CATÓLICA LISBON
SCHOOL OF BUSINESS & ECONOMICS

The implementation of an improvement process in the R&D department of a Portuguese Pharmaceutical Company

The case of Medinfar

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Dissertation submitted in partial fulfillment of requirements for the degree of MSc in Business Administration, at the Católica-Lisbon School of Business and Economics

March 2015

Abstract

Thesis Title: The implementation of an improvement process in the R&D department of a Portuguese Pharmaceutical Company

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The main objective of this dissertation is to study the benefits resulting from the implementation of an improvement process undertaken by a Portuguese Pharmaceutical Company. It was developed a case study based in Grupo Medinfar, a Portuguese Pharmaceutical Company. This case study describes a problem identified by the company in its Research and Development (R&D) department, which is related to the management process of the materials used in this unit. The case study undertakes a detailed analysis of: i) the management of materials used and activities performed in the R&D unit; ii) the main limitations found in this process; iii) Medinfar's strategy to overcome the inefficiencies identified in the process; iv) the new management processes implemented by the company; v) and the benefits resulting from the improvement process, such as improved delivery lead times and cost savings that derived mainly from higher negotiation power with suppliers acquired by the company.

This dissertation is organized in the following chapters: 1-Introduction, section that presents the dissertation subject, motivations that led to the choice of the research question and methodology used in the dissertation's writing; 2-Literature Review where it is provided the context of the Worldwide Pharmaceutical Industry landscape with a special focus on the R&D environment in Portugal and globally; 3-Case Study where is analysed the implementation of a process, addressing issues identified in the management chain of the R&D materials and the benefits for Medinfar; 4-Teaching Notes which suggests and describes questions for class discussion, providing support to students and professors; 5-Conclusion, Limitations and Future Research.

Resumo

Título da Tese: The implementation of an improvement process in the R&D department of a Portuguese Pharmaceutical Company

Autor: Nuno Gonçalves

O principal objectivo desta dissertação é estudar os benefícios resultantes da implementação de um processo de melhoramento numa empresa farmacêutica Portuguesa. Foi desenvolvido um caso de estudo, baseado no Grupo Medinfar, uma empresa farmacêutica Portuguesa. O caso explora um problema encontrado pela empresa na sua área de Investigação e Desenvolvimento (I&D), que se prende com a gestão dos materiais utilizados nessa mesma unidade. O caso de estudo analisa detalhadamente os seguintes pontos: i) gestão dos materiais utilizados e actividades realizadas na unidade de I&D; ii) principais limitações encontradas no processo; iii) estratégia da Medinfar para superar os obstáculos identificados no processo; iv) novos processos de gestão implementados pela empresa; v) e os benefícios resultantes do processo de melhoramento, tais como poupanças a nível de tempo e custos, derivados do aumento do poder negocial da empresa com os fornecedores.

A dissertação está organizada pelos seguintes capítulos: 1-Introdução, secção onde é apresentado o tema da tese, motivações que levaram à escolha da pergunta de pesquisa e metodologia utilizada na escrita da dissertação; 2-Revisão de Literatura onde é abordado o contexto do panorama Mundial da Industria Farmacêutica, com um foco especial no ambiente de Investigação e Desenvolvimento em Portugal e no Mundo; 3-Caso de Estudo onde é analisada a implementação de um projecto de gestão de material de laboratório e os seus benefícios para a Medinfar; 4-Teaching Notes que disponibiliza e analisa questões para discussão e serve de orientação para professores e alunos; 5-Conclusões, Limitações e Investigação Futura.

Preface

The motivation to choose the topic of this dissertation came as the result of the summer internship I did in June 2014 in Grupo Medinfar. I was working within the Supply Chain department and, together with another intern, was responsible for the implementation of an improvement process related with the management of products in the Research and Development department. I thought that it would be interesting to write my thesis using the learning's of my own work in Medinfar. After applying to the Healthcare Management seminar and getting the approval from my advisor, Susana Frazão Pinheiro, about the possibility to use Medinfar's case to highlight the benefits of their implementation, I knew I had made the right choice.

The next step was to start collecting all the information concerning the implementation of the improvement process.

I would like to thank everyone at Medinfar, specially to Carlos Valadas, Supply Chain Manager and Manager of the project's implementation, who was available whenever i needed to clarify any doubts or questions; my former internship colleague, Jorge Oliveira, who is now working in the Supply Chain unit at Medinfar and kept me up to date about the evolution of the process during the time I wrote my dissertation; and Mécia Frias, Chemical Analyst Technician at Medinfar's R&D unit, who also helped me in everything related to the activities performed in that area of the company. They enabled me a quick and easy access to important information that surely helped me write the case study of this successful implementation.

I would like to express my gratitude to my advisor, Susana Frazão Pinheiro, for her help and assistance during the development of my thesis, to my family for their encouragement during all this process, and finally to Rita, for her constant support and editing skills.

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Introduction

The Pharmaceutical Industry is one of the most profitable, but also capital-intensive industries in the world. The increasing costs of medicines reflect the significant expenditure incurred in the investigation and development of new products, undertaken by Pharmaceutical Companies. The combination of limited timings of commercial exclusivity provided by product patent protection with the spiraling costs of R&D, obliges Pharmaceutical Companies to be continuously investing in the research and development of new products.

This is a long process, with very high attrition rates. From millions of molecules that are tested only a few innovative products are approved by the Regulatory Authorities to be used in the treatment of patients.

There are several business models in the Pharmaceutical Industry. There are companies that undertake R&D with the objective of developing new products that provide solutions to unmet medical needs, or are better tolerated or less toxic that existing products. These are so called “Innovation“ companies. There are companies that develop less expensive copies of existing products, when they lose patent protection. These are the “Generic” companies. And there exist companies that undertake R&D aiming to improve formulations and dosages of existing products. This is the type of innovation that is made by most Portuguese Pharmaceutical Companies.

The economic crisis that affected Europe, and more specifically Portugal, had a very negative impact in the Pharmaceutical Industry with Governments implementing price cuts globally.

Almost all companies in Portugal were forced to revise their business model leading to a significant decrease of their cost base, namely via reductions on headcounts, and investments.

The smaller companies were the most affected by this crisis. And cuts in investigation, that only shows results in long term, was the norm.

Medinfar, a Portuguese Pharmaceutical Company, was also affected by this crisis and looked at processes that could be improved and improve efficiencies at all levels.

After doing a summer internship in Medinfar and having worked in the team that was responsible for studying the product's management process at the Research and Development unit to improve it, I wanted to look in more detail to the benefits that the implementation brought to the company.

This led me to the following research question:

Which were the main benefits for Medinfar resulting from the implementation of an improvement process in the R&D unit?

The implementation of the improvement process was not completed when I finished my internship in Medinfar.

Continuing working with the responsible for this project was key to collect information that allowed me to identify the benefits for the company.

Methodology

This dissertation begins with an analysis of the Pharmaceutical Industry Worldwide and R&D investments undertaken by this industry, carried out via a Literature Review. Information for this section was collected from Google Scholar, an academic database, and from reports from Pharmaceutical Companies, Consulting Companies working in the Pharmaceutical Industry and Pharmaceutical Regulatory Agencies.

It is followed by a Case Study based on Medinfar, which documents the implementation of an improvement process. It is an "analytical" case where it is described the problem identified by the company and the solutions implemented. The sources of information used to write the case study range from public and private documents to interviews to employees and personal observation, since I was involved in the implementation of the improvement process. The data used in this case was collected from June 2014 to March 2015. As the case explores the integration of an IS in a company, a technological issue that experiences a fast growth and development, it is expected that in the upcoming years the methodology used is no longer up to date.

The Case Study is complemented by four Teaching Questions, which aim to support a class discussion, approaching themes related to the conclusions of the Case Study.

Literature Review

Global Pharmaceutical Industry

Data from IMS Health shows that the Global Pharmaceutical Market in 2012 worth 962,1 billion$, with the United States leading with 38% of the Global Market, followed by Europe with 24% share. The remaining was distributed between Asia, Africa and Australia with a combined 18% share of the Market, Japan with 12% and Latin America with 8% of the Market. Europe's market value was 221,8 billion$, around 179,8 billion€.

These figures demonstrate the huge importance of the Pharmaceutical Industry in the Global Economy. It is one of the most profitable Industries in the world and, in Europe, the Health sector, including the Pharmaceutical Industry employs almost 10% of the total workforce. This Industry is accountable for the investigation, production, marketing and selling drugs licensed for usage by the Regulatory Authorities. It was responsible for several major discoveries that helped to fight some of the most deadly infectious diseases in the world such as pneumonia, tuberculosis and diarrhoea.[1]

One of Pharmaceutical Industry greatest discoveries was Vaccinnes.

Vaccination, the administration of antigenic material to stimulate an individual's immune system to develop adaptive immunity to a pathogen, is the most effective method of preventing infectious diseases. The first vaccine was produced to fight Smallpox, one of the world's most devastating diseases known to humanity caused by the variola virus. "As recently as 1967, the World Health Organization (WHO) estimated that 15 million people contracted the disease and that two million died in that year."[2] Following an immunization campaign led by the WHO, it was declared eradicated in 1980.

The development of Antibiotics was a key milestone of the Pharmaceutical Industry. Antibiotics are agents that either kill or inhibit the growth of a microorganism.

[1] United States Centers for Disease Control and Prevention (2011)

[2] http://web.archive.org/web/20070921235036/http://www.who.int/mediacentre/factsheets/smallpox/en/

The first antibiotic was discovered by Alexander Fleming in 1928 and was called penicillin. It was used widely for treating soldiers during World War II with wound infections and pneumonia. By the end of 1940's it became widely available for the general public.

The following are some key contributions of the Pharmaceutical Industry to Global Healthcare:

- Every year, medicines and vaccines prevent at least 3 million deaths from malaria and save 750,000 children from disability.
- Between 2000 and 2006, immunization campaigns helped to reduce the number of deaths from measles in Africa by 91 %.
- In 2010, there were 48 medicines in the pipeline for malaria and 81 medicines in development for HIV/AIDS.
- In 2010, International Federation of Pharmaceutical Manufacturers & Associations' (IFPMA) members had 102 on-going R&D projects related to diseases of the developing world.
- In 2009, the research-based Pharmaceutical Industry contributed around 75 % of the R&D funding for tuberculosis, malaria and dengue.

(IFPMA – The Pharmaceutical Industry and Global Health: Facts and Figures)

Pharmaceutical Industry in Europe and in Portugal

The Pharmaceutical Sector is also very important in Europe. The current healthcare expenditure in Europe, in 2012, represented 9% of its Gross Domestic Product (GDP). In Portugal, this expenditure takes an even higher share of the GDP, representing 9,5%. (OCDE Health Data 2014)

Portuguese Pharmaceutical Industry's Association "Apifarma" provides data about the European and Portuguese Markets. In 2012, the total investment in Pharmaceutical Products of the European Union 28 countries was 148,9 billion€ ; and Portugal had a market of 2,9 billion€, which represented around 2% of the total EU 28 pharmaceutical market. Unlike Europe, with a cash market growth of 3,4% from 2008

to 2012, Portugal experienced a 20,3% decrease in value in the same period. Only Greece showed a bigger decrease of 25,5%. (Apifarma, 2012)

Portugal depends mainly on foreign countries to access pharmaceutical products. This is clearly seen in the 2,19 billion€ in pharmaceutical imports contrasting with 705 million€ in exports[3]. Despite this big difference, the amount of exports increased significantly since 2008 when they valued 456 million€. (INE)

Portugal had a negative pharmaceutical trade balance of 1,34 billion€, contrasting to what happens in other major EU countries such as the UK, France and Germany.

The main export destinations for Portugal are other EU countries, representing 63% of all exports, and Portuguese-speaking African countries (13%). In what concerns to Imports, other EU countries have an even higher influence for Portugal, representing 89,3% of all Import origins, with Switzerland being the second country in terms of preference for the Portuguese, with a 7,7% share.

Europe had a positive trade balance of 55,6 billion€ in 2013[4].

