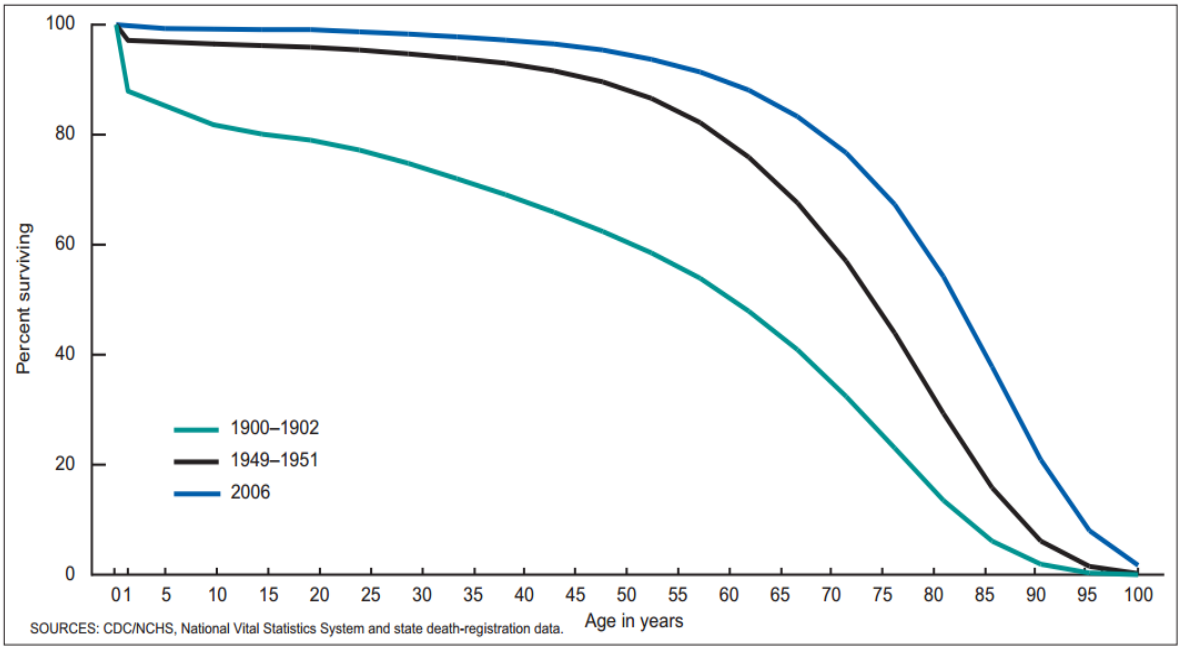

Figure 5: Percent surviving by age in 1900, 1950 and 2006
Source: www.cdc.gov

However, it is important to keep in mind what has been said before: the main goal of a pharmaceutical company is to sell products, increase profits and gain the highest share of market possible. This, obviously, represents an important source of pressure for the researchers and the company itself and it is reflected by some statistics published by The Washington Post in 2013 were it showed how the main pharmaceutical companies invested more in sales and marketing than in research and development. Some examples are Pfizer that invested 6.6 billion dollars in R&D and 11.4 billion dollars in sales and marketing or, also, Novartis invested 9.9 billion dollars in R&D and 14.6 billion dollars in sales and marketing. Finally, the statistic of the huge company such as Johnson and Johnson which invested 8.6 billion dollars in R&D and 17.5 billion dollars in sales and marketing, 100% more than R&D (precisely 104% more) (Swanson, 2015).

However, let's now get deeper in detail in the process of research and development.

When we talk about R&D in pharmaceutical companies, we must be conscious that we are considering infinite variables, phases and elements. In the figure below (Figure 6), it is possible to see which the main steps are.

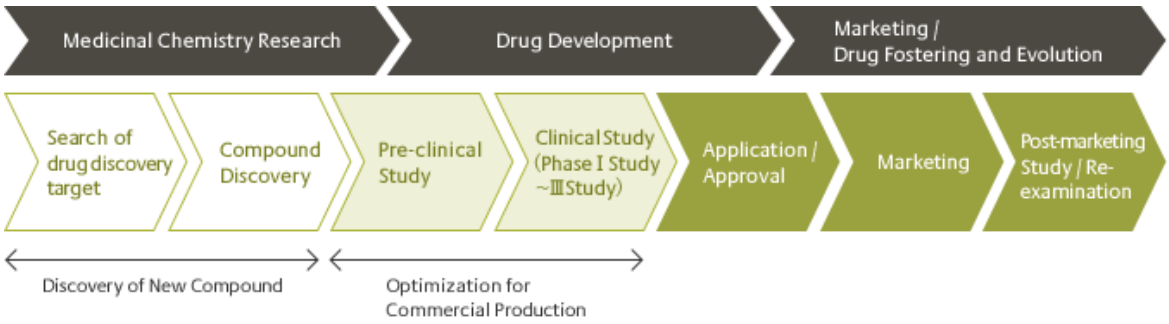

Figure 6: Drug discovery process
Source: www.takeda.com

The phase of the research can last generally seven years and it regards the "Search of a drug discovery target" and "Compound discovery". In these phases, the researchers have as objective to identify a molecular target (that causes a disease). Then, through an intensive work of the researchers, are generated an incredible number of molecular compounds that can affect the target and identify any possible element able to generate a reaction to the disease causing a stop or a reverse of its effects.

Out of thousands of molecular compounds and tests, there will be an optimization process through which the researchers will identify the most promising and potential molecular compounds that might be transformed, in the future, in possible medicines.

Those compounds that affect the only target and are completely ineffective with correlated elements represent the best result possible and the most relevant solutions.

Once identified the most promising compounds, the successive step researchers do is that one to consider already existing medicines and similar diseases to make a comparison on the effects and also a study on the dosage and the best way to provide the drug (its formula to produce it liquid or solid for example, spray or drops and so on).

Once these elements are clarified, it will begin the development process that will last approximately seven or eight years and that in Figure 5 is represented by "Pre-

clinical study" and "Clinical study" stages. The first step to undertake is the pre-clinical that is divided into two ways: *in vitro* and *in vivo.*

- *In vitro*: the molecular compound is set into a test tube with cell cultures and microorganisms and its effects are tested.
- *In vivo*: Only the molecular compounds that result to provide positive effect are then tested on animals.

The preclinical tests, as well as providing information on the toxicity, are useful also to gather information on potential side effects.

"While preclinical research answers basic questions about drug safety, it is not a substitute for studies of ways the drug will interact with the human body. "Clinical research" refers to studies, or trials, that are done in people" (U.S. Food and Drug Administration, 2016).

The clinical research is divided into three phases.

- Phase 1: in this phase there is an actual test of the active ingredient on a number that floats between twenty and one hundred volunteers (possibly young) that have, only in some cases (important diseases such as AIDS or cancer for example), the disease that the drug should be able to defeat. The purpose of this phase is to analyse the side effects and the optimal dosage by dividing the volunteers in groups and providing them always a higher quantity of the drug. It takes several months and nearly 70% of the tested drugs pass to the successive step.
- Phase 2: it is defined also the therapeutic-explorative phase. The drugs are tested on several hundreds of patients that do have the disease and it tests the effects of the drug on the target. It is still very important to consider new side effects such as, for example, the variations of blood pressure. In this phase people are divided in groups and only to some of them the drug is provided, to others will be given a *placebo* (element with no medical effects) without telling them which of the two has been given. In some cases, neither the doctor who will analyse the effects will know whether if to the patient was provided the drug or a placebo. This phase lasts longer than the previous one, generally two years and only 33% of drugs pass to the successive step.
- Phase 3: this phase is also called therapeutic-confirmatory. In this step the active ingredient is tested on a number of people varying from several

hundreds to several thousand that have the disease and it is confronted with a *placebo* and with other already existing drugs. The people on which the drug is tested are similar per age and condition, are divided in groups based on what has been provided to them and this will bring to a precise result: the differences in health will be only due to the effects of the tested drug. Side effects are still considered and adverse reactions are monitored. This phase will last a range of time that floats between the three and the five years.

Once concluded also development phases, the company will have an important dossier where all data deriving from the pre-clinical and clinical tests are collected, together with all the analysis on the relation between the efficacy of the drug and its potential risks. This last analysis, obviously, must provide extremely positive results otherwise the drug would not have even passed to the development process.

The pharmaceutical company will submit the final dossier to the competent authority (in Italy AIFA, in U.S.A. FDA) for the request of approval, registration and finally its commercialization into the market.

The entire process of R&D, starting from the search and identification of a molecular target to the approval phase, will require around fifteen or twenty years and the amount of money needed for the entire process sums up to an incredibly high amount.

This is why, for a pharmaceutical company, R&D represents a very risky unit: in the following chapter will be analysed and studied more in detail which are the main risks that a company has to face when dealing with R&D.

2.1.1 Risks of R&D processes

Beginning from what has been said at the end of the previous paragraph, when considering the main risks of research and development units it is fundamental to mention costs. The main element that counts is that the number of successes in terms of new drugs brought by the pharmaceutical companies is decreased in a meaningful way in the recent years.

Considering not only the development phases, but also the research stages of the process, the statistical number elaborated by numerous scientists is that eight drugs out of ten are not successful, bringing the projects to be abandoned.

A study brought on by Tuft Centre for the Study of Drug Development clarifies relevant numbers that might result in some way astonishing: in 2014, the cost of discovery and production of a new medicine was 2.5 billion dollars that is more than twice of the cost companies had to face in 2003.