In what concerns to employment in the Pharmaceutical Industry, Portugal doesn't follow the European Union trend. From 2008 to 2012 the number of employees in the industry decreased 22%, in Portugal, while the average of the 28 EU countries increased 1%. In 2012 there were 8000 direct employees in the Pharmaceutical Industry in Portugal, which still makes this industry a major employer in the country. Regarding Value-added tax (VAT), Portugal has one of the highest Normal VAT rates in Europe (23%) while the average in the European countries is 21,05%. Contrarily, the Portuguese medicinal products' VAT rate is one of the lowest in Europe, both for prescription and over-the-counter drugs (OTC) (6%), when compared with Europe's 8,9% for Prescription medicines and 11,2% for OTC[5]. (Units %, as of 1st January 2013).

The last available data from Portugal shows us that in 2012 there were 409 Wholesalers and, in 2013, there were 121 Pharmaceutical Companies[6].

77% of the Companies focused on the Human Health area while the rest were concentrated between Animal Health (9%), In-Vitro Diagnosis (12%) and R&D (2%). Only 34% of the companies operating in the Portuguese market are from Portugal, while the other 66% have different countries of origin.

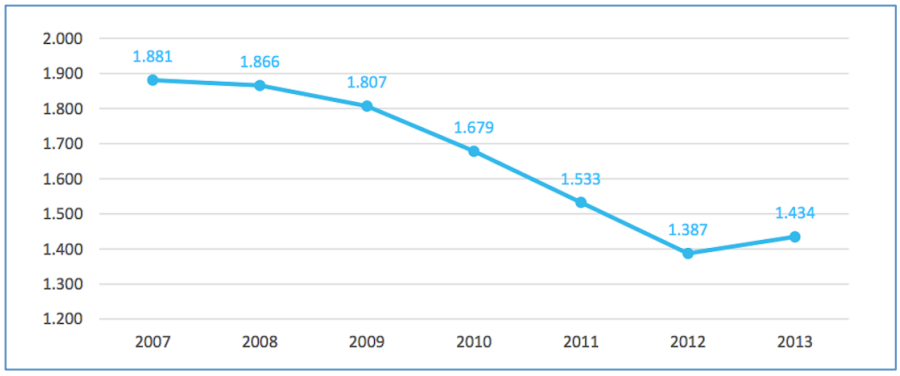
[3] Eurostat (COMEXT database – December 2013)
[4] Eurostat (COMEXT database – April 2014)
[5] EFPIA 2014
[6] Apifarma and Infarmed - Medicines Statistic 2012

Economic Crisis

The economic recession, which began in 2008, has had a mixed effect on pharmaceutical consumption, expenditures and prices. The largest changes have occurred in high-income countries and in Europe. The European region was the WHO region with the most severe decline in pharmaceutical consumption (-6%, Q3 2009 compared to Q1 2008).[7]

In Portugal, the economic crisis also had a huge impact in the Pharmaceutical Market. The manufacturing of raw materials and pharmaceutical products also suffered a decline as we can see in the picture.

Figure 1: Production evolution (M€)



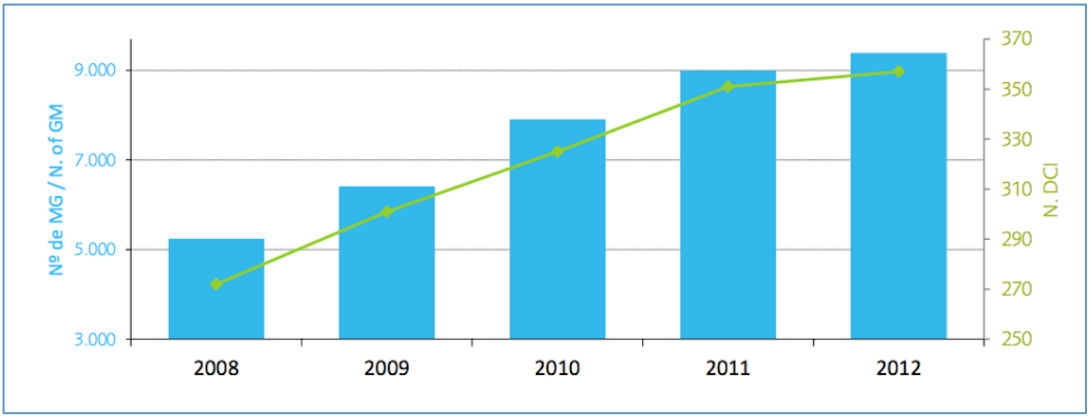
Source: INE, Infarmed, Apifarma

The annual average retail price in ambulatory for medicines also decreased from 13,01€ in 2007 to 10,11€ in 2013.

The Portuguese market had a major increase of Generic Medical Drugs, from 5.230 units in 2008 to 9.376 in 2012 accounting for 57,7% of total medicines in the market in this last year.

[7]http://www.pharmaceuticalpolicy.nl/Publications/Reports/Buysse_report%20impact%20recession_2010.pdf

Figure 2: Number of generic medical drugs evolution



Source: Infarmed

Hospital debt to Pharmaceutical Companies is a historically big issue, and it worsened with the recession in Portugal. It registered its highest value in 2011, with a total debt of 1.282,5 million€, Administrative Public Sector and Business related Public Entities combined, to the Pharmaceutical Industry.

Data form Portugal shows us that in January 2015, the National Health System Hospital's debt to Pharmaceutical Companies was around 820,9 million€, (127,4 million€ less than in the same period in the previous year) and the average payment time was 467 days, (16 days less than in the same period in the previous year).

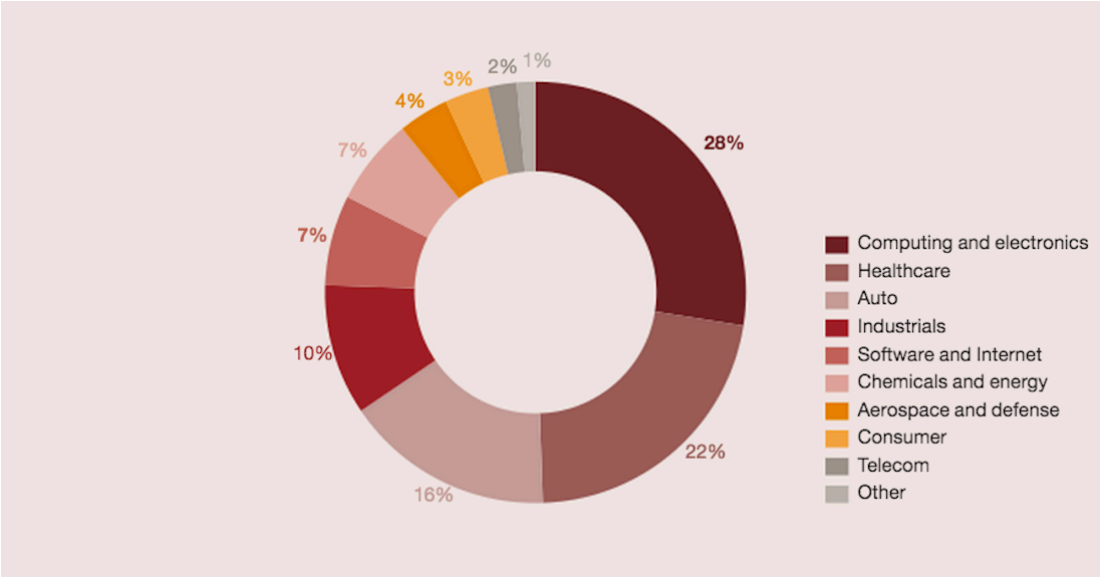
Centro Hospitalar Lisboa Norte, which is comprised by Hospital de Santa Maria and Hospital Pulido Valente, is responsible for the biggest part of the debt, owing around 126,2 million€ to Portuguese Pharmaceutical Companies. It is followed by Centro Hospitalar Lisboa Central, which has Hospital de São José, Hospital de Santo António dos Capuchos, Hospital de Santa Marta and Hospital D.Estefânia, that owes 91,8 million€. (Apifarma 2015)

Pharmaceutical Industry R&D

The Pharmaceutical Industry, or Healthcare Industry, is the second biggest R&D spending industry worldwide, only outperformed by Computing and electronics. In the last decade these two industries have been responsible by 50% of total Research and Development spending and were also the top spenders in absolute value in each of those years.

In 2014, the Healthcare Industry reduced its spending, for the first time since 2010, by 1,2%. (Bloomberg data; Capital IQ data; Strategy& analysis)

Figure 3: 2005-2014 R&D spending by industry



Sources: Bloomberg data; Capital IQ data; Strategy& analysis

U.S. Market

"The pharmaceutical industry is one of the most research-intensive industries in the United States. Pharmaceutical firms invest as much as five times more in research and development, relative to their sales, than the average U.S. manufacturing firm." (Congressional Budget Office)[8]

"Corporate venturing by multinational pharmaceutical and large biotech companies is playing an increasingly important role in financing the development of early stage innovation…[and] an essential role in the sustainability of the biotech ecosystem, advancing the future of pharmaceutical innovation and biotech entrepreneurship." (G. Von Krogh, et al.)[9]

"The Food and Drug Administration (FDA) is an agency within the U.S. Department of Health and Human Services. It consists of the Office of the Commissioner and four directorates overseeing the core functions of the agency: Medical Products and

[8] Congressional Budget Office. "Research and Development in the Pharmaceutical Industry." Washington, DC: CBO, October 2006
[9] "The Changing Face of Corporate Venturing in Biotechnology."

> Tobacco, Foods and Veterinary Medicine, Global Regulatory Operations and Policy, and Operations.
>
> FDA is responsible for:
>
> - Protecting the public health by assuring that foods (except for meat from livestock, poultry and some egg products which are regulated by the U.S. Department of Agriculture) are safe, wholesome, sanitary and properly labelled; ensuring that human and veterinary drugs, and vaccines and other biological products and medical devices intended for human use are safe and effective
> - Protecting the public from electronic product radiation;
> - Assuring cosmetics and dietary supplements are safe and properly labelled
> - Regulating tobacco products
> - Advancing the public health by helping to speed product innovations
>
> FDA's responsibilities extend to the 50 United States, the District of Columbia, Puerto Rico, Guam, the Virgin Islands, American Samoa, and other U.S. territories and possessions."
> (U.S. Food and Drug Administration, 2015)[10]

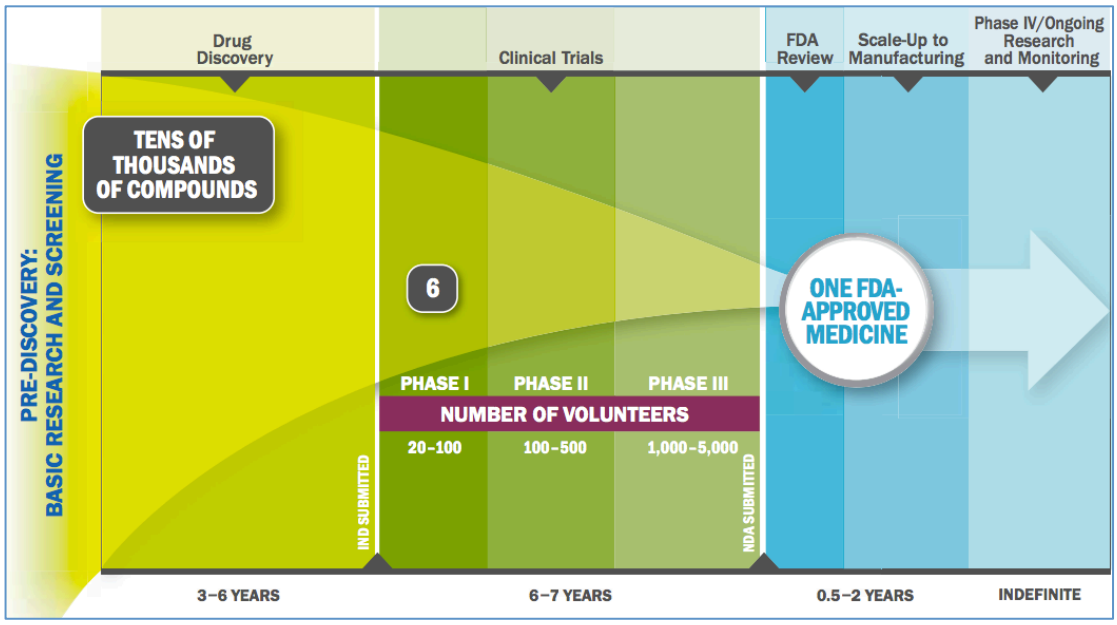
In this section we look at FDA as the agency that authorizes or not the commercialization of a new drug.

In 2013, PhRMA (Pharmaceutical research and Manufacturers of America) member companies invested an estimated 51,1 billion$ in R&D.

The R&D process in this area is very lengthy and costly and, in the majority of the cases of developing a drug, it doesn't reach "maturity". In average, 2 out of 10.000 substances in laboratories will successfully pass all stages of development required to become a marketable medicine and it takes 10 to 15 years for a new drug to be marketed. The estimated cost of researching and developing a new chemical or biological entity is 1,5 billion$ (Mestre-ferrandiz et al, 2011), including the cost of failure. Even the drugs that grasp clinical trials have only 16% probability of being accepted.

[10] http://www.fda.gov/AboutFDA/Transparency/Basics/ucm194877.htm

Figure 4: The Research and Development Process



Source: PhRMA (2014)

This image shows the numerous steps each potential new medicine goes through in order to get to patient's hands.

In the early stage of Drug Discovery researchers try to discover biological targets, such as a gene or protein, for a possible medicine. They conduct studies in cells, tissues and animal models to determine if, a specific target found in a disease, could be affected by a compound that is being studied. Then, researchers look for a lead compound —"a promising molecule that could influence the target and potentially become a medicine".

In the Preclinical Testing stage, thousands and thousands of compounds are narrowed to a few hundred promising options that will be subjected to laboratory and animal studies in order to determine if they are appropriate for human testing. This process may take many years and very few compounds move to the Clinical Trial's phase.

In the Clinical Trial's stage the compounds are tested in human volunteers.

A potential medicine must complete three important phases before being presented to the FDA for review:

Table 1: Phases of the Clinical Trials' stage

Phase I	Compound tested in a small group (20 to 100) of healthy volunteers to verify the compound's safety
Phase II	Compound tested in a larger group (100 to 500) of volunteers who have the compound's target disease. This phase determines the compound's effectiveness, risks and optimal dose
Phase III	Compound tested in a much larger group (1000 to 5000) of volunteers to produce statistically significant information about safety and efficacy and set the overall benefit-risk ratio

Source: Author, adapted from PhRMA (2014)

After finishing the clinical trials, a Pharmaceutical Company submits a New Drug Application or a Biologics License Application to the FDA for authorization to market the new drug. The FDA scientists decide whether to approve the new medicine after reviewing all the data from all the studies of the compound and measuring its benefits and risks.

Once the FDA approves the new medicine the process reaches a new phase, Manufacturing. The medicine needs to be produced at the highest quality level and meet the patient's needs so, the manufacturing facilities must be cautiously build to ensure safety in each step of the manufacturing process.

The R&D process doesn't stop once the medicine is approved by the FDA. Companies conduct post-approval research to monitor long-term side effects in patients. They also run phase IV clinical trials to assess long-term safety and effectiveness in particular patient subgroups. (PhRMA 2014)[11]

European Market

Research and Development in the Pharmaceutical area provides a precious outcome by improving life expectancy and quality of life considerably.

[11] http://www.phrma.org/sites/default/files/pdf/2014_PhRMA_PROFILE.pdf

In Western Europe, life expectancy increased from 67 years in the 1950's to 80 years in 2010, meaning that an extra life year is added every five years.

Another huge impact of R&D in this area is efficiency and cost savings.

Innovation in both drugs and devices has a decreasing effect on healthcare expenditure. Medicines support a more efficient use of resources by avoiding major health issues like surgeries. Ex: the use of aspirins or beta-blockers for patients who have experienced a heart attack, stroke or have a disease of the blood vessels in the heart may prevent a reoccurrence and avoid more expensive surgical procedures like angioplasty and bypass surgery. (Janssen Pharmaceutica N.V., Investing in European health R&D 2013)[12]

Data from 2010 shows that European Healthcare expenditure represented around 10% of GDP, a tendency that is rising and is expected to represent approximately 13% of GDP in 2030. In 2012, the Pharmaceutical Industry invested more than 30 billion€ in Europe, representing an increase of 3,2% from 2009. (EPFIA, PhRMA)[13]

Currently in Europe, 59% of the costs of providing healthcare are related to in-patient care (hospitals) and long-term care (residential and nursing homes for older people). Another efficiency achieved by the use of drugs, like long acting injections, is the reduction of time spent in hospitals. This helps cutting costs but even tough, expenditures in this specific area are projected to increase due to the ageing of populations.

R&D will remain a very important subject for Pharmaceutical Companies in the years to come, not necessarily in terms of absolute value but in the company's ability of effectively allocating money in research for new products and development of new processes which may lead to cost reductions.

> "The European Medicines Agency (EMA) is the European Union body responsible for coordinating the existing scientific resources put at its disposal by Member States for the evaluation, supervision and pharmacovigilance of medicinal products.
>
> The Agency provides the Member States and the institutions of the EU the best-possible scientific advice on any question relating to the evaluation of the quality, safety and efficacy of medicinal products for human or veterinary use referred to it in accordance with the provisions of EU legislation relating to medicinal products.

[12] http://www.janssen-emea.com/sites/default/files/Investing-in-European-Health-R&D.pdf
[13] http://www.efpia.eu/uploads/Figures_2014_Final.pdf

Principal activities

Working with the Member States and the European Commission as partners in a European medicines network, the European Medicines Agency:

- Provides independent, science-based recommendations on the quality, safety and efficacy of medicines, and on more general issues relevant to public and
- Animal health that involve medicines;
- Applies efficient and transparent evaluation procedures to help bring new medicines to the market by means of a single, EU-wide marketing authorisation granted by the European Commission;
- Implements measures for continuously supervising the quality, safety and efficacy of authorised medicines to ensure that their benefits outweigh their risks" (European Medicines Agency, 2015)[14]

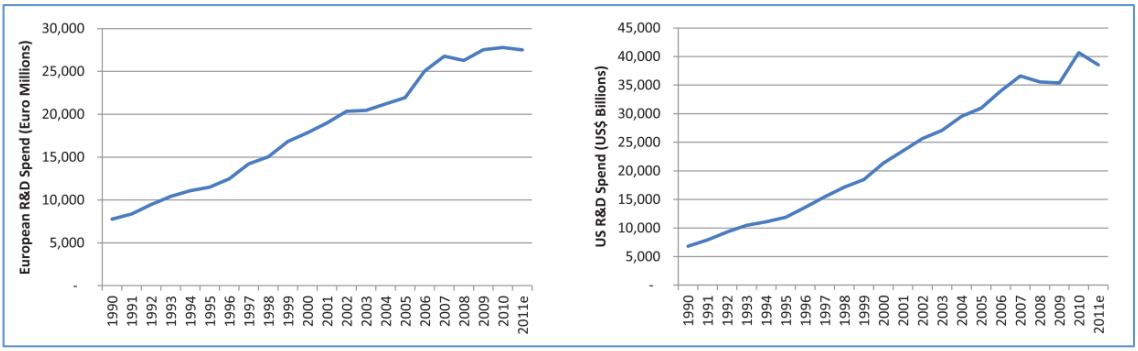
R&D Productivity (Europe vs. United States)

The total R&D costs per approved New Molecular Entity (NME) are divided in four variables: Success rates across the different phases of clinical trials; Development times from Phase I to Phase III which remained relatively constant over time, at around 6.5 years (75–79 months) on average; Out-of-pocket costs representing the cash outlay required for the development costs to produce a new drug, estimated in 220 million$ in 2011 and Cost of capital which has a huge impact on the final cost per successful NME due to the lengthiness of Pharmaceutical R&D, considered to be 11%. (Mestre-Ferrandiz, J., Sussex, J. and Towse, A.)

R&D expenditures continue to increase both in Europe and in the U.S. as we can see in the picture, while the number of new chemical or biological entities has been decreasing as shown in the table below.

[14]http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000106.jsp&mid=WC0b01ac0580028a44

Figure 5: European and US R&D Spending



Source: EFPIA (2012)

Figure 6: Number of new chemical or biological entities (1990–2009)

Number	1990–1994	1995–1999	2000–2004	2005–2009
Total	215	207	162	146
Average per year	43	41	32	29

Source: EFPIA (2010a)

If it is only compared the input (annual global Pharmaceutical R&D spending) with the output (the number of NMEs launched), it may seem that the R&D productivity of the Pharmaceutical Industry has decreased over time.

Data from previous analysis shows that the EMA approved 13 NMEs in 2010 and 23 in 2011, while the US Food and Drug Administration (FDA) approved 19 NMEs in 2010 and 32 in 2011. (Wang and McAuslane 2012)

It can also be noted that the average number of new entities launched decreased from 43 between 1990 and 1994 to 29 between 2005 and 2009.

If we consider the whole research and development process of a NME and its extensive time-length it can be perceived that the NMEs launched recently result from R&D that was done 10 to 15 ago.

By looking at these numbers is possible to say that the only way to access the true productivity of recent R&D expenditures is to wait at least 10 years and count the number of new successful entities launched.

Only through innovation can Companies discover new products that improve patient's quality of life. Companies are the main driver of change. By developing new cost-effective technologies, people can have access to cheaper and more effective

medicines. Healthcare systems around the world can also achieve savings and allocate the money to areas where productivity gains are harder to accomplish.

R&D in Portugal

In 2011, the Portuguese Pharmaceutical Industry's R&D expenditure was 87,46 million€, which represented a sharp increase of 27,4% from 2009. (OECD.Stat 2015)[15]

The only company that undertakes basic R&D in Portugal is Bial. Bial was the first and only up to now Portuguese Pharmaceutical Company to have drugs approved by the FDA and EMA.[16]

The vast majority of the other Portuguese Pharmaceutical Companies, conduct investigation to improve formulations and dosage schemes of drugs already launched in the market by originator companies. This process is very important for them, because it allows them to compete with differentiated products, based in so-called incremental innovation.

> "Incremental innovation is the process of expanding therapeutic classes, increasing the number of available dosing options, discovering new physiological interactions of known medicines, and improving other properties of existing medicines."[17]

This process contrary to the "true" innovation normally is not associated with increased costs to payers/consumers.

Examples of this incremental innovation are the development of dispersible formulations of swallow tablets and taste masked syrups in both cases with the objective of improving adhesion to therapy.

This thesis covers a specific improvement process undertaken by a Portuguese Pharmaceutical Company, Grupo Medinfar, in the context of their overall investigation area.

[15] http://stats.oecd.org/Index.aspx?DataSetCode=BERD_INDUSTRY#
[16] https://www.bial.com/pt/sala_de_imprensa.138/noticias.140/antiepiletico_da_bial_ja_esta_nas_farmacias_dos_eua.a413.html
[17] http://www.ifpma.org/fileadmin/content/Publication/2013/IFPMA_Incremental_Innovation_Feb_2013_Low-Res.pdf

Case Study

Medinfar

Grupo Medinfar is a Portuguese Pharmaceutical Group established in Portugal in 1970 with headquarters in Lisbon. It owns different companies such as Laboratório Medinfar, responsible for the distribution, marketing & sales of prescription medicines; Medinfar Consumer Health, in charge for the distribution, marketing & sales of non-prescription medicines and other health products; Medinfar Sorológico, a veterinary unit acquired in 1995, responsible for the distribution, marketing & sales of veterinary drugs, medical devices and herd vaccines; Farmalabor, a Contract Manufacturing unit with 5.350m^2 acquired in 2001; Cytothera, a Biotechnology unit established in 2005, working with isolation and cryopreservation of mesenchymal stem cells from the umbilical cord and GP – Portuguese Generics, established in 2006, responsible for the distribution, marketing & sales of generic drugs. Medinfar is dedicated to research & development, manufacturing of pharmaceutical products, distribution, marketing and sales.