The numbers instead reported by Deloitte and Thomson Reuters, that estimated a cost per drug approved and ready for the market around 1.3 billion dollars is lower because in their calculations is considered only the latest part of R&D, the development one.

John Graham (2014) in an article for the Forbes, reports that:

> Deloitte and Thompson Reuters estimate that the IRR (internal rate of return) of R&D spending has dropped in half since 2010, from 10.5 percent to 4.8 percent. Sales of new drugs are not overcoming the loss of patents, weak pricing power for older drugs, or reduced productivity of R&D. (para. 4)

What do all these numbers and statistics mean?

As it is clear now, R&D represents an incredibly volatile process, where there are required high amounts of money and investments with a really low and dangerously decreasing number of successes and an initial investment uncertainty that is incredibly high. One of the risks that the pharmaceutical companies have to face more than other companies when dealing with R&D is the time the processes require.

It is logic to imagine that a project for the search, study, development and approval of a new drug, that must also deal with very strict regulations and that demands a commitment for fifteen, twenty years, is much more risky than whatever other project of R&D which necessitates of less phases, that is quicker and, also, requires lower amount of money.

Duncan Pass and Martyn Postle (2002) tried to identify the main risks of R&D in the pharmaceutical industry and through those data, it has been possible to generate the figure below (Figure 7) and to analyse each voice in detail to better understand its correlation with R&D risks

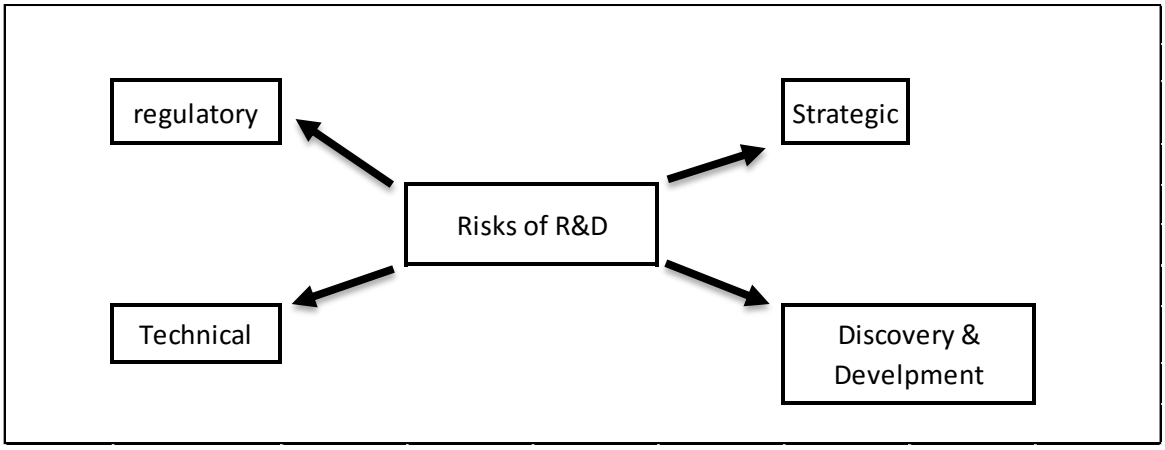

Figure 7: Overview of the risks of R&D in pharmaceutical industry
Source: Author

- ***Regulatory***: rules progressively change. The minimum standards requirements by the competent authorities of each country may in some cases be different generating eventual problems with commercialization. However, new rules, limitations and controls are continuously updated bringing possible problems to pharmaceutical companies that are investing in a project for ten years for example. These might generate stops and rejections at the moment of approval and registration.

- ***Technical***: sometimes, risks come from technical activities used in a laboratory. Let's explain more in detail. It is obviously positive to have qualified and experienced researchers, their experience and know-how in some way could bring them to produce a new drug with the correct dosage by changing simply the active ingredients. But it is not possible to predict the reactions of these in the new compound and the new formula and if problems start arising there is no way back if not to stop the process or, sometimes, stop the project with a relevant waste of resources in both cases.

- ***Strategic***: the strategic risk is a risk itself by simply considering that no company in the world can be sure its strategy will be successful, also considering its correlation with the strategic behaviour of competitors of the same industry. The business model, the R&D portfolio projects, the market share conditions and the patient population are all variable factors that do not

depend only on the work and predictions of the company, but are affected by infinite external elements.

- ***Discovery and Development***: these risks are easily linkable with R&D itself. As reported previously in this paragraph, there is no certainty in the discovery and development of a new drug because of the time and the investments the process requires. It is possible to try to make predictions, use experience, compare past results, but it is not possible to have already at the beginning of the process the certainty that all steps will be successful.

In Figure 7 it is not indicated commercialization that instead is considered very important by Pass and Postle (2002) when they stated that "it is crucial to consider the commercial element in R&D risk, because product competitiveness is the acid test of success" (p. 70).

What they state is true, commercialization of drugs is at the basis of success in the market for a company, but on the other hand, it might be more correct to consider commercialization as a problem that derives from R&D and not the opposite. If research and development is unsuccessful, the consequence is that commercialization of drugs will not take place. But if commercialization is not successful, it does not mean that the drug does not work on patients and that it has not been developed successfully. It is an inverse relation, commercialization does not represent a direct risk for R&D, while R&D might represent a risk and a variable that affects commercialization.

Previously it has been shown that also experience can have an important impact on R&D, both in a positive or negative way. It is logic to think that experience can affect much more in a positive sense than a negative one the research and development process.

But what does experience come from? Which is a good strategy for a pharmaceutical company to gain experience in R&D?

When we are considering pharmaceutical firms, we are considering firms that have as objective that one to make profit. To do so, it is important for the firm to obtain investments from third parties and for this reason, we can state that whatever investor wants to analyse the Weighted Average Cost of Capital of a firm (WACC).

The WACC considers the cost that the firm has to face to gain investments from third parties.

Now, pharmaceutical firm will have a low cost of capital for determined activities because not very risky and a very high cost of capital for more risky activities such as R&D is.

Still considering the length of time that R&D requires in its complete process, it is possible to state that investing in it from the molecular target step will undertake more risks than investing in R&D when the process is already in the development phases. All this is to say, that a high WACC will stimulate to invest in the process, and those ones that will invest from the early stages will have a higher return considering the higher risk, but not only. In fact, investing in early stages will represent an important source of experience that in the successive phases will lower the risk of the entire process of research and development, lowering also the WACC and the returns for investors. Exactly as stated by the Office of Technology Assessment (1993) "The investment in early R&D can be viewed as an investment in information that allows the firm to reduce the uncertainty of its later investments" (p. 279).

From this situation, the company can gain important information that means more experience that will lead, if well exploited in the future, to a higher rate of success and a consequent lower waste of resources.

2.2 Indicators and performance measurement of R&D in pharmaceutical companies

As depicted in the previous chapter and paragraphs, it is possible to state that R&D units in pharmaceutical industry is the unit that requires one of the highest levels of investments and that have the lowest rate of certainty in the returns and the results it is able to provide. It is for this reason that results necessary in pharmaceutical companies, when analysing Research and Development units, to monitor and interpret constantly determined indicators.

Considering first a common indicator for every R&D unit in all industries that impacts in an incredible way in the unit of the pharmaceutical sector, is the one related to the budget and expenditures. Every phase of research and development of a

new drug has an established budget according to the plans that management has made. Analysing constantly the costs of the project and they are managed is the first and probably most important and critical indicator that a company wants to monitor.

This, mainly in pharmaceutical companies, seems to be even more relevant than in other industries since the volatility of the processes is incredibly high and no precise and sure predictions can be made.

Another important asset that has been already mentioned previously in this chapter is the importance of experience.

But how can experience be seen as an indicator?

An important element considered in this sense is the time spent during a project on a particular phase. It is sure that time is a variable that is set differently according always to the type of challenge the researchers are facing, but if the work that the company is doing can be considered similar to past projects developed in the past, making an analysis of the time spent in each particular phase results to be easier.

This can, in some way, be also related to the cost indicator. Experience will allow the managers and researches in some cases to create a better plan and make it more precise in terms of analysis of the situation and on how the work has been developed so far.

Experience can lead to a reduction of time and costs of projects also thanks to the abilities researchers have gained in the past, making it possible to re-use technical knowledge (know-how) in determined phases of the process.

Other two very important indicators for managers that monitor R&D units in pharmaceutical companies is the indicator that shows the rate of discoveries and the rate of success of development.

These two indicators, however, are possible to be identified and computed only at the end of the research phases and development processes. Only when a process is concluded it is possible to state whether it has passed successfully to the following stage. Experience in these terms can represent an opportunity to increase the final rate of success, by leading researchers and management to the implementation of projects with the correct budget (with a related increase in the efficiency of its use) and the best prediction of time required.

If these two steps are well planned, also the possibilities to see and increment of the final rates of discoveries and the final rates of success will be possible.

It is still possible to make another analysis of the two rates just mentioned. There is a strong correlation between them. Let's see in which way they are linked.

The rate of discoveries is strictly linked to the success that a project has in the different phases it has faces. The possibilities that determined research projects pass the first phases is normally around 70%, while the ones that result successful in the successive stages of research decrease incredibly reaching numbers of nearly 20%. According to these percentages, we can state that these are the projects that pass the total research stages, but the indicator, for who monitors, must also be linked to the rate of success that the company achieves in every phase.