The Group has over 300 employees and a commercial presence in more than 40 countries with a subsidiary in Morocco since 2000.

Medinfar's R&D unit activities are mainly the development of new products, new galenic formulations, development of new pharmaceutical forms and the set up and development of analytical methods and process validation protocols. The R&D unit activities and services are regularly outsourced to other national and international companies, where licensed products are manufactured and marketed by Medinfar.

The case study

This Case Study covers a particular improvement process undertaken by Grupo Medinfar in their R&D unit. Throughout the case we will look at the main limitations found by the company regarding some activities performed under the R&D unit.

In order to execute all the investigation projects, Medinfar has significant costs with materials (products). Managing efficiently those products is vital, and initial assessment showed that there was considerable room for improvements. Although expenditure in this area being high, attention was not being properly given to the issue,

because when compared with expenses in other areas within the company, absolute values were almost “negligible”.

Even tough it represented a minor portion of the company’s overall costs, it started growing quickly in the last few years and Medinfar decided to look for ways to reduce those costs.

This case study analyses the management process of the R&D unit, starting with the product’s lifecycle, from their ordering process until they are consumed. It describes how these processes could be, and in some cases were, improved.

We will start by looking at the main activities carried out in the R&D unit; limitations found; what was done to solve the problem and then we will measure the benefits that resulted from the implemented solution.

R&D Unit (Activities and Products)

At Medinfar R&D is a very important area where scientists and analysts run stability studies for drugs in different climatic environments, develop new pharmaceutical formulations, develop and validate analytical methods, amongst other activities. Currently there are 18 Lab technicians working in this unit aside from managers. They work in many projects simultaneously and sometimes new projects turn up unexpectedly, that require specific products to execute them.

The activities undertaken in the R&D unit require a large number of expensive products, which represent a substantial cost.

The main sources of expenditures in R&D at Medinfar are Reagents and HPLC Columns. Reagents are used almost for every process in the Lab and Columns have a high unit cost. Those two items are responsible for the majority of the Lab’s orders.

In order to facilitate the Products’ recording and ordering processes, eight product families were created with their respective codes:

Table 2: Product Families and Codes

Code	Product	Description
ML1*	Reagents	
ML2*	Standards	
ML3*	Microbiology	Reagents used in Microbiology
ML4*	HPLC Columns	
ML5*	Glass Material	
ML6*	Consumables	Disposable Consumables, such as filters and micropipette tips
ML7*	Cytothera	Specific Reagents exclusively used by Cytothera
ML8*	Other	Every thing that is not included in any of the previous families

Source: Author, adapted from Medinfar internal report

Material's Management (Old Processes vs. New Processes Adopted)

In order to save money ordering these products throughout the year, it was necessary to estimate order points, minimum quantities and supplier's lead times to make a suitable purchasing plan.

Identifying the problem

Medinfar identified that this so-called purchasing plan was not followed in most occasions. With the urge to keep the unit's activities running, employees didn't have time to follow the process for the new projects. They were faced with the necessity to buy products immediately because they were urgently needed and any chance of planning was ruined. This disorder led to some limitations that will be highlighted later in the case study. Not only the products didn't follow a strict order plan, as their consumption records were also being neglected.

These were the main limitations found:

- High number of products with an incomplete description in the Data Base
- High number of duplicated products (same product with different codes)
- Every time a product was bought from a different supplier, a new code was inserted
- Inconsistency of data generated by all the different Data Bases for Reagents
- Incapability of measuring supplier's lead times and service levels due to the delays in the products' recording process in the Information System
- Incompatibility of the product's descriptions and codes between the System and the Laboratory

These limitations were the result of the lack of planning, and the lack of appropriate management of the products involved. Bellow we will describe the model by which orders were executed before the company found that the whole process needed a restructuration.

Old Ordering Process

Every time a product was necessary, the person responsible for the Lab's activities would order it to the "preferred" supplier. The price was not the first aspect taken into consideration. The Lab's staff focused more on their relation with the supplier, the suppliers' delivery time and the product's quality.

With the urge to reduce costs, some changes were made in some key steps that influenced the ordering process. In order to organize the Ordering Process some crucial changes needed to be implemented.

The first step was to do an inventory of all the existing products in the Lab, both in use and in stock.

The second step was to register the product's consumption so that it could be possible to estimate the necessary quantities of each product to order and then set an order point.

The main process changed was the way new products were registered in the system and how their usage was accounted. Without a good organization of the materials in the Lab it was hard to account for all the existing stock and people were constantly using new products without knowing if there was still a product in use. This

led to a lot of unnecessary orders and to excess inventory, which represents a high and unnecessary cost for the company.

Old Usage Process

Reception

As was mentioned before, the products used were not being properly registered when received. The products' reception was not following a strict plan. Products were being inserted in the System only when they were truly needed for a specific project in the Lab, not when they were delivered. This delay created a problem for the R&D Department since they were not able to estimate properly the suppliers' lead times. This also led to limitations when choosing between different suppliers as this important aspect was missing.

Storage

The Reagents were divided in three different categories: Solid, Liquid and Inflammable. The Inflammable Reagents were stored in a special container next to Solid and Liquid in a room inside the Lab. Any employee from the Lab would go there and open a new box/unit anytime they needed one. When they did that, there was no record of that action, so no one would know how many units were being used and how many were still in stock. Their usage was not being accounted.

In order to make this practice more efficient, and due to a regulation that didn't allow these materials to be located in the same space where they would be used, the Lab, the products were moved to a big container outside the Lab. One employee in the Lab was responsible for the materials. When someone needed to use a new product, because the old one finished, he/she informed the person responsible for the warehouse and that person would get the product and record that action. The process was similar, but with one person responsible, the probability of mistakes was lower.

Consumption

The first step to take after identifying every product and its quantity in stock and in use was to record its usage.

After recording the products and searching in every excel sheet for the right name and code for each product, a simple process, to register the product's consumptions, was created. In the storage room, different sheets with the names and codes of every product that existed in the Lab and products that didn't exist but were also used in the Lab, were attached. Those products were divided by categories, Solid, Liquid or Inflammable. Next to each name were columns with the existing quantities of each product. Every time a product ended and someone opened a new product, he/she would have to cross that number and write upfront the number of existing quantities. This simple process would help to account for the product's usage and set minimum quantities to order in the future.

Following the evaluation of the current situation, it was clear something needed to change. The best way to cut costs was through the implementation of an organized purchasing plan. Although some products were only used in some specific projects, for the great majority of them it was possible to estimate the quantities that would be necessary in the next planning period. Different products had very distinct types of usage and recording. In some situations the product's consumption was only registered when they finished, while for other products their consumption was recorded at the moment they arrived at the Lab. All these differences needed to be taken into consideration if the company wanted to estimate the necessary quantities for each product correctly.

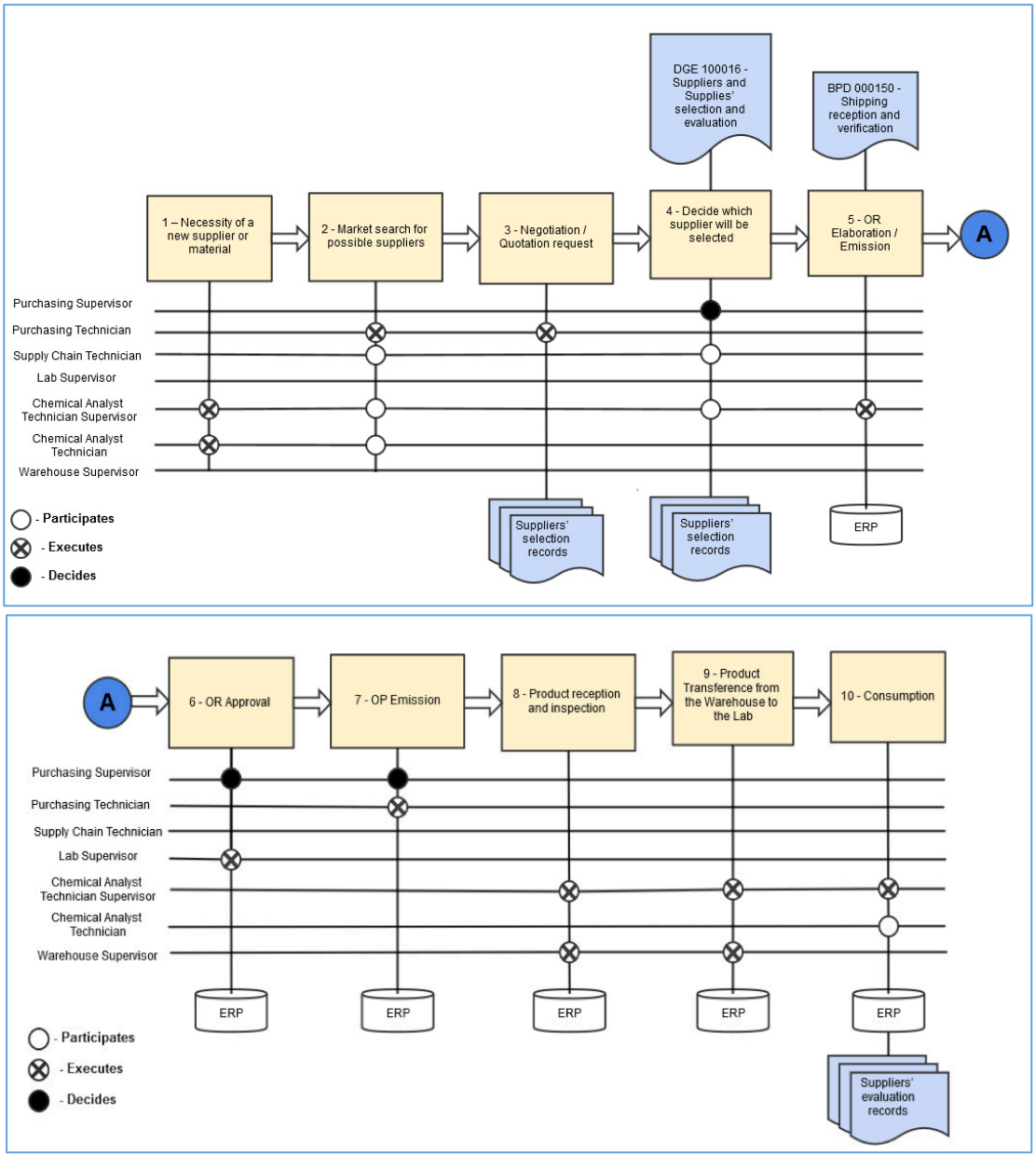
In the next section we will look at the core changes in the ordering process and in the way products were received, stored and consumed in the Lab.

New Ordering Process

Following the evaluation process, two different ways of ordering products were implemented.

The first one is called the Regular Request Process and it applies when a new product or supplier is needed.

Figure 7: Regular Request Process



Source: Adapted from Medinfar internal report

The picture shows the process' execution and the employees responsible for it.