This is exactly the level of correlation between the indicators that we are now considering. The pharmaceutical company must establish what kind of success it is considering: the one related to the projects that overcome the first phase (molecular targeting and compound discovery) and lead to the discovery of a molecular compound (that will be of a determined percentage) or the ones that overcome the also other phases, to finally reach the approval of the competent authority (and will have lower percentage of success).

A company must also establish how it wants or it thinks is the best way to monitor data collected and the proceeding of an R&D project. It is possible to distinguish the monitoring plan into two different solutions: on-site monitoring and centralized monitoring.

The on-site monitoring is made in the site were the R&D process is performed, while centralized monitoring is a remote evaluation of the data that are collected and that are reported periodically to the central site of the pharmaceutical company.

These mentioned are only some of the incredible number of indicators that managers have to consider and analyse constantly in Research and Development units of pharmaceutical companies and were the same number of a particular indicator can have completely different meanings according to the kind of project, the dimensions and the final aim of the company. These conditions will represent the way each single company will measure the performance of its R&D unit.

2.2.1 How to detect and correct a wrong path

Every company, regardless the industry it competes in, when taking a decision or establishing a strategy has the aim to improve itself and to do this, the top management must build a plan of action.

According to the type of intervention required on the firm, the plan will more or less detailed and it will be differently affected by certain elements such as experience, possibility to be monitored and opportunities to correct wrong procedures on the way.

What happens when the plan touches the R&D Units of a pharmaceutical company?

In this situation, it will be really tough for management to know where the plan will lead to. Managers can establish the final result desired, but it will be impossible for them to be sure that their aim will be achieved successfully.

As it should be clear, according from what has been stated previously in this text, when dealing with Research and Development Units in the pharmaceutical industry, results of determined practices will be obtained late. Managers and research scientists will know if the path the project is following is correct or wrong only when that specific stage of the project will reach the end. It is not possible in this situation to predict what kind of problems the project will incur into, or however, not completely. However, there are still some possibilities to manage this condition. The first step to do is to control everything that can be controlled and this will reduce the risks of taking a wrong path.

As stated in an article reported in GEN's database (2006):

> Deviation control in such a setting involves controlling the variables that can be controlled. When sources of variability cannot be identified or controlled, the work history (who, what, when, where, how) should be documented sufficiently to stand as institutional memory and a source of intelligence for future planning and study.

Also, very important is to increase, while proceeding with the stages of our project, the level of information obtained, documenting everything from the moment that proceeding with a plan means being always closer to the final aim established.

As it is possible to see from Figure 8, getting closer to the planned objective in R&D Units of pharmaceutical industries, means also an increase of critical decisions it will be necessary to take once the project finds a problem on its way.

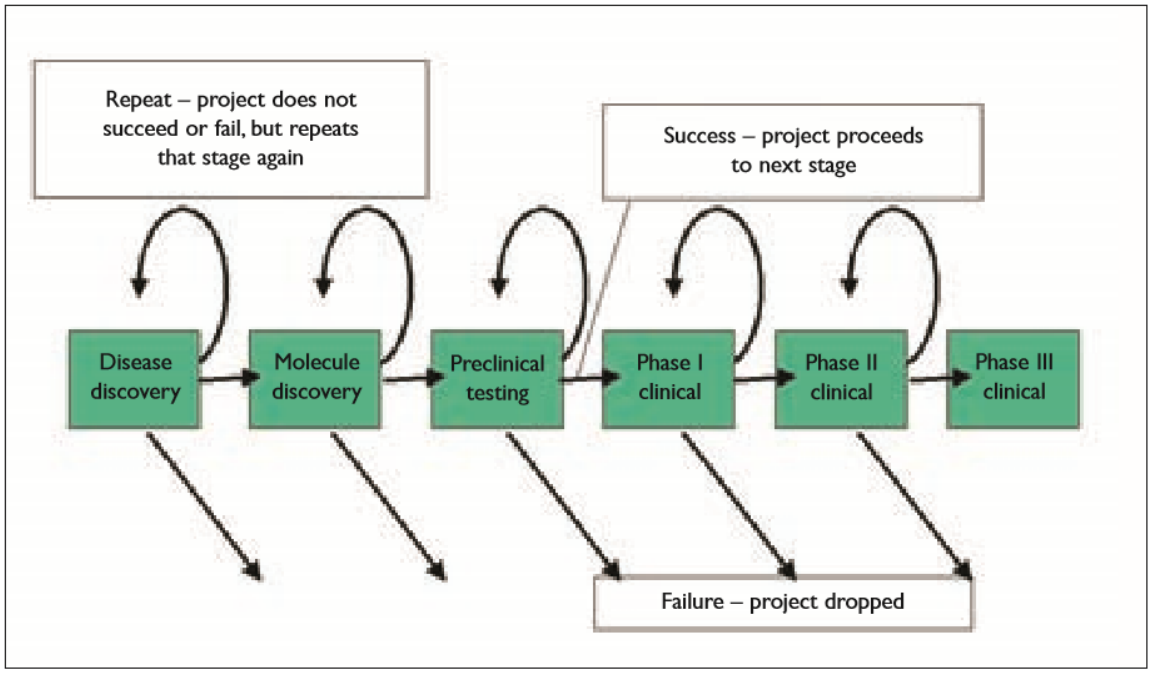

Figure 8: Consequences of discovering to have undertaken a wrong path, according to the different phases of research and development
Source: Drug Discovery World Fall, 2004

The investments made on the project by the company will be higher and will continue increasing while proceeding in the correct way and advancing to the successive step. On the other hand, this means also that in the first phases, when the company realizes that something is not going in the right way, there are possibilities to repeat the processes with more experience. Instead, it will become a relevant problem when realizing that project failed on the last stages, when a big amount of investments have been made and the project has good probabilities to drop.

This is why it is important to increase constantly the reporting of data collected during the early stages and augment the level of control while proceeding with the project and reaching the final objective.

For these critical reasons, there are particular actions that companies undertake. What they do is divide every single phase of the research into more sub-phases and try making a prediction or a plan for each of them with a studied degree of

preferences, establishing the actions to take if the most preferred plan does or does not achieve the desired goal.

Finally, for these reasons, it is possible to state that detecting a wrong path can represent, for the same project, a threat or an opportunity according to the period of identification of the problem.

A threat if detected in the last stages, making decisions become more critical and requiring a higher level of discussion since a relevant amount of resources (economical, but not only) have been invested.

An opportunity if in early stages, making it possible to learn from the failure and proceed with the other paths developed by the management before the beginning of the project, but with an increased experience.

Chapter 3
Field Research

3.1 Aim of the research

The first two chapters of this paper have an introductory function for what concerns firstly, the different performance measurement systems known and used in any kind of firm, regardless the industry expertise. Analysing which are the most common and their pros and cons according to different necessities of the firms themselves and finally a brief explanation of what KPIs are.

Lastly, with the second chapter it has been introduced the pharmaceutical industry, in particular what concern the research and development processes, their costs, how are they structured, the resources that are required and other aspects. Also, how and why firm select certain indicators.

According to this, the purpose of this text is to provide and define possible indicators and ways of working of pharmaceutical companies when analysing the performance of their Research and Development Units. Understanding how there are different methods to make analysis according to the various stages of the research and development process and the related different elements to consider when examining the level of performance.

The aim is to understand how companies behave in certain situations and why there are differences in the way of managing this Unit's performance. Interpreting and giving a meaning to these differences so to define which can be a possible common strategy of every pharmaceutical firm, considering however, different objectives, internal cultures, and strategies that lead to heterogeneous ways of working.

These differences can arise, sometimes, also within the same company from the moment that pharmaceutical firms that have incorporated an own branch of research and development, have their laboratories spread in different countries around the world according to the different objectives and functions of the laboratories themselves. A pharmaceutical firm might have a molecular target research laboratory

in India, one molecular compound laboratory in Singapore and the clinical phases' laboratories in U.S.A. and other countries (this mentioned is a random example).

Finally, the intent of this research is to understand how companies analyse the performance of their R&D Units considering the possible variables mentioned above and the introduction to R&D Units in pharmaceutical companies developed in the two previous chapters of this paper.

3.2 Methods of the research

The research, to be complete and exhaustive, required the author to obtain information and data in different ways. The methods of research have been:

- Direct, face to face interview
- Telephone interview
- Email interview
- Other data and paper consultation

The research was conducted by contacting 13 pharmaceutical companies (Angelini, Menarini, Bayer, Takeda, Eli Lilly, ITC Farma, Brystol-Myers Squibb, Novartis, Roche, GlaxoSmithKline, AbbVie, Sanofi and Anergis) and the non-profit organization TransCelerate.

The questions of the interviews were relative to the indicators that best depict the performance of Research and Development Units, how the results are evaluated and which is the system adopted by the companies to interpret results. Trying to understand how a pharmaceutical company can deal with adverse events during the R&D processes according also to the high level of investments required and if there is any possibility to predict if the process is not following the right course, how to detect these situations and which are the actions that are taken.

Not every company has answered to the questions and in the next paragraph (Understanding the results of the research) it will not be specified which company makes certain statements with the exception of Anergis.

The results will provide an overview of what is possible to understand from the answers obtained and how it is possible to interpret them so to reach an exhaustive and valuable conclusion.

3.3 Understanding the results of the research

From the various interviews to the actors of the pharmaceutical industry mentioned in the previous paragraph, it has been possible to get closer to a view of the elements that are the most representative in a performance analysis of a Research and Development Unit and the identification and meaning that must be given to the most critical and influent indicators.

According to what has been written previously in this thesis, it appears now clear that pharmaceutical companies are free to set their own indicators that best respond to their necessities and questions on the performance monitoring.