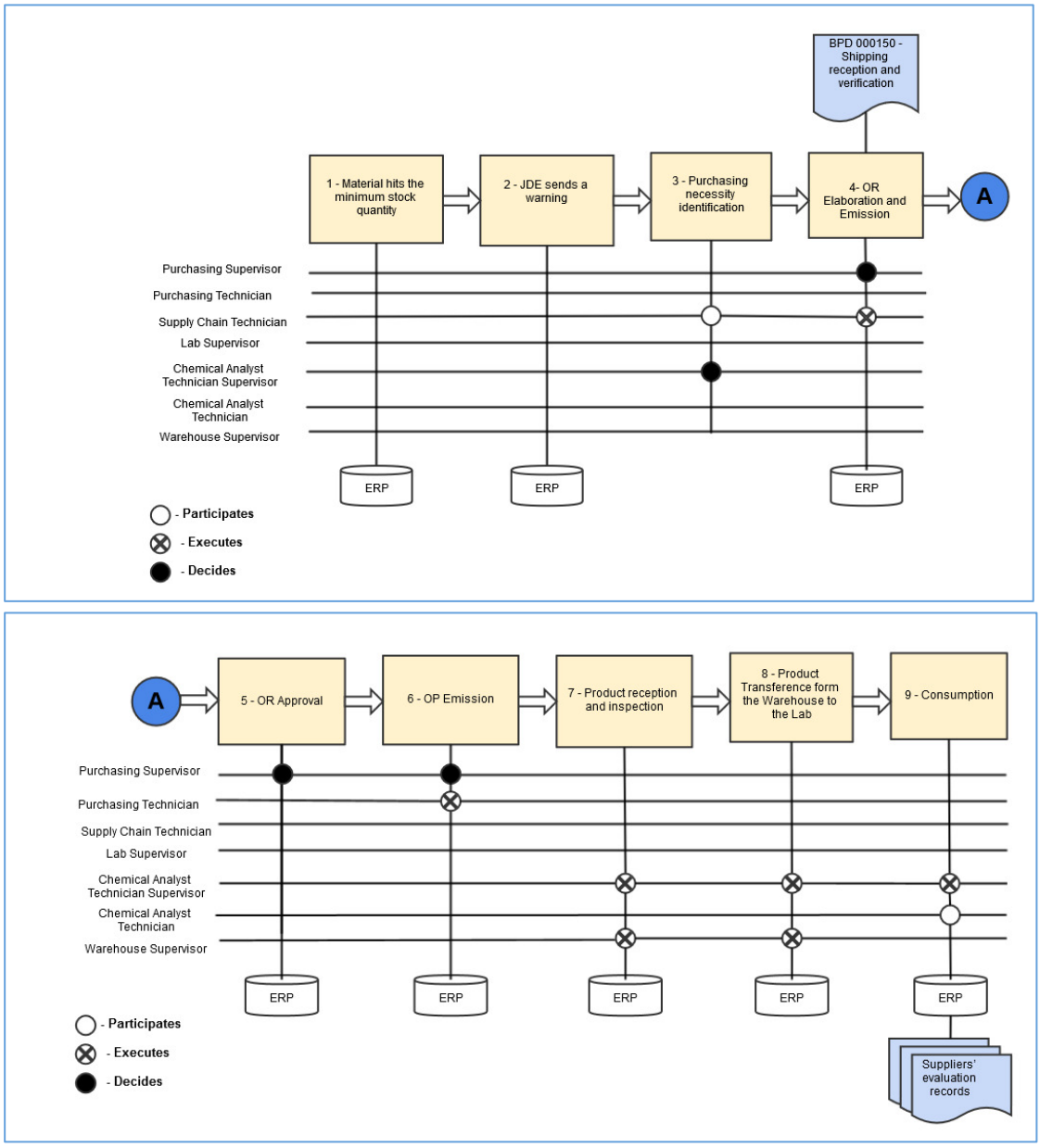
It starts when a Chemical Analyst Technician (CAT) finds the necessity of a new supplier or material and it is followed by a market research for possible suppliers executed by the Purchasing Technician (PT), who is responsible for the negotiations with interested suppliers. After the negotiation, the Purchasing Supervisor (PS) decides which supplier will be selected and then the Chemical Analyst Technician Supervisor (CATS) elaborates a Requisition Order (OR[18]). The PS approves the OR and releases

[18 & 19] Terminology used in Portugal

the Purchase Order (OP[19]). Next the CATS and the Warehouse Supervisor receive and examine the product and it is then stored in the Warehouse. When the product is needed in the Lab, they transfer it from the Warehouse to the Lab and it is finally consumed.

The second one is called the Ordering Point Process and it is responsible for establishing minimum stock quantities for each product so that the System knows when it needs to order more quantities of each product.

Figure 8: Ordering Point Process



Source: Adapted from Medinfar internal report

This Process begins when a material hits the minimum stock quantity, which triggers a warning sent by JDE (ERP Software) to the CATS, who is informed that the missing material must be bought. The PS and the Supply Chain Technician (SCT) elaborate the OR to the Supplier that was already defined in the System as the one who better met the price, quality and lead-time requirements. Then the PS approves the OR and releases the OP. Finally, as it was described in the previous process, the CATS and the Warehouse Supervisor receive and examine the product and it goes to the Warehouse. When the product is needed it is moved into the Lab and consumed.

New Usage Process

Reception/Storage

The Warehouse Supervisor is now the person responsible for receiving the products in the R&D Department. Should evaluate the material's condition and receive the Purchase Order in the System (JDE), inserting the material's batch number.

Afterwards labels the products with the specific label created for this purpose. The transfer request from the Warehouse to the Lab must be made by email by the CATS.

This employee must secure the material's physical transference and the Warehouse Supervisor must register them in System.

The System considers the moment when the materials are transferred from the Warehouse to the Lab as the material's Opening date.

The CATS is responsible for recording the Opening date and the Expiring date that is indicated in the packaging label, both in the Label and in the System.

If the Expiring date is missing in the packaging label, the CATS must assume the following rules:

- Liquid Reagents – 2 years
- Solid Reagents – 5 years
- Primary Standards – 1 year
- Work Standards – 2 years

Every time a material doesn't present the right conditions, it should be reported to the Supply Chain Technician so that a complaint can be made to the Supplier.

Consumption

The process to register the consumption of materials is now different between product families. For materials that belong to Reagents, Columns, Cytothera and Microbiology's families, the procedure is the following:

After finishing using one material, the CAT must write manually in a list the ML Code, the Product's Unique Code, the Internal Batch, the consumption's date and must sign in the end. In the end of each day, the CATS must register the daily consumptions in the System (JDE).

For Consumables, every time a material is transferred from the warehouse to the Quality Control its consumption must be registered in the System (JDE).

For Glass Material, whenever new materials are ordered, the consumptions must be registered in the System (JDE), justifying why the materials must be bought.

For Standards and Other the material's consumption must be accounted when they arrive to the Lab.

By implementing these changes, Medinfar was able to improve different procedures, which led to time and cost savings.

By registering every product and its usage on a daily basis, the System is now uploaded with the most recent information about the products, which helps in the decision making process when choosing from whom to buy. With the Ordering Point process it is now achievable to have only the necessary quantities of each product in the Lab, saving the costs of overstocking. With all the information about the price evolution linked to the suppliers uploaded in the System, Medinfar can be confident that, whenever the System identifies the need to buy a new product, it is choosing the best solution in terms of price and quality. The Supply Chain unit is responsible for updating the System with the correct supplier for whom to buy each single product. This subject will be analysed more in depth later on in the case study.

Benefits obtained by integrating the Ordering Process in the Information System (JDE)

Medinfar uses an enterprise resource planning software (ERP) called JD Edwards EnterpriseOne that allows them to integrate several processes in one single platform.

When we talk about the Ordering Process, the right utilization of the Information System brought a lot of benefits to everyone included in the process.

Medinfar was able to collect gains by keeping records of all its product's lifecycle. It helped the company save time and money by simplifying a large number of processes.

It is now possible to correctly analyse different suppliers, because all the information related to the products they sell, prices at which they sell the products, the evolution in prices and the record of transactions made between them and Medinfar is available in the System and easily accessible to the people who need this information. The person responsible for this process doesn't need to loose time contacting different suppliers every time information about a product is needed. By using CAS, a unique code addressed to a specific product, like its chemical formula, the employee can easily find an item in the system and get information about different suppliers and prices related to that product.

The system allows tracking a product's lifecycle, since the moment it was ordered, its supplier and even the project in the Lab in which it was used. If there is a problem in a project it is possible and easy to know which specific product was being used in it, from which supplier it came from and when it was bought, which helps the company to identify where the problem was originated.

Another benefit for the company is to allocate all the costs related to the projects in the final product. The costs of the reagents, the tests performed with them and the labour force are accounted in the end cost of the finished product.

It is possible to see how much value there is in stock, and make internal transferences of stock between different warehouses/companies within the Group.

"Currently the purchasing process is much cleaner. In the Lab the technicians make requisitions, which are filtered in the supply chain area, where they see if prices are correct, if Minimum Order Quantities (MOQ's) are being respected and if they are

choosing the right supplier. Only after that does the Supply chain manager revise everything and approve the purchase." (Carlos Valadas)

The main obstacle to the implementation of the IS was the resistance to change, apart from that Medinfar reduced costs, the number of invoices and the number of suppliers involved in the process.

Negotiation power with Suppliers

Medinfar saw significant gains with the implementation of this project, much of it connected with its relation with suppliers. The way different companies within the Group were related with the suppliers was not the best and it didn't create the right synergies that existed from having different units with similar necessities. As previously mentioned, the first aspect that was taken into consideration when ordering a product was the lead-time with which the materials arrived to the unit and the relationship between that unit's staff and the suppliers. The price variable was, in some way, neglected and this was done all over Medinfar's units. The laboratory technicians always preferred products from suppliers like Merck Sharp & Dohme or VWR because they transmitted confidence and safety. If we compare the two cases of the R&D unit in Lisbon and the Contract Manufacturing unit Farmalabor in Condeixa, 200 km north of Lisbon, we find they had different local suppliers for the same products that were purchased at different prices.

From each unit's point of view this was the best way to operate. For example, if Farmalabor had a stock shortage they would probably call the supplier with which they had a long trading relation, who would promptly supply them with the materials they needed. The post sales service provided by these suppliers was generally better and acted as a differentiator factor. From their perspective, it would not make sense to order something they needed urgently to someone they didn't know and who would probably take longer to supply them. There was constantly some insecurity associated with choosing a new supplier.

From the Group's standpoint this was not cost effective as Medinfar was loosing negotiation power by purchasing low volumes of the same product to different suppliers, not benefiting of the economies of scale obtained by larger purchases.

Major changes and Benefits

The necessity to centralize the decision making process in the Supply Chain area was obvious. In order to gain advantage from negotiating as a big company, Medinfar would have to restrain the freedom of each unit to choose between suppliers.

The number one rule was the price. The person responsible for this project in the Supply Chain area had to ask for supplier's quotes for each product. Medinfar analyses several parameters when evaluating a new supplier such as lead-time, post sales service, complaints service (product replacement after devolution) and, most important, the price.

After analysing each one, and getting permission from its superior, this employee would then choose the supplier who better met these requirements for each product and update all its information in the system.

With all the information, regarding the suppliers already chosen by the company, updated into the system, it was now easier for each unit to search for and order products.

The next step was to update the data about each product's consumption into the System so that the order points could be set. With all these changes being implemented, Medinfar could now organize its ordering map and get quantity discounts and better prices as a consequence of negotiating with suppliers for much bigger quantities.

One benefit from having an organized order plan is the availability to negotiate payments to suppliers, usually set to 60 days. If Medinfar defines a purchasing schedule with the orders for the next 6 – 12 months with the supplier, it will be possible to deal better payment terms which translates in more working capital being available.

Another advantage of this implementation is the ability to schedule the deliveries over time with the suppliers. This guarantees that they always have stock and meet the deadlines and it also ensures that Medinfar will not have to support the costs of excess stock. It usually means better prices to the company as well.

The tables below show the specific case of Methanol and Acetonitrile, the two Reagents with the highest consumption in the Lab, where savings are expected to be achieved in 2015 by better bargaining power Medinfar now has with suppliers:

Table 3: Supplier's prices for 2015

	Acetonitrile		Methanol		
	Price	Total	Price	Total	Total:
Supplier1	€ 16,10	€ 14 490,00	€ 8,40	€ 5 040,00	**€ 19 530,00**
Supplier2	€ 16,00	€ 14 400,00	€ 6,00	€ 3 600,00	**€ 18 000,00**
Supplier3	€ 16,58	€ 14 922,00	€ 6,20	€ 3 720,00	**€ 18 642,00**
Supplier4	€ 15,94	€ 14 346,00	€ 6,39	€ 3 834,00	**€ 18 180,00**

Source: Author, adapted from Medinfar internal report

Table 4: Expected savings for 2015 in the most used products in the Lab

Reagent	Units	Price 2014	Price 2015	Total 2014	Total 2015	Saving
Methanol	600	€ 6,56	€ 6,00	€ 3 933,60	€ 3 600,00	€ 333,60
Acetonitrile	900	€ 16,82	€ 16,00	€ 15 139,80	€ 14 400,00	€ 739,80
Total				**€ 19 073,40**	**€ 18 000,00**	**€ 1 073,40**

Source: Author, adapted from Medinfar internal report

Impact of this implementation in Group Medinfar

According to Carlos Valadas, Supply Chain Manager at Medinfar, the company always considered very important to undertake projects that allow them to monetize efforts and resources internally and also increase its production capacity. The group spends about 400 to 500 thousand € per year in laboratory material and expects savings close to 12,5% in 2015.