This kind of attitude is expandable also in an R&D Unit.

As stated by one of the Q.P. / Q.A. manager of one of the firms interviewed:

> The elements and indicators selected in an R&D Unit can be different according to the firm's kind of research work, they will always be more or less similar but each company has the will and the necessity to identify the ones more important for the representation of their performance. However, two indicators will always be common in every company. They are time and cost indicators. (Interview, April 1, 2016)

According to this statement, what is immediately clear is that the main element considered in a Research and Development Unit is the achievement of the efficiency and effectiveness.

These two elements tend to increase in terms of criticality from the moment that, as it has been stated in this thesis, the amount of money invested during the phases of the R&D process increases while getting closer to the final objective. The highest investments are necessary mainly in the clinical phases during which tests are made on humans. It is possible to see the different levels of investments required for each phase, from the pre-clinical and the target molecular one to the final phases, in Figure 9.

R&D BY FUNCTION, PhRMA MEMBER COMPANIES: 2013

(dollar figures in millions)

Function	Dollars	Share
Prehuman/Preclinical	$10,717.8	20.8%
Phase I	3,666.9	7.1
Phase II	5,351.3	10.4
Phase III	15,239.2	29.5
Approval	5,395.4	10.5
Phase IV	7,574.2	14.7
Uncategorized	3,668.7	7.1
TOTAL R&D	$51,613.6	100.0%

Figure 9: Allocation of R&D investments by functions
Source: PhRMA Annual Membership Survey

How can these numbers be interpreted? What meaning do they have and what kind of reasoning do they lead do?

As we know, clinical tests are those ones made on humans. This means that efficacy is important but not only. What companies have to consider very carefully in these steps is also another element: safety.

As one of the companies interviewed stated:

> From about 10'000 molecules synthetized in the laboratory, only one reaches commercialization, in a period going from ten to fifteen years. The influent factors are multiple and linked to the different stage of development. For the clinical part, the main indicators are efficacy and safety. (Email, May 30, 2016)

As it will be possible to see forward in the paragraph, clinical phases are effectively the most critical ones of the entire R&D process for more reasons, starting from the investments required and the time limits to respect, but also because it is the moment in which the highest level of failure is discovered.

These data are represented in Figure 10, elaborated by the author, which reflects the criticality of clinical phases and more in general, all the skimming of the molecular compounds with the proceeding of the process.

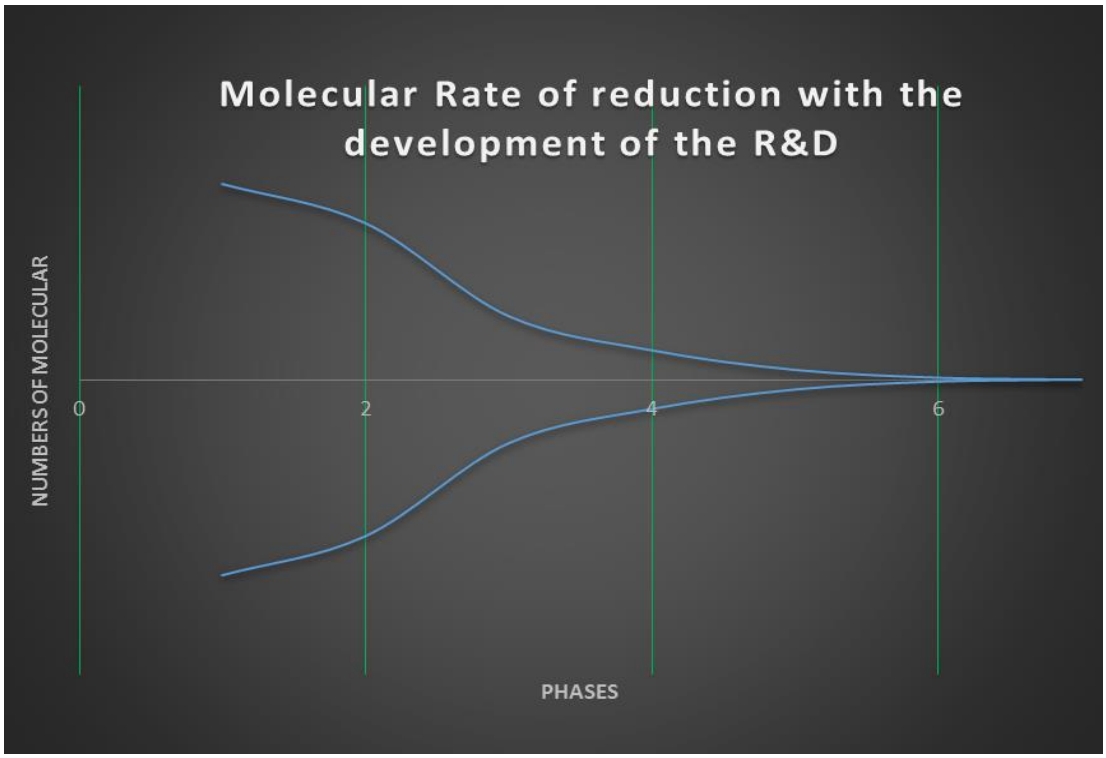

Figure 10: Molecular rate of reduction with the development of the R&D process
Source: Author

The green vertical line with indicated number 2, represents the moment in which the process passes from the preclinical phases to the clinical ones that go from number 2 to number 6. After number 6 there is the approval process from the competent authorities and the eventual commercialization of the developed drug.

The statistics provided by the statement above (from 10'000 molecules only one reaches commercialization) indicates how difficult and vital is for the managers to understand in the correct way the meaning of the results the indicators provide and the elements to keep under observation. Only 0.01% of the synthetized molecules will be successful.

There are, however, other important indicators that have to be mentioned and considered. To understand how managers measure the performance of the R&D Units of their companies, it has been very helpful the information obtained through the consultation of papers published by TransCelerate.

The data collected show that 83% of the companies interviewed use risk indicators to monitor determined R&D phases and that their results are (positive or negative) are represented by three colours (Red, Yellow, Green) or sometimes by the some pictures that represent "Thumbs down" or "Thumbs up".

This is important obviously, because it makes immediately evident for managers the elements that are not performing and CAPAs are set accordingly. Depending on the kind of indicators and their criticality, the frequency of monitoring will be different. However, only 30% of the companies state that risk indicators are predictive in terms of problems in the Good Clinical Practice (GCP). (Gough, Wilson, Zerola et al., 2016).

This means that the success or not of a determined process or phase can be seen only when this concludes and experience might become an important element to understand in a preventive way how the work is proceeding. According to the protocol, experience has a fundamental role when considering the number of deviations (problems). This means that is normally a protocol has a determined number of deviation and for the project in act the deviations are double as they normally are, experience may lead to understand the situation and take some actions. The most important and dangerous deviations to the protocol are the ones that remain unsolved.

One of the interviewed managers, when asked if there were possible indicators that could represent the actual situation of a project, stated that: “For the part of clinical research, the protocol defines the primary and secondary objectives. If these goals are achieved or not, there will be indications on how to proceed with the project” (Email, May 30, 2016).

When analysing the protocol deviations, however, it is not important only to consider the number of deviations, but also what these are representing and how relevant they are.

Deviations can be classified according to their typologies and relevance, linked to the corrective actions they require.

The kind of deviations that represent the biggest alert are the unanticipated problems that involve the high risks: they are the Emergency deviations.

The typology of deviations that instead is not so dangerous are the Minor/Administrative deviations.

According to what has been said in this thesis, the author analysed all the data and the information collected and depicted the most relevant indicators that must be considered when analysing the performance of R&D Units in pharmaceutical

companies. The elaborated indicators, represent situations at the end of a certain phase or also, can be analysed in the meanwhile, with the possibility to have a predictive view of the path the project has undertaken.

The rates can be divided into three main groups: efficacy and efficiency rates, time rates and cost rates.

Efficacy and Efficiency Rates

The Efficacy and Efficiency Rates measure the quality of the R&D process in terms of success or failure of the projects. The indicators being part of this groups are: Attrition Rate, Survival Rate, Success Rate and Expectations Rate. These kind of indicators are measured at the end of the phases.

- Attrition Rate: this rate shows how many of the projects put in act actually fail.

$$\text{Attrition Rate} = \frac{\text{molecules analysed that did not pass}}{\text{Total molecules analysed}}$$

This rate can float between 0 and 1, and the best conditions exist in the moment that this indicator is low. The most critical phases are the clinical ones, more precisely Phase II and Phase III, which present the highest value of the attrition rate. A possible way to reduce this rate is to increase the level of controls during the *in-vitro* and, mainly, the *in-vivo*, were molecular compound are tested on animals. Investing more time during the pre-clinical phases, will probably reduce the number of molecules that reach the clinical phases, but will be able in this way to reduce the failures during these stages and so the attrition rate gets lowered.

- Survival Rate: this rate is complementary of the attrition rate and measures how many of the percentage of how many of analysed molecules in one phase pass to the successive one.

$$\text{Survival Rate} = \frac{\text{molecules analysed that pass}}{\text{Total molecules analysed}}$$

Also this one floats between 0 and 1, but differently from the attrition rate, the higher it is, the better.

- The success rate measures more in general the rate of success of the total R&D project of a company

$$\text{Success Rate} = \frac{\text{Successul projects}}{\text{Total projects}}$$

This rate floats between 0 and 1 and the best the company has the best conditions when the indicator is high. This indicator depicts the general condition of the company and how its R&D Unit performs in a global view.