"After making an ABC analysis of the savings related to the most significant items in terms of purchases, Medinfar decided to do the same to all laboratory material." (Carlos Valadas)

The implementation of a System that supported the material's management was a requirement for the Lab to continue operating.

"Although representing a small part of Medinfar overall costs, the R&D area has a great influence in the company's operations." (Mécia Frias)

On a Pharmaceutical Company, the R&D unit is the core part of the mission of the company, which is invent, develop, manufacture, distribute and market drugs.

All the other departments in the company need to work in line with this central activity and depend also on the R&D unit.

New methods of production need to be developed, analysed and validated; Regulatory Authorities (Infarmed in Portugal) need to approve them. Only then will the Supply Chain area assign purchasing plans for materials; the Contract Manufacturing unit will start producing the products; and the Marketing department will be able to plan their introduction in the market.

"In the Contract Manufacturing unit, Farmalabor, quality control is performed in a small pilot sample before starting large-scale production, while in R&D quality control executed in the long term. If some material used in mass production needs to be changed, the R&D unit will have to analyse those products again to guarantee their quality." (Mécia Frias)

The investigation performed in the Lab needs to be aligned with the company's strategy for the next years.

In the specific case of Medinfar, as the short and medium term strategy is to increase exports, almost all the investigation executed in the R&D unit is directed to this objective. They need to perform stability tests to certify the stability of the products in diverse climatic zones.

"Here products are put into special containers that simulate the real climatic conditions of the area where they will be exported. The products are kept there during all its shelf life, they are only removed each 3 months to be analysed. After this, the methods still need to be validated. For cosmetic products we make in-use essays, where we simulate product opening and usage and record how much time it remains in good conditions." (Mécia Frias)

Each time Medinfar wants to commercialize a product in a different country, they need to provide the data required by local Regulatory Authorities.

The increasing number of batches that need to be analysed per month, around 300, almost the triple than in 2013, explains well the huge stake Medinfar is now making in exportations and the importance this department has in making sure that the company does not miss this business opportunity.

Teaching Notes

This section aims to provide teaching material to for classes in Pharmaceutical Management, Healthcare Management, Strategy and Innovation, and Operations Management.

Provides teaching questions that can be used by teachers to stimulate a class discussion.

Summary

Grupo Medinfar is a Portuguese Pharmaceutical Company founded in 1970.

It owns different companies and is dedicated to research & development, manufacturing distribution, marketing and sales of pharmaceutical products.

Its R&D department is responsible for the development of new pharmaceutical formulations, and validation of analytical methods, amongst other activities. This area was suffering from not having an organized purchasing plan. This created high costs for the Company and delayed the activities/projects undertaken by this unit.

The solution found was to integrate an IS already in use in Medinfar in this unit. Medinfar adopted the same purchase process they used for medicines' production materials in the products used in the Lab.

The first step necessary to start the project was to undertake an inventory of existing products and recording their consumption in the IS to identify patterns of purchases. This brought several benefits to Medinfar, as they were now able to structure the purchasing scheme in the System, buying products always at the best price and avoiding unnecessary orders.

As different companies from Medinfar consumed similar products, they centralized the purchasing process for all the companies in the Supply Chain department. By concentrating all of its companies' orders, Medinfar got better prices from suppliers and accomplished economies of scale.

Case study teaching objectives and strategies

The case study was produced with the goal of sharing with students and professionals a real-life scenario in a Company and the methodology adopted to deal with it. For professionals it shows events, which they may feel familiar with. For students it gives new insights of how a ”Company works”.

The case is intended to be used in strategic, operational, innovation and health related courses with the following teaching objectives:

- Show the importance of planning in any area of a company and how that affects business decisions.
- Help students assimilate the concept of Centralization and study its application and importance in a company like Medinfar.
- Explain how a Group of companies operates and organizes its activities to gain efficiencies.
- Describe the main activities performed in a Lab and the impacts it brings for the company of having a good management there.
- Identify simple processes that led to cost and time savings in a Pharmaceutical Company.

Teaching Questions

One suggestion to professors who may want to use the case study in a class is to provide in advance the case to students and ask them to read it and be prepared for class discussion. Bellow are described several questions that may also be given to students prior to the class; or be shown during the class to steer the discussion:

1. **What are the main consequences of not having a centralized information system in a Company? Give examples for the specific case of Medinfar.**

It is important to explain the differences between Centralized and Decentralized Information Systems (IS).

A fully centralized IS handles all data processing at a single place, upholds one single database, guarantees data consistency and supports the decision making process for all the units within the organization.

In a completely decentralized IS each organization's unit has its own data-processing activities and controls its operations.

There are advantages and disadvantages in both cases. In order to choose the model that responds better to an organization's needs, it is crucial to have a very good understanding of the organization, its structure and objectives.

For Medinfar, a group owning different companies, this was a key question. In their specific case, the necessity of having a centralized IS, covering all the business units, was vital since similar products were purchased by different companies/units within the Group.

Medinfar was suffering from not having implemented a centralized IS as described below:

- <u>No data integrity</u>

The problem of Redundancy, which violates the 1st rule of database design, appears when there is more than one place/database being fed with the same data. It is crucial to an organization to have only one place to insert data so that when something needs to be changed people don't loose time looking where that specific entry was recorded.

For Medinfar, the inexistence of a single database with the product's consumptions and orders was creating a significant number of problems.

Employees had their own excel sheets were they kept records of products used, products needed and each person did this on its own way. As example, if someone

wanted to know when it was the last time a product was ordered it had to check all the files to look for this information, which leads us to the next point.

- Difficulties in accessing data

Information Systems must provide easy access to data. When analysing the activities undertaken in a Lab, it is clear that everything needs to be planned meticulously and nothing can fail. When projects are running in the Lab, if some product is missing, investigators need to check urgently if they still have them in stock or if they need to order them. In the absence of a single database, a unique place where they can go and be sure that if the product is not there they don't have it, time will be lost and that may as well affect the results of the project.

- Lack of consistency and out-dated information

Two other issues that may arise from the existence of multiple databases are lack of consistent information and outdated information that may lead to wrong decisions.

The objective of recording every purchase and usage of products is to be able to assess not only price evolution or to control expenses over time, but also to forecast future expenses and set a purchasing plan. If a company doesn't keep track of all its activities, or if it does it incorrectly, business decisions will be ill informed. Medinfar couldn't benefit from the data they collected on the Lab because it was not consistently updated.

- Failure to achieve economies of scale

Without having a centralized IS where all units' purchases can be planned and executed at the same time, companies loose the opportunity to achieve economies of scale. Medinfar was experiencing this problem. It was considered a priority to aggregate all the unit's orders since they were similar in many cases.

This would allow reducing costs through getting better prices by buying the products in larger volumes.

2. What were the major benefits of the improvement process implemented in Medinfar? How did they affect the Company's operations?

The improvement process implemented in Medinfar was responsible for numerous benefits across units within the Group. The Lab's material management System, as this solution was called, came primarily as a necessity to reduce costs in the R&D unit but the benefits obtained by its implementation had a much significant reach.

These were the major benefits obtained at Medinfar:

- Time and cost savings through simplified processes

This was one of the first changes being noticed. With a unique platform that allowed lab technicians to search for products with detailed and updated information, many mistakes were avoided, which led to a more efficient flow of operations in the Lab.

Specific roles were assigned to different employees within the R&D unit. This was a very important step to improve the organization in the activities performed in this area.

Similarly having a unique database with all the information related to products and suppliers simplified the search process, having different employees responsible for the product's reception, consumption, storage and purchasing avoided unnecessary errors, and reduced the time spent executing those actions.

Another outcome of these changes was the decrease in the number of wasted products. The tighter control around product's expiry dates led to a more precise management and helped prevent unrequired orders, which represented a significant cost for the company.

- Stronger negotiation power and achievement of economies of scale

These were the main drivers for cost reduction in the R&D unit. Medinfar was able to make better deals with suppliers with the support of a restructured IS where detailed information about them was constantly updated. With the correct information

available it was now easier to choose between different suppliers, with the confidence that the Company was making the right decisions.

By aggregating all companies' purchasing plans and centralizing the decisions related to which suppliers to choose, Medinfar increased its negotiation power and was able to achieve economies of scale. Products were now being purchased in much bigger quantities, which decreased the unitary price for each product.

- Better control of all the companies within the group

One of the main objectives of this project was to consolidate all companies' operations in one single platform. With all the similarities in terms of products used it was very important to combine some procedures that were being undertaken individually by each company. Currently, with all the information about the companies' transactions inputted in a unique database, it is easier and faster to track any inconsistency that may occur. If something wrong related to any purchase happens in one unit it is easy to see if the same happened in the other. If some process common to all areas needs to be changed, it can now be executed much simply since they are integrated in the same IS.

One advantage that derived from this integration was communication between units. If one unit is missing an important product, it is possible and easy to look for that product in other unit and proceed with the transaction.

The operations around different units are now considerably tightly synchronized and controlled. With constant access to the information concerning all companies' purchases it is possible to predict expenses and set budgets to each unit.

3. Comment on the importance of having an integrated R&D unit with the overall company's strategy and objectives.

"On a Pharmaceutical Company, the R&D unit is the core part of the mission of the company, which is invent, develop, manufacture, distribute and market drugs.

All the other departments in the company need to work in line with this central activity and depend also on the R&D unit.

New methods of production need to be developed, analysed and validated; Regulatory Authorities (Infarmed in Portugal) need to approve them. Only then will the Supply Chain area assign purchasing plans for materials; the Contract Manufacturing unit will start producing the products; and the Marketing department will be able to plan their introduction in the market.

The investigation performed in the Lab needs to be aligned with the company's strategy for the next years.

In the specific case of Medinfar, as the short and medium term strategy is to increase exports, almost all the investigation executed in the R&D unit is directed to this objective. They need to perform stability tests to certify the stability of the products in diverse climatic zones. Each time Medinfar wants to commercialize a product in a different country, they need to provide the data required by local Regulatory Authorities. Starting large-scale production, it is conditional to having positive quality control tests that are performed in a small pilot sample". Case Study Medinfar

All business areas of the Group depend on the investigation undertaken by Medinfar. And they have to adapt to the outputs of the R&D unit.

4. Identify the main factors that lead to a project's implementation success. Apply them to Medinfar's specific case.

Before starting discussing the success factors for the implementation of a process it is important to define what is a successful project implementation. It needs to respect a pre-defined schedule and budget; achieve the set objectives; and be accepted and used by its "clients".

The first success factor is the Project Mission.

The project's goals need to be clear and understood both by the team involved in the project and by other areas in the company.

The main objectives of this improvement process in Medinfar were to achieve cost and time savings in the R&D department. Everyone in the Supply Chain unit, as well as in the R&D unit, was well aware of these objectives.

The second one is Top Management Support.

It is very important for a project to succeed to have the top management~~'s~~ approval and support during all its stages.

According to Carlos Valadas, Supply Chain Manager at Medinfar, "the company always considered very important to undertake projects that allow them to monetize efforts and resources internally and also increase its production capacity".

Not only the company's top management considered them important, but also gave the needed support such as allocating sufficient resources (financial resources by hiring an external IT consultancy company to integrate the IS in the company's needs; manpower by employing two full time interns in the project); and being available to discuss the key challenges during all the implementation.

The third success factor is Project Schedule/Plans.

This is probably one of the most relevant factors for the success of a project implementation. It should be a detailed specification of all the actions that need to occur during the implementation of the project. Without a Plan, many things that were identified in the beginning and expected to be done, end up being forgotten. It is crucial to describe in which stages of the implementation different actions need to be taken.