- Expectations Rate: this rate is particular and if does it not provide a value that can be considered positively, might represent a critical situation in the quality of work of the research scientists. This indicator represents the positive expectations that researchers have on a number of molecules they are treating and their effective success at the end of the phase.

$$\text{Expectations Rate} = \frac{\text{Number of compound molecules considered promising that pass to successive phase}}{\text{Total number of compound molecules considered promising}}$$

This indicator requires a collection of data during the phases and that researchers report the most promising compounds. The value of this indicator floats between 0 and 1 and, obviously, the higher it is, the better.

Time Rates

A time rate considers the time invested on a project and how the company is able to respect the deadlines established at the beginning of the R&D project. The indicator identified by the author that might be taken into account, is the so called

Phase's Time Weight Rate. This indicator analyses the time required by one single phase over the total time invested in the R&D process. The important thing of this rate is that it helps the managers to understand which phases are requiring more time and were if necessary, an intervention is asked.

$$\text{Phase's Time Weight Rate} = \frac{\text{Time invested on the phase}}{\text{Total time invested on the project}}$$

Cost Rates

The cost rates measure the way the company is managing the budget established at the beginning of the R&D project during the different phases of the process. The important element of the cost rates is that, differently form the ones analysed previously, these can be monitored during the phases and not just and the end of them, making it easier for the managers to understand how the expenditures are managed and were is possible to take preventive actions, avoiding negative situations at the end of the stages.

The cost indicators are the Discovery, Phase I, Phase II and so on allocation Rate, the Expenses' Development Rate and the Cost of Failure Rate.

- Discovery and Phases Allocation Rate: these rates depict the expenses required in a particular phase related to the total budget established for the entire process. Here below we will see the Discovery Allocation Rate, but only by changing the numerator, it is possible to adapt the rate to whatever phase.

$$\text{Discovery Allocation Rate} = \frac{\text{Expenses required by the discovery phase}}{\text{Total budget of the project}}$$

These kind of rates are very useful to monitor how much the considered phase is affecting the entire project's budget.

- Expenses' Development Rate: this rate, differently from the previous one, allows the managers to control how the entire budget established at the beginning of the process has been spent so far and undertake eventual actions to improve the situation or not.

$$\text{Expenses' Development Rate} = \frac{\text{Total expenses incurred so far}}{\text{Total budget of the project}}$$

- Cost of Failure Rate: this rate depicts how much did the failed molecular test impact on the total of the budget.

$$\text{Cost of Failure Rate} = \frac{\text{Total cost of failed moleculars}}{\text{Total budget of the project}}$$

This is an indicator that should be always as low as possible. It is important to consider that a certain value will have different meanings according to the phase that we are considering. It the value of the Cost of Failure Rate is the same both for the pre-clinical tests and for the clinical tests, perhaps in phase II, considering the much higher investments required in this last phase mentioned, it is possible to give two meanings to the value. On one hand, it is excessively high in the pre-clinical tests and it would mean that something is definitely going wrong; alternatively, the situation is particularly good in the clinical phase II.

These indicators have been developed by the author and can be considered, through the data collected during the study for the thesis, the ones that can provide the most critical and relevant information during the R&D process of Pharmaceutical company.

Here below in Figure 11, are summarized the indicators analysed in this paragraph, divided into the three macro-groups to which they belong.

Efficacy and Efficiency Rates	Time Rates	Cost Rates
- Attrition Rate	- Phase's Time Weight Rate	- Discovery Allocation Rate
- Survival Rate		- Phases (I,II,III,IV) Allocation Rate
- Success Rate		- Expenses' Develpment Rate
- Expectations Rate		- Cost of Failure Rate

Figure 11: Indicators classification of R&D Units in the Pharmaceutical Industry
Source: Author

The question that could arise now, is if there are possibilities to link these indicators to the performance measurement systems and what affects the different selection of indicators between the companies.

The answer is that it depends. The performance measurement systems have a pre-set schedule which means that it has already planned how the indicators have to be divided and organized. This might be a useful procedure when talking about units that are not R&D, Even more in pharmaceutical companies, where as we have seen, there is nearly nothing of secure. According to this, it is possible to state a pre-set matrix, for example a balanced scorecard, should not be taken exactly as it is because it would not represent, maybe, in the best way the actual situation of the R&D Unit of the firm.

It is also true, that some indicators and their selection are deeply influenced by the dimension, market share, economic potential of the firm, in one word, by its strategy. The indicators shown in Figure 11 can be adopted by every company, but their meaning and their specific weight changes according to the strategy. A huge company with many economic resources will have more possibilities to decide not to drop a project, for example and try anyway to develop it and see if it will lead to future positive results. Differently, a small medium pharmaceutical company, with a limited number of projects and economic capabilities with respect to a multinational

firm, will decide to drop or interrupt the project it is carrying on rather than risk losing its resources.

During an interview to Alexander Kettner, Director Head of Research of Anergis, when he was asked about the link between strategy and R&D, according to the different timings and necessities that a company has with respect to those of a research process that can last 20 years, he stated that:

> (…) we also drive our research according to the kind of partners we might find, so to become more attractive to them. Therefore, we make in a certain sense a short term job for this activity. However, I believe that all this is true mainly for a small company. For us, we can state that R&D is almost our core business. For example, we do not have products on the market yet and so our revenues cannot derive from this. Also, being a small company our investors require higher returns because of a higher risk, and so our strategy is not only linked to the product development but also to the exits of our investors and differently from big companies, we have to adapt our R&D goals in this direction. (Interview, June 17, 2016)

This depicts the strong relation between strategy and R&D Units processes. What is clear is the importance, as described before, of the dimensions and the market share of the company we are considering.

Following, instead, when the Director was asked how they measure R&D performance, the answer was very interesting stating that the publications and participations to scientific events represents a good feedback on the quality of their work:

> Publications can have different topics and what you can see is how many publications you have, so quantify numerically your work. You can also measure the quality of publications according to which journal is publishing it. In scientific conferences that we attend, we describe the data we collect and our feedback is the interest that arises on what we are reporting. (Interview, June 17, 2016)

To conclude, the performance measurement systems can have an important role, but the best solution might be to select first of all the indicators combined to the overall strategy of the firm and in particular of the R&D Unit, regardless the systems

available, and then establish if there is a system that best fits with the indicators selected and can be helpful for the Unit to monitor the situation.

It is difficult that a performance measurement system can be taken exactly as it is. It is better to adapt it to the conditions and necessities of the firm, eventually dividing the indicators identified in groups according to the type of values they represent.

Conclusions

The aim of this thesis is to understand the way managers measure the performance of the R&D Units in pharmaceutical companies.

In the first chapter, we have analysed different performance measurement systems pre-set and widely used by many companies, not only in being part of the pharmaceutical industry, that can be adapted to the own necessities and elements that must be measured for the firm.

It also described with a brief analysis, how KPIs are set and the corrective and preventive actions that might be taken when required, according mainly to documents provided from the literature.

The second chapter introduced and analysed more in detailed how the pharmaceutical Research and Development Units work and the different relevant elements that affect its performance.

Finally, in the third chapter have been elaborated by the author, through a personal research on the field, the results and the answers obtained by the managers of different pharmaceutical companies of the world that have been interviewed.

What this research leads to is the conclusion that actually there are no pre-set matrixes or performance measurement systems that are used and adapted exactly as they are built in the company. Their adaptation process is something that does not follow strict rules. The most important thing for managers is to identify those indicators that are able to provide the information that are required during the R&D process or during a particular phase of it.

The first thing that the study brought to light was that actually, each company, even if in the same industry, had its own ways of monitoring and according to its dimension, market share, internationalization and so on, could set certain indicators and monitor particular elements, important for them.

As reported in Chapter 3, during an interview it had been said that according to the different characteristics of the firms, each one would set its own indicators depending on the type of work of R&D the particular firm performed.

However, through the answers obtained, it was possible to identify which are considered, for every the pharmaceutical companies, the most relevant criticalities

that affect the research and development process. This allowed the author to identify and suggest those indicators that may be the most representative of the current situation and that can touch every R&D Unit of any pharmaceutical company, regardless its dimensions, market share, internationalization and so on.

These indicators measure the cost, time and efficacy and efficiency performance of the firm and once defined them, it is possible to give them, eventually, a location in the performance measurement system that perhaps the firm wants to adopt.

It would be restrictive and rigid to first identify a performance measurement system and then decide how to fill it.

Each company should understand which indicators are the most helpful to measure their R&D Unit performance and then, eventually, divide them, as the author of this thesis did in chapter 3, into macro-groups that could be adapted to the performance system selected.

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Interviews transcript

Company 1:

Question: “We know that the R&D process in a pharmaceutical company is long and complex, there are many phases that require different kinds of work. Which are the most representative indicators for the different phases?”

Answer: “Well, every phase of an R&D project is an individual project itself. With its own indicators linked to its necessities and those ones of the company.”

Q: “Okay. And how does the company define these indicators? Is it possible for me to understand if something is going wrong during the project?”

A: “When an objective has been defined, the managers must establish a project plan to follow. First, thing to understand is how do I reach my goal? How do I define a correct formula? Then define the economic resources that are necessary. The time required for that particular phase of the project. Trying also to predict which the most relevant criticalities are.”

Q: “So, once I have defined my project, it will begin the monitoring of each phase of it. How do you set the indicators to monitor? Which are the elements that are more critical for the managers?”