In Medinfar's case, all the parts affected by the process needed to be described. By defining exactly which materials would be studied; where to look for them; the employees who would be responsible for specific tasks and proposing a time frame to finish each stage of the project, the company was tracking all its steps and reducing the probability of missing important parts.

The fourth success factor is Client Consultation.

The best way to assure the success of a project's implementation is by taking into account its users' needs. The degree to which users are involved in the implementation process affects directly the support they will be giving to that project in the future. By talking with the employees that will be more affected by the implementations, companies can get some significant personal insights. Someone who works daily in a specific process has certainly the capacity to provide suggestions for its improvement.

Medinfar worked directly with the employees in the Lab, the most affected by this improvement, to identify the main limitations in the current process and to search for ways to overcome them.

As the IS would be used by some of those employees and by employees in the Supply Chain unit, they received regular feedback on the changes implemented in the System. They were also asked to provide feedback about their experience working with it so that new improvements could be applied.

The fifth success factor is Human Resources.

It is decisive to have the best team possible working in the project. The process of recruitment, selection and training is essential to develop a good team with the necessary skills to perform the required tasks.

Medinfar recruited two full time interns to work on this implementation. The company also communicated with its employees the objectives of this project and its importance in terms of costs savings. Employees in the Supply Chain and R&D areas, who would be directly affected by this project, knew what role they would have to perform during the implementation.

The sixth success factor is Technical Tasks.

To implement a technological project it is necessary that the employees involved have the needed technological skills; and that the adequate technology that the implementation requires will be available.

Medinfar met these two criteria with qualified employees, both in the Supply Chain unit, who already had the necessary skills to work with the implemented IS; and in the R&D unit, with the employees who needed to work directly with the system being trained for that. The implementation was an improvement in the system that was already being used. Therefore it was considered that the technology needed was available; and that was necessary only to change some processes using the same technology.

The seventh success factor is Client Acceptance.

This factor evaluates the overall efficacy of the implementation, as the most affected parts (users) are the ones that need to confirm that the results are the ones expected. This step cannot be avoided because, although respecting all the previous steps, it is possible that there is something missing; or that parts could be improved from the consumers' point of view. Not only client consultation at an earlier stage is important, but also client acceptance in the end, as things don't always work exactly as expected.

The most affected employees in Medinfar were the responsible for the material's purchases in the R&D department and the employees in the Supply Chain unit. The improvement process will help them save time in their daily tasks. But they are still adapting themselves to the changes, and it is possible that they may not accept or like the modifications before being comfortable with them, and experiencing their benefits.

They provided regular feedback throughout the project's implementation and, when it was finished, they tested the process to see if anything still needed to be modified.

The eighth success factor is Monitoring and Feedback.

These two aspects relate to the project's control processes that constantly compare each stage of the implementation to its initial projections. By making provisions of control information at each stage of the project, the team manager is able to anticipate difficulties and apply corrective procedures. They also refer to the monitoring of the performance of each team member's. These two aspects must be present in all the previously mentioned factors. They don't come after client acceptance in the project's implementation flow but are considered a critical success factor common to all the implementation stages. In Medinfar, monitoring and feedback were crucial as the IS implementation needed to be as functional as possible. The budget and time restrictions also needed to be followed strictly, which highlights the importance of always monitoring the evolution of the project.

Success factor number nine is Communication.

This is one of the most important factors that lead to success in any type of implementation. Having the right communication channels within the project team but also between the team and the other areas in the company is critical to assure that the project goals, status and achievements are shared with all the parts involved.

Communication has always been a concern in Medinfar, as all areas share knowledge and information between each other, essential to their daily activities. The communication during this implementation was also a very important aspect as the project supervisor had weekly meetings with the two interns responsible for the project to get a status report. Employees from the R&D unit also communicated constantly with

the Supply Chain employees to discuss different aspects of the System's implementation.

The tenth success factor is Troubleshooting.

Even the most well planned implementation cannot predict every future problem that could possibly occur. It is very important for the project manager to have "troubleshooting procedures" to better react to possible problems. This procedure is now responsibility of an employee in the Supply Chain unit. He was responsible for this implementation and now works directly with the responsible for purchases in the R&D unit, trying to solve the problems that may arise from the utilization of the System.

Conclusion

The literature review carried out in this dissertation clearly demonstrates that the business model of the Pharmaceutical Industry is based on Research and Development of new medicines. This constitutes the "social contract" of the Pharmaceutical Industry with society. Big investments made by the Pharmaceutical Industry led to the discovery of medicines that helped to reduce morbidity and mortality of most diseases over the last 6 decades; and increased life expectancy from 67 to 80 years in developed countries, during the same period. From a patient's perspective, these investments in innovation were very positive as they allow people to live longer and have better lives.

The Pharmaceutical Industry environment is extremely competitive, requiring highly skilled human resources, access to advanced technology, and high capital investment. The R&D process of new drugs has extremely high churn rate, as new drugs to be approved for usage, need to show at least non-inferiority in efficacy to existing standard of care; associated with improvements in tolerability and toxicity profiles. And in most countries today they also have to show that they are more cost effective than existing therapeutic alternatives.

The increase in R&D costs over the recent years, together with the growth of "Generic" companies, created a very challenging environment to the Pharmaceutical "Innovation" companies, and has led to a significant concentration in the sector with Mergers and Acquisitions over the last 15 years.

The economic crisis that affected the World over the last 8 years, combined with an ageing population and a significant increase in the innovation offered by the Pharmaceutical Industry, led Governments to implement price cuts in drugs and to reduce the entry pace of innovation. That had a significant impact in the Pharmaceutical Industry, mainly in Europe and particularly in Portugal. And companies were obliged to reduce costs, including investments in R&D.

The case study covers the benefits achieved from an improvement process undertaken by Medinfar, a Portuguese Pharmaceutical Company that was affected by the same crisis.

The implementation of this improvement process was considered a success by the company because all the objectives that were set, were achieved.

The integration of an Enterprise Resource Planning software (JD Edwards EnterpriseOne) in the process of material purchasing in the R&D unit, which was then applied in other units, and a rigorous monitoring of consumption, storage and reception of products, enabled Medinfar to gain a better grasp of their necessities in terms of products, and a better knowledge of their potential suppliers.

By setting ordering points to the great majority of products purchased, the company increased the efficiency of the processes. The aggregation of the different companies' purchases within Grupo Medinfar was another key accomplishment since the company increased its negotiation power upon suppliers by purchasing materials in bigger quantities. Medinfar is expecting to save around 50 to 60 thousand€ in laboratory material purchases in 2015. Similar improvement processes were already adopted by Medinfar in areas like stationary material and office supplies.

Limitations and Future Research

As this dissertation follows the case study structure, more specifically the implementation of an improvement process in a particular Pharmaceutical Company, it should not be inferred that it would deliver similar results if applied in another company or another sector of activity.

In the process of data collection some issues were found such as the difficulty in accessing the material's consumptions and making an initial inventory of products used in the R&D unit's Laboratory due to the lack of organization in the process of monitoring dates and volumes of consumptions. An initial objective of the study was to have reliable forecasts of consumptions of those materials. This has required a significant amount of work prior to the initiation of the improvement process.

One of the main limitations of the case study was not being able to follow directly all the implementation of the process due to the termination of the internship. This was mitigated by all the support and access to information provided by the Medinfar team.

For further investigation, I suggest areas such as: the study of the procurement processes in the Portuguese Pharmaceutical Industry in order to improve efficiencies

and profitability; and the study of information knowledge of business processes in the Pharmaceutical Industry, namely in R&D in order to improve productivity in terms of new product outputs.

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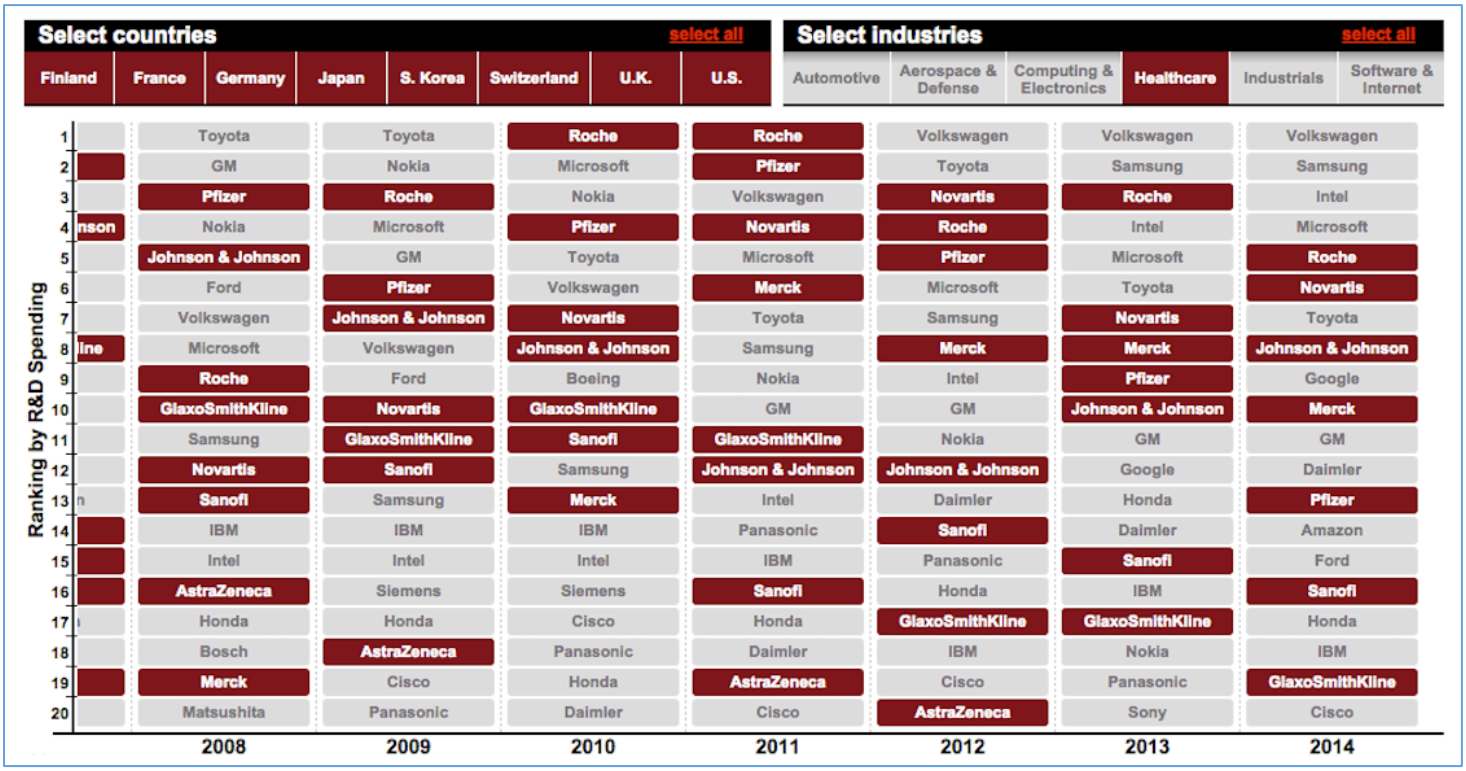
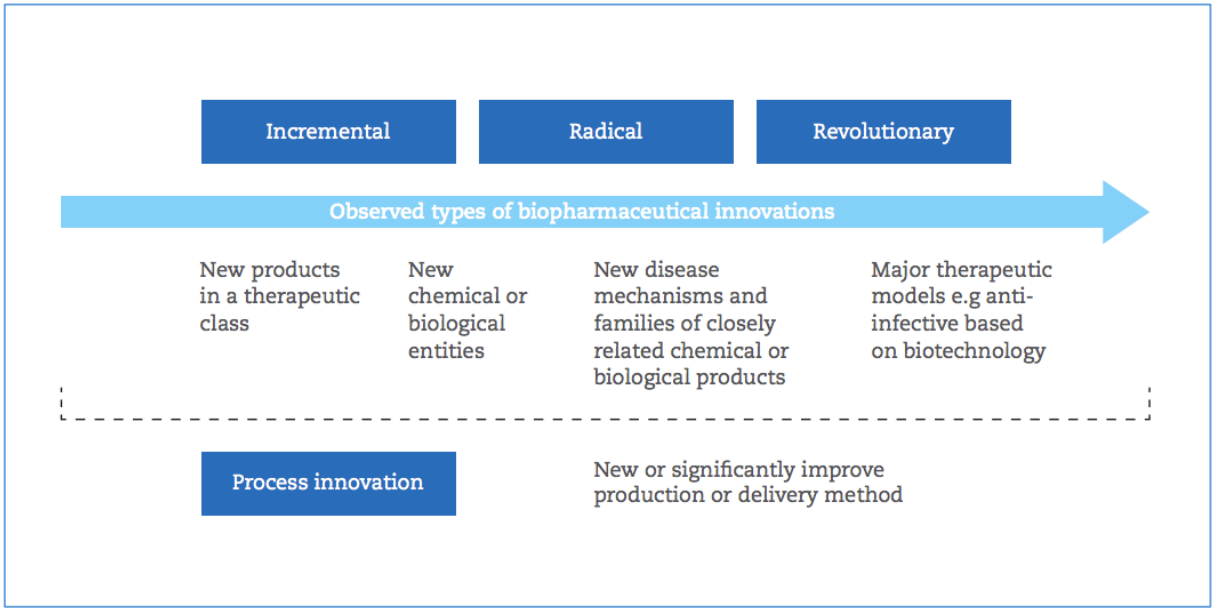
Appendices