A: “Well, in any case the manager has to ask himself if the time schedule planned is respected, both for the project while proceeding but also for each single step of the phases; understand if the costs predicted are respected; if the predicted result of each phase is obtained and so on. This is how it works the monitoring process.”

Q: “Okay, this is clear. Are there possibilities that, for example, time schedule and costs are respected, but the final result is not achieved? If yes, can I detect this situation before the end of the phase?”

A: “Sure it can happen. We are talking about projects. It means that the idea of the project does not reflect a realistic opportunity under the conditions that were set.”

Q: “It means there was an underlying problem, right?”

A: “Exactly. It is a project. It can fit as it can go wrong.”

Q: “And how is a similar situation managed?”

A: “A project is composed by a really high number of sub-phases that allow a more precise monitoring. I immediately know, in this way if I am having problems in a single sub-phase, and according to the problem the management defines the actions. Should the project be interrupted? Should it be definitively dropped? Another solution can also be to modify what has been set for the other phases to allow the project to continue. For example, I am having problems with phase one and I still want to proceed? The managers can decide to establish a plan for phase one *bis* and phase one *tris.* You see, thing can change during the project according to the conditions that are created.”

Q: “So, making a final statement on the indicators for the R&D, we can say that each company sets its own based on the necessities and there are no fixed indicators that every company sets them regardless, is it correct?”

A: “The elements and indicators selected in an R&D Unit can be different according to the firm’s kind of research work, they will always be more or less similar but each company has the will and the necessity to identify the ones more important for the representation of their performance. However, two indicators will always be common in every company. They are time and cost indicators.”

Q: “Okay. Well this is all. Thank you very much for your kind availability.”

A: “Thanks to you.”

Company 2

Q: “Considering the complexity of R&D processes in the pharmaceutical companies and its related necessity of monitoring, through which indicators is it possible to measure the results of R&D Units during the various stages of the research?”

A: “For the part of clinical research, when a drug has already been established as such, the results of the research phases, and so the indicators to monitor, are different for the different phases of the testing.”

Q: “What elements have a greater impact on the success or failure of a research project? Which are the most sensitive indicators to detect?”

A: “From about 10’000 molecules synthetized in the laboratory, only one reaches commercialization, in a period going from ten to fifteen years. The influent factors are multiple and linked to the different stage of development. For the clinical part, the main indicators are efficacy and safety.”

Q: “Is it possible to understand through certain indicators (if yes, which are they?) if a research project is producing the desired results or not?”

A: “For the part of clinical research, the protocol defines the primary and secondary objectives. If these goals are achieved or not, there will be indications on how to proceed with the project.”

Q: “Which ones (if any) are the corrective actions to change a path that seems to be going wrong?”

A: “There are possibilities to change a study protocol if new elements emerge.”

Anergis

Q: “From the studies I have made, what I realized is that an R&D Unit is a unit in which volatility is high and where you cannot be certain of what is coming out. You cannot be sure that what you are looking for will be achieved, is this correct?”

A: “Exactly. For example, efficacy and safety of a drug are endpoints. They do not measure really how R&D is performing during the process.”

Q: “And in this sense, we know that R&D is divided into many phases. Is there a way to measure the performance during the process, before the end of it?”

A: “Actually, we do not have defined indicators that measure costs and resources in our company. What we do is to define the process and set the milestones. Then we have a process in which we have an idea of our drugs and we do a first set of experiments, we analyse them and then we continue and this is iterative. So for us measure is also about understanding how many times do we have to come back to the start of the process.”

Q: “Okay.”

A: “Also, another indication is how much time and how many resources it takes to reach the milestones we define.”

Q: “Yes. I suppose that time and resources that I invest are important elements I always need to consider.”

A: “Sure, because it is not only the costs that must be under control, you also must consider, if you redo the process, what kind of elements you must deal with and manage. According to every phase that represents our framing in which we operate, we analyse how much time it took and how many resources did we invest for it.”

Q: “Which are the actions that the company can undertake when it realizes that it will not reach the goal it wanted to achieve?”

A: “During the development of the project we try to see which the bottlenecks are and we do a risk analysis. Obviously, it depends also in which phase you are in: if it is purely the research phase, than you might just drop the project because you can evaluate if it is taking too much time or if it is technically impossible. Alternatively, we may try to understand if we can go on with what we have. This means that the situation is not ideal, but maybe we can improve it during the development process. And for the risk analysis, what we might do is to see which can be the difficulties by studying the previous tracks and extrapolate what happened, trying to predict costs, time and risks we might be dealing with.”

Q: “So is it correct to say that experience is fundamental?”

A: “Yes. It is the past data accumulated that can provide an idea of how fast and how cost-efficiently you can develop your product. You try to anticipate technical problems so you might try different approaches, also for budget planning, and you make reallocations according to what is needed for the success of the process.”

Q: “Okay. We know that going on with the phases, the success rate decreases continuously and the biggest jump in this sense is from pre-clinical phases to clinical ones. Everything is obviously reported, but can we use the same data of some molecules to generate another drug?”

A: “Well, we start from a known molecule and modify it and have specific readouts to see if it is working or not, but we cannot take the same molecule for another application. What we gain is knowledge, how to design and then make a connection between design and experimental, but we do not use the same molecule for another application. This might be different from other, big, pharmaceutical companies that might have many molecules ready and make a screening and see which might potentially be positive. This can happen for example for the development of cancer drugs.”

Q: "Okay."

A: "But for us the development process is different. We have a report and when we want to proceed with the development of a new drug, what we do is to get the report and try to understand, from the indications and the results, what can we do better. Can we jump a step? Can we try with more molecules from the beginning? This is what we can do, but we do not really take back the molecule itself."

Q: "Okay. Perfect. Talking now about strategy that can vary according to the different companies, what I believe from my economic studies background, is that firms have certain necessities that cannot wait the time required by an R&D process, that can last 15/20 years. So what I can think, and maybe I am wrong, is that R&D Units have an own strategy that is in some way independent from the overall strategy of the company, since they inevitably have different timings. Is it correct?"

A: "Well, in general it might be right, but for us that do not exist from 20 years, the R&D strategy is very market-driven. We are in the allergies treatment sector. Let's say first that not all countries have the same allergies and, being a small company, our strategy is to look for partners in different countries according to the allergy that exists in that place. In this way, we attract investors and financings from the place where the allergy is common. In addition, we develop for example a treatment against dust mites, which are global, and so attract investors from all over the world. This because for us, in this moment, the risk would be too high to develop a product on our own."

Q: "This is really interesting. So, your company's strategy and R&D Unit are strictly linked."

A: "Exactly. For this reason we also drive our research according to the kind of partners we might find, so to become more attractive to them. Therefore, we make in a certain sense a short term job for this activity. However, I believe that all this is true mainly for a small company. For us, we can state that R&D is almost our core

business. For example, we do not have products on the market yet and so our revenues cannot derive from this. Also, being a small company our investors require higher returns because of a higher risk, and so our strategy is not only linked to the product development but also to the exits of our investors and differently from big companies, we have to adapt our R&D goals in this direction."

Q: "Okay, this kind of interaction between strategy and R&D is very interesting to analyse."

A: "Another thing I might add is that for us, R&D performance indicators can be represented by the publications that we have, the scientific conferences or the presentations. We also see how many companies are interested in our technologies and the number of confidential agreements we have and this gives us important feedbacks on the quality of our work."

Q: "In which way publications and the other elements you mentioned, can represent indicators of performance measurement?"

A: "Publications can have different topics and what you can see is how many publications you have, so quantify numerically your work. You can also measure the quality of publications according to which journal is publishing it. In scientific conferences that we attend, we describe the data we collect and our feedback is the interest that arises on what we are reporting."

Q: "Is it also a communication strategy?"

A: "Sure. It is also a way to make other now us. We have to convince our clients that out products work. To be clear, you are not a client for us, you are a patient. Doctors that make you use our products are our clients. Therefore, we must convince the scientific community, make publications and generate interest on our results. This because in our field, publication means that a peer of experts who work for the journal review and analyse your data and see if it is scientifically valuable. This is known as a peer review process."

Q: “This is very interesting. This does actually mean that publications are performance indicators.”

A: “Sure.”

Q: “Well, this is all for me. Thank you very much for your availability. It has been a really interesting interview and it has been extremely helpful.”

A: “I am very happy for that. Thanks to you.”

Summary of Thesis

Performance measurement and evaluation of R&D units in pharmaceutical companies

Table of contents

Introduction

This thesis will analyse the way pharmaceutical companies evaluate and understand the performance of their Research and Development (R&D) Units.

The decision to make a study on this subject sees its birth in difficulties R&D Units lead to in terms of performance analysis and data interpretation for managers.

Evaluating an R&D Unit in pharmaceutical companies is extremely complex from the moment that the entire process required to develop a drug from its first phases (the molecular targeting) to the last ones (approval of the drug from the competent authority) lasts between fifteen and twenty years, requiring incredibly high amounts of investments without having any reassurance on the success of the project.

The research, to be complete and exhaustive, required the author to obtain information and data in different ways. The methods of research have been:

- Direct, face to face interview
- Telephone interview
- Email interview
- Other data and paper consultation

The research was conducted by contacting 13 pharmaceutical companies (Angelini, Menarini, Bayer, Takeda, Eli Lilly, ITC Farma, Brystol-Myers Squibb, Novartis, Roche, GlaxoSmithKline, AbbVie, Sanofi and Anergis) and the non-profit organization TransCelerate.

The thesis is structured in three chapters.

The first one describes the different performance measurement systems known and that might be adopted from the companies of any industry to make analysis and have a picture of their current situation by adapting these systems to their own necessities. It will then be explained what Key Performance Indicators are, their importance for the companies and the characteristics that these must have to be effective in a managerial analysis and from a generic explanation of the KPIs it will be depicted how they can be adapted and set to a Research and Development Unit of a pharmaceutical industry and the correct way to interpret them.

Following, the second chapter goes more in detail with the pharmaceutical industry and its R&D Units. The objective of the chapter is to understand how the

research and development process works and is structured, which are the main risks that a pharmaceutical company deals with when working on a project.

Finally, the second chapter will analyse the way managers can understand (and if this is actually possible) if the process put in place is leading to the desired results or not and the eventual preventive (or corrective) actions that might be undertaken to try reducing the damages the wrong path may generate.

Lastly, the third and final chapter will provide the results obtained by the personal research on the field by the author getting to the final elaboration of data collected through interviews. The information collected will be analysed and interpreted so to depict which common indicators can provide the most critical information to the companies when evaluating R&D Units performances and how managers practically interpret them during the phases of the process.

Every company will have an individual way of monitoring and will give an individual meaning to the results obtained and the aim of this thesis is to use the data collected from the different companies interviewed to develop and identify a common behaviour related to the most critical and determining indicators.

Chapter 1

Performance measurement systems

Literature and years of economic evolution brought experts to create and study an incredible number of systems useful to obtain determined indicators that represent certain results and every result must be always, with no exception, quantifiable. This last consideration represents one of the toughest challenges for managers: it is a crucial step to be able to represent whatever element in a numerical way and make sure that that value is the exact image of the situation the company is in. However, there is one thing that has to be kept constantly under consideration: indicators are numbers. These ones are irrelevant if other elements are not considered; the same numerical value of an indicator can have completely different meanings in companies of different age, industry and so on. The fact that values must be chosen carefully and subsequently interpreted lead to the logical conclusion of how important it is for a firm to have a skilled managerial team, able to interpret the indicators' results and

determine a strategy according to these. Kazandjian and Lied (1999) state this by saying: “performance indicators do not measure performance, people do” (p.2).

As said previously, many factors can affect the meaning of a certain indicator and its value and this is why is fundamental to use the performance measurement system that best fits with the information that the company is looking for. This is a factor of vital importance from the moment that decisions and strategies taken by managers must follow the data collected, “a performance measurement system is only as good as the outcome it tracks” (Hatry, 2006, p.43).

Which are the most common performance measurement systems used?

The first that must be mentioned is for sure the balanced scorecard developed by Kaplan and Norton.

The aim of the balanced scorecard is to divide the performance measurement into four different perspectives: financial, customer, internal business process and learning and growth. Each of these perspectives are linked with each other and are all related to a common vision and strategy that is the one of the firm. In fact, what the balance scorecard does is to drive and translate vision and strategy through the perspectives into performance measures (Kaplan & Norton, 1996).

Each perspective has to answer to certain questions that make it possible to analyse in the correct way the performance we want to obtain:

- Financial: To succeed financially, how should we appear to our shareholders?
- Customer: To achieve our vision, how should we appear to our customers?
- Internal business processes: To satisfy our shareholders and customers, what business processes must we excel at?
- Learning and growth: To achieve our vision, how will we sustain our ability to change and improve?

It is possible, however, to identify some elements that result lacking with this performance measurement system such as the level of competition of the industry. When the management of a firm has to determine a strategy to follow, that as we can see influences the entire matrix, it is of vital importance to know how competitors move and act. Having a benchmark is necessary and being able to identify the correct one fundamental and with the balanced scorecard this theme is not treated properly. However, it is evident that if we contextualize this problem in R&D units, where the

level of uncertainty is high, certain processes are pre-set and according to different industries, companies that compete with each other tend to follow the same steps when investing in the R&D.

Another important performance measurement system is the performance prism elaborated by Andy Neely and Chris Adams, which consists in the interrelated analysis of five different facets that must be able to answer certain questions:

- Stakeholder satisfaction: who are the stakeholders and what do they want?
- Stakeholder contribution: what do we want and need from our stakeholders?
- Strategies: what strategies do we need to put in place to satisfy the wants and needs of our stakeholders while satisfying our own requirements too?
- Processes: what processes do we need to put in place to enable us to execute our strategies?

Capabilities: what capabilities do we need to put in place to allow us to operate our processes?

Differently from the balanced scorecard, with the performance prism Neely and Adams understood that the environment in which a firm finds itself is big and complex, with many actors affecting its decisions and so it is not enough to consider only customers and shareholders as the stakeholders but also regulators, employees and suppliers.

It possible to analyse the EFQM model also as a performance measurement tool. This excellence model was founded with the aim "to stimulate and assist organizations throughout Europe to participate to improvement activities, leading ultimately to excellence in customer and employee satisfaction, and to result in changes to society and business" (Klazinga, 2000, as cited in Legido-Quigley, McKee, Nolte & Glinos, 2009, p. 34).

During the years, an increasing number of companies from different country in Europe started adopting the EFQM Excellence model as performance tool. The relevance of the framework has its basis on the fundamental concepts that together bring to what it can be considered an excellent organization.

The EFQM model is based on five enablers for excellence: leadership, people, strategy, partnership and resources and processes, products and services that "provide

ways to assess what has been done in the organization" (Hakes, 2007, p. 16) and four results criteria: people results, customer results, society results and business results that "provide ways to assess what has been achieved" (Hakes, 2007, p. 16).

Finally, we can consider as a particular performance tool the Tableau de bord that is "a reporting device, making it possible to control the realization of previously fixed objectives, as well as a tool for diagnosis, reaction and hierarchical dialogue" (Ardoin, Michel and Schmidt, 1986, as cited in Raynus, 2012, p. 226).

To generate a tableau de bord and establish the key performance indicators (KPIs) the management of a firm has to define clearly a strategy and a plan to follow, so to be able to understand exactly what is the result that must be achieved. The indicators can be both monetary or not, but what is important is that they must be quantifiable also if representing quality and not quantity measures; its aim is not only to provide financial results but also efficiency ones. For this reason, the management has to establish only the critical elements that best represent the situation by setting a minimum level of result that can be controlled in the clearest way possible.

This makes us understand how the tableau de bord is not a pre-set matrix or framework, but is a system that is developed and studied according to the necessities of each firm.

From this basis, it is possible to state that companies not always have to use pre-set matrixes but have their aim is to identify where its strategy goes and through which system is it possible to monitor it.

Chapter 2

R&D units in the pharmaceutical companies

When we talk about pharmaceutical industry, we are talking about that industry that involves different phases such as the research, the production of medical products in different solutions (i.e. syrup, tablet, spray, for injection, etc.) and finally its commercialization. Every company, obviously, has as principal goal that one to increase its profit as much as possible to survive and gain the highest share of the market possible.

However, let's now get deeper in detail in the process of research and development.

When we talk about R&D in pharmaceutical companies, we must be conscious that we are considering infinite variables, phases and elements. In the figure below (Figure 1), it is possible to see which the main steps are.

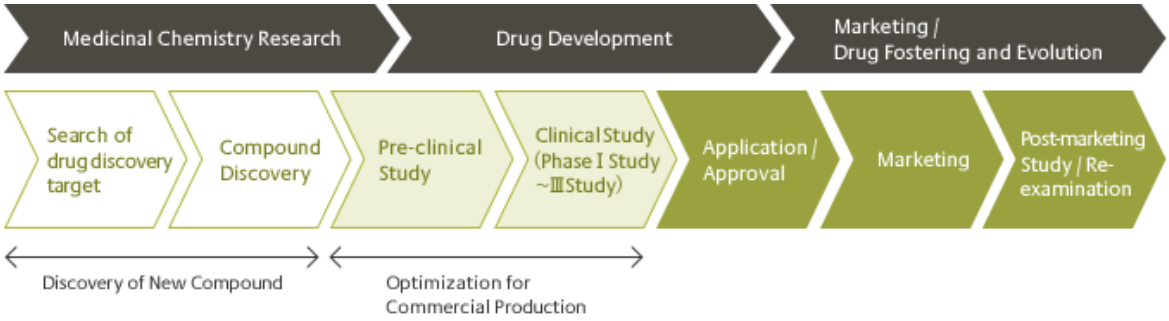

Figure 1: Drug discovery process
Source: www.takeda.com

The phase of the research can last generally seven years and it regards the "Search of a drug discovery target" and "Compound discovery". In these phases, the researchers have as objective to identify a molecular target (that causes a disease). Then, through an intensive work of the researchers, are generated an incredible number of molecular compounds that can affect the target and identify any possible element able to generate a reaction to the disease causing a stop or a reverse of its effects.

Out of thousands of molecular compounds and tests, there will be an optimization process through which the researchers will identify the most promising and potential molecular compounds that might be transformed, in the future, in possible medicines.

Those compounds that affect the only target and are completely ineffective with correlated elements represent the best result possible and the most relevant solutions.

Once identified the most promising compounds, the successive step researchers do is that one to consider already existing medicines and similar diseases to make a comparison on the effects and also a study on the dosage and the best way to provide the drug (its formula to produce it liquid or solid for example, spray or drops and so on).

Once these elements are clarified, it will begin the development process that will last approximately seven or eight years and that in Figure 2 is represented by "Pre-clinical study" and "Clinical study" stages. The preclinical tests, as well as providing information on the toxicity, are useful also to gather information on potential side effects.