Annex 1: Top 20 R&D Spenders 2008-2014



Source: Bloomberg data; Capital IQ data; Strategy& 2014 Global Innovation 1000 survey data and analysis

Annex 2: Categories of pharmaceutical innovation



Source: IFPMA 2013 Incremental Innovation: Adapting to patient needs

Annex 3: Interview to Carlos Valadas (Supply Chain Manager at Medinfar)

1. **Why did the company see the need to implement a Lab's Material Management System?**

This need came from the fact that Medinfar is a big group, with several companies that buy the same type of materials and there was the intention to aggregate all that bargaining power. The profit starts in the early stage of purchasing.

2. **Which level of importance does Medinfar give to projects like this?**

The company privileges and always gave big importance to projects that allow the monetization of effort and resources internally and increase the company's' production capacity. With the austerity scenario Portugal is going through right now, the key word is "Savings".

3. **Is it possible to quantify the gains obtained through this solution's implementation?**

Medinfar is spending around 400 to 500 thousand € per year in Laboratory material and we are expecting a saving of around 12,5% in 2015, which will be very good for us. The fact that we have an employee controlling the purchases and negotiating with suppliers reduces the number of complaints from the R&D unit's employees related to suppliers' selection. The level of discipline in this area increased considerably taking into account that we need to boost savings.

This project already started to show savings in January facing the standard values we have from 2014. We expect to save about 50 to 60 thousand €.

4. **Which were the main limitations identified by the Supply Chain area when the Information System was implemented in Medinfar?**

The main barrier to the implementation of the IS was resistance to change.

We have a Quality Control centre in Farmalabor, in the Contract Manufacturing unit in Condeixa and we have an R&D department in Venda Nova, which performs Galenic formulation and development and other Quality Control activities. Normally the

pharmaceutical technicians don't need to be concerned with prices of materials and other variables that we are responsible for in the Supply Chain area.

The pharmaceutical technicians feel more safe buying products to well known suppliers like Merck Sharp & Dohme or VWR, and accepting a new supplier, who's manufacturer is sometimes the same or has the same quality level of the current suppliers' manufacturer, is difficult.

They think that if everything always worked well with one supplier, there is no need to choose another one.

Medinfar always buys products to suppliers with the most competitive prices. Farmalabor, with a slightly different culture, always stayed with the most traditional suppliers but will now start buying to the suppliers we chose.

We can't only look at prices, we also need to take into account the suppliers' responsiveness. Sometimes we urgently need a Reagent and we can't jeopardize an analysis or a future production by not having that product.

The resistance to change was really the principal obstacle to this implementation, because apart from that we are reducing the number of invoices, costs and the number of suppliers involved in the process. Currently the purchasing process is much cleaner. In the Lab the technicians make requisitions, which are filtered in the supply chain area, where they see if prices are correct, if Minimum Order Quantities (MOQ's) are being respected and if they are choosing the right supplier. Only after that does the Supply chain manager revise everything and approve the purchase.

From now on the employee responsible for the material's requisitions will start using as request date the real day when they will be needing those materials in the Lab and not be asking for the materials for the same day the requisition was made.

With supplier's lead times uploaded in the System it is much easier for the employees responsible for the requisitions, both in the R&D department and in Farmalabor, to know better when they will be needing those products. This forces them to better manage their stocks upstream, taking into account that they now have daily access to each product's existing stock.

These technicians have nowadays more responsibility. They were given management responsibilities, they are no longer focused only on the analysis and studies they did before.

5. What is for you the main reason for different companies within Medinfar to buy products to local suppliers, disregarding the price?

Better financing conditions I'm sure it is not. In some cases the post sales assistance, from local suppliers, is better and that is the differentiating factor. Medinfar's units can't achieve better lead times, flexibility or financing conditions by choosing these local suppliers.

When we analyse a new supplier we take the following aspects into consideration: price; lead-time; post-sales assistance; complaints service and product replacement in case of devolution.

This new supplier must present equal or better conditions compared with our actual supplier in order to be chosen.

For these companies, the relation they have with their suppliers is very important. If their suppliers have always been professional with deliveries of materials and their prices are not significantly higher than the competition's, for them there is no need to change.

If these companies are presented a supplier with a 30% lower price, their first reaction is that its quality is inferior and the new supplier must not have the same availability to solve their problems as the previous.

All the Laboratory material suppliers' have a licensed warehouse with pharmacists and they don't work like grocery stores, but they usually have small quantities of all the products to assure their clients, in an urgency case, that their analyses or productions will not stop because they are missing a product.

The main reason must be described as the long-term relations these companies have with their suppliers. For the companies it doesn't make sense to ruin a relation like these, unless the price difference really justifies it.

It is normal that suppliers with which Medinfar has a longer business relation start decreasing their prices when facing other cheaper suppliers.

It is somehow unfair that they only lower their prices when faced with competition, but it is also understandable because these products they sold us were never negotiated. The laboratory material was always bought as something really urgent, it was considered an SOS purchase.

At the same time this kind of material was considered in Medinfar a Z purchase in terms of significance.

After making an ABC analysis of the savings related to the most significant items in terms of purchases, Medinfar decided to do the same to all laboratory material.

We also did it in stationary material and office supplies.

The advantage for Medinfar to choose suppliers like VWR or Laborspirit is that they have been supplying us for many years and we have a good professional relation with them. We also buy them excipients and active ingredients of a medication. If they can aggregate lab material to this "selling cake" they will do everything they can to do it.

6. Do you think this improvement process will translate in a better negotiation power with suppliers? How do you expect Medinfar's relation with them to be affected?

Medinfar's relation with suppliers will be affected because it will now be possible to negotiate bigger quantities. We will be able to do a one shot purchase and then internally divide the products by the different Medinfar's companies.

Medinfar already has a very good negotiating power in the market, with worldwide partnerships at the highest level with MSD, Pfizer, Astra Zeneca, Novartis, amongst other. All these aspects give us a great credibility in the market. If these companies want to work with us it is because of our quality.

Annex 4: Interview to Mécia Frias (Chemical Analyst Technician at Medinfar's R&D unit)

1. Which are the main activities performed in Medinfar's R&D centre?

We perform Stability Tests for our products manufactured in Farmalabor and in other factories. We have more or less ten analysts performing this kind of work. These tests are done for products in which we want to increase validity times, or for products, which we want to export, and there is the necessity to study its stability in a different climatic zone. We also need to execute these tests if there is necessary to change something in a production method.

We also do Galenic Formulations, not so much as Stability Tests, and Development and Validation of Analytic Methods, which is what I do most, together with other five analysts.

Stability Tests represent roughly 70% of all the work performed in the R&D unit.

2. Which are the biggest challenges concerning the management of these daily activities?

The biggest challenge of all is to be able to manage all the activities simultaneously. In my particular case, the greatest issue is to find time to manage all the purchases at the same time I need to focus on my main activity, which is the development and validation of analytic methods.

In terms of stability tests, we have a monthly map with all the product batches that need to be tested. Each month we receive a new map with the needs in terms of tests.

We also have clients that ask us to perform test on their products in our unit. There is also the need to validate the analytic methods of products each time the international area wants to sell those products to a foreign country.

There is a group of employees in the R&D unit responsible for stability tests and other one who performs the development and validation of analytic methods.

The stability tests are already planed until 2020, while development and validation of analytic methods doesn't follow a strict schedule. Sometimes it is necessary to perform additional validations and the group of employees from stability tests must stop their work and focus on this activity.

3. **Did employees in the R&D unit felt that the material's management process needed to change?**

We had the notion that the management of Lab materials had to change. We knew that it would be hard for us to be responsible for that change because there was always so much work to do that we just let the situation continue unchanged.

The perception that the process needed to change was more patent for employees that were directly related to the management of materials.

4. **In which way did the implementation of a Laboratory Material Management System helped to simplify the work performed in the R&D unit?**

This implementation helped me in terms of products with order points because I no longer need to concern with those purchases. Before this change in the purchasing process, anytime a product was needed, the analysts inserted the name of the product in a list and I was responsible for ordering them. If I was busy with work and couldn't see the requests, the product would end and I would need to start calling to suppliers.

At this moment I only execute the orders related to products that don't have ordering points, which are really few.

Meanwhile there are still some flaws in some menus. The System was attributing different validities to products in the beginning, a very important aspect for us that needed to be corrected.

In the end I tend to save considerable time with the ordering process.

For the rest of the employees this implementation brought many benefits, taking into account that they don't need to concern with the orders, they lose less time performing their daily activities.

5. **Which were the main difficulties found while using this, already existing but not totally integrated, System?**

One of the biggest struggles I have now while ordering different products using the System is the fact that now there are different menus for different types of products. If I want to order laboratory material I need to use one menu, whereas if I want to order consumable products like paper rolls or syringes I need to use another one. In my opinion this last group of products should also have an order point because their consumption is usually constant.

Some modifications in the System are still being implemented, which makes its utilization somewhat disorganized.

6. How did the attribution of specific tasks to employees in the R&D unit help in controlling errors and maintaining the order in the activities performed?

By attributing the responsibility of registering the products' reception in the system to a specific employee, it is now easier to evaluate suppliers, knowing if they meet the deadlines previously set.

7. How important is the R&D unit for the core business of Medinfar?

Although representing a small part of Medinfar overall costs, the R&D area has a great influence in the company's operations.

The great majority of the work performed in the R&D unit is Stability Tests to products manufactured in Farmalabor in order to export them.

Here products are put into special containers that simulate the real climatic conditions of the area where they will be exported. The products are kept there during all its shelf life, they are only removed each 3 months to be analysed. After this, the methods still need to be validated. For cosmetic products we make in-use essays, where we simulate product opening and usage and record how much time it remains in good conditions.

For example, some countries don't like the essences we use in our products, so we need to test new formulations here in the R&D unit, so in Farmalabor they can produce respecting client's preferences.

In the Contract Manufacturing unit, Farmalabor, quality control is performed in a small pilot sample before starting large-scale production, while in R&D quality control executed in the long term. If some material used in mass production needs to be changed, the R&D unit will have to analyse those products again to guarantee their quality. For example, if Medinfar wants to produce pills in Farmalabor, here in the R&D unit we do the formulation and it is tested in a small sample. Then they produce a pilot sample, which is analysed again here in R&D, and if everything is ok they can start producing in large scale.

Every time we want to change something in the production or formulation of a product those modifications need to be submitted to Infarmed (Regulatory Authority).

If we don't perform the Stability Tests and the Development and Validation of Analytic Methods, taking into consideration that now we want to sell all our products to foreign countries, it is impossible to export products. This explains why the number of batches that need to be analysed each month triplicated since 2013 and are now 300.