"While preclinical research answers basic questions about drug safety, it is not a substitute for studies of ways the drug will interact with the human body. "Clinical research" refers to studies, or trials, that are done in people" (U.S. Food and Drug Administration, 2016).

Once concluded also development phases, the company will have an important dossier where all data deriving from the pre-clinical and clinical tests are collected, that will be submitted to the competent authority (in Italy AIFA, in U.S.A. FDA) for the request of approval, registration and finally its commercialization into the market.

R&D in pharmaceutical companies represents an incredibly volatile process, where there are required high amounts of money and investments with a low and dangerously decreasing number of successes and an initial investment uncertainty that is incredibly high. The main risks that can be identified are: regulatory, technical, strategic and discovery and development. These risks however, can be in someway controlled through the setting, from the management of determined Key Performance Indicators that will allow the management to know whether something is not performing as it should.

To be sure that KPIs are correct, they must have four characteristics. They must be quantifiable, practical, real and relevant. For this reason, the indicators selected for the monitoring of each unit will float in a number between 3 and 10.

Between the various measures and indicators that must be monitored during the R&D process, one of the most important is the one related to the budget and expenditures. Every phase of research and development of a new drug has an established budget according to the plans that management has made. Analysing constantly the costs of the project and they are managed is the first and probably most important and critical indicator that a company wants to monitor. This, mainly in pharmaceutical companies, seems to be even more relevant than in other industries

since the volatility of the processes is incredibly high and no precise and sure predictions can be made.

The cost indicator can be considered related also to the experience developed in the Unit, since experience means more know-how and a better way of understanding what is going on, increasing the possibilities to reduce the waste of resources.

Other two very important indicators for managers that monitor R&D units in pharmaceutical companies is the indicator that shows the rate of discoveries and the rate of success of development.

These two indicators, however, are possible to be identified and computed only at the end of the research phases and development processes. Only when a process is concluded it is possible to state whether it has passed successfully to the following stage.

A company must also establish how it wants or it thinks is the best way to monitor data collected and the proceeding of an R&D project. It is possible to distinguish the monitoring plan into two different solutions: on-site monitoring and centralized monitoring.

The on-site monitoring is made in the site were the R&D process is performed, while centralized monitoring is a remote evaluation of the data that are collected and that are reported periodically to the central site of the pharmaceutical company.

These mentioned are only some of the incredible number of indicators that managers have to consider and analyse constantly in Research and Development units of pharmaceutical companies.

Every company, regardless the industry it competes in, when taking a decision or establishing a strategy has the aim to improve itself and to do this, the top management must build a plan of action

As it should be clear, according from what has been stated previously in this text, when dealing with Research and Development Units in the pharmaceutical industry, results of determined practices will be obtained late. Managers and research scientists will know if the path the project is following is correct or wrong only when that specific stage of the project will reach the end. It is not possible in this situation to predict what kind of problems the project will incur into, or however, not completely. However, there are still some possibilities to manage this condition. The first step to

do is to control everything that can be controlled and this will reduce the risks of taking a wrong path.

As stated in an article reported in GEN's database (2006):

> Deviation control in such a setting involves controlling the variables that can be controlled. When sources of variability cannot be identified or controlled, the work history (who, what, when, where, how) should be documented sufficiently to stand as institutional memory and a source of intelligence for future planning and study.

Very important is to increase, while proceeding with the stages of the project, the level of information obtained, documenting everything from the moment that proceeding with a plan means being always closer to the final aim established, meaning that decisions taken will get always more critical according also to the fact that investments grow with the progress of the project

For these critical reasons, there are particular actions that companies undertake. What they do is divide every single phase of the research into more sub-phases and try making a prediction or a plan for each of them with a studied degree of preferences, establishing the actions to take if the most preferred plan does or does not achieve the desired goal.

Finally, for these reasons, it is possible to state that detecting a wrong path can represent, for the same project, a threat or an opportunity according to the period of identification of the problem.

Chapter 3

Field Research

According to the work of research on the field described in the introduction, it is important to say that not every company has answered to the questions and it will not be specified which company makes certain statements with exception of Anergis.

The results will provide an overview of what is possible to understand from the answers obtained and how it is possible to interpret them so to obtain exhaustive and valuable final conclusion.

According to the answers obtained in the interviews, what is immediately clear is that the main element considered in a Research and Development Unit is the achievement of the efficiency and effectiveness and, in the clinical phases, of safety. The first two elements tend to increase in terms of criticality from the moment that, as it has been stated in this thesis, the amount of money invested during the phases of the R&D process increase while getting closer to the final objective and the rate of success of the molecules decreases drastically. One of the companies interviewed states that only 0.01% of the synthetized molecules will be successful.

There are, however, other important indicators that have to be mentioned and considered. The data collected show that 83% of the companies interviewed use risk indicators to monitor determined R&D phases, however, only 30% of the companies state that risk indicators are predictive in terms of problems in the Good Clinical Practice (GCP). (Gough, Wilson, Zerola et al., 2016).

One of the interviewed managers, when asked if there were possible indicators that could represent the actual situation of a project, stated that: "For the part of clinical research, the protocol defines the primary and secondary objectives. If these goals are achieved or not, there will be indications on how to proceed with the project" (Email, May 30, 2016).

When analysing the protocol deviations, however, it is not important only to consider the number of deviations, but also what these are representing and how relevant they are. Deviations can be classified according to their typologies and relevance, linked to the corrective actions they require.

The kind of deviations that represent the biggest alert are the unanticipated problems that involve the high risks: they are the Emergency deviations.

The typology of deviations that instead is not so dangerous are the Minor/Administrative deviations.

Interviews brought to light also that strategy is linked to R&D Units mainly for small companies, that might have a market driven R&D strategy, following the necessities of the partners who decide to invest in their projects.

According to what has been said in this thesis, the author analysed all the data and the information collected and depicted the most relevant indicators that must be considered when analysing the performance of R&D Units in pharmaceutical

companies. The elaborated indicators, represent situations at the end of a certain phase or also, can be analysed in the meanwhile, with the possibility to have a predictive view of the path the project has undertaken.

The rates can be divided into three main groups: efficacy and efficiency rates, time rates and cost rates.

The Efficacy and Efficiency Rates measure the quality of the R&D process in terms of success or failure of the projects. The indicators being part of this groups are: Attrition Rate, Survival Rate, Success Rate and Expectations Rate. These kind of indicators are measured at the end of the phases.

A time rate considers the time invested on a project and how the company is able to respect the deadlines established at the beginning of the R&D project. The indicator identified by the author that might be taken into account, is the so called Phase's Time Weight Rate. This indicator analyses the time required by one single phase over the total time invested in the R&D process. The important thing of this rate is that it helps the managers to understand which phases are requiring more time and were if necessary, an intervention is asked.

The cost rates measure the way the company is managing the budget established at the beginning of the R&D project during the different phases of the process. The important element of the cost rates is that, differently form the ones analysed previously, these can be monitored during the phases and not just and the end of them, making it easier for the managers to understand how the expenditures are managed and were is possible to take preventive actions, avoiding negative situations at the end of the stages.

The cost indicators are the Discovery, Phase I, Phase II and so on allocation Rate, the Expenses' Development Rate and the Cost of Failure Rate.

The number of publications and the quality and relevance of the journal that decided to publish the research results can represent other performance indicators as reported by the Director Head of Research of Anergis.

Conclusions

The aim of this thesis is to understand the way managers measure the performance of the R&D Units in pharmaceutical companies.

In the first chapter, we have analysed different performance measurement systems pre-set and widely used by many companies, not only in being part of the pharmaceutical industry, that can be adapted to the own necessities and elements that must be measured for the firm.

It also described with a brief analysis, how KPIs are set and the corrective and preventive actions that might be taken when required, according mainly to documents provided from the literature.

The second chapter introduced and analysed more in detailed how the pharmaceutical Research and Development Units work and the different relevant elements that affect its performance.

Finally, in the third chapter have been elaborated by the author, through a personal research on the field, the results and the answers obtained by the managers of different pharmaceutical companies of the world that have been interviewed.

What this research leads to is the conclusion that actually there are no pre-set matrixes or performance measurement systems that are used and adapted exactly as they are built in the company. Their adaptation process is something that does not follow strict rules. The most important thing for managers is to identify those indicators that are able to provide the information that are required during the R&D process or during a particular phase of it.

The first thing that the study brought to light was that actually, each company, even if in the same industry, had its own ways of monitoring and according to its dimension, market share, internationalization and so on, could set certain indicators and monitor particular elements, important for them.

As reported in Chapter 3, during an interview it had been said that according to the different characteristics of the firms, each one would set its own indicators depending on the type of work of R&D the particular firm performed.

However, through the answers obtained, it was possible to identify which are considered, for every the pharmaceutical companies, the most relevant criticalities that affect the research and development process. This allowed the author to identify and suggest those indicators that may be the most representative of the current situation and that can touch every R&D Unit of any pharmaceutical company, regardless its dimensions, market share, internationalization and so on.

These indicators measure the cost, time and efficacy and efficiency performance of the firm and once defined them, it is possible to give them, eventually, a location in the performance measurement system that perhaps the firm wants to adopt.

It would be restrictive and rigid to first identify a performance measurement system and then decide how to fill it.

Each company should understand which indicators are the most helpful to measure their R&D Unit performance and then, eventually, divide them, as the author of this thesis did in chapter 3, into macro-groups that could be adapted to the performance system selected.